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ABSTRACTS

ADRENAL DISORDERS

Abstract #100

NORTH AMERICAN EXPERIENCE OF ROBOTIC ADRENALECTOMY IN OBESE PATIENTS

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Tulane

Objective: Laparoscopic approach (LA) is a well-described technique for adrenal surgery. However, it can be challenging in obese patients. It is unclear whether robotic assisted surgery has advantages over the traditional laparoscopic approach for surgical management of benign adrenal lesions. The aim of this study is to analyze perioperative outcomes related to robotic versus laparoscopic trans-abdominal adrenalectomy. We hypothesize that the robotic approach is more beneficial in obese patients.

Methods: This is a retrospective analysis of our surgical experience with endoscopic adrenal surgery in which 75 patients were included. Forty-five patients were in the laparoscopic group and 30 in the robotic group. Patients demographics, operative time, length of hospital stay and morbidity encountered were evaluated. The effect of learning curve on the operative time and feasibility of robotic assisted procedure in obese patients was examined.

Results: Seventy-five consecutive laparoscopic and robotic assisted adrenalectomy were performed. Both groups were similar in terms of age, gender and tumor size (p >0.05 for all). BMI was (29.3 ± 0.74 kg/m²) in the robotic group versus (31.1 ± 1.43 kg/m²) in the laparoscopic (p = 0.29). Robotic approach has longer total operative time (211 ± 19.37 min vs. 123 .84 ± 8.07 min; p < 0.01). Improvement in the length of time to perform components of the robotic procedure was noted after 15 cases. The intraoperative blood loss between the robotic approach and laparoscopic approach was reported to be 54 ± 22.7 ml and 157.4± 14.6 ml (P = 0.04) respectively. the hospital stay was shorter in robotic group compared to the laparoscopic group (1.57 ± 0.3 day versus 2.53 ± 0.12) (P<0.01).

In obese patient, laparoscopic approach showed positive association between BMI and a longer total operative time (p = 0.03), whereas robotic group did not show any association (p = 0.32).

Discussion: In this study, we will be discussing the potential benefits of robotic adrenalectomy approach in obese patients. Furthermore, comparing that to laparoscopic adrenalectomy approach.

Conclusion: Robotic assisted transperitoneal adrenal surgery is safe and feasible. The use of robotic approach was associated with shorter hospital stay and was most critical in obese patients. Further studies with larger number are warranted to brace our result

Abstract #101

ACTH-INDEPENDENT MACRONODULAR ADRENAL HYPERPLASIA CAUSING SUBCLINICAL CUSHING SYNDROME - RARITY UNVEILED

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Objective: Adrenocorticotropicin (ACTH) - Independent macronodular adrenal hyperplasia (AIMAH) is a rare cause of Cushing syndrome. AIMAH is characterized by benign, hyperplastic, macronodular, and bilateral involvement of adrenal glands. We present a rare case of AIMAH causing subclinical Cushing syndrome.

Case Presentation: A 57 year old Caucasian female was found to have bilateral adrenal masses on MRI of the abdomen performed for investigating elevated liver enzymes. The patient has type 2 diabetes mellitus for the last 10 years treated with metformin and basal insulin. She was a former smoker, with no history of alcohol abuse or illicit drug use. Family history was significant for diabetes mellitus in both parents. Physical examination showed body mass index of 39.3, normal blood pressure and no clinical signs of Cushing syndrome. Laboratory data showed fasting blood glucose 133, HbA1c 8.0%, AST 105, ALT 142, normal lipid panel and thyroid function test. Abdominal ultrasound revealed hepatic steatosis with hepatomegaly. Iron studies, acute hepatitis panel and serum copper level were normal. Additional work up showed an AM cortisol of 23.7 (6.2-19.4 mcg/dl), ACTH level of 1.2 (7.2-63.3 pg/ml) and non-suppressible cortisol after administration of 1mg dexamethasone. Plasma metanephrines were normal and dehydroepiandrosterone (DHEA) sulfate level was 17 (26-200 mcg/dl). Twenty-four hour urinary free cortisol and midnight salivary cortisol were in the normal range. Adrenal dedicated abdominal CT scan
demonstrated bilateral adrenal nodules with a 1.9x1.1 cm on the right and a 3.6x2.8 cm bilobed nodule on the left. CT morphology was consistent with benign adenosomas based on the Hounsfield units and rapid washout studies. Non-suppressible cortisol, low ACTH and low DHEA sulfate levels confirmed the diagnosis of subclinical Cushing syndrome. Adrenal venous sampling showed cortisol production from both adrenal nodules, but production from the left was greater than the right. Thus diagnosis of AIMAH was made. She was scheduled for a left adrenalectomy.

Discussion: AIMAH is an unusual cause of Cushing syndrome, with most patients presenting in the fifth and sixth decades of life. Although bilateral adrenalectomy will cure the disease, unilateral adrenalectomy of the larger adenoma has been reported to cause significant improvement in clinical and biochemical features. It would be very interesting to follow the patient postoperative for weight loss, improvement in glycemic status and liver steatosis.

Conclusion: This case illustrates a rare case of AIMAH leading to subclinical Cushing syndrome.

Abstract #102

ATYPICAL FINDING IN PATIENT WITH RESPIRATORY SYMPTOMS

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Case Presentation: 64yo man with hx of smoking, hypertension and 4-vessel CAD, developed respiratory symptoms and thought to have left lower lobe pneumonia that was treated on and off with antibiotics. He denied weight change, fever, chills, or night sweats. He reported throbbing headache, facial flushing and occasional palpitations. PET/CT scan, reported a tumor in the posteromedial aspect of the left lower lobe about 5 cm with increased uptake and a lesions right above the bifurcation of the aorta into the iliacs about 3.5cm, which is PET positive. The patient had a needle biopsy of the lung mass, which was an adenocarcinoma. Percutaneous biopsy of the abdominal mass pathology reported small fragments of malignant epithelial neoplasm compatible with a paraganglioma, given that the tumor stained strongly for S100. Carotene HCA, CEA, RCA, inhibin, and CD10 were all negative. Evaluation in 2 occasions revealed: a 24-hour urine metanephrines of 800 mcg, normetanephrine of 485 and total metanephrines of 1285, epinephrine of 37, normormetanephrine of 65, dopamine of 267, and VMA of 7.1. Additional evaluation included 24-hour urine metanephrines of 800 mcg, and normetanephrine of 485, and a total metanephrine level of 1285. An MIBG excluded additional foci of neuroendocrine tumors. An octreotide scan revealed focal increase accumulation of the tracer in the midabdomen corresponding to the CT images of a periaortic retroperitoneal mid-abdominal tissue measuring 3.3 x 2.3 cm. The diagnosis of paraganglioma was made. Patient was started on doxazocin and the abdominal mass was removed. Pathology confirmed the diagnosis.

Discussion: Paragangliomas are catecholamine-secreting tumors arising from the chromaffin cells of the sympathetic ganglia, and are known as extraadrenal pheochromocytomas. These tumors commonly present with episodic hypertension, tachycardia, headache, and diaphoresis, and can be either benign or malignant. The diagnosis made by serum and urine analysis for catecholamines, metanephrines and confirmed with imaging studies that include CT MRI, or NM. Although the majority of PGs are sporadic, a growing percentage of cases are part of a familial genetic syndrome. Management of PG is predicated on surgical resection, and careful perioperative management with alpha- and beta-adrenergic blockade is imperative for optimal outcomes. The majority of these tumors are benign, but for patients with malignant disease, chemotherapy, and radiation therapy may provide modest benefit. Long-term follow-up is essential, as PGs can recur many years after initial diagnosis.

Conclusion: Pheochromocytomas and paragangliomas can have atypical presentations.

Abstract #103

ADRENAL HEMORRHAGE IN A PATIENT ON DABIGATRAN

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Objective: Dabigatran is an oral anticoagulant that acts as a direct thrombin inhibitor and can be used for the prevention of stroke in patients with non valvular atrial fibrillation. Dabigatran is as efficacious as warfarin for prevention of stroke in patients with non valvular atrial fibrillation. Unlike its predecessors of warfarin and heparin, there is currently no commercially available agent to reverse the anticoagulant effect of dabigatran in the event of clinically significant bleeding.
Case Presentation: A 71 year old male presented with persistent atrial fibrillation and was treated initially with warfarin until 2011 when he was transitioned to dabigatran due to difficulty in regulating INR. The atrial fibrillation was refractory to ablation, antiarrhythmic medications and multiple cardioversion attempts. He subsequently presented to his cardiologist for consideration of a maze procedure with left atrial appendage ligation.

Pre-procedural chest CTA was performed and a 3.5 x 4.0 cm right adrenal mass with internal flecks of calcification was noted incidentally. Follow up non-contrast CT scan of the adrenals showed the mass to be 4.4 x 3.3 cm with hounsfield unit density of 33.1.

Endocrine evaluation ruled out pheochromocytoma, primary hyperaldosteronism, and hypercortisolism. Because the mass was >4cm with indeterminate imaging characteristics, surgical removal for definitive diagnosis was elected. The patient underwent uncomplicated laproscopic right adrenalectomy. Pathology showed adrenal hemorrhage with central necrosis and no evidence of neoplasm.

Discussion: This case illustrates the potential for spontaneous hemorrhage within the adrenal gland with newer classes of anticoagulant therapies such as dabigatran.

Conclusion: To our knowledge, this is the first reported case of unilateral, asymptomatic adrenal hemorrhage related to dabigatran treatment in a patient presenting with an incidentally discovered adrenal mass.
medications, prior to the procedure. Post-hysterectomy, the patient had extreme variations in blood pressure (systolic blood pressures ranging from 90 to 220 mmHg) as well as left arm numbness and mild dyspnea. EKG demonstrated marked ST depression in the anterior precordial and lateral limb leads. Troponins were significantly elevated (11.5 ng/mL) and the outside hospital transferred the patient to our facility for cardiac catheterization. During the procedure, she had recurrent episodes of a narrow complex tachycardia and labile blood pressures. There was no evidence of coronary artery disease, and left ventricular function was normal.

After catheterization, the patient complained of abdominal pain with difficulty passing gas. Computed tomography of the abdomen and pelvis with contrast revealed a heterogeneously enhancing 4.3 x 5 cm mass in close relation to the left adrenal gland. Plasma fractionated metanephrines were more than 4 times the upper limit of normal and 24-hour urine fractionated catecholamines and metanephrines were more than 2 times the upper limit of normal. We scheduled the patient for left adrenalectomy and administered phenoxybenzamine and labetalol for 10 days prior to surgery. She tolerated the procedure well, and pathology revealed a 5 cm pheochromocytoma of the adrenal medulla.

At 3-month follow-up, she was asymptomatic and only required one agent for blood pressure control. Repeat plasma metanephrines were within normal limits. She continues to do well and remains symptom-free to this day.

**Discussion:** Studies have shown patients with a pheochromocytoma have a 14-fold higher rate of cardiovascular events than patients with essential hypertension. Myocardial infarction as initial manifestation of pheochromocytoma occurs in only 3.9% of cases. Acute catecholamine secretion may induce chest pain and segmental myocardial dysfunction, mimicking an acute ischemic event, in patients with pheochromocytomas. Prompt diagnosis and preoperative management are key, but can be a challenge as demonstrated in this case.

**Conclusion:** Suspecting pheochromocytoma in patients with an unexpected myocardial event and labile hypertension can lead to prompt diagnosis and management resulting in a successful outcome.

**Abstract #106**

**AN UNUSUAL PAIN: A CASE OF AN ADRENAL REST TUMOR**

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**Case Presentation:** A 28 year old white male with a history of classic CAH presented for evaluation of a testicular mass. The patient had a history of severe adrenal insufficiency since infancy. He had run out of his medications three years previously, and had never sought to re-establish care as he did not experience any symptoms. Two months prior to evaluation, he developed severe pain and swelling in his left testicle. He saw a urologist who felt that it represented primary testicular cancer, and recommended orchiectomy. He then presented to an endocrinology clinic seeking a second opinion. Physical exam revealed a tender, 1 cm nodule on the left testicle. Ultrasound revealed a 1 cm mass with surrounding orchitis. Laboratory evaluation showed an elevated ACTH and 17-OH progesterone. Alpha feto-protein and beta-HCG were undetectable. Hormone replacement therapy with prednisone was initiated, and at 6-week follow up he reported that the pain and swelling was significantly improved. Laboratory evaluation showed normalization of ACTH, and suppression of 17-OH progesterone. Repeat ultrasonography was performed, and did not show any evidence of a mass, with complete resolution of orchitis.

**Discussion:** Gonadal tumors, known as adrenal rest tumors, in patients with classic Congenital Adrenal Hyperplasia (21-hydroxylase deficiency) have been well described in current literature, but are not frequently seen in clinical practice. This case demonstrates the classic presentation of an adrenal rest tumor. As testicular masses in young men have a high likelihood of malignancy, recognition of this condition is important in preventing unnecessary procedures and the morbidity associated with them.

**Conclusion:** An adrenal rest tumor should be considered in men with classic CAH presenting with a testicular mass or infertility.

**Abstract #107**

**ALDOSTERONE PRECURSORS IN THE DIAGNOSIS OF PRIMARY ALDOSTERONISM**

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**Objective:** Primary aldosteronism (PA) is an adrenal disorder which is characterized by the overproduction of the mineralocorticoid hormones by the adrenal glands when not as a result of excessive renin secretion. The importance of case detection of PA among hypertensive patients is not a matter of controversy presently. In our study we evaluated the value of different mineralocorticoids in the diagnosis of PA. The main attention was paid to 11-deoxycorticosterone (DOC) and 18-hydroxy cortisol (18OHB) which are precursors of aldosterone with various affinity to the mineralocorticoid receptor.
Methods: We evaluated 128 low-renin hypertensive patients and 30 normotensive subjects. We measured serum aldosterone and renin activity by radioimmuno assay; serum corticosterone (B), 18OHB, DOC and urinary 18-hydroxycorticosterone (u18OHB) by means of high-performance liquid chromatography. All patients underwent saline infusion test (SIT) and computed tomography (CT).

Results: Positive ARR had 76 low-renin hypertensive patients. Diagnosis of PA among them was based on SIT and CT. 14 patients suspected on bilateral adrenal hyperplasia (BAH) underwent AVS. All patients with positive ARR were subsequently divided into 3 groups: low-renin essential hypertensives (LREH), patients with aldosterone-producing adenoma (APA) and BAH. They were 43, 21, 12 patients, respectively.

Discussion: Patients with PA (both APA and BAH) displayed significantly higher levels of serum B, 18OHB, DOC and u18OHB compared with LREH. Furthermore, APA patients displayed higher levels of serum DOC and 18OHB and u18OHB compared with patients with BAH. In our groups we identified a cutoff value useful for the distinction among LREH and PA. In our data PA was confirmed in patients with DOC level more than 4 ng/ml, serum 18OHB more than 2 ng/ml and u18OHB higher than 35 mkg/sec.

We observed a significant correlation between serum aldosterone levels and serum 18OHB and DOC, u18OHB levels (p<0.05 for all three comparisons), correlation between serum B and aldosterone was not significant. Furthermore, after subdivision of patients into LREH, APA and BAH groups, correlation between serum and urinary 18OHB and aldosterone, and DOC and aldosterone remained significant in all three groups.

Conclusion: The measurements of serum and urinary 18OHB and DOC in patients with a positive ARR could be additional tests in confirmation and subtype differentiation of PA. This data will be useful to identify alternative strategies to AVS which is not readily available in many clinics.

Abstract #108

PHYSICIAN BEWARE: CORTICOSTEROIDS MASQUERADING AS MEXICAN OTC PAIN MEDICATIONS CAN CAUSE ADRENAL INSUFFICIENCY

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Objective: We report a series of Cushingoid-appearing patients with adrenal insufficiency secondary to corticosteroids contained in over the counter (OTC) pain medications from Mexico.

Case Presentation: A 54 year old Hispanic man with diabetes presented with weakness, frequent falls and back pain for 2 months. Exam noted moon facies, abdominal striae, central obesity and ecchymoses. Investigations noted T7 compression fracture, suppressed cortisol (1.9 ug/dL) after 1 mg overnight dexamethasone suppression test, and undetectable 24 hour urine free cortisol (<5 ug/24 hr). Further probing revealed he had taken Artridol, a betamethasone-containing OTC pain medication from Mexico, for gout for several months prior. Onset of weakness coincided with cessation of Artridol. A 250 mcg ACTH stimulation test was consistent with adrenal insufficiency with baseline cortisol of 2.6 ug/dL, ACTH <1.1 pg/mL and peak cortisol of 10 ug/dL. His symptoms resolved with replacement dose hydrocortisone.

A 50 year old Hispanic woman with osteoporosis and L1 compression fracture presented with 1 week history of nausea, vomiting, diarrhea, malaise and fever. She reported taking Artridol from Mexico for rheumatoid arthritis but had stopped 1 month prior. She was febrile, tachycardic and had diffuse abdominal tenderness and ecchymoses. Infectious and rheumatologic etiology of fever was ruled out. A 250 mcg ACTH stimulation test revealed baseline cortisol of 2.2 ug/dL, peak cortisol 12.6 ug/dL and ACTH 3.2 pg/mL. Her symptoms resolved with stress dose hydrocortisone. She was discharged home on replacement dose hydrocortisone.

A 50 year old Hispanic man presented with chronic leukocytosis. He reported taking Rumoquin, a dexamethasone-containing OTC pain medication from Mexico, for 10 years for gout. Upon stopping Rumoquin, his leukocytosis resolved and he noted a 10 lb unintentional weight loss but no other symptoms of adrenal insufficiency. Exam noted central obesity and abdominal striae. Morning cortisol was <0.2 ug/dL. He failed a 1 mcg ACTH stimulation test with baseline cortisol of 2.6 ug/dL, ACTH 6.7 pg/mL and peak cortisol of 3.5 ug/dL. He was started on replacement dose hydrocortisone.

Discussion: Our series highlights the incidence and morbidity of adrenal insufficiency secondary to chronic use of steroid-containing OTC pain medications obtained from outside the U.S. and the importance of a thorough history for accurate clinical diagnosis. Our patients appeared Cushingoid yet presented with adrenal insufficiency. None were aware that their pain medication contained steroids.

Conclusion: Physicians need to be aware of this to avoid the morbidity associated with adrenal suppression from exogenous steroids.
Abstract #109

SCHWANNOMA PRESENTING AS AN INCIDENTAL ADRENAL MASS

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Objective: To report an unusual pathology of adrenal incidentaloma.

Case Presentation: A 51-year-old man presented with episodic dizziness, nausea, vomiting, and diaphoresis. He was on a multiple antihypertensive drug regimen. He had an unremarkable family history. Physical examination was normal. CT abdomen revealed an incidental 5 cm mass within or adjacent to the left adrenal gland which was confirmed to be of adrenal origin on MRI. Hormonal workup was negative and it was felt to be a non-functioning lesion. The patient underwent a complete laparoscopic left adrenalectomy. Histopathological diagnosis pointed to a benign nerve sheath tumor. Tumor cells stained positive for S-100 and negative for CD34 and epithelial membrane antigen with overall morphologic features and immunohistochemical profile consistent with a diagnosis of schwannoma. The tissue specimens were evaluated by two histopathologists who concurred with the diagnosis. Blood pressure improved significantly after adrenalectomy. Four months after surgery, the patient remained well and without evidence of recurrence or metastasis.

Discussion: Retroperitoneal neural sheath tumors, which include benign and malignant schwannomas, are a rare clinical entity with a variable and non-specific presentation. Patients with tumors of adrenal origin commonly complain of vague symptoms of mild abdominal pain and distension, thus frequently contributing to a delay in diagnosis. Atypical presentations may include dysesthesia, dyskinesis, headache, secondary hypertension, flank pain, hematuria, or recurrent renal colic. Schwannomas are generally benign, solitary lesions usually occurring in the head and neck region. They can also arise from the retroperitoneal fat tissue, psoas muscle, pancreas, or adrenal glands. The diagnosis of adrenal schwannoma is extremely difficult to make on imaging alone. Surgical resection is the primary means of management as it is not possible to distinguish benign from malignant lesions based on imaging appearance. Histopathologic features of adrenal schwannomas are similar to those found at other sites.

Conclusion: Although adrenal incidentalomas are being increasingly identified with recent advances and proliferation in imaging techniques, only a few cases of adrenal schwannoma have been reported. Our patient did not present with symptoms classically associated with this condition. Management of hypertension has been documented to be easier after surgical removal, however the exact mechanism is not known. Schwannomas are rarely malignant and can recur.

Abstract #110

CORRECTION OF A PSEUDO-PHEOCHROMOCYTOMA LIKE SYNDROME PRESENTING WITH PAROXYSMAL REFRACTORY HYPERTENSION AND TACHYCARDIA FOLLOWING TREATMENT WITH DEXTROAMPHETAMINE SULFATE

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Objective: To determine if a pseudo-pheochromocytoma like syndrome could be another manifestation of the large variety of chronic treatment refractory conditions related to sympathetic nervous system hypofunction (referred to as the sympathetic neural hyperalgesia edema syndrome) and thus could respond to treatment with dextroamphetamine sulfate similar to its efficacy in alleviating symptoms of the many other chronic disorders related to increased cellular permeability.

Case Presentation: A 42 year old female developed episodes of incapacitating paroxysmal sinus tachycardia with heart rate sometimes at 200 beats/minute and sudden rise of blood pressure sometimes as high as 220/160. She was evaluated for a pheochromocytoma by 3 different endocrinologists but each time both urine and serum metanephrines and catecholamines were negative. Serum free T4 and TSH were normal. A CT-scan of the abdomen showed a subcentimeter nodule in the left adrenal but MRI suggested it to probably be a small non-functioning adenoma of the adrenal cortex. Therapy with standard medication prescribed by cardiologists or renal hypertensive experts, e.g., beta blockers and calcium channel blockers failed to control her symptoms. One cardiologist considered atrioventricular nodal re-entry tachycardia and recommended ablation. Before surgery she sought an opinion from our group. We considered that she could have sympathetic nervous system hypofunction which allowed absorption of chemicals into a certain defective area of the heart precipitated by the increase in hydrostatic pressure which occurs in the standing position (which seemed to precipitate these attacks) similar to the mechanism of causing edema. She showed dramatic improvement with just 15mg of dextroamphetamine...
sulfate extended release capsules which has been shown to quickly correct a multitude of chronic refractory disorders probably by replacing the deficient sympathetic nervous system neurotransmitter. She remained asymptomatic for over 2 years. Circumstances prevented her from returning to our office for prescriptions for 5 months and all her symptoms quickly returned. The tachycardia and hypertension abated within 2 days after re-starting 20mg dextroamphetamine sulfate.

Discussion: The sympathetic neural hyperalgesia edema syndrome is relatively common but many physicians are unaware of its existence. It can manifest in many ways depending on certain weaknesses in specific tissues such that it can cause severe headaches in some people and Crohn’s disease in others.

Conclusion: Thus we report the first case of the sympathetic neural hyperalgesia edema syndrome presenting as a pseudo-pheochromocytoma.

Abstract #111
MORE THAN AN ADRENAL INCIDENTALOMA: A CASE OF PRIMARY ADRENAL B-CELL LYMPHOMA PRESENTING WITH PRIMARY ADRENAL INSUFFICIENCY

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Objective: We describe a patient with primary adrenal lymphoma (PAL) who presented with subtle clinical symptoms of primary adrenal insufficiency (PAI) and bilateral progression of a left adrenal incidentaloma.

Case Presentation: A 74-year-old woman with type 2 diabetes mellitus, hypertension, cardiovascular disease, a pacemaker for complete heart block, and chronic renal disease was incidentally found to have a 2.1-cm left adrenal nodule on a non-contrast computed tomography (CT) scan with pre-contrast Hounsfield units (HU) of 19. Biochemical studies ordered by her primary provider were unremarkable for adrenal hypersecretion. A 250-μg cosyntropin stimulation test revealed baseline, 30- and 60-minute cortisol levels of 13.4, 15.8, and 16.1 μg/dl, respectively. Baseline adrenocorticotropic hormone was 230 (reference 6-48 pg/ml). Because these results were consistent with PAI, she was placed on hydrocortisone 20 mg daily in divided doses and fludrocortisone 50 μg daily. Plasma fractionated metanephrines, serum histoplasma antigen and quantiferon test results were negative. A CT-guided right adrenal mass biopsy revealed large B-cell lymphoma consistent with PAL. Fluorodeoxyglucose (FDG) positron emission tomography demonstrated intensely FDG-avid bilateral adrenal lesions without evidence for FDG-avid disease elsewhere. A head CT showed neither brain lesions nor lymphadenopathy. Lactate dehydrogenase was 171 (reference 84-246 U/L). She has been initiated on R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) chemotherapy for Ann Arbor stage IV PAL.

Discussion: PAL is a rare aggressive extranodal hematologic malignancy accounting for <1% of non-Hodgkin lymphomas. Patients may present with adrenal insufficiency, B symptoms (fevers, sweats, weight loss) and abdominal/flank pain. PAL may infrequently present as an incidental adrenal finding with a high incidence of bilateral involvement.

Conclusion: PAL, although rare, is one of the differential diagnoses for an adrenal incidentaloma. Strong clinical suspicion is important for early recognition and intervention in this aggressive malignancy, particularly when bilateral adrenal masses occur synchronously with primary adrenal insufficiency.

Abstract #112
A CASE OF ADRENAL CUSHING SYNDROME WITH A DETECTABLE ACTH FROM AN UNEXPECTED SOURCE

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Objective: There are only 17 reported cases in literature of mixed corticomedullary adrenal tumors. The majority of patients are females presenting with Cushing syndrome. We describe the second reported case of a male patient diagnosed with a mixed corticomedullary tumor, presenting with Cushing syndrome and hypertension.

Methods: Medical records were reviewed, and a review of the literature was performed.

Case Presentation: A 48-year-old man presented with hypertension and overt clinical manifestations of
Cushing syndrome. A 24-hour urine cortisol revealed hypercortisolemia (787 μg/dL), with a detectable ACTH (24 pmol/L). A high dose dexamethasone suppression test indicated an adrenal or ectopic source of cortisol. A 3 cm left adrenal mass was identified on imaging. Plasma metanephrines were within normal limits. Computed tomography of the chest, abdomen and pelvis revealed no potential ectopic sources of ACTH, and there was no evidence of right adrenal hyperplasia. A Laparoscopic left adrenalectomy was therefore planned. During induction of general anesthesia, the patient developed resistant hypertension with a SBP of 210 mmHg after perioperative stress dose hydrocortisone was administered. The surgery was cancelled and repeat laboratory testing revealed elevation of plasma metanephrines. Alpha blockade and fluid resuscitation were administered for 7 days for presumed simultaneous pheochromocytoma, and the patient subsequently underwent an uneventful laparoscopic adrenalectomy. Pathology revealed a mixed corticomedullary tumor, likely the source of cortisol, catecholamine, and ACTH in this patient.

Discussion: Mixed corticomedullary tumor is distinguished as a single tumor mass of the adrenal gland composed of intermixed cortex cells and pheochromocytes. The clinical presentations are unique to the hormones secreted by the tumor and may mimic other conditions. This case highlights the importance of a comprehensive preoperative evaluation to rule out an ectopic source of ACTH production in patients with likely adrenal Cushing syndrome and an unexpected detectable ACTH.

Conclusion: Mixed corticomedullary adrenal tumor is a rare condition defined by histological findings with a variation of clinical presentations. Although rare, they illustrate the importance of a thorough biochemical evaluation for each patient to rule out co-existing functioning tumors.

Abstract #113

ACUTE ANEMIA BY UNILATERAL ADRENAL HAEMORRHAGE: THREE CASES

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Objective: Adrenal haemorrhage is uncommon in adults occurring in association with trauma, severe physical stress, surgery, anticoagulant therapy, sepsicaemia, hypotension or tumor. We report three cases of unilateral adrenal haemorrhage (AH) presenting as acute anemia with abdominal pain.

Methods: Clinical and biochemical data of the patients are presented and the pertinent literature is reviewed.

Case Presentation: A 28-years-old woman was admitted to the Emergency Room because of abdominal pain, nausea and fever. US abdomen showed a 130 mm right liquid adrenal mass, with signs of recent bleeding. Labs disclosed severe anemia (Hb 7.3 g/dl). Hormonal evaluation excluded glandular dysfunction, blood pressure was normal. She underwent adrenalectomy by laparotomy. Histology revealed an adrenal pseudocyst. The second case is a 52-years-old man with history of untreated mild hypertension, complained of flank pain and syncope. Abdomen TC showed a large retroperitoneal hematoma from arterial bleeding involving the right adrenal gland. Labs showed acute anemia (Hb 9.4 g/dl) treated with transfusion. After hemodynamic stabilization, the patient underwent selective embolization of the right adrenal artery. Our third case concerns a 60-year-old woman, who came to the Emergency Room complaining of right flank pain. She was on anticoagulant therapy because of a valve replacement, INR was 3.4 and Hb was 9.2 g/l. Abdomen CT showed a 75 mm adrenal hematoma. The embolization of the right adrenal artery was performed.

Discussion: Adrenal pseudocyst is a rare, usually incidentally diagnosed condition, mostly in the 4th and 5th decades of life, with female predominance. Patients are asymptomatic until the tumor becomes large enough to compress adjacent organs. So far, literature reported only few cases of large unilateral adrenal cysts presenting with acute abdomen and hypovolemic shock or anemia, due to adrenal bleeding. Idiopathic unilateral AH is a rare entity that either may have an acute presentation (e.g., idiopathic adrenal rupture) or may present as an asymptomatic adrenal mass. AH is a rare but insidious complication of anticoagulant therapy, often bilateral, presenting as Addisonian crisis. If unilateral, it may be asymptomatic or presenting as flank pain and/or anemia.

Conclusion: Acute unilateral adrenal haemorrhage is a rare but life-threatening event and must be considered in the differential diagnosis of patients with abdominal symptoms and unexplained anemia. Embolization may be a lifesaving temporizing measure. Acute surgical intervention should be considered in selected patients. Earlier diagnosis and treatment of these lesions is curative.
Abstract #114

THE VALUE OF CHROMOGRAFIN A FUNCTION OF TUMOR SIZE IN PHEOCHROMOCYTOMAS

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Objective: Chromogranin A value is bigger in pheochromocytomas with bigger tumor size compared with smaller pheochromocytomas and its value increases with tumor size.

Methods: We realized a retrospective study with 35 isolated pheochromocytomas which had been diagnosed in National Institute of Endocrinology C.I.Parhon Bucharest between 1985-2005 on the basis of plasma and urinary methanephrenes and normethanephrenes and the diagnosis has been confirmed by imaging and pathologically examination. We have determined the value of Chromogranin A in pheochromocytomas with tumor size < 5 cm and tumor size > 5 cm.

Results: In our study there have been 14 pheochromocytomas with tumor size < 5 cm and 21 pheochromocytomas with tumor size > 5 cm. For patients with pheochromocytoma and tumor size < 5 cm chromogranin A value was between 257-700 ng/ml with a median value of 462,857±109,957 ng/ml. For patients with tumor size >5 cm chromogranin A value was between 724-1410 ng/ml with a median value of 909,429±189,44 ng/ml. Patients with pheochromocytomas > 5 cm had bigger chromogranin A value than patients with pheochromocytomas < 5 cm and this difference was statistically significant (p<0,01). To identify the existence of a significant relationship between tumor size and the value of chromogranin A we have used the Pearson coefficient which indicated a statistically significant difference between tumor size of pheochromocytoma and Chromogranin value (p<0,01). This coefficient was 0,95 very close of 1 which is considered the maximum value of this coefficient and this indicates a strongly positive correlation between the two variables (tumor size and the value of chromogranin A). The association relationship between the two variables indicates that an increase in tumor size is followed by an increase of Chromogranin A value. Simple linear regression procedure revealed that tumor size explain 82% of the variation of Chromogranin A value.

Discussion: Chromogranin A is important in the diagnosis of pheochromocytomas and it can predict tumor size and the extension of the tumor in malignant pheochromocytomas.

Conclusion: In our study the value of Chromogranin A is bigger in pheochromocytomas with larger tumor size compared with smaller pheochromocytomas and it increases with tumor size.

Abstract #115

AUTOIMMUNE POLYGLANDULAR SYNDROME II IN A PATIENT WITH TAKOTSUBO’S CARDIOMYOPATHY

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1. Akron General Medical Center, 2. Northeast Ohio Medical University

Objective: Autoimmune Polyglandular Syndrome (APS) is a rare condition involving multiple endocrinopathies and associated autoimmune disorders. It is preceded by adrenal failure in almost 50% of cases. Takotsubo Cardiomyopathy (TCM) is a disorder with a poorly understood pathogenesis, leading to transient dysfunction of the middle segments/apex of the left ventricle and subsequent apical systolic dilatation. We report a case of APS type II in a 65-year-old female with recent history of TCM.

Case Presentation: A 65-year-old female diagnosed with TCM based on cardiac catheterization consulted seven months later for progressive and chronic fatigue, hair loss, nail problems, insomnia, eczema and multiple hypopigmented patches. She was being maintained on hormone replacement therapy for hypothyroidism and low sex hormone levels. Workup revealed thyroid peroxidase antibodies present but was unremarkable for other autoimmune antibodies (anti-thyroglobulin, anti-tissue transglutaminase, anti-cardiolipin, anti-phosphatidylserine, anti-glutamic acid decarboxylase, anti-islet cell, and anti-21 alpha hydroxylase antibodies). Cosyntropin stimulation test suggested possible primary adrenal insufficiency. Despite the sensitivity of anti-21 alpha hydroxylase antibody testing, negative results have been documented in diagnosed cases of Addison’s disease. Autoimmune Polyglandular Syndrome was suspected based on symptomatology, laboratory findings of hypothyroidism, primary adrenal insufficiency and recent clinical findings consistent with dermatomyositis. The patient was then started on hydrocortisone, with good response to treatment.

Discussion: This is a case of Takotsubo Cardiomyopathy with hypothyroidism and low sex hormone levels, later presenting with clinical and laboratory findings consistent with Autoimmune Polyglandular Syndrome type II. Three
other cases of APS with concomitant TCM have been reported. While TCM is currently of unclear etiology, if related to APS it may be an early sign of the latter disease, as seen in this case. One plausible theory argues that TCM may be triggered by potentiated catecholamine release in APS II due to elevated ACTH levels. Other authors cited possible hormonal preconditioning combined with the patient being in distress as factors contributing to the coexistence of these two diseases. 

**Conclusion:** This case report supports the possibility that APS II and TCM may share common pathogenetic pathways which may include autoimmunity, hormonal factors, and genetic factors. Further studies are recommended to establish correlation.

Abstract #116

**ADRENAL CORTICAL ADENOMA TRANSFORMING INTO ADRENOCORTICAL CARCINOMA IN A PATIENT WITHOUT CUSHING’S FEATURES**

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**Objective:** Adrenocortical carcinoma (ACC) is a rare heterogeneous tumor with an annual incidence of 0.7-2 cases per million and poor prognosis. In Cushing’s Syndrome, 10% of cases are caused by ACC, which manifests under conditions of steroid excess in 60% of the cases. We report a case of adrenal adenoma without manifestation of Cushing-like features, progressing to metastatic ACC.

**Case Presentation:** A 76 year old Caucasian female, with a history of right adrenal cortical adenoma without Cushing’s features having underwent laparoscopic adrenalectomy one year prior, presented with complaints of progressive weakness, lower back pain and hyperglycemia. Physical examination was significant for bilateral lower extremity edema. Laboratory investigation revealed normal values of norepinephrine (609 pg/mL; supine), free metanephrine (<25 pg/mL), free normetanephrine (54 pg/mL) and serum creatinine (0.86 mg/dL). Renin activity (12.07 ng/mL/h), glucose (309 mg/dL) and HbA1c (8.6%) were elevated. Cortisol levels were obtained, but the sample was inadequate for interpretation. A diagnosis of new-onset Diabetes Mellitus Type II was made. An MRI of the abdomen and pelvis with contrast showed multiple retroperitoneal masses in the areas of the infra-hepatic vena cava (IVC) and the right kidney, with the largest measuring 7.5 x 6.0 x 5.5cm. Renal biopsy showed tumor necrosis and fewer than 25% of the tumor cells showing clear neoplasm favoring metastatic ACC. The patient was subsequently scheduled for palliative chemotherapy, radiation and surgical intervention including right nephrectomy and IVC stenting; however, the patient demised before the contemplated interventions.

**Discussion:** This report describes a rare case of benign adenoma transforming into metastatic ACC. ACC presents with Cushing’s syndrome in 60% of the cases, along with metastasis. This patient did not initially have the typical Cushing-like features of a cortisol-producing tumor, and presented only with fatigue and uncontrolled hyperglycemia one year after adrenalectomy for adenoma. In this case, the new onset of diabetes is secondary to elevated levels of cortisol from metastatic ACC. Furthermore, tumor extension into the renal artery and/or IVC caused compression symptoms. Other rare manifestations of ACC include virilization, feminization and Conn’s syndrome.

**Conclusion:** It is recommended that clinicians should have a high index of suspicion for ACC in previously diagnosed cases of adrenal cortical adenoma to include routine screening and follow-up.

Abstract #117

**WEIGHT LOSS, HYPERPIGMENTATION WITH BILATERAL ADRENAL ENLARGEMENT: PRESENTATION OF TWO CASES**

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**Objective:** To present two cases of cortisol deficiency with bilateral adrenal enlargement, creating a diagnostic dilemma.

**Case Presentation:** Recently, two patients were admitted in our Department with similar features. Both the patients were middle aged male and presented with weight loss, anorexia, generalized weakness and hyperpigmentation more marked in the sun exposed areas, skin creases and also involving oral mucosa. They had biochemical evidence of Addison’s disease and imaging revealed bilateral adrenal enlargement. CT guided FNAC of adrenal gave similar results showing granulomatous lesions. As they had no pulmonary lesion, history of exposure to smear positive tuberculosis patient, very high ESR or positive tuberculin test, antibody against Histoplasma capsulatum was sent and found positive in both the cases. Moreover, in one case biopsy from nodular lesion in gum showed histoplasma
capsulatum within histiocytes and also extracellularly. So, after excluding other possible causes of Addison’s disease with bilateral adrenal enlargement we started treatment with replacement dose of hydrocortisone along with Itraconazole. Both the patients are now under regular follow up and they are gradually improving.

**Discussion:** Bilateral adrenal enlargement with adrenal insufficiency may be seen with tuberculosis, cytomegalovirus, malignant and nonmalignant infiltrative diseases, adrenal hemorrhage and deep fungal infections like histoplasmosis. Adrenal involvement by histoplasmosis resulting in adrenal insufficiency is uncommon as patient with disseminated disease present early and clinical adrenal insufficiency results when almost 90% of the adrenal tissue is destroyed.

**Conclusion:** Histoplasmosis needs to be kept in differential diagnoses in patients presenting with adrenocortical insufficiency, bilateral adrenal enlargement and granulomatous lesion in cytology.

Abstract #118

**A 19-YEAR-OLD LADY WITH VIRILIZATION**

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Bangabandhu Sheikh Mujib Medical University

**Objective:** The objective of this presentation is to highlight a rare cause of androgen excess due to adrenal adenoma.

**Case Presentation:** A 19-year-old lady presented to Endocrinology Department, BSMMU with primary amenorrhea, hirsutism, masculinization of body without deepening of voice, enlarged clitoris & no thalarche. On examination, she had hirsutism, the clitoris had 2 cm length, breast development at Tanner stage-B1, vital signs were normal. Our provisional diagnosis was androgen secreting malignant tumor. Hormonal evaluation revealed high levels of testosterone (1115 ngm/dl) & dehydroepiandrosterone sulfate (DHEAS- 560µgm/dl). Serum cortisol, ACTH &17-OH progesterone were normal. Her karyotype was 46XX. At pelvic ultrasound the uterus was small and multiple tiny follicles were noted in both ovaries. Initial CT scan of abdomen revealed bilateral adrenal enlargement with multiple tiny follicles in both ovaries. As the findings failed to correspond with the biochemical reports, an expert radiologist consultation was sought who advice a repeat CT scan. Repeat CT revealed a left adrenal mass (4x3cm). Open adrenalectomy followed by histopathological examination of the adrenal mass indicated a benign adrenal adenoma. The patient post operative progress was satisfactory with normalization of DHEAS & testosterone level and onset of menstruation.

**Discussion:** Pure virilizing benign adrenal adenoma is rare, with approximately 50 cases reported in the literature. Such tumors have to be considered in the differential diagnosis of CAH in patients presenting during childhood. In females, most patients present before the menopause with marked hirsutism, deepening of the voice, and amenorrhea. Clitoromegaly is found in 80% of cases. Tumors vary in size and should be treated surgically. Postoperatively, clinical features invariably improve, and normal menses return.

**Conclusion:** Virilization usually indicates a malignant adrenal tumor, but surprisingly the cause may be a benign one.

Abstract #119

**DISSEMINATED TUBERCULOSIS CAUSING ADDISON’S DISEASE IN ADULT DIABETIC PATIENT.**

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**Objective:** The aim of this report is to describe a case of Addison’s disease caused by disseminated tuberculosis which presented with crisis lead by add-on bacterial pneumonia.

**Methods:** History, clinical features and investigation reports were analyzed.

**Case Presentation:** In January 2010, 45-year-old Bangladeshi diabetic male previously on insulin presented at BIRDEM for recurrent hypoglycemia, hypotension leading to recurrent syncope past 4 months. History of common inciting causes for hypoglycemia or hypotension was negative. He lost 6 kg weight, had low grade fever, paroxysmal productive cough with no response to antibiotics. Previous TB close contact or infection were negative. He noticed pigmentation of skin, oral cavity shortly. Clinical examination revealed: pale conjunctiva, BP 90/60 mmHg with postural drop, pulse 92/bpm, temperature 99.50F, BMI 17.56kg/m2. Hyperpigmented palmar creases, knuckles, recent scars, buccal mucosa, bronchial sound in left front chest and bilateral crackles in upper areas. Investigations revealed: hemoglobin 10.5 gm/dl, TC 11,400/cmm, ESR 84,CRP 12 mg/L, HbA1C-6.1%. Na126mmol/L, K 5.7 mmol/L, Ca 9.3 mg/dl), S. cortisol 83.44nmol/L, S. ACTH 98.0 pg/ml, negative sputum AFB, Sputum C/S: S. aureus, rapid ACTH stimulation
ABSTRACTS – Adrenal Disorders

A 67-year-old normotensive female laboratory investigations and ultrasonography of abdomen recent onset upper abdominal pain and vomiting. Initial evaluation of acute pancreatitis. Cushing's with adrenal incidentaloma was revealed during a 67-year-old female are reported in whom subclinical hypertriglyceridaemia. Methods: diabetic woman who presented with acute pancreatitis and revealed subclinical Cushing's syndrome with adrenal incidentaloma in an elderly objective:

Discussion: The diagnosis of adrenal TB is challenging. At present in developed countries, 75-80% of cases of AD are caused by autoimmune destruction followed by TB (7-20%). However, in developing countries tuberculosis still remains the main cause of Addison’s disease. In adrenal tuberculosis, typical granulomatous inflammation with Langhan’s giant cells is found in less than half of the cases which may be related to necrosis and local suppressive effect of steroids. Conclusion: This case presented with features of progressive primary adrenal insufficiency due to disseminated tuberculosis and adrenal crisis was caused by add-on bacterial pneumonia which summoned stress on the background of chronic adrenal insufficiency.

Abstract #120

SUBCLINICAL CUSHING’S SYNDROME WITH ADRENAL INCIDENTALOMA IN AN ELDERLY DIABETIC WOMAN PRESENTED WITH PANCREATITIS.

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Objective: to report a case of subclinical Cushing’s syndrome with adrenal incidentaloma in an elderly diabetic woman who presented with acute pancreatitis and hypertriglyceridaemia.

Methods: Clinical, biochemical and radiological data of a 67-year-old female are reported in whom subclinical Cushing’s with adrenal incidentaloma was revealed during evaluation of acute pancreatitis.

Case Presentation: A 67-year-old normotensive female with type 2 diabetes and BMI 22.4kg/m2 presented with recent onset upper abdominal pain and vomiting. Initial laboratory investigations and ultrasonography of abdomen revealed features suggestive of acute pancreatitis. Later, for better evaluation of pancreatitis and to document any complication if any, CT abdomen with oral contrast was done that revealed a homogenous nodular (21 mm X 20 mm) right adrenal mass and contralateral adrenal gland was normal. After resolution of pancreatitis and relief of stress, evaluation of the adrenal incidentaloma was carried out that revealed UFC as 198mmol/24h (N<280mmol), after overnight 1mg dexamethasone suppression test Serum cortisol (9am) not suppressed 135.24nmol/L(<50mmol/L), Serum ACTH level as 6 ng/L. DHEA-S, 24h urinary VMA were within normal range. Other investigations revealed Na:137mmol/L, K:3.64mmol/L, HbA1c:6.9%, serum total cholesterol:225mg/dl, HDL:16.5mg/dl, LDL:179mg/dl, triglyceride:416mg/dl, DEXA scan: osteopenia (T score -2.1). As patient had no clinical features suggestive of overt Cushing’s syndrome and with a right adrenal incidentaloma and results of adrenal hormonal assessment, the diagnosis was consistent with subclinical Cushing’s syndrome.

Discussion: With increasing use of various imaging techniques such as USG, CT and MRI, adrenal masses are being detected with increased frequencies. Autopsy studies suggest an incidence of adrenal incidentaloma of 1 to 6% while imaging studies suggest incidence of 3.5%. A substantial proportion of these incidentalomas are hormone producing and most are cortisol producing resulting into Cushing’s syndrome or subclinical Cushing’s syndrome (5%-20%). Estimated prevalence of subclinical Cushing’s syndrome is 79 cases per 100,000 persons. The condition is characterized by clinically unapparent adrenal mass with subtle autonomous and dysregulated cortisol secretion not fully restrained by pituitary feedback. The condition is often associated with hypertension, glucose intolerance, dyslipidemia and osteopenia. Management includes surgical approach and non-surgical approach encompassing treating metabolic conditions if any and routine follow-up.

Conclusion: Patient with asymptomatic adrenal incidentaloma should be routinely screened for hormone overproduction especially for cortisol excess.

Abstract #121

17α-HYDROXYLASE DEFICIENCY IN THREE 46,XY PHENOTYPIC FEMALE PATIENTS

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Objective: 17α-Hydroxylase deficiency (17OHD), a rare autosomal recessive form of congenital adrenal hyperplasia (CAH), is caused by mutations in the gene encoding cytochrome P450c17 (CYP17). We aim to describe the presentation, unique genetic findings, and
management of three patients with 17OHD.

Case Presentation: Three phenotypic females, a 21 year old from Mexico (proband A) and two siblings from Kuwait, age 23 (proband B) and 17 years respectively, presented with primary amenorrhea, lack of secondary sexual characteristics, and hypertension. None had clinical manifestations of adrenal insufficiency. Due to long standing uncontrolled hypertension, proband A had narrowing of the retinal arterioles with focal constriction and proband B had left ventricular hypertrophy. All patients came from consanguineous families. Endocrine investigation revealed low or undetectable levels of the steroids requiring 17-hydroxylation for biosynthesis (cortisol, testosterone, estrogen, DHEAS, 17-hydroxyprogesterone), while those not requiring 17-hydroxylation (progesterone, deoxycorticosterone, corticosterone) were high. ACTH, FSH, and LH levels were elevated. All patients had suppressed plasma renin activity and low aldosterone level, but only proband A was hypokalemic. A 46,XY karyotype was found in all patients. Imaging revealed the absence of uterus and adnexal structures. PCR failed to amplify exons 1 through 6 of the CYP17 gene which contains 8 exons. The patients’ hypertension resolved after combining glucocorticoid therapy with spironolactone.

Discussion: 17OHD defects in the biosynthesis of cortisol and sex steroids result in mineralocorticoid excess, hypertension typically with hypokalemia, and sexual abnormalities such as primary amenorrhea or pseudohermaphroditism in genotypic males. Phenotypic differences have been described. The disease is usually diagnosed at puberty. The probands’ condition was diagnosed late and the lack of timely adequate therapy resulted in complications. To date, more than 80 mutations in the CYP17 gene associated with CAH have been described. Interestingly, only a part of our patients’ CYP17 sequence could be determined by currently available commercial testing. This raises the possibility of homozygous intragenic deletion of exons 1 through 6 of the gene, which is not reported yet in 17OHD. Genomic hybridization microarray targeting the CYP17 gene is considered to confirm our suspicion.

Conclusion: The combination of hypertension, hypokalemia, and lack of secondary sexual development could point towards the diagnosis of 17OHD. Genetic testing and family member screening may be warranted. Prompt implementation of appropriate therapy is important to avoid complications.

Abstract #122

SUBCLINICAL CUSHING’S SYNDROME: IS IT CLINICALLY SILENT AND DETRIMENTAL?

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Objective: Subclinical Cushing’s Syndrome (SCS) has not received the clinical attention it deserves due to lack of well-defined diagnostic criteria and clear guidance on clinical management. We would like to describe a patient with SCS who underwent successful curative surgery.

Case Presentation: A 75-year-old male was evaluated for a 2.2 cm left adrenal mass discovered incidentally. Medical history included metabolic syndrome, IFG, hypertension, hyperlipidemia, asthma, GERD, OSA, partial empty sella. Medications included metformin, levothyroxine, testosterone gel, furosemide, lisinopril, felodipine, metoprolol XL, atorvastatin, fluticasone/salmeterol, montelukast, esomeprazole, ranitidine, duloxetine, gabapentin, mirtazapine, and uroxatral. Besides poorly controlled hypertension, his BMI was 35-37 kg/m2. Review of system was pertinent for easy bruising, weight gain, and fatigue. Examination did not reveal stigmata for Cushing’s syndrome. Laboratory revealed suppressed ACTH on 3 occasions (< 5 pg/mL; normal 6-50), failed 1mg and 2mg overnight DST (cortisol 10 and 7.7 mcg/dL, respectively), normal CBG level, normal 24-h free cortisol level on 3 occasions, abnormal midnight salivary cortisol (0.16 and 0.14 mcg/dL; normal <0.09), and abnormal midnight serum cortisol while asleep (6.2 mcg/dL; normal <5). Screening for pheochromocytoma and primary hyperaldosteronism was negative. The patient underwent laparoscopic left adrenalectomy receiving perioperative stress dose steroid with pathology confirming adrenocortical adenoma. Six weeks after surgery, his blood pressure completely normalized; ACTH level rose to 11 pg/mL. Postoperatively, the patient developed adrenal insufficiency requiring corticosteroid replacement therapy. He also reported 15-pound weight loss and improvement in skin bruising.

Discussion: SCS has long been a debate whether or not it is clinically significant. There has recently been a resurgence of interest due to emerging data on its strong association with clinical factors that increase cardiovascular risk. It has also been shown to increase prevalent and incident osteoporotic fractures. In addition, there are recent data that favor surgery over observation. Our patient met at least 3 diagnostic criteria with sensitivity of 85.7% and
specificity of 72.7% (accuracy 77.8, p-value=0.0382). Following surgery, his clinical improvement was already evident at 6-week follow up. In addition, the resultant post-operative adrenal insufficiency further confirms the diagnosis of SCS.

**Conclusion:** SCS is a true clinical entity and can be clinically detrimental despite mild degree of hypercortisolemia. Early detection and surgery can improve and possibly reverse the underlying metabolic abnormalities.

**Abstract #123**

**RAPID DEVELOPMENT OF A FUNCTIONAL ADRENOCORTICAL CARCINOMA IN A 56-YEAR OLD WOMAN WITH HISTORY OF AN APPARENTLY BENIGN ADRENAL NODULE: SIGNIFICANCE OF 1-MG OVERNIGHT DEXAMETHASONE SUPPRESSION TEST**

Samuel Olatunbosun, MD, FACP, FACE, Gabriella Cardoza-Favarato, MD

**Case Presentation:** A 56-year old woman, referred by primary physician, presented with 5-month history of weight gain and development of a “moon face”. Per records, an apparently benign 1 cm Lt adrenal nodule was incidentally discovered on MRI 10 months earlier after ESWL. The plan then was to repeat adrenal MRI in 1 year, because she was noted to have had CT imaging for nephrolithiasis, at least twice within 9 months preceding the MRI with no interval growth of the incidentaloma. Urine metanephrines and PAC/PRA were normal. UFC was obtained 14.2 mcg/24hrs; noted not to be the ideal test, but level described as “low”, hence “reassuring”. There were no reported clinical features of Cushing’s syndrome or hyperandrogenism. DST (dexamethasone suppression test) was deferred till next annual evaluation. Past medical history of Rt breast cancer s/p lumpectomy and XRT 5 years ago; Rt leg DVT, 6 months after knee replacement. Significant family history of cancer on paternal side; dad had lung, liver and brain tumors; uncles also had lung cancer; but were all smokers; paternal aunt had breast cancer. On examination: BP 158/92, HR 69, Wt 240 lbs, BMI 33.47 kg/m2; round face, facial plethora and hirsutism; dorsocervical fat pad; truncal obesity. Cortisol 27.9 mg/dL from 1-mg overnight DST; 24-hr UFC 717.3; ACTH < 1 pg/ml. Urine metanephrines and PAC/PRA were normal; FBG - normal. Adrenal MRI showed a Lt adrenal 5.5 x 5.5 x 5.8 cm mass with high T2 signal intensity; minimally heterogeneous; no signal dropout was seen on out of phase images. Additional labs -Testosterone 103 ng/dL; DHEAS 117.0 mcg/dL; 17-OHP 250 ng/dL; FSH 0.3 mIU/mL, LH 0.1 mIU/mL. Impression: ACTH-independent Cushing’s syndrome with concerns for ACC; androgen cosecretion. She underwent an open Lt adrenalectomy with a 7.5 cm tumor removed. Histopathology was consistent with ACC; tumor was close to surgical margin. Postop 24-hr UFC 42.2 mcg; Testosterone 2.6 ng/dl; DHEAS 22.65 mcg/dl. CT Chest/Abd/Pelvis did not reveal any mass lesions or lymphadenopathy suggestive of metastasis; hence stage 3 ACC. Adjuvant mitotane therapy was started, reasonably tolerated. Radiation therapy also was instituted; received a total of 50.4 Gy.

**Discussion:** Early detection of subclinical Cushing’s syndrome with DST when the adrenal nodule was initially discovered could have altered the clinical course of this patient’s tumor. Occurrence of ACC and breast cancer in the patient, and her family history of cancer raise concern for Li Fraumeni syndrome.

**Conclusion:** For an adrenal incidentaloma the screening test of choice for SCS is 1-mg overnight DST. Considering the rarity of ACC, and clustering of cancers in this patient’s family, genetic evaluation is reasonable.

**Abstract #124**

**ADRENAL CUSHING IN A GRAVES DISEASE PATIENT WITH ORBITAL LYMPHOMA**

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**Objective:** Despite known association between Hashimoto thyroiditis with thyroid lymphoma, orbital lymphoma is rare in a patient with previous Graves disease, making the etiologic diagnosis of exophthalmic syndrome more difficult.

**Case Presentation:** A 64-year-old woman with a 19-years history of Graves disease with asymmetrical ophthalmopathy (Reye 21 mm, Leye 19 mm) for which she received treatment with antithyroid drugs and corticosteroids, presented with worsening right eye symptoms simultaneously with the development of a right preauricular tumor. Approximately 9 years before, a diagnosis of right orbital tumour had been made by an orbital MRI with a follow-up CT scan after 2 years showing no progression. She was diagnosed with diabetes 4 years before, on insulin glargine, metformin with HbA1c of 7.5% at presentation. Physical examination reveals right eye exophthalmia, swelling of periorbital tissues, chemosis, redness and limitation of eye movements. The thyroid function was normal. Cushing’s syndrome was
suggested by supraclavicular and dorsocervical fat and facial rounding with minimal hirsutism. Basal ACTH levels were suppressed (<1 pg/mL), despite normal cortisol levels 14 ug/dl; cortisol rhythm was impaired (midnight cortisol = 10.3 ug/dl) and didn’t suppressed after 2 mg 2d dexamethasone (13.4 ug/dl). The CT scan showed a left adrenal mass, 27/29 mm diameter; and the head MRI showed right orbital infiltrative lesion involving the lacrimal gland and optic nerve with intracranial extension and multiple parotid lymph nodes. Excisional biopsy of the preauricular nodule suggested lymphomatous infiltration, while bone marrow biopsy revealed involvement.

Discussion: Treatment will include left adrenalectomy followed by corticosteroid replacement therapy and then radiotherapy and chemotherapy for lymphoma. The approach order of this strange combination of disorders is discussed.

Conclusion: This case shed light on the importance of differential diagnosis between inflammatory lesion and orbital tumor in patients with unilateral proptosis in the course of Graves’ ophthalmopathy and the importance of a detailed evaluation of patients with suspected hypercortisolism even without typical Cushing’s syndrome.

Abstract #125

SUBCUTANEOUS METASTASIS AS INITIAL PRESENTATION OF PRIMARY ADRENOCORTICAL CARCINOMA (ACC)

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Objective: Primary Adrenocortical Carcinoma (ACC) is a very rare and aggressive malignancy with an annual incidence of 1 per 1 million people. Patients often have metastatic disease at initial presentation with the most common at the liver, lungs, lymph nodes and bone. While cutaneous metastasis of ACC is uncommon with currently two reported cases, in a 6-year old boy and a 52-year old woman.

Case Presentation: An 84-year old women initially presented with right upper quadrant pain and CT scan of the abdomen showed: Cholelithiasis, pancreatic head mass and right adrenal gland mass 5.2x3x4.1cm, left adrenal gland was nodular without discrete mass. Workup done showed: normal 1mg Dexamethasone suppression test (cortisol 48.6 nmol/L, N<50nmol/L), elevated serum cortisol (812.7 nmol/L, N 138-690 nmol/L), normal aldosterone (upright 11.8 ng/dl, N 4-31 ng/dl), renin (upright 5.03 ng/mL, N 1.9-6 ng/mL), and PAA/PRA 2.3, normal DHEA-S 49.3μg/dl. Impression was: Bilateral nodular adrenal adenoma, rule out Cushing’s Syndrome. One month after, patient started to have palpable isolated masses on right, subcostal area and left upper arm measuring 1-2cm diameter, firm, movable, non erythematous and tender on palpation subcutaneous nodules. It was accompanied with intermittent fever, decreased appetite and weight loss (6kg in 1 month). Excisional biopsy of subcutaneous nodules was done and patient was discharged stable.

Five days after discharge, she developed obstructive symptoms and started to be jaundiced. Repeat CT scan of abdomen showed: Interval increase in pancreatic head mass, significant increase in size of right adrenal mass, 6.3x4.7x7.2 cm (from 5.2x3x4.1 cm done last month) now extends partly in adjacent right hepatic lobe and 2.1x1.4 cm right lower perihepatic mass. ERCP with stent insertion was done. Histopathology report of the excised subcutaneous nodules showed: malignancy metastatic to subcutaneous tissue, Primary Adrenocortical CA is highly considered. Immunohistochemistry staining showed positive for Cytokeratin and Vimentin, negative for Synaptophysin and CA 19-9, results showed Metastasis from Primary Adrenocortical Carcinoma. Final diagnosis: Primary ACC with metastasis to subcutaneous tissue, pancreas and liver.

Discussion: The prognosis of ACC is poor with an overall-year survival rate of 15-47%. When metastatic disease is present at initial presentation, death usually occurs within one year. Surgical resection is the treatment of choice and the only potential cure for ACC.

Conclusion: Skin is a rare site of metastatic disease in patients with Primary ACC. Therefore, it is of paramount importance to recognize that the tumor is a metastatic presentation of an underlying carcinoma.

Abstract #126

AN UNUSUAL PRESENTATION OF THE “GREAT MASQUERADER”

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Objective: To present a case of transient ischemic attack (TIA) caused by undiagnosed pheochromocytoma.

Case Presentation: A 62-year-old Caucasian woman presented after a fall. In the emergency department, she complained of chest pain and dyspnea. Multiple rib fractures and a large heterogeneous solid and cystic retroperitoneal mass measuring 8.1 x 9.8 x 10.2 cm were found on CT. On the fourth day of hospitalization, she developed confusion, dysarthria, and right facial droop.
Acute infarcts to the left thalamus and MCA territory were found on the CT of the head. An ultrasound-guided biopsy of the mass indicated a neuroendocrine neoplasm. Following the biopsy, blood analysis revealed chromogranin 33 nmol/L (0-6 nmol/L), plasma normetanephrines 1092 pg/mL (0-145 pg/mL), and metanephrines 377 pg/mL (0-62 pg/mL) suggestive of pheochromocytoma. She had no further complications during her hospital stay and was transferred to acute inpatient rehabilitation. An outpatient MRI of the abdomen revealed a 10 cm left retroperitoneal periaortic mass consistent with neuroendocrine neoplasm. Pathology of the mass reported tumor cells positive for a neoplasm suggestive of endocrine/neuroendocrine origin from the pancreas or less likely gastrointestinal tract or lung. Endocrinology conducted outpatient preoperative management with phenoxybenzamine and frequent blood pressure monitoring. Six weeks later the mass was excised. Following a difficult postoperative state, the patient recovered nicely with normalized normetanephrines 94 pg/mL, and metanephrines 33 pg/mL levels. 

Discussion: Pheochromocytoma's myriad of clinical manifestations has led to the name “great masquerader.” Its diagnosis is challenging since the classic symptomatic triad of headaches, sweating, and palpitations in conjunction with episodic hypertension may not be the presentation. Other presentations may include cerebrovascular event or a myocardial infarction. Proposed mechanisms of neurological injury in pheochromocytoma include hypertension and vasospasm that overwhelm the cerebrovascular autoregulation causing transient impairment of the circulation or infarction. 

Conclusion: Pheochromocytoma should be in the differential of an incidentally found abdominal mass in order to avoid complications of biopsy. TIA and strokes can be caused by hemodynamic instability and can be the primary presentation of pheochromocytoma.

Abstract #127

A CASE OF CUSHING SYNDROME CAUSED BY PHEOCHROMOCYTOMA

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UAMS

Objective: We present a rare case of ectopic Cushing syndrome due to ACTH producing pheochromocytoma. 

Case Presentation: A 50 year-old male was admitted with hypertensive emergency, acute renal failure, leukocytosis, hypokalemia (K 1.6 mEq/L) and new onset diabetes mellitus. Physical exam was significant for diffuse abdominal tenderness, bilateral pitting edema of the lower extremities and multiple bruises and ecchymosis on the upper limbs. CT scan and MRI of the abdomen showed a right adrenal mass measuring 4.1 x 3.8 cm and left adrenal gland hyperplasia. The hormonal work up revealed elevated plasma metanephrine at 2.3 nmol/L (0.0-0.49), and normetanephrine 7.2 nmol/L (0.0-0.89), 24-hour urine metanephrine 1556 µg/gr creatinine (0-300) and normetanephrine 2306 µg/gr creatinine (0-400). Plasma cortisol was 102.3 µg/dL with no circadian rhythm; 24 hour urine cortisol was 3625 µg/g cr (< 24) with elevated ACTH at 1073 pg/ml (7-69). MRI of the sella did not show any pituitary mass and octreotide scan was negative. PET scan showed hypermetabolic activity in both adrenal glands. The uncontrolled hypertension was treated with Phenoxybenzamine, Labetalol, Hydralazine and Lisinopril. He was also treated with Metyrapone and Ketokonazole, which normalized the cortisol level. The patient was submitted to laparoscopic right adrenalectomy with no complications. Pathology report showed a 5 cm pheochromocytoma with negative margins and immunohistochemical staining positive for chromogranin and synaptophysin, with patchy positivity for ACTH. After the surgery, he was initially started on stress dose hydrocortisone and then switched to oral dexamethasone followed by oral hydrocortisone. The follow up hormonal evaluation showed normal plasma metanephrine and normetanephrine, normal 24 hour urine metanephrine and minimally elevated urine normetanephrine at 607 µg/gr creatinine, ACTH level was < 5 pg/ml with low cortisol.

Discussion: CS is ACTH-dependent in 80% of cases and 10% of these are due to ectopic production of corticotrophin. Ectopic CS is caused by a pheochromocytoma in 3.4% of the cases. The incidence of ectopic hormone secretion in pheochromocytoma is present in approximately 1% of the cases. Most ectopic hormone-secreting pheochromocytoma cause hypercortisolism due to ACTH production. CRH has also been implicated. Most of these pheochromocytomas are neither malignant nor familial.

Conclusion: The presence of both hypercortisolism and pheochromocytoma constitute a diagnostic and therapeutic challenge. Ectopic hormonal secretion often presents with unusual symptoms. Early diagnosis of pheochromocytoma and Cushing syndrome requires a high index of suspicion.
Abstract #128

ENDOGENOUS ACTH-DEPENDENT CUSHING SYNDROME AND REFRACTORY HYPOKALEMIA CAUSED BY GASTRIC ADENOCARCINOMA

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Objective: To present a case of Cushing syndrome caused by ectopic ACTH secretion secondary to gastric adenocarcinoma.

Case Presentation: A 42 year-old woman presented with a two day history of palpitations, fatigue and peripheral edema. Her potassium was 2.0 meq/l and she was hypertensive and hyperglycemic. Rest of the physical examination was normal. CT scan showed bilateral adrenal hyperplasia and lymphadenopathy in the upper abdomen. Her morning serum cortisol, ACTH, androstrenedione and DHEA-Sulfate levels were 5 times the upper limit. High-dose dexamethasone did not suppress ACTH production. Aldosterone, 11-desoxycortisol and 17-A (OH) progesterone levels were normal. Abdominal MRI with Gadolinium showed an enhancing mass along the greater curvature of the stomach. MRI of the brain excluded pituitary disease. Liver biopsy revealed metastatic poorly differentiated adenocarcinoma which stained positive for ACTH. She was diagnosed with ectopic ACTH syndrome caused by gastric adenocarcinoma. She was started on spironolactone, mitotane and ketoconazole. She developed gastric and duodenal recurrent perforations. Refractory hypokalemia complicated her course. She remained hypokalemic despite concomitant use of high-dose spironolactone and intravenous potassium.

Discussion: ACTH-dependent Cushing represents 80% of the cases of endogenous Cushing; only 20% are due to non-pituitary causes. Among non-pituitary causes, small-cell lung carcinoma is the most common. Gastric adenocarcinoma is an extremely rare case of non-pituitary ACTH-dependent endogenous Cushing Syndrome. In our patient, mineralocorticoid excess was excluded. Hypokalemia is very common in patients with non-pituitary ectopic ACTH syndrome. Its incidence is directly proportional to cortisol levels. At very high levels, cortisol can activate mineralocorticoid receptors. Hypokalemia can also be explained by intermediary adrenal steroids with mineralocorticoid activity. Surgical removal of the primary tumor is the treatment of choice. Other interventions are aimed at blocking steroid biosynthesis or antagonizing glucocorticoid receptors. In the setting of metastatic disease, adrenalectomy is the best option.

Conclusion: Non-pituitary ectopic-ACTH Syndrome caused by gastric adenocarcinoma is extremely rare. Hypokalemia could be explained by direct activation of mineralocorticoid receptors by excessive cortisol levels. Surgical excision of the tumor is the treatment of choice, accompanied by medical therapy to block glucocorticoid production.

Abstract #129

A CASE OF A TESTOSTERONE-PRODUCING ONCOCYTIC ADRENOCORTICAL ADENOMA

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Objective: Oncocytic neoplasms of the adrenal gland are rare, typically benign and non-functioning. Histologically, they are characterized by epithelial cells with abundant eosinophilic, granular cytoplasm. The number of reported cases of functioning adrenocortical oncocytomas have increased in recent years.

Case Presentation: A 59 year female with history of hypertension presented with a 14 x 14 cm left suprarenal mass that was found incidentally on a CT of the abdomen. Physical examination revealed severe, diffuse hirsutism in a male distribution pattern, hypertrichosis, and severe virilization. With the exception of mild left upper quadrant fullness and hirsutism, she had no other complaints. Liver/renal function, electrolytes, and complete blood counts were within normal values. Hormonal testing as follows: testosterone 842 ng/dL, DHEA-S >1000 ug/dL, androstenedione 852 ng/dL, progesterone 11.78 ng/ml, estradiol 39 pg/mL, cortisol 15.8 ug/dL, 24 hour urine metanephrines, normetanephrines and cortisol levels were within normal limits. A left open adrenalectomy was performed and the mass was resected showing no adjacent tissue invasion. Immunohistological evaluation demonstrated cortical oncocytic adenoma of borderline malignant potential with clear margins. In addition to no angiolymphatic invasion, there were infrequent mitoses (<1/50 hpf), apoptotic figures exceeded 50 per 50 hpf, no necrosis, occasional atypical cells. Classified as borderline malignant potential as it met one minor Weiss criteria.

Discussion: Postsurgical recovery was uneventful and follow up laboratory at 7 weeks revealed testosterone level <3 ng/dL and DHEA-S 42.8 ug/dL. The patient reported hot flashes and reduction in the male hair distribution. Oncological consultation recommended repeat CT scans of the chest, abdomen/pelvis 6 months post-op which
revealed no recurrence. Follow up every 3 months since has demonstrated almost disappearance of the hirsutism. Oncocytomas are extremely rare, mostly found in the kidneys, thyroid, parathyroid, pituitary or adrenal glands. Oncocytomas are most commonly nonfunctioning and are typically found incidentally. The incidence of these tumors is about 1-2 per million population annually. Diagnosis is made by histological evaluation using the Weiss criteria. Treatment depends on the tumor’s size; adrenalectomy being the treatment of choice.

**Conclusion:** Because of the rarity of these adenomas, diagnosis and management rely almost entirely on anecdotal case reports and review of the existing literature. More cases should be published to help create guidelines for the management of this rare but sometimes life-threatening tumors.

**Abstract #130**

**CLINICALLY CHALLENGING CARDIAC MANIFESTATIONS OF PHEOCHROMOCYTOMA**

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North Shore Medical Center

**Objective:** This case illustrates the atypical presentations of Pheochromocytomas, including cardiac manifestations mimicking myocardial infarction and labile hypertension.

**Case Presentation:** A 71 year old male with hypertension, presented to ER with dizziness, pain radiating to the shoulders and history of recent episodes of panic and palpitations. He had tachyarrythymia and EKG showed ST segment elevation in inferior leads. Coronary angiography showed non critical stenosis and no intervention was performed. He continued having EKG changes and systolic BP over 200s. Re-catherisation showed unchanged vessel anatomy, but due to dynamic EKG changes, the artery was stented. Later he developed wide complex tachycardia and hypertensive crisis with blood pressure of 200/128. BP was very labile ranging from systolic of 200s, then dropping to 80s with heart rate of 140s. The hemodynamic instability gave rise to the suspicion of Pheochromocytoma. In hospital he had terrible headaches with diaphoretic spells and was cold, clammy & sweaty. Lab workup showed high urine free epinephrine of 2063, norepinephrine of 1240, metanephrine 11030. CT abdomen showed 5.0 x 4.3cm mass in the right adrenal gland. He was managed by alpha-blockade with phenoxybenzamine followed by beta blockade. 4 weeks later, after adequate alpha blockade was achieved, surgery was performed. Histology showed nests of large tumor cells with eosinophilic cytoplasm and a delicate fibrovascular stroma classic for pheochromocytoma. Following surgery, his condition stabilized.

**Discussion:** Pheochromocytomas are rare catecholamine-secreting, chromaffin cell tumors. They classically present with the triad of episodic headache, sweating and tachycardia. Some patients present with symptoms associated with myocardial infarction, and very few of these are found to have significant coronary atherosclerosis indicating that the myocardial injury is likely due to direct toxic effects of catecholamine including accelerated cell death and fibrosis. Rare cardiac presentations include ACS, ST elevation, rhythm disturbances, QT prolongation and Takotsubo cardiomyopathy. Evaluation includes urinary fractionated catecholamine and metanephrine levels (most sensitive), followed by imaging, MRI or CT scan. All patients should undergo surgical resection. Preoperative management includes BP control, with combined alpha and beta adrenergic blockade. Alpha blocker is given for 10-14 days preop and longer in cardiac manifestations.

**Conclusion:** To recognize and diagnose the atypical cardiac manifestations of Pheochromocytomas. The management includes control of high blood pressure, followed by surgery.

**Abstract #131**

**A RARE ASSOCIATION OF PHEOCHROMOCYTOMA AND INTRACARDIAC THROMBUS**

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UCSF-Fresno Medical Education Program

**Objective:** To report a patient with pheochromocytoma who presented with pulmonary embolism due to intracardiac thrombus

**Case Presentation:** A 40-year-old Asian female with history of diabetes mellitus type 2 and hypertension presented to ED with shortness of breath of 5-day duration. Initials vitals were BP 152/114 mm Hg, HR 97, T’ 36.6 °C. CT chest showed a large pulmonary embolus involving the right main, lobar and segmental pulmonary arteries. There was normal bilateral lower extremity venous duplex ultrasound with no evidence of deep venous thrombosis. However, there was left ventricular and right atrial thrombus at echocardiogram. MRI abdomen revealed a 12.3cm left adrenal mass. 24 hour urine studies showed significantly elevated total metanephrines 32205 (NR < 900 ug/24hr), metanephrines 25680 (NR< 300 ug/24hr) and normetanephrines 6528 (NR< 600 ug/24hr). She was anti-coagulated and underwent left adrenalectomy 2 months later. Surgical pathology confirmed pheochromocytoma of left adrenal gland. At follow-up visit 3 months after
operation, she was well and her 24 hour urine results all returned to within normal ranges.

**Discussion:** Pheochromocytomas are catecholamine-producing tumors arising from the chromaffin cells in the sympathoadrenal system with the prevalence of 0.1% to 0.6%. Thromboembolic events have been reported in patients with pheochromocytoma but the association of intracardiac thrombus and pheochromocytoma is extremely rare. The exact mechanism of thrombosis in pheochromocytoma remains unknown.

**Conclusion:** This case illustrated that patients with pheochromocytoma may present with pulmonary embolism due to intracardiac thrombus. Early recognition of this association and appropriate management will result in improvement in the outcome.

Abstract #132

**BILATERAL ADRENAL HEMORRHAGE WITHOUT ADRENAL INSUFFICIENCY**

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**Case Presentation:** A 76 yo male, with a history of COPD and PUD, was admitted with a 1 week history of vague abdominal pain, decreased appetite, nausea, emesis, weakness, and fatigue. On the day of admission, he had abrupt onset of 10/10 midepigastric abdominal pain. In the ED he was afebrile, BP 157/72, pulse 87, RR 18 and O2 Sat 95% RA. Exam: Mild discomfort to palpation in the mid epigastrum without guarding, rebound or masses. Labs: WBC 22k, no left shift, HCT 39.6, Na 133, K 3.7, BUN/Cr 25/1.5, Amylase and lipase normal. Imaging: GB U/S: sludge; CT abd: RLL 1.4 cm stellate lung lesion, and prominent adrenal glands without masses. Working diagnosis was acute cholecystitis vs PUD. HIDA was negative. Treated empirically with antibiotics. On the 3rd hospital day a CT chest was done to evaluate the lung lesion. It showed bilateral enlargement of the adrenals: R 2.8; L 3.7. HU 30’s. The patient’s symptoms from admission were improving and hemodynamics, including orthostatics, were normal. An ACTH Stim Test done on the 3rd hospital day: Bo-16.4; 30’-18.6; 60’-19.1, was considered normal. Patient was d/c’d on small dose of hydrocortisone (10 am , 5 pm) “just in case.” 2 weeks after discharge he had another ACTH Stim Test done (off hydrocortisone) and it too was normal: Bo-12.9; 30’-19.2; 60’-20.6. Hydrocortisone was d/c’d. Follow up CT and 2 months after d/c showed a 1.2 cm nonspecific right adrenal nodule. The left was normal.

**Discussion:** Bilateral adrenal hemorrhage is uncommon and may present with vague, nonspecific signs and symptoms similar to this case. When it does occur though, especially if it is unrecognized and massive, destroying 90% of the adrenal cortex, it can lead to hemodynamic collapse and potentially death. We believe our patient had radiographic evidence of significant bilateral adrenal hemorrhage based upon the rapid fluctuations in the size of the adrenal glands as described above. Despite this seemingly significant intraadrenal bleed, our patient did not display clinical nor chemical evidence of adrenal insufficiency, the latter based upon the ACTH Stim Tests done during the admission and 2 weeks after the patient’s discharge. The literature describes, and this case demonstrates nicely, that not all cases of bilateral adrenal hemorrhage results in loss of adrenal cortical function.

**Conclusion:** This is a case that clearly demonstrates, and confirms the literature, that not all cases of bilateral adrenal hemorrhage results in primary adrenal insufficiency (AI). One certainly needs to assess for adrenal insufficiency in each case given the potential catastrophic risks of missing AI.
DAPAGLIFLOZIN REDUCES POSTPRANDIAL PLASMA GLUCOSE CONCENTRATION AS ADD-ON THERAPY IN PATIENTS WITH TYPE 2 DIABETES

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1. AstraZeneca, 2. Bristol-Myers Squibb

Objective: Postprandial plasma glucose (PPG) concentration is a major determinant of HbA1C when it is 7%-8%, but with worsening HbA1C control, the contribution of fasting hyperglycemia increases. This implies that control of fasting hyperglycemia alone may not be optimal to achieve HbA1C <7.0% in patients with type 2 diabetes mellitus (T2DM). Dapagliflozin (DAPA) is a sodium-glucose cotransporter 2 (SGLT2) inhibitor that reduces plasma glucose concentration independently of insulin secretion or action by increasing renal glucose excretion. In this analysis, we assessed the effect of DAPA on PPG as add-on therapy to commonly used antidiabetic medications in three phase 3, 24-week clinical trials.

Methods: Patients with T2DM were randomized to receive either DAPA or placebo (PBO) as add-on to glimepiride (GLIM) (NCT00680745, N=596), pioglitazone (PIO) (NCT00683878, N=420), or sitagliptin (SITA) ± metformin (NCT00984867, N=451). 2-h PPG was assessed as a secondary end point following an oral glucose or liquid meal tolerance test. An ANOVA model was used for change from baseline in 2-h PPG with treatment and strata (where applicable) as fixed effects and baseline value as a covariate. Safety was evaluated from reported adverse events (AEs).

Results: PBO-corrected mean changes (95% CI) from baseline at 24 weeks in 2-h PPG for DAPA 10 mg/d were -49.1 (-64.1, -34.1) mg/dL (P<0.0001) as add-on to GLIM; -53.3 (-71.1, -35.6) mg/dL (P<0.0001) as add-on to PIO; and -42.9 (-52.1, -33.8) mg/dL as add-on to SITA. The proportion of patients with ≥1 AE was generally similar between DAPA 10 mg/d and PBO groups. Events suggestive of urinary tract infections were also similar between DAPA (4%-5%) and PBO groups (4%-8%). Events suggestive of genital infections were more frequent with DAPA (7%-9%) than with PBO (0-3%). Hypoglycemic events were infrequent and similar between DAPA and PBO in the add-on to PIO (0 vs 1%) and add-on to SITA studies (3% vs 2%), but more frequent with DAPA vs PBO in the add-on to GLIM study (8% vs 5%). No patients discontinued from the studies as a result of hypoglycemia.

Discussion: Observational studies suggest that PPG may be more predictive of cardiovascular morbidity and mortality and microvascular complications than fasting plasma glucose. Higher postprandial blood glucose concentrations may lead to increased glucose filtration, allowing for greater glucose excretion with SGLT2 inhibition and effective PPG lowering, thus potentially preventing vascular complications.

Conclusion: DAPA produced significant reductions in PPG in patients with T2DM when used as add-on therapy to a sulfonylurea, thiazolidinedione, or DPP-4 inhibitor.

HIGH RESISTIN LEVELS ARE ASSOCIATED WITH FUTURE CARDIOVASCULAR EVENTS IN TYPE 2 DIABETIC PATIENTS

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Objective: The purpose of this study was to determine whether plasma levels of resistin could predict occurrence of future cardiovascular (CV) events in patients with type 2 diabetes mellitus.

Methods: We consecutively evaluated 216 patients (age 73.2±9.3, male 55%), who presented with a type 2 diabetes. Patients were followed up for 36±3 months. The primary outcome was major adverse cardiac events (MACEs). Baseline concentrations of circulating levels of resistin, leptin, adiponectin, and hsCRP were determined by enzyme-linked immunosorbent assay (ELISA).

Results: Patients were divided into two groups based on the median of each biomarker. MACEs developed in a total of 89 patients (41%). In Kaplan-Meier analyses, high-leptin (P = 0.004) and high-resistin (P = 0.036), but not high-adiponectin or high-hsCRP, were significantly associated with MACEs. When we stratified patients into four groups based on leptin and resistin, the high-leptin/high-resistin group had a 4.9-fold higher MACE risk compared with the low-leptin/low-resistin group (P = 0.0005). The Cox proportional hazards analysis including established risk factors, log-leptin and log-resistin, revealed that log-leptin (P = 0.0001, HR (95%CI): 1.7 (1.3-2.1)) and log-resistin (P = 0.006, HR (95%CI): 1.5 (1.1-2.1)) were independently associated with MACEs. Multivariate Cox analysis with the forced inclusion model with the previously identified prognostic factors demonstrated resistin as a significant predictor of the future CV events (HR 1.23, 95%CI 1.09-1.38, P<0.001).

Discussion: Proteins secreted from adipocytes - so-called adipocytokines - influence metabolic and vascular function. Resistin has been linked to obesity, type 2 diabetes mellitus, inflammation and atherosclerosis. Recent data suggest that various adipocytokines are dysregulated in type 2 diabetes.
mellitus and might be of pathophysiological and prognostic significance in cardiovascular complications. **Conclusion:** Elevated plasma levels of resistin independently correlated with the future CV events in type 2 diabetes mellitus. High resistin value may serve as a predictive marker of MACEs in combination with leptin and provide useful information in managing patients with type 2 diabetes mellitus.

**Abstract #202**

RELATIONSHIP OF ELEVATED LEVELS OF VISFATIN WITH INSULIN RESISTANCE AND PROTHROMBOTIC STATE IN TYPE 2 DIABETIC PATIENTS

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**Objective:** The purpose of this study was to examine the relationship between visfatin and prothrombotic factors in patients with type 2 diabetes mellitus. **Methods:** We consecutively evaluated 223 patients, who presented with a type 2 diabetes. We measured anthropometric and biochemical variables including renal function, plasma lipid profile, fasting glucose, insulin and C-peptide, PAI-1, prothrombin fragment 1+2 (F1+2), and D-dimer as markers of a prothrombotic state, and C-reactive protein (CRP) as a marker of proinflammatory state. The Homeostatic Model Assessment (HOMA) index was calculated as an index of sensitivity to insulin. **Results:** Type 2 diabetic patients had significantly higher levels of visfatin, D-dimer, PAI-1, F1+2 compared with healthy men. On univariate regression analysis, visfatin was directly related with PAI-1 (r = 0.173, P<0.05) and duration of diabetes (r = 0.141, P<0.05), BMI (r = 0.214, P < 0.01), HOMA index (r = 0.347, P < 0.001), CRP (r = 0.375, P < 0.001), triglycerides (r = 0.193, P<0.01) and LDL-cholesterol (r = 0.190, P < 0.01), and inversely related with HDL-cholesterol (r = -0.179, P<0.01). A multivariate analysis included demographic and anthropometric variables, alcohol intake and smoking habit, duration of diabetes, use of antihypertensive drugs, renal function and plasma lipid levels, HOMA index and CRP indicated that visfatin levels are independently related with D-dimer (β=0.203, P<0.01), PAI-1 and duration of diabetes (respectively: β=0.195 and β=0.157, both P<0.05), LDL cholesterol (β = 0.164, P<0.05), HOMA index (β = 0.236, P<0.001), and CRP (β=0.278, P<0.001). **Discussion:** Recent data suggest that various adipocytokines are dysregulated in type 2 diabetes mellitus and might be of pathophysiological and prognostic significance in cardiovascular complications. Visfatin has been linked to obesity, type 2 diabetes mellitus, inflammation and atherosclerosis. **Conclusion:** These results indicate that a prothrombotic state is associated with elevated visfatin level and duration of disease, insulin resistance and a proinflammatory status in type 2 diabetes mellitus. Intriguingly, high plasma level of adipokine seem to modulate platelet activation. These results suggest that increased visfatin levels in diabetes mellitus may be novel biochemical risk factors for atherothrombotic complications, promoting to procoaculant reactions.

**Abstract #203**

HOSPITAL ADMISSIONS AND EMERGENCY DEPARTMENT UTILIZATION AMONG PATIENTS RECEIVING DIABETES SELF-MANAGEMENT EDUCATION

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**Objective:** Approximately 25.8 million Americans live with diabetes with an estimated 176 billion dollar direct medical cost in 2012. Diabetes self-management education (DSME) aims to improve clinical outcomes and health status. It may also result in decreased rates of emergency department (ED) utilization, hospitalization, and health care costs. We sought to find the relationship between participation in DSME and subsequent ED visitation and hospitalization for any cause. We hypothesized that compared to a control group, patients who participated in DSME would have lower rates in both categories. **Methods:** This is a retrospective study of 572 diabetic patients over 6.5 years. Inclusion criteria included adult patients with type 1 or 2 diabetes who received care in our outpatient clinics. Billing data was used to identify hospital discharge and ED visit data. The total number of hospitalizations and ED visits at our facility were recorded from 3 months after the time of enrollment to the end of the study. Hospitalization and ED visit rates were evaluated at short-term (1 year) and long-term intervals (total) as the number per year. Differences in the rates between groups were tested with Poisson regression. **Results:** We identified 266 DSME participants and 306 controls. Of the total participants, 96.6% had type 2 diabetes with a mean HbA1c of 7.7. The mean number...
of DSME visits was 8.1 at a mean rate of 2.8 visits per year. There was no statistical difference in the rate of hospitalizations or ED visits between control and DSME patients. The mean short-term and long-term ED visit rate was 0.14 and 0.17 in the control group versus 0.21 and 0.22 in the DSME group. The mean short-term and long-term hospitalization rate was 0.25 and 0.23 in the control group versus 0.19 and 0.25 in the DSME group. There was also no significant difference in the ED visit or hospitalization rate when evaluated by total number DSME visits.

Discussion: Several limitations may explain these findings. Hemoglobin A1c was significantly higher in the DSME group. Patients with more severe diabetes may have been selected for DSME by their physicians, introducing selection bias. This study is also limited by retrospective design. Finally, we did not account for hospitalizations or ED visits at other facilities. A prospective study would be helpful to evaluate these trends further.

Conclusion: Though our results did not find a significant difference in hospital resource utilization with DSME, it is still an important tool in diabetes management. In the future, additional studies would be useful to evaluate long term benefits.

Abstract #204

ASPIRE CLINICAL TRIAL VERSUS CARELINK REAL-WORLD EXPERIENCES WITH INSULIN PUMP SUSPENSION FOR MITIGATION OF IATROGENIC HYPOGLYCEMIA

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Objective: Suspension of insulin delivery during hypoglycemia may improve outcomes in type 1 diabetes. In the US, Threshold Suspend (TS) - elsewhere known as Low Glucose Suspend (LGS) - was evaluated in two randomized clinical trials. We compared glucose excursions following pump suspensions lasting for 2 hours (“events”) mediated by the TS feature in the clinical trial setting with those following events mediated by the LGS feature in the real-world setting.

Methods: The TS feature was evaluated in the ASPIRE In-Clinic study (50 subjects, 48 events) by measuring plasma glucose concentrations with YSI measurements. The TS feature was evaluated in the ASPIRE In-Home study (121 subjects in the TS-ON group, 1438 events) with sensor glucose (SG) data. The LGS feature was evaluated using SG data uploaded by Veo users to the CareLink database (26,207 users, 161,809 events).

Results: At the beginning of TS/LGS events, mean ± SD glucose values were 70±0.2, 66±7, and 62±13 mg/dL in the ASPIRE In-Clinic, ASPIRE In-Home, and CareLink data sets, respectively. At 60 min, glucose values were 68±13, 70±25, and 76±36 mg/dL, respectively. At 120 min (the time basal insulin delivery resumed), glucose values had recovered to 77±29, 93±41, and 100±52 mg/dL, respectively. Severe hyperglycemia 240 min after the start of the TS/LGS event (i.e., 120 min after resumption of basal insulin delivery) was never noted, with glucose values of 91±38, 169±65, and 160±75 mg/dL in the ASPIRE In-Clinic, ASPIRE In-Home, and CareLink data sets, respectively. In the ASPIRE In-Home data set, the prevalence of SG values ≤50 mg/dL was 57% lower in the group using the TS feature than in the Control group, while in the CareLink data set, the prevalence of SG values ≤50 mg/dL was 43% lower on days that the LGS feature was in use than on days it was not in use. No significant increase in A1C was associated with TS use in ASPIRE In-Home, or estimated A1C with real-world LGS use in the CareLink data set.

Discussion: Clinical trial data from the TS feature in the ASPIRE In-Clinic and ASPIRE In-Home studies were consistent with data uploaded from the real-world users of the LGS feature.

Conclusion: Recovery from hypoglycemia during and after 2-hour pump suspensions was similar in clinical trials and real-world settings. Use of the TS/LGS feature reduced the prevalence of hypoglycemia, which is a major deterrent in patients trying to achieve optimal glycemic control.

Abstract #205

PREVALENCE AND RISK FACTORS OF PRE-DIABETES IN A RURAL COMMUNITY IN SOUTH-EAST NIGERIA

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Objective: Pre-diabetes refers to the intermediate state between normal and diabetic glucose homeostasis, usually clinically silent, but with far-reaching adverse effects on various organ systems often heralds Type 2 Diabetes Mellitus. The increasing prevalence of diabetes has been noted in both rural and urban areas in Nigeria. The aim of the study was to determine the prevalence of pre-diabetes in a rural community in South East Nigeria and determine
ABSTRACTS – Diabetes Mellitus/Prediabetes

Methods: A cross-sectional study was done on 824 consenting adults in Ihuokpara a rural community in Nkanu East LGA of Enugu State. Questionnaires were used to obtain demographic data, family history of diabetes and awareness of diabetes. Fasting and 2-hour post glucose load levels were measured after subject’s blood pressure and anthropometric parameters were obtained. Homeostatic assessment of insulin resistance (HOMA-IR) was used to estimate insulin resistance. Fasting lipid profile was measured. The results were analysed using SPSS v 17.

Results: There were 286 males and 538 females. Majority of the subjects were aged 45-65 years. The predominant occupation was farming. Generalised obesity was present in 16.7% and abdominal obesity in 35.9%, with females more obese than males (p<0.001). The overall prevalence of prediabetes was 24%, the prevalence of impaired fasting glucose (IFG) was 9.2% and that of impaired glucose tolerance (IGT) was 20.4%. Of the subjects, 22.5% had both IFG and IGT. Insulin resistance was present in 13.7%. Predictors of pre-diabetes were sleep duration less than 5.5 hours on most nights and hypertension. Insulin resistance did not predict pre-diabetes.

Discussion: There was a high prevalence of pre-diabetes in this rural Nigerian community. Poor sleep was the most significant risk factor as has been documented in a few studies. The inability of insulin resistance to predict pre-diabetes may have been due to the low prevalence of obesity in this population. It is worrisome that pre-diabetes was so prevalent despite the highly active lifestyle of the residents. This will have to be considered in future preventive measures.

Conclusion: Prevalence of prediabetes was high in the community and was associated with poor sleep duration and hypertension and not obesity or insulin resistance.

Abstract #206

ROLE OF LANGERHANS CELLS IN DIABETIC NEUROPATHY

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Objective: Langerhans cells (LCs) are dendritic cells that are integral to immune function in the epidermis. They mediate vasodilation via release of prostaglandin D2 (PGD2) upon binding of nicotinic acid with the GPR109A receptor expressed on the LCs. PGD2 binds to DP1 receptor on blood vessels causing vasodilation. We have previously shown that defective microvascular function is a sine qua non in diabetic neuropathy (DN) and precedes the onset of diabetes. We hypothesize that abnormalities in LC structure and function may be a significant contributor to defective vasodilation in the pathogenesis of microvascular insufficiency in DN.

Methods: Skin punch biopsies from matching sites (25 healthy controls vs 25 subjects with diabetic neuropathy) were obtained and processed for indirect immunofluorescence using anti-Langerin/CD 207 as primary antibody with an appropriate TRITC-conjugated secondary. Stained sections were scanned using confocal microscopy, and images quantitated using Neurolucida software. Statistical comparisons were performed using Student’s t-test or analysis of variance.

Results: LC density (LC/mm epidermis) was significantly greater in the proximal leg in patients with DN (p=0.0049) compared to controls. The cell body area (μm2) was significantly greater in the proximal (p= 0.0006) and distal leg (p= 0.0017) in DN compared to controls. LC perimeter was significantly higher in the proximal (p=<0.0001) and distal leg (p= <0.0001) in DN compared to controls. Mean LC number (p=0.0002), body area (p=<0.0001) and perimeter (p<0.0001) independent of biopsy site were significantly different in patients with DN compared to controls.

Discussion: Here we clearly demonstrate that DN is associated with an increase in LC density and size. Our findings suggest that defective LC function may be central to the pathogenesis of DN. Since abnormalities of LC have been reported in the eye, it seems likely that abnormalities in LC function may contribute to both DN and retinopathy and thus constitute a common pathogenetic mechanism for at least two of the major microvascular complications of diabetes.

Conclusion: This study demonstrates a novel observation that in DN, there are major significant differences in LCs, suggesting that LCs could play a role in the pathogenesis of altered vasodilation and possibly neuropathy itself. Since LCs play a key role on prostaglandin mediated vasodilation which is potentially treatable, future studies focused on the function of LCs in prostaglandin mediated vasodilation could provide further insight into the relationship between vascular dysfunction and DN and provide a new avenue for therapeutic intervention for DN for which there is currently no pathogenetic treatment.
Abstract #207

EVOLUTION OF ALBUMINURIA AND THE EFFECT OF GLP-1 AGONISTS ON ITS PROGRESSION IN TYPE 2 DIABETES

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Objective: Albuminuria is an indicator of glomerular and endothelial damage in patients with diabetes mellitus. We compared the evolution of albuminuria in patients at our center (DECWNY) with that from the largest database on albuminuria derived from Internal medicine and Endocrinology practices in the Kaiser Permanente Health System (KPHS). In addition, we hypothesized that the use of GLP-1 agonists resulted in a greater reversal in microalbuminuria than that in non-users of GLP-1 agonists.

Results: Over a 5.4 year follow up, the data from KPHS show that microalbuminuria progresses to macroalbuminuria in 20% i.e. 4% per annum (pa) and to normoalbuminuria in 20%(4% pa) with 0.3% progressing to ESRD. Macroalbuminuria regressed to microalbuminuria in 33% (6% pa), remained as macroalbuminuria in 62% and progressed to ESRD in 4% (0.8% pa). 40% of patients with normoalbuminuria progressed to microalbuminuria, 6.3% to macroalbuminuria and 0.08% to ESRD over 5.4 years. In comparison, the data from our center demonstrate that over a period of 2.3 years, 57% of patients with microalbuminuria regressed to normoalbuminuria(24.7% pa), 6% progressed to macroalbuminuria (2.6% pa) and 37% continued with microalbuminuria (p <0.0001 as compared to data from KPHS). On the other hand, 37% of macroalbuminuric patients became normoalbuminuric (16% pa) and 24% became microalbuminuric (10.4% pa) while 39% remained macroalbuminuric (p<0.0001 as compared to data from KPHS). 13% of patients with normoalbuminuria progressed to microalbuminuria(5.6% pa) and 0.3% to macroalbuminuria(0.05% pa)(p =0.0003 as compared to data from KPHS).

The use of GLP-1 agonists resulted in regression of microalbuminuria to normoalbuminuria in 67%(38% pa) with no progression to macroalbuminuria; as compared to 42% regression to normal (25% pa) with 11% progression to macroalbuminuria in the non GLP users (6% pa) (p<0.0001).

Discussion: The differences in the evolution of albuminuria between KPHS and our center are highly significant and demonstrate that albuminuria can be reversed by aggressive control of glycaemia, blood pressure, dyslipidemia and the use of RAAS inhibitors. Furthermore, GLP-1 agonists are associated with a significant decrease in the progression of microalbuminuria, also with a significantly greater reversal to normoalbuminuria with no progression to macroalbuminuria.

Conclusion: We conclude that microalbuminuria should be monitored routinely to assess the evolution of microvascular complications of diabetes and to ensure that the recommended therapeutic targets of glycaemia, blood pressure and drug are being met. In addition to preventing progression, GLP 1 agonists may have a role in the regression of diabetic nephropathy.

Abstract #208

POINT OF CARE GLYCATED HEMOGLOBIN IN THE DIAGNOSIS OF DM- A PRELIMINARY SURVEY FROM A RESOURCE LIMITED SETTING

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Objective: Prevalence of Diabetes Mellitus is expected to rise to 592 million by 2035, over 80% of this number live in low and middle-income countries. Prevalence of DM in Nigeria increasing with attendant huge burden on already scarce economic resources. Glycated Hemoglobin (HbA1C) predict development and progression of DM complications, recommended as a tool in the diagnosis of DM. Although recommendation stipulates high-pressure liquid chromatography for diagnosis, cost of this is exorbitant, unaffordable and not readily accessible for majority of our patients. We set out to determine the usefulness of the cheaper and more readily available point of care (POC) HbA1c test as a tool for DM diagnosis in referral center in southwestern Nigeria.

Methods: Prospective Study carried out over a period of four months at the DM Centre of LASUTH. Inclusion-treatment naive persons newly referred to the DM clinic with repeated FPG levels≥7.1mmol/L. We sought for, Hx of DM symptoms, family Hx of DM, Drug Hx, anthropometric indices, BP. Plasma samples under fasted conditions: glucose, lipid profile and HbA1c. HbA1c levels determined using liquid chromatography method. Capillary blood for POC HbA1c levels using Clover A1c machine employs use of boronate affinity method. Specificity and sensitivity ,correlation levels. An HbA1c of 48 mmol/mol (6.5%) recommended cut point for diagnosis diabetes. Test statistics used included Student t- test; χ², and correlation. SPSS for data anal.
Results: 22 subjects have been recruited till date. Mean age (SD) is 54.59(14.54) years, ages ranged from 25-78 years. Majority (59%) were females which was statistically significant ($p = 0.001$). First degree family history of DM was documented in 23% of the Study subjects. 82% were in the overweight/obese category. 63% had evidence of dyslipidemia. Mean HbA1c values were 9.6(2.7) range 5.8 to 13.6% for POC group while that of Liq Chromatography was 6.6(2.1) % range from 2.18 to 9.87%. Yield for DM in the POC group was higher than the liquid chromatography group $p = 0.025$. Sensitivity/specificity was 97%/ 99% and 60%/97% for POCA1c and Liq Chromatographic HbA1c method respectively. Correlation $r = 0.7$ $p< 0.001$.

Discussion: The increasing prevalence of DM makes it important to develop means of early and accurate diagnosis. In this study, the yield for DM was higher in the POCA1c group confirming earlier reports that led to the recommendation of glycated hemoglobin as a diagnostic tool for DM.

Conclusion: POC HbA(1c) as a single screening test is adequate to detect newly diagnosed diabetes in our locale and is fortunately readily accessible and affordable.

Abstract #209

ERECTILE DYSFUNCTION IN NIGERIAN MALES WITH TYPE 2 DIABETES MELLITUS

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Objective: Erectile Dysfunction is a well-recognized complication of Type 2 Diabetes Mellitus (T2DM). This condition impacts negatively on the psychosocial wellbeing of the affected persons. The objective of this study was to determine the prevalence of erectile dysfunction in males with Type 2 Diabetes and the associated risk factors in these persons.

Methods: This was a cross-sectional comparative study of 160 male patients with T2DM (study subjects). Erectile dysfunction (ED) was evaluated with the International Index of Erectile Function (IIEF-5) questionnaire. Clinical data and laboratory analysis was done for the study subjects. Chi-square analysis was used for comparison of proportions while the independent samples t-test was used to compare means. Multiple regressions were used to determine the strength of the risk factors.

Results: The age range of the study subjects was between 40-79 years. (Mean age 58.2±10.1 years). The prevalence of erectile dysfunction in the study subjects was 73.8% and the severity of erectile dysfunction increased with age. Statistically significant risk factors for erectile dysfunction in men with Type 2 Diabetes mellitus were; duration of diabetes (7.5±7.0 years in those with ED compared to 3.8±3.7 years in those without ED), positive history of cigarette smoking (27.1% of those with ED compared with 9.5 % of those without ED); increasing age(59.6±9.47 years in those with ED compared to 54.1±10.6 years in those without ED), peripheral neuropathy(33.9% of those with ED compared to 4.8% of those without ED), postural hypotension(13.6% of those with ED compared with 0% of those without ED) and low level of plasma free testosterone levels(15.9±6.8 pg/ml in those with ED compared to 19.6±5.4 pg/ml in those without ED).

Discussion: This study showed that erectile dysfunction is very common in men with type 2 diabetes with a prevalence rate of 73.8%. Significant risk factors for ED in diabetic men were; duration of DM, smoking, increasing age, low plasma free testosterone level, presence of peripheral neuropathy and postural hypotension.

Conclusion: Management of diabetic men should include assessment of erectile function for early detection and treatment.

Abstract #210

RAMADAN FASTING IN DIABETIC SUBJECTS WITH CHRONIC KIDNEY DISEASE: CLINICAL AND BIOCHEMICAL EFFECTS

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BIRDEM

Objective: Ramadan fasting is a pillar of Islam. Muslim diabetic subjects with chronic kidney disease (CKD) usually want to fast this month. The effect of fasting during the month of Ramadan on patients with renal impairment is still a matter of controversy. This study was planned to determine the effects of fasting on renal function in CKD patients.

Methods: The study subjects were studied during two phases: when the subjects were drinking and eating freely before the start of Ramadan and a second phase after the end of Ramadan of the year 2012(1434 Hijri). A total 106 subjects were included in this study but among them only 50 subjects completed the 2nd visit. So the final analysis was done with these 50 subjects.

Results: Among the 50 patients studied mean (±SD) age was 54.96 (±10.55) years with a duration of Diabetes of 10.55(±6.09) years. Among the study subjects; 38% were managed with insulin, 30% with oral drugs, 28% with both and 4% with lifestyle only. This study demonstrates a good tolerance and safety of fasting Ramadan in CKD patients.
glycemic control did not show any significant difference pre and post Ramadan (p = .952, .575 and .368 respectively). Pre and post Ramadan S. creatinine, S. sodium and S. Potassium level did not show any significant difference between the two time period (p = .661, .106 and .064 respectively). There was no significant difference (p = .533) in eGFR among the study subjects pre and post Ramadan.

**Discussion:** All patients in our study tolerated fasting of Ramadan very well. One of the clinical finding, in our study was the tendency of weight reduction. This weight reduction has also been documented in several studies and it is attributed to the reduction of meal frequency during Ramadan. There was no significant decline in the estimated GFR. This study did not find any serum electrolyte disturbances during fasting. In a large epidemiological study conducted in 13 Islamic countries on 12,243 individuals with diabetes, those who fasted during Ramadan had a high rate of acute complications, mainly hypo and hyperglycemia. None of our diabetic patients revealed such metabolic complications during fasting. Despite that Hb A1C was changed in pre and post Ramadan visits but its changes during this study periods was not significant.

**Conclusion:** Ramadan fasting is safe in stable CKD patients. This study did not find any significant alteration in glycemic control or decline in eGFR during the study period. However, fasting should be medically supervised in diabetic CKD subjects with special attention to fluid intake, daily activity, and adjustment of drug regimens.

**Abstract #212**

**DEPRESSION IN DIABETICS AND ITS RELATION WITH CARDIOVASCULAR RISK FACTORS AND MARKERS: CROSS SECTIONAL STUDY IN TAIF, SAUDI ARABIA**

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**Objective:** The International Diabetes Federation has released an estimates numbers of 382 million people with diabetes in 2013 and forecasts for 2035 of 592 million.
Recent studies showed that the risk of depression in diabetics was twice that of non-diabetics which did not differ by sex, type of diabetes, or assessment method. The presence of depression as a co-morbid condition with diabetes is associated with a significantly increased CV mortality rate. Limited data evaluated the relationship between depression in diabetics and cardiovascular risk factors and markers. The primary goal of this study is to evaluate the incidence of depression and its relationship with the cardiovascular risk factors.

**Methods:** We conducted a cross-sectional study at King Abdulaziz Specialist Hospital, Taif, Saudi Arabia, Division of Endocrinology. Type 2 diabetics above age of 18 years who had a routine visit to the Endocrine clinic from Jun-Dec 2013 were asked to participate. Baseline characteristics and measurement were collected. Laboratory data was collected from the patient’s electronic record. We excluded diabetics with existing psychiatric illness, untreated hypothyroidism and with history of malignancy. We used PHQ-9 to screen for depression which was administered by the investigators.

**Results:** Total of 215 patients participated, 103 (48%) were male and 112 (52%) were female with mean age 56.6 years old, mean A1c 8.6%, mean duration of diabetes of 10.93 yrs, mean BMI 31.8%, 88.4% were married, 42.3% were on oral medications only, 52.1% were on insulin +/- oral and 5.6% were on diet control. 40.9% met the diagnostic criteria for depression. Compare to non-depressed, depressed diabetics mean age 57.4 yrs vs 56 yrs, 58% were female vs 48%, 84.1% vs 91.3% were married, and 70.5% vs 61.4% reported low income.

80.7% of the depressed diabetics report sedentary lifestyle compared to 70.1% in the non-depressed. 9.1% of the depressed were active smoker compared to 6.3%. Passive smoking reported in 35.1% in the depressed diabetics compared to 29.7%.

Depressed mean A1c of 8.7 vs 8.6%, BMI 32.8 vs 31.04 (p=0.04), mean systolic BP 143 vs 138.2, mean diastolic 81.6 vs 80.7, and mean resting HR 82.37 vs 80.6. 77.3% and 69.3% of the depressed have dyslipidemia and hypertension compared to 65.4% and 52% in non-depressed (p value 0.061 and 0.011), respectively.

**Discussion:** Incident of depression was high in our study, Clinicians should made aware about this finding and screen diabetics at risk.

**Conclusion:** The incidence of depression was 40.9% which is higher than previously reported. Depressed diabetics have higher cardiovascular risk factors and do have worse cardiovascular marker compared to non-depressed.

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**Abstract #213**

**SELF BLOOD GLUCOSE MONITORING AMONG DIABETES PATIENTS IN UNIVERSITY OF NIGERIA TEACHING HOSPITAL ENUGU**

Ekenechukwu Young, MBBS, FWACP, Michael Abonyi, MBBS, Christian Okafor, MBBS, FMCP; Belonwu Onyenekwe, MBBS, FMCP; Esther Ofoegbu, MBBCh, FWACP, MSc

**Objective:** Self-monitoring of blood glucose (SMBG) is encouraged in all patients with diabetes. It encourages patient adherence to medication and enables the health care provider to make necessary adjustments in the patient’s treatment regimen. The study aimed to determine the frequency and methods of SMBG in patients with diabetes.

**Methods:** The study was cross-sectional and conducted in the diabetes outpatient clinic. Questionnaires were administered to obtain demographic data, and information on use of glucometers, frequency and timing of monitoring. Data were analyzed using SPSSv17.

**Results:** There were 146 patients of which 92(63%) were female and 54(37%) were male with a mean age and duration of diabetes of 65.8 ± 12.3 years and 15.9 ± 10.4 years respectively. Majority had type2 diabetes (97.2%). Only 66(45.2%) had tertiary education while 16(11%) had no formal education. A total of 103(70.5%) had owned a glucometer for a mean duration of 26.4 ±18.6 months. There were 103(70.5%) on oral drugs, 39(26.7%) on oral and insulin combination and 4 on insulin alone. The most common frequency of monitoring was less than 3 times a week in 49(33.6%), while 12(8.2%) used it daily. The most (64.4%) tested only fasting blood glucose. There was no difference in frequency of monitoring between those on oral drugs and those on insulin (p=0.45). Blood glucose records were kept by 62(42.5%) patients who owned glucometers. Their mean FBG was 126.1±43.8 mg/dl and HbA1c 8.4±1.8%. Those who owned glucometers had lower mean fasting blood glucose than those without (142±68.5mg/dl, vs 174.2 ± 73.6 mg/dl), p = 0.016.

**Discussion:** The lower mean duration of glucometer ownership in comparison with duration of diabetes suggests that most patients acquired glucometers much later after diagnosis. It was however noted that most of them used their glucometers less than three times a week despite their overall poor glycaemic status. It is likely that more frequent monitoring may have helped to improve their glycaemic control. However for many patients this is difficult due to the added financial burden of obtaining glucometer strips in addition to the cost of their drugs, as health care in this part of the world is largely patient-funded without health insurance. It was not surprising to note the
better glycaemic status of those who owned glucometers as this has been documented in earlier studies. 

**Conclusion:** Blood glucose monitoring was common in the patients though with low frequency of monitoring and associated with better glycaemic control.

**Abstract #214**

**OUTCOME OF DIABETIC FOOT ULCER ADMISSIONS AT THE UNIVERSITY OF NIGERIA TEACHING HOSPITAL ENUGU NIGERIA**

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**Objective:** Diabetic foot ulcer (DFU) is associated with a high rate of morbidity, prolonged hospital stay and serious complications, including osteomyelitis and amputation. Prevention and healing of DFU remains a challenge. The objective of the study was to determine the outcome of DFU among in-patients in the University of Nigeria Teaching Hospital Enugu, Nigeria.

**Methods:** Admission records of diabetes-related admissions in the medical wards of the University of Nigeria Teaching Hospital Enugu between January 2009 and December 2012 were analyzed. Case records of patients admitted with diabetic foot ulcer during the same period were examined. Data obtained included age, gender, duration of hospital stay and outcome. In addition, duration of diabetes, ulcer stage and presence of peripheral vascular disease or peripheral neuropathy was sought for from the case records. Statistical analysis was done using SPSS v17.

**Results:** Out of 696 DM related admissions, there were 393(56.5%) males, females were 303(43.5%) and DFU accounted for 113(16.2%). Of this number there were 68(60.2%) males and 45(39.8%) females. The mean duration of diabetes was 7.2 ± 6.8 years while the median (Interquartile range) duration of ulcer before presentation was 24(14-60) days. Mean age of patients with DFU was 55.2years, duration of hospital stay ranged from 2 days to 98 days with a median of 36days. Out of the 113 DFU admissions, 84(74.3%) were discharged, 15(13.3%) died while 14(12.4%) discharged against medical advice. Of those who were discharged, about 75% were discharged with non-healed ulcers either for outpatient care or to surgical units. The most common Wagner grade of ulcer was grade 3(41.5%). Features of peripheral neuropathy occurred in 58.9% of those with foot ulcer while peripheral arterial disease was seen in 45%. The total mortality for all DM admissions was 141 hence DFU mortality accounted for 10.6% of all diabetes mortality.

**Discussion:** Diabetic foot ulcer was a common reason for admission and characterized by late presentation and advanced ulcer stage. Though a high proportion of the patients were discharged, their final outcome could not be determined as most were discharged with non-healed ulcers for continuing outpatient or surgical care. Early discharge is usually due to high costs of in-patient care. Foot ulcer-related mortality was high and may have been under-estimated due to insufficient follow-up data.

**Conclusion:** Diabetes foot ulcer was associated with long duration of hospitalization and high mortality.

**Abstract #215**

**INPATIENT MANAGEMENT OF HYPERGLYCEMIA: EFFECT OF EDUCATION AND A COMPUTERIZED INSULIN ORDER ENTRY PROTOCOL**

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**Objective:** 1) Assess the impact of an intervention on inpatient hyperglycemia and protocol adherence, and 2) Describe challenges in protocol adherence specific to a teaching hospital setting.

The link between uncontrolled hyperglycemia and increased patient morbidity and mortality is well established. Even though there are widely available insulin protocols and computerized insulin order sets, blood sugar control among in-patients remains a challenge. We performed a multi-year intervention in a teaching community hospital to improve hyperglycemia management among inpatients by using a computer order entry protocol for insulin.

**Methods:** As part of this prospective study, we performed a chart review for hyperglycemia from 2010 to 2013. A computerized order entry set for insulin was introduced in May 2013 to address inpatient blood sugar control. Education of medical staff on the insulin computerized order protocol was done on regular intervals since 2010 and adherence was monitored by recording the proportion of eligible patients who were on the recommended insulin protocol. Data on protocol adherence were compared over time as well as before and after the end of the academic year using descriptive analyses, t-tests, and repeated measures ANOVA.

**Results:** There was an increasing trend in protocol adherence from June 2010 to December 2013, with an overall improvement from 20% to 56% of patients on recommended protocols. There was a significant difference in proportion of inpatients on recommended
protocol from 2011-2013 (F = 4.76; df= 2,33; P<0.05). Surprisingly, the protocol adherence trend showed cyclical variation with highs in December-January of each year and lows in June-July, coinciding with the academic year and entry of new residents in the hospital system. There was a significant difference before/after June 30 in the proportion of inpatients on recommended protocol in 2011 (t = 2.5; df= 8; P<0.05) and 2013 (t = 4.6; df= 10; P<0.05).

**Discussion:** Introduction of a computerized order entry set for insulin, education and monitoring helped to improve protocol adherence in non-ICU inpatients in our hospital setting. However, there are some unforeseen challenges in maintaining improvement based on the yearly influx of new staff. Future directions in hyperglycemia management protocol adherence need to focus on more intense education and training of medical staff during specific times of the academic year to prevent an increase in morbidity outcomes during specific times of the year.

**Conclusion:** Computerized insulin order entry protocols and education on use of such protocols can be essential in improving hyperglycemia and inpatient outcomes.

**Abstract #216**

**A CASE OF NECROTIZING PANCREATITIS DUE TO A GLP 1 ANALOG.**

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North Central Bronx Hospital

**Objective:** An uncommon case of necrotizing pancreatitis in a patient on Exenatide.

**Methods:** Clinical exam, laboratory tests, imaging, literature review

**Case Presentation:** A 50 year old african american male with a medical history of uncomplicated diabetes mellitus type II (on daily 5 mg subcutaneous exenetide for 2 years and NPH Insulin) and hypertension (on lisinopril), presented to the emergency room with severe epigastric pain radiating to the back, associated with multiple episodes of bilious non bloody vomiting. No significant alcohol intake prior to presentation. In the ER he was afebrile, tachycardiac and saturating at 92% and had severe epigastric tenderness. His laboratory results were significant for a wbc 23K, lipase 30k, amylase 800, AST 415, ALT 171, alkaline phosphatase 166, gamma glutamyl transferase 251, total bilirubin 2.2. A CT scan of the abdomen and pelvis was significant for acute pancreatitis without necrosis or hemmorhage and a contracted gall bladder without radio-opaque stones. He had normal triglycerides. The admitting diagnosis was acute pancreatitis most likely secondary to exenatide. He was discharged in a stable condition and exenetide was discontinued. Patient was re-admitted after 2 weeks due to recurrent abdominal pain. A repeat CT scan of abdomen showed 75% necrosis of pancreas and a large pseudocyst with mildly elevated lipase and amy lase. Surgical and gastroenterology services were consulted and the patient was managed conservatively and remains symptom free.

**Discussion:** Glucagon-like peptide-1 is a hormone that is released by the small intestine in response to ingestion of food and has an inhibitory effect on gastric emptying, glucagon release and appetite, while promoting glucose-dependent insulin secretion. Exenatide is a synthetic hormone that shares 53% sequence identity with GLP-1. Exenatide induced pancreatitis is a diagnosis of exclusion and has remained a controversy. Only 7 cases of necrotizing pancreatitis have been reported so far. Mechanism is not fully understood and studies in animal models have shown conflicting results. Recently, studies have shown increased exocrine cell proliferation and dysplasia in pancreas from age matched organ donors with type 2 DM and treated with incretin therapy.

**Conclusion:** Our case of Exenetide induced necrotizing pancreatitis is very rare. Exenetide and its association with pancreatitis has surfaced in post marketing reports and many more studies are needed to confirm this association. It is important for physicians to counsel their patients regarding this side effect and patients with high risk for pancreatitis should not be put on incretin mimetics. The use of both Exenetide and Sitagliptin should be avoided.

**Abstract #217**

**BURDEN AND PATTERN OF MICROVASCULAR COMPLICATIONS IN TYPE 2 DIABETES IN A TERTIARY HEALTH INSTITUTION IN NIGERIA**

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**Objective:** The objectives of this study were to report the burden of various microvascular complications in T2DM and to identify various factors associated with these complications in subjects with T2DM attending the diabetes outpatients’ clinic.
Methods: Ninety (90) patients with T2DM who have attended diabetes clinic for at least 3 months were recruited for this study. Detailed history, physical examination and biochemical analysis was done in each of the subjects. All subjects underwent a detailed standard evaluation to detect diabetic retinopathy (fundoscopy), neuropathy (10g monofilament and/or diabetes neuropathy scores), and nephropathy (microalbuminuria, macroalbuminuria, serum creatinine and estimated glomerular filtration rate).

Results: There was high prevalence of microvascular complications among patients with T2DM. Almost half of subjects with T2DM had some form of microvascular complications; diabetic neuropathy being the commonest (69.6%), followed by nephropathy (54.5%) and retinopathy (48.9%). The factors associated with developing these complications were increasing age, duration of diabetes, hypertension and dyslipidaemia for nephropathy and neuropathy.

Discussion: In this hospital-based study, the prevalence of different microvascular complications of diabetes was similar to figures from other populations in Africa, but much higher than those reported by Kumar et al in India. The reason for this may be due to poor control of glycaemia among our patients; only 41% of our patients had target goal of blood sugar.

In our study, 55.4% of the patients had nephropathy. This is much higher than value obtained by Alebiosu et al who obtained 25%. DM nephropathy is now the leading cause of ESRD worldwide and is responsible for about 1/3 of patients who undergo dialysis. In Nigeria, DM nephropathy as a cause of nephropathy is also high, representing 15-25%. As previous studies, have indicated, this study also found age, hypertension, and male sex as important risk factors for DM nephropathy.

Conclusion: There is a high burden of microvascular complications in patients with type 2 diabetes. Age, male gender, hypertension, glycaemic control, BMI duration of diabetes, and glycaemic control were factors associated with microvascular complications.

Abstract #218

ASSESSMENT OF DIABETES-RELATED KNOWLEDGE AMONG DOCTORS AND NURSES IN A TERTIARY INSTITUTION IN NIGERIA

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Objective: This study aimed to assess diabetes-related knowledge of health care professionals in a tertiary institution with particular emphasis on inpatient diabetes management skills and insulin therapy.

Methods: This is a cross-sectional study that used a 42-item multiple choice questionnaire to assess diabetes-related knowledge of specialists, resident doctors and nurses in departments of medicine, surgery and gynecology.

Results: Of the 185 subjects approached 155 completed the questionnaire. Knowledge was highest among specialists and lowest among nurses. Participants from Medicine department (specialists, residents and nurses) had the highest level of knowledge (44±12%) and the lowest level of knowledge was found among final year medical students (p<0.001). The percentage mean score of knowledge on insulin therapy was 36%; highest among specialists in medicine (55%) and lowest among nurses in gynecology (27%). Same low knowledge base was found among participants on ketoacidosis (38%) and hypoglycaemia (34%). There was a significant difference between resident doctors in medicine (55%) and residents doctors in gynecology (55% vs. 39%, p<0.05) in the knowledge of diabetic ketoacidosis. Although comfort level was highest among specialist in gynecology (5.09), this did not translate to better knowledge in most domains assessed.

Discussion: This study identified significant lack of knowledge of doctors, nurses, medical and nursing students regarding treatment of diabetic inpatients. The results obtained in this study were even lower in almost all domains assessed, when compared; with results obtained with same instrument by Roman Tripp et al in Switzerland, and similar study done in the UK.

The better results obtained among residents and specialists in internal medicine department affirm the fact that
ABSTRACTS – Diabetes Mellitus/Prediabetes

Doctors in internal medicine are primarily responsible for the management of diabetes. However, this performance is average as only about 50% of questions were answered correctly, by those who manage majority of diabetic patients—both inpatients and outpatients.

**Conclusion:** There was significantly low knowledge on inpatient management of diabetes among specialists and resident doctors in other fields/specialties but moderate knowledge among specialists and resident doctors in medicine department. Nurses as well as medical and nursing students also had very low knowledge in diabetes. This correlated with comfort levels (except in gynecology) in dealing with diabetes.

**Abstract #219**

**PREVALENCE AND RISK FACTORS ASSOCIATED WITH PERIPHERAL ARTERIAL DISEASE AMONG TYPE 2 DIABETES PERUVIAN PATIENTS**

*Harold Torres, MD, Rosa Agüero, MD, Hugo Arbanil-Huaman, MD, Rosa Pando, MD, Dante Gamarra, MD, Jaime Pajuelo, MD*

*Dos de Mayo Hospital*

**Objective:** Peripheral arterial disease (PAD) is a serious complication of type 2 diabetes mellitus associated with not only increased risk of lower limb amputation but also cardiovascular morbi-mortality.

In a previous Peruvian study, Quiroz et al. found a significantly higher prevalence of PAD compared to international reports. The objective of this study was to determine the prevalence and risk factors associated with PAD diagnosed by the ankle brachial index (ABI), among type 2 diabetes patients in Dos de Mayo Hospital - Lima, Peru - between March and December 2013. These patients came for a routine foot examination and risk assessment.

**Methods:** Cross-sectional study. Patients were consecutively enrolled. HbA1c, lipid profile, BMI, waist circumference and length of illness of diabetes were assessed. ABI was measured using ultrasonic Doppler flow detector. A cut off of < 0.9 was used to define peripheral arterial disease. Means, standard deviations and frequencies were described. Pearson correlation coefficient was used to estimate the correlation between ABI and the others variables. A generalized linear model was performed in order to analyze an association between ABI and the significant variables. The study was approved by an institutional review committee.

**Results:** We evaluated 188 patients, 125 females (66.5%). Mean age was 61.7±10.3 years. The mean length of illness of diabetes was 8.6±8.4 years. The prevalence of PAD was 14.9% with men having a higher prevalence (17.5%), as compared to women (13.6%) (p=0.483). ABI values were negatively correlated with age (r = -0.226, p=0.002), length of illness (r = -0.173, p=0.018) and LDL cholesterol (r = -0.173, p=0.036). A generalized linear model adjusted for sex and age revealed that length of illness of diabetes and LDL cholesterol contributed significantly to the variance of ABI (p=0.019 and p=0.043, respectively).

**Discussion:** We found a prevalence of PAD similar to international reports. PAD was more frequent in men but it was not statistically significant.

**Conclusion:** The prevalence of PAD diagnosed by ABI among type 2 diabetes Peruvian patients was 14.9%. Risk factors significantly associated were age, length of illness of diabetes and LDL cholesterol.

**Abstract #220**

**ABSENT OF PEDAL PULSE VERSUS EDINBURGH CLAUDICATION QUESTIONNAIRE FOR DETECTION OF PERIPHERAL ARTERIAL DISEASE IN TYPE 2 DIABETIC PATIENTS**

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**Objective:** Diabetic patients are at high risk for peripheral arterial disease (PAD) characterized by diminished or absent peripheral pulses, and symptoms of intermittent claudication.

Our aim was to determine the diagnostic accuracy of finding absent of pedal pulse versus the Edinburgh Claudication Questionnaire (ECQ) for PAD diagnosed by the ankle brachial index (ABI), among type 2 diabetes patients who came for a routine foot examination and risk assessment in Dos de Mayo Hospital - Lima, Peru - between March and December 2013.

**Methods:** We performed a cross-sectional study and patients were consecutively enrolled. ABI was measured using ultrasonic Doppler flow detector. A cut off of < 0.9 was used to define peripheral arterial disease. Face-to-face interviews were conducted using the ECQ for the presence of intermittent claudication. Furthermore, pedal pulse palpation was performed for each foot. For the patients who screened positive for PAD by ABI, we determined the sensitivity, specificity, negative and positive predictive value of having at least an absent pedal pulse and the ECQ.

**Results:** 185 patients were evaluated, 123 females (66.5%). The prevalence of PAD was 14.6% (27 patients). Among these patients with PAD, seventeen (63.0%) had symptoms of intermittent claudication based on the ECQ.
Abstract #221

IMPROVING ACCESS TO SHARED DECISION MAKING FOR LATINOS WITH INADEQUATELY CONTROLLED TYPE 2 DIABETES MELLITUS

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Objective: Diabetes is a significant problem in Latinos with prevalence rates more than double non-Latino whites. Shared Decision Making (SDM) is a collaborative process that allows patients and their providers to make health decisions together taking into account the best scientific evidence available as well as the patient’s preferences. Patient Decision Aids (PDAs) are tools that communicate information on treatment options and facilitate patient choice consistent with values/preferences. Well-designed evidence-based PDAs to assist people with type 2 diabetes (T2DM) with inadequate glycemic control on metformin as additional medication options are considered have been developed in English. Materials targeting Latinos are a priority and an integral part of outreach efforts to improve outcomes. However, disparities exist in availability of PDAs for Spanish-speaking Latinos. We describe cultural and linguistic adaptation of a PDA for Latinos with T2DM, a group at high risk for complications.

Case Presentation: A Steering Committee consisting of 2 endocrinologists, a primary care physician, certified diabetes educator and dietician, each providing care to Latinos was convened to assess a PDA developed for an English-speaking audience of patients with T2DM not controlled on metformin. Content was reviewed for focus, cultural sensitivity and appropriateness for a Latino population. A consensus building process consisting of teleconferences and iterative version edits incorporated perspective of clinicians. Attention was paid to content consistent with traditional precepts of communication in Latino cultures, (e.g. avoidance of hostile confrontation; value of warm interaction; respect for authority figures, including health care providers; value of family in supporting decisions). The PDA next underwent a forward and backward translation by translators with clinical expertise. Language was tested in cognitive interviews with 10 Spanish-speaking Latinos with T2DM. Also tested were clinical terminology to assure that content in the final PDA is reflective of the experience, understanding and language Latinos use to describe their diabetes and treatment. Final edits to the script were made and the content was produced into an online video format for dissemination.

Discussion: Access to high quality, well-developed tools to facilitate shared decision making in populations with less access to culturally sensitive information can narrow gaps and better align care with individual patient values.

Conclusion: A newly developed PDA culturally appropriate for Latinos with T2DM and inadequately controlled on metformin is now available for SDM. The impact of this PDA on overall management of T2DM requires further study.

Abstract #222

EFFICACY AND SAFETY OF CANAGLIFLOZIN (CANA) IN PATIENTS WITH TYPE 2 DIABETES MELLITUS (T2DM) BY HISPANIC/LATINO ETHNICITY

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Objective: CANA is a sodium glucose co-transporter 2 (SGLT2) inhibitor approved for the treatment of patients with T2DM. This analysis assessed whether ethnic origin had any impact on CANA’s efficacy as measured by changes from baseline in A1C, body weight (BW), and systolic blood pressure (SBP), as well as its safety profile.
**Methods:** Pooled data from the 4 placebo (PBO)-controlled Phase 3 studies that enroled a general population of patients with T2DM (N = 2,313; mean age, 56.0 y; BMI, 32.1 kg/m2) were analyzed based on ethnicity (Hispanic/Latino [n = 609; mean A1C, 8.1%; BW, 80.5 kg; SBP, 126.1 mmHg], non-Hispanic/Latino [n = 1,695; mean A1C, 8.0%; BW, 92.3 kg; SBP, 129.3 mmHg], not reported or unknown [n = 9]). LS mean changes from baseline in A1C, BW, and SBP were assessed at Week 26. Least squares (LS) mean changes were calculated and PBO-subtracted differences (95% confidence interval [CI]) are reported.

**Results:** CANA 100 and 300 mg were associated with significant reductions in A1C, BW, and SBP versus PBO in Hispanic/Latino and non-Hispanic/Latino patients. The A1C-lowering response was similar for both CANA doses compared with PBO in Hispanic/Latino versus non-Hispanic/Latino patients. PBO-subtracted A1C reductions were -0.82% (-1.01, -0.63) and -0.94% (-1.12, -0.75) with CANA 100 and 300 mg, respectively, in the Hispanic/Latino group, compared with -0.70% (-0.80, -0.60) and -0.91% (-1.00, -0.81), respectively, in the non-Hispanic/Latino group. Dose-related mean percent reductions in BW were observed with CANA 100 and 300 mg in both subgroups (PBO-subtracted differences of -2.1% [-2.8, -1.4] and -2.8% [-3.5, -2.1], respectively for Hispanic/Latino; non-Hispanic/Latino: -2.3% [-2.7, -1.9] and -3.0% [-3.4, -2.5], respectively). A dose-dependent reduction in SBP was seen with CANA versus PBO in the Hispanic/Latino group (PBO-subtracted differences of -4.2 mmHg [-6.3, -2.1] with CANA 100 mg and -6.8 mmHg [-8.8, -4.7] with CANA 300 mg). In the non-Hispanic/Latino group, the PBO-subtracted reduction seen with CANA 100 mg (-4.0 mmHg [-5.4, -2.7]) and CANA 300 mg (-3.9 mmHg [-5.2, -2.5]) was similar. In Hispanic/Latino patients, the overall incidence of adverse events (AEs) was 59%, 57%, and 56%, with CANA 100 and 300 mg and PBO, respectively; rates were similar across groups in non-Hispanic/Latino patients (60%, 60%, and 61%, respectively). The incidences of serious AEs and AEs leading to discontinuation were generally low across groups in both Hispanic/Latino and non-Hispanic/Latino patients.

**Conclusion:** CANA provided improvements in A1C, BW, and SBP, and was generally well tolerated in both Hispanic/Latino and non-Hispanic/Latino patients with T2DM.

**Abstract #223**

**THE 2 WEEK FASTING GLUCOSE AS A PREDICTOR OF RESPONSE TO ONCE WEEKLY DULAGLUTIDE 1.5 MG**

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**Objective:** To assess whether laboratory fasting blood glucose (FBG) in patients with type 2 diabetes mellitus (T2DM) measured early in treatment with the once weekly GLP-1 receptor agonist dulaglutide (DU) 1.5 mg predicts treatment response.

**Methods:** Post hoc analyses were conducted separately for 2 double-blind, randomized Phase 3 studies (AWARD-5, in combination with metformin, and AWARD-1, in combination with metformin and pioglitazone) in patients with T2DM assigned to once weekly DU 1.5 mg. In AWARD-5, FBG values were categorized at baseline as follows (using tertiles): Low (L, <142 mg/dL); Intermediate (I, ≥142 to <185 mg/dL); and High (H, ≥185 mg/dL). Treatment response was assessed at week 12 (AWARD-5) or 13 (AWARD-1) and 26 (AWARD-5, AWARD-1) by the following composite efficacy endpoint (CEE): A1c <7.0% or A1c reduction from baseline >0.8% (if baseline A1c <8.0%); >1.1% (if baseline A1c ≥8.0% and <9.0%); or >1.6% (if baseline A1c ≥9.0%). Association between FBG categories and the CEE was analyzed using chi-square tests.

**Results:** In AWARD-5, mean baseline A1c for DU 1.5 mg (N=304) was 8.1%. At baseline, mean FBG was 176 mg/dL, and 33% (n=99), 32% (n=97), and 36% (n=108) of patients had FBG in L, I, and H categories, respectively. After 2 weeks of treatment, mean FBG was 129 mg/dL, and 68% (n=208), 21% (n=64), and 11% (n=32) of patients had FBG in L, I, and H categories, respectively. At week 26, mean A1c was 6.9%. There was a strong association between FBG at week 2 and achieving the CEE at week 26 (p<0.001). A significantly higher percentage of patients in FBG category L (83% [172/208]) at week 2 met the CEE at week 26 compared to patients in FBG categories I (61% [39/64]), p<0.001, and H (34% [11/32]), p<0.001. CEE results at week 12 were consistent with those at week 26. Similar findings were seen using AWARD-1 data.

**Discussion:** The identification of patients most likely to
respond to a specific treatment is important when attempting to individualize patient care. Predictors of treatment success for other weekly GLP-1 receptor agonists have, to date, not been reported. In patients treated with once weekly DU 1.5 mg in AWARD-5 and AWARD-1, FBG values at week 2 were strongly associated with treatment response at week 26 as measured by a CEE. The probability of achieving treatment response at week 26 was greatest for patients in the lower FBG categories at week 2.

Conclusion: FBG values at week 2 may be an early and useful measurement for predicting response to once weekly DU 1.5 mg treatment in patients with T2DM.

Abstract #224

INITIATING V-GO® IN PATIENTS USING LONG ACTING INSULIN

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Objective: Most patients (pts) initiating insulin therapy start with long acting insulin injections (LAI). V-Go is a disposable 24-hour device that provides a continuous rate of insulin infusion and on-demand bolus dosing. V-Go delivers preset basal rates of 20, 30 and 40 U/d and may facilitate transition to a basal-bolus insulin regimen. The purpose of this analysis is to describe therapeutic response when pts with uncontrolled glycemia currently receiving LAI start using V-Go.

Methods: A prospective, observational, open-label, multicenter study (SIMPLE) is being conducted in pts with uncontrolled type 2 diabetes initiating the V-Go. Insulin management was left up to the physician without forced titration. V-Go devices, but no other supplies, were provided to pts for up to 6 mos. An analysis of therapeutic response was conducted stratifying pts by the initial V-Go basal rate (20, 30, 40 U/d). Data up to 6 mos are reported.

Results: A total of 59 pts initiated therapy of which 40 have completed 6 mos of treatment using the V-Go to date. Mean pt age was 59 yrs with diabetes duration of 14 yrs and insulin use of 4 yrs. Mean prior total daily insulin dose (TDD) was 46 U/day overall and 33, 51 and 58 U/d for pts initiating V-Go 20, 30 and 40, respectively. The corresponding A1C was 8.9% overall and 8.9%, 8.5% and 10.2%. At 6 mos the mean TDD was 49 U/d overall and 48, 48 and 53 U/d for pts initiating V-Go 20, 30 and 40; and the corresponding mean A1C was 7.9% overall (p<0.001 compared to baseline) and 8.3%, 7.7% and 7.8%. Pts starting V-Go 20 had the greatest bolus insulin change, initiating 7 U/d and increasing to 19 U/d, contrasting with pts starting V-Go 40 initiating at 10 U/d and receiving 15 U/d at 6 mos. Five hypoglycemic events occurred (<70 mg/dl). No severe hypoglycemic events were reported.

Discussion: At 6 mos the A1C and TDD were similar across the population despite differences at baseline and initial V-Go basal rates. The V-Go 40 starting cohort, that had the highest baseline A1C and LAI dose, had the largest A1C drop while lowering the TDD.

Conclusion: Patients receiving LAI safely initiated V-Go with a very low risk of hypoglycemia. Initiating basal-bolus insulin regimen using V-Go after LAI therapy may be an effective and safe strategy.

Abstract #225

EFFICACY OF CANAGLIFLOZIN (CANA) IN PATIENTS WITH TYPE 2 DIABETES MELLITUS (T2DM) BY BASELINE BODY MASS INDEX (BMI)

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Objective: The sodium glucose co-transporter 2 (SGLT2) inhibitor CANA has demonstrated glycemic efficacy and reduction in body weight and systolic blood pressure (SBP) in patients with T2DM in Phase 3 clinical trials. The current analysis, across 4 clinical trials of patients with T2DM, evaluated the effect of CANA versus placebo (PBO) on changes in A1C, body weight, and SBP stratified by baseline BMI.

Methods: Data were pooled from the 4 PBO-controlled Phase 3 studies that enrolled a general population of patients with T2DM (N = 2,313; mean age, 56.0 y; A1C, 8.0%; BMI, 32.1 kg/m2; SBP, 128.4 mmHg). Changes in A1C, body weight, and SBP at 26 weeks (last observation carried forward [LOCF]) were evaluated in subgroups by baseline BMI (<25 kg/m2 [n = 236], 25 to <30 kg/m2 [n = 728], 30 to <35 kg/m2 [n = 703], and ≥35 kg/m2 [n = 645]). Least squares (LS) mean changes were calculated within each subgroup, and PBO-subtracted differences in LS mean changes (95% confidence interval [CI]) are reported.
Results: At Week 26 (LOCF), LS mean reductions from baseline in A1C levels, body weight, and SBP were greater with CANA versus PBO regardless of baseline BMI, with CANA 300 mg generally providing greater reductions in all 3 parameters than CANA 100 mg for most BMI subgroups. PBO-subtracted A1C reductions with CANA 100 and 300 mg, respectively, were similar across subgroups (BMI <25 kg/m², -0.73% [-1.05, -0.41] and -0.91% [-1.23, -0.58]; BMI 25-<30 kg/m², -0.74% [-0.90, -0.59] and -0.90% [-1.05, -0.75]; BMI 30-<35 kg/m², -0.71% [-0.87, -0.56] and -0.85% [-1.01, -0.70]; BMI ≥35 kg/m², -0.73% [-0.88, -0.57] and -1.00% [-1.16, -0.85]). PBO-subtracted body weight reductions with CANA 100 and 300 mg, respectively, were also consistent across subgroups (BMI <25 kg/m², -2.2% [-3.5, -1.0] and -3.5% [-4.8, -2.3]; BMI 25-<30 kg/m², -2.4% [-3.0, -1.8] and -3.2% [-3.8, -2.7]; BMI 30-<35 kg/m², -2.1% [-2.7, -1.4] and -2.2% [-2.8, -1.5]; BMI ≥35 kg/m², -2.2% [-3.0, -1.5] and -3.2% [-3.9, -2.4]). PBO-subtracted SBP reductions with CANA 100 and 300 mg, respectively, decreased with increasing baseline BMI (BMI <25 kg/m², -5.7 mmHg [-9.4, -2.0] and -7.7 mmHg [-11.5, -4.0]; BMI 25-<30 kg/m², -4.2 mmHg [-6.3, -2.2] and -5.3 mmHg [-7.3, -3.3]; BMI 30-<35 kg/m², -4.6 mmHg [-6.6, -2.5] and -4.2 mmHg [-6.2, -2.1]; BMI ≥35 kg/m², -2.5 mmHg [-4.7, -0.3] and -3.4 mmHg [-5.6, -1.1]). Overall, both CANA doses were generally well tolerated, with a safety profile consistent with previous reports from individual studies.

Conclusion: In summary, CANA 100 and 300 mg were associated with improvement in A1C, body weight, and SBP versus PBO and were generally well tolerated over 26 weeks in patients with T2DM regardless of baseline BMI.

GLYCEMIC EFFICACY OF CANAGLIFLOZIN (CANA) BY BASELINE A1C AND KNOWN DURATION OF TYPE 2 DIABETES MELLITUS (T2DM)

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Objective: CANA is a sodium glucose co-transporter 2 (SGLT2) inhibitor with demonstrated glycemc efficacy across a range of T2DM patient populations. This analysis evaluated the effects of CANA versus placebo (PBO) on changes in A1C based on baseline A1C and duration of T2DM.

Methods: Pooled data from the 4 PBO-controlled Phase 3 studies that enrolled a general population of patients with T2DM (N = 2,313; mean age, 56.0 y; A1C, 8.0%; BMI, 32.1 kg/m²; mean known T2DM duration, 7.3 y) were analyzed. Change in A1C at 26 weeks (last observation carried forward [LOCF]) was evaluated in subgroups by baseline A1C (<8.0%, 8.0%-<9.0%, and ≥9.0%; mean baseline A1C of 7.3%, 8.4%, and 9.6%, respectively, in the total population) and T2DM duration (<5 y, 5-<10 y, and ≥10 y; mean baseline A1C of 7.9%, 8.1%, and 8.1%, respectively, in the total population). Least squares (LS) mean changes (standard error [SE]) were calculated and PBO-subtracted differences (95% confidence interval [CI]) are reported.

Results: CANA 100 and 300 mg were associated with progressively greater PBO-subtracted LS mean reductions in A1C as baseline A1C increased (A1C <8.0%: -0.45% [-0.55, -0.35] and -0.65% [-0.74, -0.55]; A1C 8.0%-<9.0%: -0.91% [-1.07, -0.75] and -1.07% [-1.24, -0.91]; A1C ≥9.0%: -1.25% [-1.54, -0.97] and -1.48% [-1.77, -1.20], respectively). PBO-subtracted A1C reductions with CANA 100 and 300 mg were -0.70% (-0.84, -0.56) and -0.96% (-1.10, -0.82), respectively, for patients in early stages of T2DM (<5 y). In patients with 5-<10 y T2DM duration, PBO-subtracted A1C differences were -0.74% (-0.90, -0.59) and -0.91% (-1.06, -0.75) with CANA 100 and 300 mg, respectively; differences were -0.74% (-0.89, -0.58) and -0.85% (-1.00, -0.70), respectively, in patients with ≥10 y T2DM duration. Overall, both CANA doses were generally well tolerated across subgroups based on baseline A1C and duration of T2DM, with a safety profile consistent with previous reports from individual studies, including increased incidences of genital mycotic infections and AEs related to osmotic diuresis with CANA compared with PBO.

Conclusion: CANA provided glycemic improvements in patients with T2DM regardless of baseline A1C or duration of T2DM. Greater reductions in A1C with CANA were seen in patients with higher baseline A1C, similar to what has been observed with other antihyperglycemic agents.

Abstract #226

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Objective: CANA is a sodium glucose co-transporter 2 (SGLT2) inhibitor with demonstrated glycemc efficacy across a range of T2DM patient populations. This analysis evaluated the effects of CANA versus placebo (PBO) on changes in A1C based on baseline A1C and duration of T2DM. CANA 100 and 300 mg were associated with progressively greater PBO-subtracted LS mean reductions in A1C as baseline A1C increased (A1C <8.0%: -0.45% [-0.55, -0.35] and -0.65% [-0.74, -0.55]; A1C 8.0%-<9.0%: -0.91% [-1.07, -0.75] and -1.07% [-1.24, -0.91]; A1C ≥9.0%: -1.25% [-1.54, -0.97] and -1.48% [-1.77, -1.20], respectively). PBO-subtracted A1C reductions with CANA 100 and 300 mg were -0.70% (-0.84, -0.56) and -0.96% (-1.10, -0.82), respectively, for patients in early stages of T2DM (<5 y). In patients with 5-<10 y T2DM duration, PBO-subtracted A1C differences were -0.74% (-0.90, -0.59) and -0.91% (-1.06, -0.75) with CANA 100 and 300 mg, respectively; differences were -0.74% (-0.89, -0.58) and -0.85% (-1.00, -0.70), respectively, in patients with ≥10 y T2DM duration. Overall, both CANA doses were generally well tolerated across subgroups based on baseline A1C and duration of T2DM, with a safety profile consistent with previous reports from individual studies, including increased incidences of genital mycotic infections and AEs related to osmotic diuresis with CANA compared with PBO.

Conclusion: CANA provided glycemic improvements in patients with T2DM regardless of baseline A1C or duration of T2DM. Greater reductions in A1C with CANA were seen in patients with higher baseline A1C, similar to what has been observed with other antihyperglycemic agents.
Abstract #227

ASSOCIATION OF SERUM INSULIN AND URINARY ALBUMIN WITH OCCULT CAD IN TYPE 2 DIABETES

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Objective: To study the association of occult coronary artery disease with fasting serum insulin level, albuminuria and other classical risk factors in patients suffering from type 2 diabetes.

Methods: Patients suffering from type 2 diabetes with no history and no sign-symptoms of ischemic heart disease were included in two arms of the study. 120 patients with high fasting serum insulin level were taken in arm A, while arm B contained 60 patients with normal fasting serum insulin level. Both arms were further subdivided into three subgroups according to the duration of disease. All patients were subjected to the detailed medical history, demography, anthropometric measurements, blood investigations, urine investigations and radiological imaging. CT angiography was performed to detect coronary artery disease and immunoprecipitation test was used for the quantitative determination of microalbuminuria.

Results: Data was analysed with the help of chi-square test and student ‘t’ test. In the group of patients with high serum insulin level 80% were found to be suffering from coronary artery disease while normal serum insulin level group had only 56.6% of such cases. 38 patients out of 120 were found to have microalbuminuria associated with high serum insulin level which was significantly higher (more than double) if compared with the group of normal serum insulin level. Dyslipidemia was higher in hyperinsulinemic group. 72 out of 120 patients in hyperinsulinemic group had high low density lipoproteins in compare to 30 patients of normal serum insulin group.

Discussion: Microalbuminuria was initially demonstrated in patients with diabetes mellitus, it was shown to be associated with atherogenic changes in the cardiovascular risk profile and to predict increased mortality and cardiovascular disease. Several studies have demonstrated an association between slightly increased urinary albumin excretion and cardiovascular risk factors, even in the general population. Urinary albumin excretion and the fasting serum insulin levels were directly related to angiographic evidence of CAD.

Conclusion: This study is much more relevant in developing countries. Even in the absence of CT angiography, a documented hyperinsulinemia and microalbuminuria in an asymptomatic diabetic could be considered as a reasonable clue for underlying atherosclerosis. This would help us coronary artery disease prevention in type 2 diabetes patients which is a biggest cause of mortality and morbidity. More studies are needed for further conclusion.

Abstract #228

CORRELATION OF METABOLIC SYNDROME WITH IHD (BASED ON CT ANGIOGRAPHY OF CORONARY VESSELS) IN TYPE 2 DIABETES MELLITUS

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Objective: To study the incidence of IHD as a result of metabolic syndrome in type 2 Diabetes

Methods: It was a hospital based cross sectional study conducted in a 2200 bedded multi-specialty teaching hospital’s medical department. All Type II DM patients (150), including male (50%), mean age 47.70 years and female (50%) mean age 54.28, reported to the medicine department during Apr 2012 to Oct 2013 were included in this study. BP, sr. lipid profile, waist Circumference, CTMT, ECG, CT Angiography of Coronary vessels along with socioeconomic profile. Glycated haemoglobin (HbA1c) test was used to confirm Type II DM among the new cases. Metabolic Syndrome was diagnosed using modified NCEP.ATP-III criteria. As all patients were Type2 DM, so already fulfil one criteria for Metabolic Syndrome, Criteria for Ischemic heart disease by CT Angiography of coronary was >50% obstruction in coronary vessels.

Results: Among 150 diabetic patients, metabolic syndrome was present in 103 (66.66%), patients. The Ischemic heart disease was present in 55 among all 150, among these 55 patients42 (28%) patients (21 males and 21 females) belongs to MS positive group and 13(8.66) patients (11 males and 2 females) belongs to MS negative group. The incidence of IHD was highest between 50-60 years age group. The difference of SBP,DBP,TG in MS vs MS negative group was statistically significant(p<.05).Analysis of IHD by CT Angiography of coronary vessels shows 20% IHD patients in 1-5 years of duration of disease .28% IHD patients in 5-10 years of disease and 42% IHD patient showed IHD after 10
years of diabetes. Among these IHD patients 60% showed double vessel disease, 30% showed single vessel disease and 10% showed triple vessel disease.

**Discussion:** In our study MS with type 2 DM had complications as IHD. Our studies shows 36.66% MS positive and only 8.66% MS negative group have IHD. Thus it indicates more cardiovascular complications associated with MS and type 2 DM. In Carolle A et al study result showed 17.7% of angina, 13.8% of MI, and 4.3 of stroke cases. In Giovanni et al study result showed 23.75% and 26.7% of angina and MI respectively, similar observation in our study. Timothi et al study showed 3 fold cardiovascular morbidity and mortality risk when both MS and Type 2 DM patients combined together. hence other studies had similar results of CVS complications when compared to our study in MS and type 2 DM patients.

**Conclusion:** Based on this study we find that Metabolic syndrome is a major determinant (three times in MS positive patients) of Ischemic heart disease among middle age Indian males and females, in particular among smokers in type II DM.

Abstract #229

**ASSOCIATION BETWEEN RISK FACTORS OF GDM AND GLUCOSE CHALLENGE TEST STATUS AMONG URBAN PREGNANT WOMEN IN BANGLADESH: A TERTIARY CARE HOSPITAL EXPERIENCE.**

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**Objective:** To see frequency of risk factors of GDM among urban women and to find out association between risk factors of GDM and glucose challenge test (GCT) status.

**Methods:** Descriptive study conducted among randomly sampled women with 24 weeks gestation. Subjects were assessed for risk factors of GDM from history, clinical examination, and medical records. GCT was done at 24 weeks of gestation.

**Results:** Total 149 subjects had mean± SD (SE) for pre-gestational age (years) as 27.19±3.31 (0.27), BMI (kg/m²) as 23.86±1.95(0.16), SBP (mmHg) as 109.19±12.53(1.03), DBP (mmHg) as 70.12±9.96(0.82) and GCT-VPG (mmol/L) as 7.09±1.19(0.09).

GDM Risk factors frequencies (%) and GCT-VPG (mmol/L) as mean± SD (SE) between risk factor positive vs negative groups were as follows: age>25yrs 73.8% and 7.21±1.30(0.12) vs 6.74±0.71(0.11)[p<0.03], exercise<150min/wk 65.8% and 7.23±1.30(0.13) vs 6.71±0.82(0.11) [p<0.01], DM family history 61.1% and 7.55±1.31(0.14) vs 6.68±0.83(0.11)[p<0.01], BMI>25kg/m² 25.5% and 7.83±1.59(0.25) vs 6.82±0.87(0.08)[p<0.01], PCOS 22.8% and 7.57±1.70(0.29) vs 6.94±0.95(0.08) [p<0.01], bad obstetric history 20.8% and 7.72±1.50(0.27) vs 6.92±1.04(0.09)[p<0.01], acanthosis negricans 12.8% and 7.86±1.57(0.36) vs 6.98±1.09(0.09)[p<0.01], macroamia 2.7% and 7.32±1.25(0.63) vs 7.09±1.19(0.09) [p<0.69], previous GDM 11.4% and 8.41±1.43(0.35) vs 6.92±1.05(0.09)[p<0.01], IGT 5.4% and 9.35±0.94(0.33) vs 6.96±1.07(0.09)[p<0.01], IFG 4% and 9.46±1.08(0.44) vs 6.99±1.09(0.09)[p<0.01].

GCT was positive (≥7.8mmol/L) in 18.8% subjects. GCT positive(%) between risk factor positive vs negative groups were in: age>25yrs as 22.7 vs 7.7[p<0.02], exercise<150min/wk as 25.5 vs 5.9[p<0.01], DM family history as 27.5 vs 5.2[p<0.01], BMI>25kg/m² as 42.5 vs 10.1[p<0.01], PCOS as 29.4 vs 15.7[p<0.07], obstetric history as 45.2 vs 11.9[p<0.01], acanthosis negricans as 36.8 vs 16.2[p<0.03], obstetric history as 25 vs 18.6[p<0.74], previous GDM as 64.7 vs 12.9 [p<0.01], IGT as 100 vs 14.2[p<0.01], IFG as 100 vs 15.4[p<0.01].

**Discussion:** Age>25yrs was the most frequent (73.8%) risk factor followed by physical inactivity, DM family history, BMI>25kg/m², PCOS etc. Mean GCT-VPG (mmol/L) was significantly higher among risk factor positive subjects, mostly those with Previous GDM, IFG, IGT, BMI>25kg/m², acanthosis negricans etc. GCT was positive among 18.8% subjects. GCT was significantly positive among risk factor positive subjects than negative ones mostly those with GDM, IFG, IGT, BMI>25kg/m², DM family history, physical inactivity etc.

**Conclusion:** Risk factors of GDM were highly frequent. GCT status was significantly associated with risk factors. All urban pregnant Bangladeshi women should be routinely assessed and screened for GDM.

Abstract #230

**MAGNESIUM STATUS IN ADVANCED STAGES OF CKD IN ADULTS WITH DIABETIC NEPHROPATHY AND ASSOCIATION OF HBA1C% WITH MAGNESIUM STATUS**

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**Objective:** To find out whether serum magnesium varies among CKD stage 3-5 in adults with diabetic nephropathy and whether HbA1c% varies with magnesium status.
Methods: Cross-sectional observational study conducted among 106 adult (age>18 years) having diabetic nephropathy CKD stage 3-5. Serum electrolyte including magnesium (normal range: 0.7-1.0 mmol/L), HbA1c%, serum creatinine, eGFR and CKD stages (as per eGFR; stage 5: <15 or dialysis, stage 4: 15-29 and stage 3: 30-59) were assessed. Data were analyzed with SSPS version 20.

Results: 106 diabetic nephropathy subjects (male=49, female=57 with 23, 42 and 41 subjects having CKD stage 3,4 and 5 respectively) had mean± SD (SE) for age (years) as 67.54±11.10(1.08), BMI (kg/m2) as 23.29±2.99(0.29), SBP (mmHg) as 134.19±16.02(1.55), DBP (mmHg) as 79.62±9.12(0.88), HbA1c% as 7.62±0.75(0.07), serum creatinine (mg/dl) as 4.17±2.90(0.28), eGFR(ml/min/1.73m2) as 21.40±14.13(1.37), S. Na (mmol/L) as 132.04±7.04(0.68), S. K (mmol/L) as 4.11±0.95(0.09) and S. magnesium(mmol/L) as 0.76±0.15(0.01). Age of subjects with CKD stage 3 [74.61±8.73(1.82)] were significantly different than that of stage 4 (p 0.00) and 5 (p 0.02). BMI, SBP, DBP, HbA1c%, serum Na, K were not significantly different between CKD stage 3,4 and 5. Serum creatinine and eGFR were significantly different among CKD stages (p=0.00). S. Mg was not significantly different among male and female subjects [0.80±0.15(0.02) vs 0.73±0.15(0.02), p=0.66]. Serum Magnesium level as mean± SD (SE) and (95% CI) were as 0.73±0.14(0.03) and (0.67-0.79) in CKD 3, 0.75±0.13(0.02) and (0.71-0.79) in CKD 4 and 0.79±0.17(0.03) and (0.74-0.84) in CKD stage 5 which were not different among groups (p 0.26). Among subjects 35(33%) and 8(7.5%) had hypomagnesaemia and hypermagnesaemia respectively. HbA1c% as mean±SD (SE) were 7.70±0.52(0.08), 7.61±0.85(0.10) and 7.40±0.83(0.29) among subjects with hypomagnesaemia, normomagnesaemia and hypermagnesaemia (p 0.58).

Discussion: Renal function is the major regulator of serum Mg level and in advanced CKD overt hypermagnesaemia develops. Insulin is required for Mg reabsorption at loop of Henle. In diabetes, insulin resistance or deficiency promote Mg loss at thick ascending limb & may resist development of hypermagnesaemia or even result into hypomagnesaemia. Mg deficiency is associated with poor glycemic control. This study found no significance with Mg level with increased GFR level and HbA1c% levels in diabetic subjects.

Conclusion: A significant negative association between advanced CKD stages and serum Mg levels was not found with those with diabetic nephropathy and glycemic status was not different with Mg status.

Abstract #231

ANEMIA AND IRON STATUS IN DIABETES WITH ADVANCED STAGES OF CKD

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Objective: A study was done to determine association of anemia-iron status among diabetic subjects with CKD stage 3 onwards.

Methods: This cross section descriptive study (2009-10) was conducted among diabetic subjects with eGFR <60ml/min/1.73m2 sampled purposively, with written informed consent and ethical permission, from nephrology and endocrinology units of BIRDEM. Pregnant, children, subjects with other hematological disorder or other disorders causing CKD were excluded.

Results: Age group 48-58 years constituted the highest proportion (32.5%) of respondents. Anemia was found in 89% (male= 86.0%, female= 92.1%) subjects with frequency of mild (Hb:9-12gm/dl), moderate (Hb:7-9 gm/dl) and severe anemia (Hb:<7 gm/dl) as 60.5%, 29.5% and 10% respectively. Among subjects 15.5%, 5.0% and 1.5% received blood transfusion, subcutaneous erythropoietin and intravenous iron. CKD stages 3, 4 and 5 were found among 52%, 38% and 10% subjects respectively with of BMI (kg/m2) as 25.45± 4.25, 24.28±4.67 and 23.00±4.21 (p 0.039 ). SBP (p 0.074), DBP (p 0.099), HbA1c (p 0.263) did not differ significantly among stages. Among CKD stages 3, 4 and 5, Hemoglobin (gm/dl) as mean±SD were 10.24±4.25, 9.24±4.67 and 9.04±4.21 (p 0.039 ). S. iron (µmol/L) as mean±SD were 13.55±6.53, 11.08±5.75 and 10.84±7.57 (p 0.021), S. Ferritin (ng/m) as mean±SD were 145.83±96.95, 214.67±270.56 and 292.45±342.487 (p 0.006), TIBC as mean±SD were 39.37±15.96, 34.29±11.53 and 39.84±11.98 (p 0.043) respectively.

Discussion: Anemia was very frequent among diabetic patients having advanced CKD. Level of Hemoglobin, serum iron, serum ferritin and TIBC were significantly different in different stages of CKD.

Conclusion: This study indicates that anemia-iron profile significantly differs among diabetic subjects with advanced stages of CKD. Therapeutic approaches for diabetics with CKD should include identification and treatment anemia and correction iron status.
Abstract #232

CLINICAL AND SUB-CLINICAL HYPOTHYROIDISM IN TYPE 2 DIABETES WITH MICROVASCULAR COMPLICATIONS

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Objective: To compare between frequency of clinical, sub-clinical hypothyroidism (SCH) and diabetic microvascular complications.

Methods: Cross-sectional descriptive study was conducted in Endocrinology unit of BIRDEM from 2009-2010 among purposively sampled 156 type 2 diabetic subjects having chronic microvascular complication(s) after taking written informed consent and with ethical permission. FT4 and TSH were done to evaluate hypothyroidism. TSH level 4.5-10 µIU/ml and a normal FT4 defined diagnosis of SCH. High TSH (>4.5µIU/ml) and low FT4 (<10.3 pmol/L) defined clinical primary hypothyroidism. To evaluate retinopathy ophthalmoscopy with or without retinal photography, for neuropathy sensory, motor, autonomic function tests and to evaluate nephropathy urine for protein, serum creatinine, CCR, 24 hour UTP, urine for microalbumin were done.

Results: Subjects (male 54, female 102) had age as mean± SD (SE): 56.21± 12.12(97), HbA1c as mean± SD (SE) and (95% CI): 9.95±2.25.(18) and (9.6-10.3). FT4 (in pmol/ml) was as mean± SD (SE) and (95% CI): 12.74±2.79.(22) and (12.3-13.19) and TSH (in IU/ml) was as mean± SD(SE) and (95% CI): 4.73±8.14.(65) and (3.44 - 6.0). Fifty four (34.6%) of them were hypothyroid [clinical n=26(16.7%), SCH n=28(17.9%)] and rest 102 (65.4%) were euthyroid. Hypothyroid cases had FT4: 10.51±2.7 (.37) and (9.7-11.27) and TSH: 9.72±1.23(1.68) and (6.35 -13.10). Euthyroid subjects had FT4: 13.9 ±1.97 (.19) and (9.7-11.27) and TSH (in IU/l/ml) was as mean± SD(SE) and (95% CI): 9.95±2.25(18) and (9.6-10.3). Euthyroid subjects had FT4: 13.9 ±1.97 (.19) and (9.7-11.27) and TSH (in IU/l/ml) was as mean± SD(SE) and (95% CI): 9.95±2.25(18) and (9.6-10.3). FT4 (in pmol/L) was as mean± SD (SE) and (95% CI): 12.74±2.79.(22) and (12.3-13.19) and TSH (in IU/ml) was as mean± SD(SE) and (95% CI): 4.73±8.14.(65) and (3.44 - 6.0). Fifty four (34.6%) of them were hypothyroid [clinical n=26(16.7%), SCH n=28(17.9%)] and rest 102 (65.4%) were euthyroid. Hypothyroid cases had FT4: 10.51±2.7 (.37) and (9.7-11.27) and TSH: 9.72±1.23(1.68) and (6.35 -13.10). Euthyroid subjects had FT4: 13.9 ±1.97 (.19) and (9.7-11.27) and TSH (in IU/l/ml) was as mean± SD(SE) and (95% CI): 9.95±2.25(18) and (9.6-10.3). Euthyroid subjects had FT4: 13.9 ±1.97 (.19) and (9.7-11.27) and TSH (in IU/l/ml) was as mean± SD(SE) and (95% CI): 9.95±2.25(18) and (9.6-10.3).

Discussion: Common contributing factors (hypertension, dyslipidemia, obesity, insulin resistance), found in both hypothyroidism and diabetes mellitus, may worsen the chronic vascular complications if hypothyroidism is overlooked and not treated in patients having both type 2 diabetes and hypothyroidism. Though subjects might not represent whole community, the study revealed that clinical and SCH were significantly associated with diabetic retinopathy but not with nephropathy or neuropathy among type 2 diabetic subjects.

Conclusion: Type 2 diabetic patients with microvascular complication(s) should be screened for hypothyroidism.

Abstract #233

INTERESTING CASE OF INSULIN RESISTANCE IN A TYPE 1 DIABETIC PATIENT DURING DIABETIC KETOACIDOSIS ASSOCIATED WITH RHABDOMYOLYSIS.

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Case Presentation: Diabetes ketoacidosis (DKA) is a serious hyperglycemic emergency associated with significant morbidity and mortality. Rhabdomyolysis is associated with destruction of muscle tissue that can lead to pigment-induced acute kidney injury. Rhabdomyolysis has not previously been reported to be associated with insulin resistance. We report the first case of transient insulin resistance in a patient with both DKA and rhabdomyolysis.

33 year-old Caucasian male poorly controlled type 1 diabetic was admitted to the hospital in a comatose state. According to his family members, he was not using his insulin pump for the last 3-4 days, and there was no previous use of statins in his medical reconciliation. He was found lying on the floor for an unknown period of time. His initial evaluation in the emergency room showed a clear picture of DKA coma with elevated blood sugars, low bicarbonate, elevated beta-hydroxybutyric acid and elevated anion gap. Total CPK levels on admission were markedly elevated 22789 U/L (20-200 U/L) with mild troponins elevations 0.093 ng/ml (0.006-0.026 ng/ml). His troponins became undetectable in the next 20 hrs.

He was treated with IV normal saline (NS) and insulin infusion followed by continuous IV NS with IV Dextrose 5% (D5%) for the next 12 hrs once he reached a blood glucose below 250 mg/dl. His anion gap closed and his D5% drip was switched to an insulin infusion with blood glucose monitoring every hour and hourly correction of insulin rate according to blood sugar changes. Serum potassium corrections were performed with a goal of 4 mmol/dl. His insulin infusion rate was very high during the first 24 hrs oscillating between 5-8 units/hr and stabilizing at 3.3 units/hr at next 36 hrs, followed by 2.1
units/hr at 48 hrs and then decreasing to his usual home basal insulin requirements of 1-0.8 units/hr at about 60 hrs after his presentation.

**Discussion:** This patient showed an association between the decline in serum CPK and the insulin requirements.

**Conclusion:** Muscle tissue plays an important role in insulin metabolism and the treatment of diabetic patients. This case raises the interesting possibility that transient insulin resistance occurs with rhabdomyolysis. This association may have not been previously appreciated since in non-diabetics there is adequate endogenous insulin production to overcome the resistance.

**Abstract #234**

**SEVERE INSULIN RESISTANCE IN TYPE 2 DIABETES PATIENTS TREATED WITH U500 INSULIN USING CGMS AS A TOOL IN EVALUATION**

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**Objective:** To evaluate the clinical effect of U500 insulin in severely Insulin-resistant Type 2 Diabetes patients on glycemic control using Continuous Glucose Monitoring System (CGMS) as a tool in management.

**Methods:** A retrospective chart review was performed of patients using different regimen of U100 insulin with poor glycemic control whom were switched to U500 insulin three times daily. Glycosylated hemoglobin (HbA1c), body weight and Total Daily Dose (TDD) were documented before and after change in treatment. CGMS was performed during follow up visits for monitoring minute to minute glycemic control, hypoglycemia risk and for dose adjustment.

**Results:** From January, 2010 to January 2013, 97 patients (mean age 57.9±1.1, BMI 38.8±0.9 and TDD 168.2±7.4) were identified. Mean HbA1c has decreased after average of 6 months on U500 from 10.3±0.2 to 8.5 ± 0.2 (p < 0.001). Weight change was proportional to the TDD of insulin across all patients regardless of insulin type, however the mean TDD of insulin while on U500 has insignificantly increased from 168.2±7.4 to 179.9±7.5 (P=0.506). CGMS gathered from 17 patients on U100 and 83 patients on U500 showed significant drop in time spent in hyperglycemia (BG>140 mg/dl) (P <0.001 and P=0.001 respectively). However, no significant difference in time spent in hypoglycemia (BG<70mg/dl) (p=0.31), and more importantly, no nocturnal hypoglycemia has been observed.

**Discussion:** There is no specific guideline recommendation or consensus in practice about use of U500 insulin, and the cut off value of 200 units or more of daily insulin dosage recognized to switch patients to higher concentration insulin is arbitrary used. We observed in our cohort that the benefit of better glycemic control is preserved when using a lower cut off value (average 168.2±7.4) and an earlier consideration of U500 insulin significantly improve glycemic control with no significant increase in TDD. The concerning risk for hypoglycemia episodes or nocturnal hypoglycemia with high concentration insulin was not seen and confirmed by CGMS monitoring. This is the first study to our knowledge to show the advantage of using CGMS results of treatment with U500 insulin.

**Conclusion:** Patients with T2D with severe insulin resistance requiring very high dose of insulin benefit from switching to U500 insulin 3 times daily with better glycemic control and no significant increase in TDD or risk of hypoglycemia.

**Abstract #235**

**NEW EMERGING PROMISING THERAPEUTIC TARGET: ROLE OF 11β-HYDROXY STEROID DEHYDROGENASE 1 (11β-HSD1) IN GLUCOCORTICOSTEROIDS INDUCED DIABETES AND ASSOCIATED VASCULAR COMPLICATION**

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**Objective:** 1) To Elucidate role of 11β-HSD1 in Glucocorticosteroid induced Diabetes and associated vascular complication.

2) To evaluate safety and efficacy of Metlyrapone along with Metformin in STZ-HFF Induced Diabetic Rat.

**Methods:** 11β-Hydroxysteroid Dehydrogenase type 1 (11β-HSD1) catalyse the inactive cortisone to active cortisol. Elevated glucocorticoids are a key risk factor for metabolic diseases, so, glucocorticoids activating enzyme 11β-HSD1 represents a promising therapeutic target. Induction of diabetes with 35 mg / kg Streptozotocin (STZ) - High Fat Fed (HFF) (STZ-HFF) leads to increased level of 11β-HSD1 enzyme. The effects of 11β-HSD1 on diabetic vascular complication in STZ-HFF diabetic rats were examined. Metyrapone is a selective 11β-HSD1 inhibitor. Upon the Metyrapone treatment leads to the downregulation of the 11β-HSD1 activities result in abnormal cortisol metabolic clearance rate would lead to stimulation of the Hypothalamus Pitutary Adrenal (HPA)
axis in an attempt to normalise serum cortisol levels, and might account for the Adrenocorticotropic hormone (ACTH) mediated hyperandrogenism in such patients, condition termed as a “Cortisone Reductase Deficiency syndrome”. Metformin play a very protective role in Cortisone Reductase Deficiency syndrome. STZ-HFF induced diabetic rats were treated with Metyrapone (50 mg/kg, i.p), Metformin (50 mg/ kg, orally) as well as combination of Metyrapone with Metformin for 4 weeks. Fasting blood glucose, lipid parameters, Serum cortisol, Serum Testosterone, Antioxidant enzyme, vascular reactivity study, Blood pressure and gluconeogenesis activity were measured.

**Results:** Metyrapone treated Diabetic rats showed significant decreased (p < 0.001) in blood glucose levels, serum Cholesterol (p < 0.05), Serum LDL (p < 0.05) and serum VLDL (p < 0.05) as well significant increased Serum HDL (p < 0.01) compare to diabetic control rats. Metyrapone treated diabetic rats showed significant restoration of antioxidant enzyme compared to diabetic animals. Testosterone level was found significantly lower (p < 0.05) in metformin and Metyrapone combination treated HFF-STZ diabetic animals. From Invitro and invivo vascular reactivity showed Significant increased (p < 0.01) in pD2 and Rmax of acetylcholine were found in Metyrapone treated diabetic animals. As well as Metyrapone showed significant restored (p<0.01) gluconeogenesis pathway.

**Discussion:** Excessive glucocorticosteroids is a highly risk factor for pathogenesis of Diabetes and associated vascular complication.

**Conclusion:** 11β-HSD1 is a new promising target to treat Glucocorticosteroids induced Diabetes and associated metabolic risk factor.

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**Abstract #236**

**DIABETIC CARDIOVASCULAR AUTONOMIC NEUROPATHY IN NEWLY DETECTED TYPE 2 DIABETES PATIENTS**

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**Objective:** 1.To evaluate newly diagnosed type 2 diabetes patients(NDD) for presence of cardiac autonomic neuropathy(CAN)

2.To evaluate correlation of CAN with other parameters of diabetic peripheral neuropathy(DPN) in these patients

**Methods:** Fifty three NDD patients(diagnosis of type 2 diabetes established using ADA criteria) were evaluated for presence of DPN and CAN. All patients were subjected to monofilament testing, testing of vibration perception threshold (VPT) potentials, and for tests for CAN including resting heart rate(RHR), beat to beat heart rate(HR) variability measured as expiration to inspiration ratio of R-R interval(E:I ratio), HR response to standing measured as 30:15 ratio, HR response to valsalva manoeuvre, systolic BP response to standing and diastolic BP response to handgrip exercise.

**Results:** Study included a total of 30 male (M) and 23 female (F) patients with NDD in the age group 23-71 years with mean age 48.1(+10.35) years. Average BMI was 30.3(+7.17) kg/m2 with 48(27M, 21F) patients having a BMI more than 23kg/m2. Average A1c was 9.85% (+2.50). Evaluation for DPN showed monofilament test positive in 17(32.07%) patients while mild impairment of VPTs was present in only 6 (11.3%) patients. Evaluation of CAN showed abnormal E:I ratio(<1.2) as the commonest abnormality present in 29 of 53 patients ( 54.7%) , followed by abnormal diastolic BP response (<10mm rise) to handgrip exercise(21/53 patients,39.62%) and impaired HR response to Valsalva (valsalva ratio<1.10) manoeuvre (18/53 patients, 33.96%). Only 7 patients (13.2%) had RHR more than 90 beats/min, 13 patients (24.53%) had impaired 30:15 ratio (<1.0), and only 9 patients (16.98%) had mildly abnormal systolic BP drop (10-30mmHg) in response to standing. Parameters of CAN(abnormal E:I ratio, abnormal diastolic BP response, abnormal HR response to valsalva) showed no or poor correlation with abnormal monofilament test and impaired VPTs.

**Discussion:** Diabetic CAN may be present at the time of diagnosis of type 2 diabetes, and is associated with increased mortality and risk of silent myocardial ischemia in these patients. However, very little information exists about frequency of CAN in diabetic population, especially in NDD patients.

Our study shows that CAN was present in more than 50% of the newly detected type 2 diabetes patients and may be an early indicator of presence of diabetic neuropathy.

**Conclusion:** Evaluation for presence of cardiac autonomic neuropathy in newly detected type 2 diabetes patients may be helpful in detecting more patients with diabetic neuropathy at an early stage of disease and also in identifying type 2 diabetes patients with higher cardiovascular risk.
Abstract #237

SIMPLIFYING SCREENING METHODS FOR IDENTIFYING THE RISK OF FOOT ULCERATION AMONG DIABETICS. IS IPSWICH TOUCH TEST THE ANSWER? THE SAUDI EXPERIENCE

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Objective: To compare the performance of Ipswich Touch Test (IpTT) with the neuropathy disability score (NDS), vibration perception threshold (VPT) and 10-g monofilament (10g-MF) for identifying the risk of foot ulceration (FU) among Saudi patients with diabetes mellitus (DM) in an outpatient setting.

Methods: A cross-sectional study was conducted on a sample of 184 Saudi diabetic patients referred for the first time from primary health care centers to a specialized diabetes care centre at Prince Salman Hospital-MOH, in Riyadh-KSA. Informed consent was obtained. Patients underwent clinical evaluation including detailed feet assessment. The presence of diabetic peripheral polyneuropathy (DPN), its severity and the risk of FU were determined using NDS. VPT assessed using neurostesiometer. IpTT was performed by touching the tips of first, third and 5th toes of both feet, and defined the presence of neuropathy as IpTT score ≥2 insensate of the 6 sites. The sensitivity and specificity for IpTT to detect neuropathy was calculated against NDS and VPT. Comparison of IpTT and 10-g MF was also performed. SPSS17 was used for statistical analysis.

Results: Mean age 47.4±11 years.92.4% of patients had type 2 DM. Duration of DM was 7.4±7.5years. History of foot ulcer and amputation accounted for 4.3%, 1.1% respectively. IpTT score showed negative correlation with the duration of DM, history of FU and amputation. DPN detected by IpTT correlated significantly with that detected by NDS 0.568** P<0.0001, by VPT 0.463** P<0.0001, and 10-gMF 0.659** P<0.0001. Sensitivity & specificity for the IpTT to detect neuropathy was calculated against NDS and VPT. Comparison of IpTT and 10-g MF was also performed. SPSS17 was used for statistical analysis.

Discussion: Our results demonstrated that IpTT is highly specific when compared to established screening tests for identifying feet at high risk of ulceration such as NDS and VPT and 10-g MF. IpTT exhibited substantial agreement and reliability when directly compared to10-g MF test. The study showed that the test can be easily performed in an outpatient setting as the procedure is simple, quick and doesn’t require special equipment.

Conclusion: IpTT is a simple, inexpensive and reliable screening test for identifying the risk of foot ulceration among diabetic patients.

Abstract #238

EFFECT OF PIOGLITAZONE ON SEVERE HYPERTRIGLYCERIDEMIA IN PATIENTS WITH DIABETES: A CASE SERIES

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Objective: Studies have shown that pioglitazone causes reduction in triglyceride (TG) levels in addition to its effect on glycemic control. Most of these studies were done in patients with average TG levels and therefore effect of pioglitazone on individual cases of severe hypertriglyceridemia (HTG) remains inadequately documented. We report 3 cases where adding pioglitazone led to significant improvement of therapy-resistant severe HTG in patients with diabetes mellitus (DM).

Case Presentation: Case 1: A 53-year-old woman with type 2 DM (T2DM) and HTG was managed with insulin, glipizide and sitagliptin. Her HbA1c ranged 7.8-8.8%. Her TG levels ranged 730-810 mg/dL (normal <150 mg/dL) for about a year despite treatment with statins, ezetimibe and fish oil. Patient did not tolerate fenofibrate. We started pioglitazone 15 mg daily and stopped sitagliptin. Her TG levels dropped from 806 to 260 mg/dL within 2 months. Follow-up showed further drop of TG to 156 mg/dL while on the same dose of pioglitazone.

Case 2: A 30-year-old woman with T2DM and HTG presented to our clinic on insulin, metformin and rosiglitazone. Her HbA1c ranged 5.9-7.5%. Her TG levels ranged 730-810 mg/dL (normal <150 mg/dL) for about a year despite treatment with statins, ezetimibe and fish oil. Patient did not tolerate fenofibrate. We started pioglitazone 15 mg daily and stopped sitagliptin. Her TG levels dropped from 806 to 260 mg/dL within 2 months. Follow-up showed further drop of TG to 156 mg/dL while on the same dose of pioglitazone.

Case 3: A 63-year-old woman with T2DM and HTG presented to our clinic on insulin, metformin and rosiglitazone. Her HbA1c ranged 5.9-7.5%. Her TG levels ranged 500-2000 mg/dL over 6 years despite treatment with fibrates and niacin. We continued the fenofibrate she was taking (160 mg daily) and replaced rosiglitazone with pioglitazone 15 mg daily. Her TG levels dropped from 806 to 260 mg/dL within 2 months. Follow-up showed further drop of TG to 156 mg/dL while on the same dose of pioglitazone.
ABSTRACTS – Diabetes Mellitus/Prediabetes

statins, and niacin. Her TG levels ranged 650-2000 mg/dL over the previous 2 years. HbA1c ranged from 5.1 to 6.8%. We added pioglitazone 15 mg daily to her regimen, which consisted of gemfibrozil 600 mg twice a day. Her TG levels dropped from 800 to 227 mg/dL within 2 months. Subsequently, increasing the dose of pioglitazone to 30 mg daily led to further drop of TG level to 156 mg/dL. Further follow-up showed that TG levels stayed <160 mg/dL after almost 2 years.

Discussion: Pioglitazone was effective in lowering very high TG levels in our cases. This could be due to the induction of increased lipoprotein lipase activity, leading to increased fractional clearance rate of VLDL TG. Also the insulin sensitizing effects of pioglitazone may help restore hypertriglyceridemia and postprandial lipemia.

Conclusion: Our 3 cases demonstrate that pioglitazone can lead to dramatic drop and near normalization of TG in patients with very high TG levels who failed other therapeutic agents.

Abstract #239

IMPACT OF PRESCRIBED AND MONITORED MEDIUM-INTENSITY PHYSICAL ACTIVITY ON DIABETES, OBESITY, CARDIOVASCULAR PROFILES AND QUALITY OF LIFE

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Objective: Demonstrate benefit of monitored, structured exercise in overweight or obese patients with Diabetes Mellitus (DM).

Methods: Randomized and controlled trial of patients from Scripps Clinic, San Diego, CA. Inclusion criteria: age 18-70 years; prior diagnosis of Pre-DM, Type 1 or Type 2 DM; BMI 25-45kg/m2. Exclusion criteria: severe DM complications; uncontrolled psychiatric illness; nonEnglish speaker; unable to exercise 150 minutes a week; unable to complete a 1-mile walk test. At screening, patients were randomized to the experimental group (EG) or control group (CG), and completed a health survey and activity assessment. Physical fitness was assessed with a 1-mile walk test. Both groups received nutrition and DM education. The EG participated in a monitored moderate-intensity exercise class, taught by a qualified instructor, for 150 minutes a week for 12 weeks. The CG was counseled to perform 150 minutes of unguided, medium-intensity exercise per week. Vitals, glucose logs, and adverse events were reviewed monthly by a physician. Fasting blood glucose (FBG), A1C, LDL and health-related quality of life surveys were evaluated at screening and 12 weeks.

Results: Baseline characteristics of the two groups (n=17) were similar. Weight loss was significant in the EG (12.9 vs. 2.6 lbs, p=0.01), as was lower BMI (2.2 vs. 0.5 kg/m2, p=0.03). There was a favorable decreasing trend in A1C, FBG, and waist circumference in the EG. Health-related quality of life scores improved in both groups. Lipid profiles and systolic blood pressure (BP) reduction were not observed in either group.

Discussion: The cardio-metabolic benefits of exercise include BP and LDL reduction, weight loss, enhanced glycemic control, and insulin sensitivity. The promising results of the LOOK Ahead trial revealed that intensive lifestyle intervention improves physical fitness, glycemic control, and cardiovascular risk factors relative to diabetes support and education. Other studies have shown that exercise is enhanced when behavioral strategies parallel supervised exercise. Such approaches may be cost-effective in the management of DM and obesity, and should prompt further attention towards observed structured exercise programs to enhance compliance.

Conclusion: Our study has shown that monitored and structured exercise positively affects weight, DM control, and health-related quality of life scores. With our second group of patients, we hope to prove statistical significance in cardiovascular benefit, with both BP and LDL reduction.

Abstract #240

GLYCOGEN STORAGE DISEASE TYPE (GSD-1) AND PREDIABETES - CAN THEY COEXIST?

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Objective: There has been growing concern in the US about the increasing incidence of prediabetes and dyslipidemia because of its association with increased cardiovascular risk. Patients with increased LDL or triglycerides are often screened for diabetes or prediabetes. We present a unique case of a patient who was diagnosed with prediabetes but also had a coexisting metabolic disorder characterized by postprandial hypoglycemia.

Case Presentation: A 39 yr old man was referred for evaluation of an elevated HbA1c. PMH was significant for a diagnosis of (GSD-1) at age 5 months and 2 episodes of pancreatitis at age 29 and 34 years. Medications included enalapril, gemfibrozil and allopurinol. Past surgical and family history were non contributory. PE was significant for an alert man who looked younger than his stated age with normal vital signs and a BMI of 29. Lab studies showed a Hba1c of 5.8, triglycerides of 661, LDL of 124, HDL of 27 and a 24 hr urine protein excretion of 0.84...
The management questions that arose were whether the HbA1c needed to be treated and whether this patient was at risk of atherosclerosis in the future because of the dyslipidemia and microalbuminuria.

**Discussion:** GSD-1 is a dysfunction of glycogen breakdown characterized by a defect in either the G-6-Pase catalytic unit or the G-6-P transporter in the endoplasmic reticulum. In adulthood, patients usually resort to frequent feedings of uncooked cornstarch to avoid hypoglycemia. A literature search did not reveal any cases with coexistent prediabetes and glycogen storage disease. There have been studies showing 50-66% values of normal endogenous glucose production in adolescent patients reaching near normal in adults with GSD but the mechanism is still unclear. Metformin in this patient would be absolutely contraindicated because of the coexisting lactic acidosis. As for the issue of atherosclerosis, a study comparing 9 adolescent GSD-1a patients with healthy weight matched controls revealed that the study cohort had a thinner max intima thickness as compared to controls. Other factors contributing to a possible decreased risk of atherosclerosis might be decreased platelet aggregation and the increased uric acid acting as a potent free radical scavenger. On the other hand, as GSD patients live longer, development of worsening renal function may increase the risk of atherosclerosis.

**Conclusion:** This case illustrates that we do not fully understand glucose metabolism as well the predisposing factors for atherosclerosis. Furthermore, the underlying glycogen storage disease precludes the use of metformin and emphasizes the need for a thorough history and physical exam prior to deciding treatment for new onset hyperglycemia.

**Abstract #241**

**QUALITY IMPROVEMENT IN INPATIENT DIABETES CARE DECREASES WASTEFUL HBA1C TESTING**

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**Objective:** Excessive laboratory testing is a well-known problem in medical practice, particularly in the inpatient setting. In the past, the high incidence of wasteful HbA1c testing has been attributed to the implementation of HbA1c based performance measures. In 2009, our 591-bed teaching hospital began a quality improvement process that culminated in February 2013 when the hospital was awarded Joint Commission Accreditation in Advanced Inpatient Diabetes Care. One of the requirements was that all patients with diabetes have a HbA1c test on admission unless there was another HbA1c available from the previous 90 days. The hospital embarked on multiple electronic and educational performance improvement activities to meet this requirement. Our goal was to study the influence of quality improvement on wasteful laboratory testing by examining the change in the rate of unnecessary repeat HbA1c tests over this four-year period.

**Methods:** We performed a retrospective analysis using data from our computerized laboratory system. We obtained all HbA1c results from tests performed on inpatients from 2009 through 2012. Our primary outcome measure was the repeat rate, or the proportion of total HbA1c tests that were performed less than 90 days from a previous test.

**Results:** Overall, 17.7% of the total testing was unnecessary. Notably, there was a trend toward a decrease in the monthly repeat testing rate from the baseline period to the culmination of the quality improvement process. In the beginning of 2009, 21.44% of the HbA1c tests were performed less than 90 days from a previous test, with that number decreasing to 13.04% (p< .0001) by the end of 2012, just prior to the Joint Commission site visit. This decrease occurred without any interventions intentionally targeting the reduction of wasteful ordering.

**Discussion:** Our results are compatible with previously published reports that have shown a similarly high rate of unnecessary repeat HbA1c testing. However, contrary to published speculation, we found that quality improvement did not increase the rate of wasteful HbA1c testing; in fact there was a statistically significant decrease in wastefulness. Though quality improvement processes tend to penalize the underutilization of resources without rewarding the avoidance of overutilization, we believe that in this case the efficiency and reliability introduced by the quality improvement process led to an overall decrease in the rate of unnecessary testing.

**Conclusion:** In conclusion, though previous studies have linked implementation of quality performance metrics to wasteful ordering practices, our study demonstrates that the quality improvement process can actually decrease wasteful resource utilization.
Abstract #242

A CASE OF ACUTE HYPERGLYCEMIA AFTER INITIATION OF EVEROLIMUS FOR METASTATIC BREAST CANCER

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Objective: To report a case of severe hyperglycemia associated with the initiation of Everolimus in a patient with metastatic breast cancer.

Case Presentation: A 64 year old female with a six year history of well controlled diabetes and metastatic breast cancer presented for management of diabetes. She was initiated on Everolimus six weeks prior and her glucometer download revealed abrupt changes in mean blood glucose from 95 to 275 mg/dL. The patient reported polyuria, fatigue and weight loss of twelve pounds in the past six weeks. Vitals and exam were unremarkable except for tachycardia. Her HbA1c was 5.9 % three weeks prior to the initiation of Everolimus. After six weeks of use, the HbA1c increased to 6.6 %. Seven weeks after this, the level was 8.8 %. After significant changes in lifestyle and diet, her blood sugars remained elevated despite augmentation of her oral diabetic medications. Within eight weeks of starting Everolimus, she required the initiation of multidose insulin regimen. She was eventually controlled on a total daily dose of 34 units of insulin.

Discussion: This case illustrates the potential for severe hyperglycemia with the use of Everolimus and the importance of expeditious management. As mTOR inhibitors have been shown to significantly improve clinical efficacy in patients with advanced breast cancer, careful monitoring and treatment of potential adverse events such as acute hyperglycemia are critical. Current literature describes the need for initiation of oral anti-diabetic medications for management of Everolimus induced hyperglycemia. Patients in phase III trials show that 4-20 % of patients on Everolimus have Grade 3-4 hyperglycemia, and Common Terminology Criteria for Adverse Events guidelines call for the interruption of Everolimus treatment in these populations.

Conclusion: This case emphasizes the need for early recognition and aggressive use of insulin to manage glucose toxicity associated with Everolimus use, especially in patients with underlying diabetes.

Abstract #243

GASTRIC EMPTYING EFFECTS OF DULAGLUTIDE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Objective: To evaluate the effect of once weekly dulaglutide on gastric emptying (GE) using scintigraphy; and the effect of dulaglutide coadministration on the pharmacokinetics (PK) of metformin, used as a secondary marker to correlate the effect of dulaglutide on GE.

Methods: Thirty-one male and 7 female patients (18-75 years; body mass index 25.7-39.9 kg/m2) with type 2 diabetes mellitus (T2DM) participated in a placebo-controlled, multiple-dose scintigraphy study. Patients received placebo on Week 1 (Day 1) followed by once-weekly subcutaneous (SC) injections of either placebo or dulaglutide 1.5 mg on Weeks 2 to 5 (on Days 8, 15, 22 and 29). Patients taking metformin immediate release stayed on a stable dose throughout the study. GE was evaluated using scintigraphy following a radiolabeled solid breakfast on Days 3, 10, 17, 24 and 31. The primary endpoint was the time required for 50% of radioactivity to empty from the stomach (t50). Metformin PK (n=23) were evaluated in parallel with the scintigraphy assessments on Days 3, 17 and 31. Serum glucose and plasma insulin were also quantified.

Results: The GE delay was approximately 2 hours, with a mean delay in t50 from 1.72 hours on Day 3 (after placebo administration) to 3.77 hours on Day 10 (after the first dulaglutide dose). The mean t50 values on Days 17, 24 and 31 were 3.32, 3.28 and 3.15 hours, respectively. There were no statistically significant changes in the PK parameters of metformin when coadministered with dulaglutide at steady state (on Day 31), relative to placebo. Mean serum glucose levels decreased over time in patients administered 1.5 mg dulaglutide; while there were marked increases in mean plasma insulin levels at 2 days postdose, corresponding to peak dulaglutide levels. Gastrointestinal (GI) events were the most commonly reported type of adverse event.

Discussion: Although statistically significant delays in GE compared to baseline were observed in patients administered 4 once-weekly doses of dulaglutide 1.5 mg, the effect showed a trend to decrease with each subsequent dose, suggesting a potential tolerance to the effect. There was no clinically relevant impact of steady state dulaglutide coadministration on the PK of metformin immediate release. There was a decrease in serum glucose; accompanied by marked increases in plasma insulin,
consistent with glucose-dependent insulin secretion. **Conclusion:** The dulaglutide-induced GE effect was largest after the first dose, with a trend of diminishing effect following subsequent doses of dulaglutide. Based on metformin PK, no dose adjustment is recommended for metformin when coadministered with once weekly dulaglutide.

**Abstract #244**

**SRI LANKA DIABETES DIET STUDY:**
**GLYCAEMIC RESPONSE OF STRING HOPPERS WITH TYPICAL SRI LANKAN CURRIES IN HEALTHY VOLUNTEERS**

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**Objective:** Objective of the study was to study the glycaemic response of white and red rice string hoppers consumed with typical Sri Lankan curries in healthy volunteers.

**Methods:** 30 healthy volunteers (20-60yrs, M:F 13:17) were given white and red rice string hoppers meals with changing curries, making 8 types of meals. All 30 were given all 8 menus on different days, containing 50g of available carbohydrates. String hoppers (white and red rice flour) were given with one of the following curries on one occasion: coconut gravy with coconut sambol, lentil (Dhal) curry, bean (legume) curry and fish curry. Subjects came fasting for 12hrs. A fasting glucose was done and after consuming the food, blood glucose was tested every half hour till 2hours. Glycaemic index (GI) was calculated by standard method.

**Results:** The GI of string hoppers made of white rice flour had significantly higher GI values compared to red rice flour string hoppers, except when consumed with beans (legume) curry. Highest GI (69.2±9.47) was seen with string hoppers and coconut gravy/coconut sambol. However there was significant difference between white and red rice (69.20 ± 9.47 vs 50.46 ± 9.74). Lowest GI was seen, when string hoppers were eaten with legume curry, irrespective of whether the rice flour was white or red (39.93 ± 8.14 vs 41.96 ± 9.86).

**Discussion:** String hoppers when eaten with various curries, have different GI values for same quantity of available carbohydrate. Coconut gravy with string hoppers gave the highest GI. Legume curry combined with red or white rice string hoppers give the lowest GI value. Adding high fibre vegetables seem to reduce the glycaemic response of carbohydrate meal in normal subjects. This phenomena has to be tested in diabetes patients.

**Conclusion:** String hoppers when eaten with various curries, have different GI values for same quantity of available carbohydrate. Coconut gravy with string hoppers gave the highest GI. Legume curry combined with red or white rice string hoppers give the lowest GI value. Adding high fibre vegetables seem to reduce the glycaemic response of carbohydrate meal in normal subjects. This phenomena has to be tested in diabetes patients.

**Abstract #245**

**HEPATIC STEATOSIS AND THE DIABETES EPIDEMIC: BIRDS OF A FEATHER**

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**Objective:** Describe quantitative liver SPECT analysis to assess hepatic steatosis and aid with its follow-up and treatment.

**Methods:** SPECT liver-spleen scans were used for liver disease related to hepatotoxins or endocrinopathy including insulin resistance (IR), Cushing’s syndrome (CS), diabetes mellitus (DM), thyroid disease (TD) or obesity. Modified fractal analysis used A=(average/peak) counts within hepatic isocontours, I. Regression analysis of Ln(I) vs. Ln(A) yields a near (0,0) intercept-limiting slope, M and normalized Mn = M(L)(S)/70 for vertical liver (L) and spleen (S) span in cm. Liver disease was confirmed by CT, ultrasound or biopsy; cognitive function by Montreat Cognitive Assessment, IR by HbA1c, CS by high serum cortisol and obesity by BMI.

**Results:** Among 65 patients, 37 female, 28 male, age 50+-14 years, were untreated: 9/46 (20%) near normal with Mn 0.96+-0.10; 14/46 (30%) hepatic steatosis with Mn 1.51+-0.15; 13/46 (28%) hepatic fibrosis with Mn 2.05+-0.17 and 10/46 (22%) cirrhosis with Mn 2.78+-0.27. Only 6/53 (11%) with Mn > 1.16 had high liver enzymes. Comorbidities included: obesity 55/65 (85%); hypertension, portal 20/65 (31%), pulmonary 4/65 (6.2%) or systemic 35/65 (54%); IR 20/65 (31%); DM 26/65 (40%); TD 19/65 (29%); CS 4/65 (6.2%); coronary disease 10/65 (16%); heart failure 7/65 (11%); hyperlipidemia 32/65 (49%); TIA or stroke 8/65 (12%), renal disease 5/65 (7.7%); depression, unipolar 19/65 (29%), or bipolar 4/65 (6.1%); chronic anxiety 4/65 (6.2%) or PTSD 2/65 (3.1%), opiate-dependent chronic pain 12/65 (18%); cognitive impairment 18/39 (46.1%); and substance abuse, alcohol 8/65 (12%) or nonalcohol 4/65 (6.2%). Treatment with > 3600 mg omega 3 fish oil, 400 units vitamin E and/or phenteramine/topiramate 7.5/46 mg oral daily for > 6
months tended to reduce Mn with stability or improvement in all comorbidities, even in a cirrhotic patient whose Mn decreased from 4.4 to 2.9.

Discussion: Liver SPECT is more sensitive than liver enzymes, noninvasive, and less expensive than combined CT for hepatic steatosis and MRI for hepatic fibrosis. Although liver SPECT may be nonspecific, epidemic hepatic steatosis will nonetheless account for the preponderance of abnormalities. Liver disease is intrinsic to obesity-related IR, its progression to DM and its comorbidities. Medical therapy for weight loss or mifepristone for mild, often unrecognized CS, may be cost effective vs. invasive, bariatric surgery.

Conclusion: Liver SPECT heterogeneity is readily quantified to sensitively assess liver function; moreover, its use to monitor effective therapy of early liver disease may help to control the epidemic of obesity-related medical and neuropsychiatric comorbidities.

Abstract #246

EFFICACY AND SAFETY OF LINAGLIPTIN IN BLACK/AFRICAN AMERICAN PATIENTS WITH TYPE 2 DIABETES (T2D): POOLED ANALYSIS FROM 8 RANDOMIZED, PLACEBO-CONTROLLED PHASE 3 TRIALS

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Objective: In the US, Black/African Americans have an increased risk of T2D and its associated complications compared to white adults. This group is also less likely to achieve glycemic targets. However, clinical evidence specifically targeting this population is lacking. To address this need, we pooled data from a large clinical development program to assess the efficacy and safety of the dipeptidyl peptidase-4 inhibitor linagliptin in this population.

Methods: This retrospective analysis identified self-reported Black/African Americans in North and South America from 8 randomized, placebo-controlled linagliptin trials. The primary endpoint was change from baseline in HbA1c after 18 (2 trials) or 24 (6 trials) wks.

Results: Of 336 Black/African American T2D patients, 173 received linagliptin 5 mg/day and 163 received placebo (as monotherapy or add-on to various glucose-lowering regimens). Age and BMI were similar across groups. Mean (SD) baseline values of the efficacy variables in the full analysis set (linagliptin n=163; placebo n=152) also were comparable: HbA1c, 8.53 (0.98) and 8.61 (1.13%); fasting plasma glucose (FPG), 163.8 (56.4) and 177.3 (60.2) mg/dL with linagliptin and placebo, respectively. Overall, 67% had T2D for >5 years. Placebo-adjusted mean change (95% CI) in HbA1c from baseline was -0.69% (-0.92, -0.46; P<0.0001) at wk 18 (8 trials) and -0.64% (-0.90, -0.39; P<0.0001) at wk 24 (6 trials). For FPG, placebo-adjusted mean change (95% CI) was -11.7 mg/dL (-23.1, -0.3; P=0.0446) at wk 18 (8 trials) and -14.7 mg/dL (-25.7, -3.8; P=0.0087) at wk 24 (6 trials). Safety profiles were similar in both groups, with adverse events (AEs) in 65.3% of patients on linagliptin and 68.1% on placebo. Fewer patients on linagliptin had drug-related AEs (9.2% vs 13.5% with placebo). Of 9 serious AEs with linagliptin, 2 were considered drug-related by investigators (1 increased CPK; 1 adjudicated unstable angina); both patients recovered. Incidence of hypoglycemia was comparable across groups (12.1% on linagliptin, 11.7% on placebo), with most hypoglycemic events being mild in intensity and occurring in an add-on to basal insulin study (only one severe hypoglycemic event requiring assistance occurred with linagliptin). Both treatments were weight neutral.

Discussion: The availability of effective oral glucose-lowering drugs is of particular importance to Black/African American patients. We show here that linagliptin significantly improved glycemic control in this highly burdened group and was well-tolerated with a low risk of hypoglycemia and no weight gain.

Conclusion: These data support linagliptin as a useful T2D therapy option in Black/African Americans.

Abstract #247

ASSOCIATION OF GLYCEMIC CONTROL PARAMETERS WITH CLINICAL OUTCOMES IN CHRONIC CRITICAL ILLNESS

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Objective: Chronic Critical Illness (CCI) designates a subset of patients requiring prolonged mechanical ventilation and tracheostomy, with associated poor outcomes. Our study assessed the impact of glycemic parameters on outcomes in a CCI population.

Methods: A retrospective case series was performed on 148 patients.
patients admitted to The Mount Sinai Hospital Respiratory Care Unit between 2009-2010. A semi-parametric mixture model identified trajectories for the daily mean blood glucose (BG) and range over time. Patients with both low-stable daily BG mean and range were classified as the low-risk hyperglycemia group (n=87) with the remainder classified as the high-risk group (n=61). Utilizing the same model, patients were classified into low- (n=90) or high-risk hypoglycemia groups (n=58). The cohort was also grouped into diabetes (DM) [n=48], stress hyperglycemia (SH) [n=85], and normal glucose (n=15) groups.

Results: Hospital mortality was significantly greater in the high- (28%) compared to the low-risk hyperglycemia group (13%); RR 2.20 [1.11-4.37] (p=0.0199). One-year mortality was significantly greater in the high- (66%) vs. low-risk hyperglycemia group (46%); RR 1.46 [1.07-1.91] (p=0.0185). Low-risk hypoglycemia patients were 29% less likely to expire within 1 year of discharge (p=0.0215). The rate of hypoglycemia (BG < 70 mg/dL) was lower among ventilator-liberated patients compared to those who failed to liberate (0.092 vs. 0.130; p<0.0001). When assessing high- and low-risk hyperglycemia only in the DM patients, hospital and 1-year mortality no longer showed significance, while hypoglycemia continued to show an association. In the SH group, both hospital and mortality (high-risk hyperglycemia 48%, low-risk hyperglycemia 15%; p=0.0013) and 1-year mortality (high-risk 74%, low-risk 50%; p=0.0482) remained significantly different. The hypoglycemia (<70 mg/dL) and severe hypoglycemia (<40 mg/dL) rates were lower in the SH group than the DM group (0.086 vs. 0.182; p=0.0001 and 0.012 and 0.022; p=0.0118, respectively).

Discussion: Our study demonstrated an association of mean BG, range and hypoglycemia with outcomes in a CCI population. Diabetic status as a modulator of optimal BG targets has been demonstrated recently in other critically ill populations. In our cohort, tighter glycemic control was associated with improved outcomes in patients with SH, but not with DM. Avoidance of hypoglycemia was important for both groups.

Conclusion: Glycemic parameters were associated with outcomes in a CCI cohort. Diabetic status was found to be an important contributing factor. Confirmation of these findings may lead to stratified glycemic control protocols in CCI patients based on the presence or absence of diabetes.

Abstract #248

LABORATORY VERIFICATION OF STEATOSIS IN PATIENTS WITH TYPE 2 DIABETES CO-MORBID WITH CHRONIC HEPATITIS C

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Objective: To study and create a method of non-puncturing biopsy with measurements of biochemical markers of hepatic steatosis in patients with type 2 diabetes combined CHC.

Methods: We observed 29 patients with type 2 diabetes, combined with CHC, aged 38 to 54 years (17 men and 12 women). The diagnosis of CHC was on the basis of complex clinical and biochemical parameters, confirmed by detection of antibodies with anti-HCV polymerase chain reaction - HCV-RNA and an ultrasound of the abdominal cavity. Type 2 diabetes was verified according to the ICD-10 with a certain level of blood glucose, glycosylated hemoglobin, C-peptide and immuno-reactive insulin. Patients underwent clinical and laboratory examination of biochemical markers of cytolysis, cholestasis, dyslipidemia and dysproteinemia, peroxide-induced chemiluminescence of blood serum and liver biopsy. Statistical processing was done by Statistica 8 (StatSoft, USA).

Results: In patients with CHC, liver steatosis was verified in 18 of 29 patients (62.1%). Microscopic examination found that the initial degree of steatosis is accompanied by the deposition of lipids mainly in the centro-lobular area. With the progression of steatosis, microgranular steatosis of the centrolobular area transform to macrogranular and in the periportal zone to microgranular steatosis. With progression to the third degree of steatosis its character changes to macrogranular not only in the area, but also in the periportal zone.

Discussion: For laboratory verification of the presence of hepatic steatosis in patients with chronic hepatitis C, we carried out morphological and biochemical studies and proposed discriminant equation:

S1 = 7.83 * A + 5.19 * B + 0.79 * C - 25.7
S2 = 9.89 * A + 3.94 * B + 0.86 * C - 28.1

where A - the concentration of cholesterol, mmol / L, B - triglycerides, mmol / L, C - CL intensity peroxide induced serum conv.

Conclusion: In patients with CHC, liver steatosis was verified in 62.1% cases. Exceeding S1 over S2 CHC patients ascertain the presence of hepatic steatosis with a diagnostic accuracy of 79.8%.
Abstract #249

DETECTION OF TYPE 2 DIABETES MELLITUS IN MEDICAL STUDENTS

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Objective: According to World Health Organisation, a disease of the middle-aged and elderly, type 2 diabetes has recently escalated in all age groups and is now being identified in younger and younger age groups, including adolescents and children, especially in high-risk population. This underscores the need for mass awareness and screening programmes to detect diabetes at an early stage and early age. So purpose of the study is to find risk of type 2 diabetes mellitus at an early age using IDRS. To assess Random Capillary Blood Glucose (RCBG) in students having high IDRS score.

Methods: All the students of Bharati Vidyapeeth Deemed University Medical College will be screened using IDRS which includes age, family history of diabetes, exercise status and Waist circumference. After scoring them they will be categorised into mild, moderate and high risk group. In students who are having score more than 50, Random Capillary Blood Glucose (RCBG) will be assessed with the help of glucometer.

Results: We have assessed 403 students till now. It was observed that 9%, 36% & 55% students in high, Moderate & Low risk group respectively for developing type 2 D.M. Mean abdominal obesity in high risk students was 98.19 ± 10.42 as compared to 78.52 ± 12.25 in moderate and low risk students (p<0.0001). Family history of diabetes in either or both parents was present in 28.% students. 72% students were having sedentary lifestyle. Mean RCBG in students having score more than 50 was 95.10 ± 11.63 mg/dl. Also, 4 students were having RCBG >103mg/dl.

Discussion: This underscores the need for further investigations to detect diabetes at an early stage and to overcome the disease burden of diabetes in future. IDRS is the simplest way to screen large population. Conclusion: RCBG is a simple and practicable test which can be used to predict the risk of type 2 diabetes mellitus. To prevent and to postpone the risk of type 2 diabetes mellitus, health education programme, exercise and diet planning can be recommended for these students.

Abstract #250

EMPAGLIFLOZIN REDUCES BLOOD PRESSURE IN PATIENTS WITH TYPE 2 DIABETES AND HYPERTENSION: A PHASE III, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL (EMPA-REG BPTM)

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Objective: To investigate the efficacy and safety of empagliflozin in patients with type 2 diabetes and hypertension (mean seated systolic blood pressure [SBP] 130-159 mmHg and diastolic BP [DBP] 80-99 mmHg).

Methods: In this study (NCT01370005), patients (mean [SD] age 60.2 [9.0] years, BMI 32.6 [5.1] kg/m2) received empagliflozin 10 mg (n=276), empagliflozin 25 mg (n=276) or placebo (n=271) once daily for 12 weeks. Co-primary endpoints were changes from baseline in HbA1c and mean 24-hour SBP (ambulatory BP monitoring [ABPM]) at week 12. Key secondary endpoint was change from baseline in mean 24-hour DBP (ABPM) at week 12.

Results: Mean (95% CI) differences vs placebo in changes from baseline in HbA1c were −0.62% (−0.72%, −0.52%) and −0.65% (−0.75%, −0.55%) with empagliflozin 10 mg and 25 mg, respectively (both p<0.001), in mean 24-hour SBP were −3.44 mmHg (−4.78, −2.09) and −4.16 mmHg (−5.50, −2.83) with empagliflozin 10 mg and 25 mg, respectively (both p<0.001), and in mean 24-hour DBP were −1.36 mmHg (−2.15, −0.56) and −1.72 mmHg (−2.51, −0.93) with empagliflozin 10 mg and 25 mg, respectively (both p<0.01). Adverse events were reported by 48.9%, 51.4%, and 52.6% of patients on empagliflozin 10 mg, 25 mg, and placebo, respectively. Events consistent with volume depletion were reported in 1 patient each on empagliflozin 10 mg and placebo.

Discussion: In patients with type 2 diabetes, hypertension is a common comorbidity and enhances the risk of cardiovascular complications, thus a treatment approach that includes control of BP and glycemia may reduce the risk of cardiovascular complications and mortality. Conclusion: Empagliflozin significantly reduced BP and was well tolerated in patients with type 2 diabetes and hypertension.
Abstract #251

OVERALL TOLERABILITY OF LINAGLIPTIN IN A LARGE COHORT OF PATIENTS WITH TYPE 2 DIABETES: A POOLED ANALYSIS OF PROSPECTIVE SAFETY DATA FROM PLACEBO-CONTROLLED STUDIES

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Objective: Numerous glucose-lowering drugs are available for the management of type 2 diabetes mellitus (T2DM) and drug safety is a key consideration. We aimed to assess the safety and tolerability of the dipeptidyl peptidase-4 inhibitor linagliptin in patients with T2DM who participated in a large global clinical development program.

Methods: Safety data were pooled from a comprehensive trial database comprising all available randomized, double-blind, placebo-controlled, clinical trials with linagliptin lasting up to 102 weeks. Incidences of predefined adverse events (AE) were calculated with descriptive statistics and results are summarized by treatment group (linagliptin, placebo) overall and by age category (<65 years, 65-74 years, >75 years). Hypoglycemia was assessed descriptively and with an exploratory analysis based on the risk ratio, the respective 95% confidence interval (CI), and Fisher’s exact test.

Results: In total, 22 trials were included in the analysis involving 7400 patients (age >65 years: 30.0%) of whom 4810 received linagliptin 5 mg total daily and 2590 received placebo. The overall incidence of AEs or serious AEs (SAE) including cardiac disorders, vascular disorders, infections and infestations, gastrointestinal disorders (including pancreatitis) with linagliptin was similar to placebo (AE 57.3% vs. 61.8%; SAEs 4.8% vs. 6.4%, respectively). As expected, with advancing age, aggregate incidences of AE and SAE numerically increased, but the incidences comparing linagliptin to placebo remained similar.

Discussion: Because patients with T2DM are likely to be on antidiabetes treatment for several years, establishing the safety of therapeutic agents is important. This pooled comprehensive safety analysis supports previous evidence that linagliptin is well tolerated overall and across all age groups, with a low incidence of hypoglycemic events. Ongoing large outcome trials will provide further insights into the long-term safety profile of linagliptin.

Conclusion: This analysis supports linagliptin as a well-tolerated therapy for the management of hyperglycemia in patients with T2DM.

Abstract #252

PREVALENCE OF GLUTAMIC ACID DECARBOXYLASE-65 ANTIBODIES IN A PREDOMINANTLY AFRICAN AMERICAN URBAN POPULATION WITH APPARENT TYPE 2 DIABETES

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Objective: To identify the prevalence of glutamic acid decarboxylase-65 antibodies (GADA) in a predominantly African American (AA) population with apparent type 2 diabetes (T2DM) in our diabetes treatment center.

Methods: Retrospective data analysis was conducted on all patients with apparent T2DM upon initial presentation to our clinic between 6/2007 through 11/2013. GADA along with other variables were reviewed which included A1C, insulin therapy, hypertension, BMI and HDL level. Our lab reference range for positive GADA was greater than 1 U/ml.

Results: Out of 858 patients with T2DM who were tested for GADA, 127 (14.8%) were found to be positive. Out of the 127, 91.13% were AA with a median age of 54 years ranging from 20-86 years. Females accounted for 62.4 %. At initial presentation, mean A1C was found to be 9.37±2.77% and 58.1% of the patients were on insulin therapy. The mean BMI was 32.45±9.91 kg/m2 and 67.5% of patients were hypertensive. HDL level was found to be 53.27±20.36 mg/dL.

Discussion: T2DM is by far more common than type 1 diabetes (T1DM) accounting for more than 90% of diabetes in the US. Insulin resistance is the main pathophysiologic mechanism in T2DM, while the hallmark of T1DM is autoimmune destruction of beta cells of the pancreas. Islet cell, GADA, tyrosine phosphatases, IA-2 and IA-2β autoantibodies have been described as the immunologic markers with GADA being the most sensitive and specific. Other studies showed that patients with high titers of GADA
tended to be associated with a lower BMI and progressed more quickly to insulin deficiency and dependence. Our study population did not follow this BMI trend.

**Conclusion:** GADA were common among AA with typical obese and hypertensive T2DM phenotype. Further studies are warranted in our population to assess the clinical course of patients with GADA and the need for early initiation of insulin. Meanwhile, we recommend all newly diagnosed AA patients with apparent T2DM be screened for auto antibodies, especially GADA.

**Abstract #253**

**CHARACTERISTICS AND HABITS OF DIABETICS WHO ARE AT HIGH RISK FOR SLEEP APNEA: CROSS SECTIONAL STUDY**

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**Objective:** Obstructive sleep apnea (OSA) has been associated with insulin resistance and glucose intolerance. Recent reports have indicated that the majority of patients with type 2 diabetes are also have OSA. It been suggested that over 80% of patients with moderate to severe OSA go undiagnosed. Poor glycemic control was reported in diabetics with untreated OSA. The primary goal of this study was to evaluate the prevalence of diabetic individuals with high risk for OSA and their characteristics and habits.

**Methods:** A cross-sectional study conducted at the King Abdulaziz Specialist Hospital, Taif, Saudi Arabia. Type 2 diabetics age 18 years and older who had a routine follow up to the Diabetes clinic from Jun-Dec 2013 were asked to participate. Baseline characteristics, laboratory data and measurement were collected by the investigators. We excluded patients with existed psychiatric illness and those with history of diagnosed OSA. We used Berlin Questionnaire to screen for OSA risk which was administered by the investigators.

**Results:** Total of 215 patients participated, 103 (48%) were male and 112 (52%) were female with mean age 56.6 yrs, mean A1c 8.6%, mean duration of diabetes of 10.93 yrs, mean BMI of 31.8, 88.4% were married, 42.3% were on oral medications only, 52.1% were on insulin +/- oral and 5.6% were on diet control. 48.8% are at high risk for OSA. Compare to the low risk, diabetics with high risk for OSA has mean age of 57.3 yrs vs 55.8 yrs (p=0.38), 40.6% were male vs 47.9% (P=0.034), 85.8% vs 88.4% were married, and 67% vs 65.1% reported low income.

High risk diabetics for OSA has mean A1C of 8.6 vs 8.7 (p=0.51), BMI of 33.8 vs 29.8 (p=0.000), mean systolic BP of 144 vs 137 mmHg (p = 0.02), mean diastolic of 82.5 vs 80 mmHg (p=0.12), and mean resting HR of 84 vs 80.6 bpm (p=0.005) compare to low risk. Regarding the diabetes related complications, high risk diabetics for OSA have high prevalence of neuropathy 69.8% vs 56.4% (p=0.05), HHS 13.2% vs 5.5% (p=0.026), retinopathy 29.2% vs 20.9% (p=0.17) and nephropathy 3.8% vs 0.9% (p=0.16) compare to low risk individuals. 81.1% who are at high risk for OSA reports sedentary lifestyle compare to 67.3% (p=0.045). 84.0% of the high risk group were active smokers compare to 71.8% in the low risk group (p=0.012).

**Discussion:** Almost half of the group screened are at high risk for OSA.

**Conclusion:** High risk diabetics for OSA tend to be older and have significantly higher mean of BMI, systolic BP and resting heart rate. Also, they tend to have significantly higher risk for neuropathy and HHS despite non-significantly lower A1c. They have more risky habits compare to the low risk group.

**Abstract #254**

**ROLE OF OSAS (OBSTRUCTIVE SLEEP APNEA SYNDROME) ON GLUCOSE VARIABILITY IN DIABETES**

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**Objective:** Glucose variability is considered an ominous contributor to the high rate of cardiovascular death in diabetic subjects. There are many recent data pointing to a disruptive role of Sleep Apnea and or disturbed sleep on glucose control. We evaluated the role of Sleep Apnea and sleep disturbance on glucose variability in diabetes.

**Methods:** 24 diabetic type subjects 2 with suspected OSAS underwent continuous blood glucose monitoring for seven days. All the common physical and biochemical parameters were recorded. None of these subjects was on insulin treatment. During this week they also underwent a home polysomnographic recording. Two of them were eliminated due to technical artifacts. The common
indexes of OSAS, Apnea/Hypopnea Index (AHI), Oxygen Disturbance Index (ODI), Respiratory Disturbance Index (ODI), the Nadir of Oxygen desaturation, the time spent sleeping and the % of time spent in REM sleep, were entered into a partial correlations with the most common indexes of glucose variability, Continuous Overall Net Glycemic Action (Conga) 1, 2, 4, the number accounting for the time period in hours being considered.

Results: There was a positive correlation between the time spent in REM Sleep (p=.001) and the three indexes of Glucose Variability. The correlation was positive also with the Nadir of Oxygen desaturation (p=.001), and to a lower level (p<.05) with the three indexed of respiratory disturbance, AHI, RDI, ODI during the REM phase of sleep.

Discussion: This is the first report linking the respiratory disturbance to the indexes of glucose variability studied with a sophisticated technology. The results clearly point to an effect of the respiratory disturbance occurring during the REM sleep on the short term (1-4 hours) glucose variability.

Conclusion: Monitoring of sleep and respiration should be included among the tests needed in subjects with high glucose variability.

Abstract #255

REVERSAL OF SEVERE INSULIN RESISTANCE IMMEDIATELY AFTER BARIATRIC SURGERY

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Objective: Obesity may accelerate the age-related decline in insulin sensitivity and is associated with a risk of type 2 Diabetes (T2DM). Elevated insulin levels may additionally contribute to more weight gain. The Homeostasis Model Assessment of insulin resistance (HOMA-IR) is a widely validated clinical tool that estimates insulin sensitivity based on fasting plasma glucose and insulin. We report herein a case of morbid obesity with severe insulin resistance (IR) showing tremendous improvement directly after bariatric surgery based on the HOMA assessment.

Case Presentation: Mr. NS is a 49 yo gentleman with longstanding history of morbid obesity (BMI 59 kg/m2), T2DM, obstructive sleep apnea and hypertension. He has been diabetic for more than 5 years, insulin dependent for at least 3 years with severe insulin resistance requiring a total of 300 units of insulin U-500 per day and Metformin 1000 mg BID. He enrolled in the medical weight management program (dietitian supervised calorie count and regular exercise) for 6 months during which he lost 40 lbs (8.9 % of his initial body weight) and his insulin requirements decreased to a total of 55 units of U-500 per day. After that, he underwent a sleeve gastrectomy. Postoperatively, he required only 2 units of regular insulin subcutaneously at 1 hour postop. His fasting blood glucose, fasting insulin level and C-peptide were measured at 24, 48 and 72 hours postop and HOMA-IR was calculated and the results were 18.82, 11.43 and 5.84 respectively. During his hospital stay no further insulin was needed and he was discharged home on no DM medications. He came for follow up 2 weeks later during which he has been on a liquid diet. His fasting glucose was 113 mg/dl with a simultaneous insulin level of 16.5 (uiU/ml), his HOMA was 4.6. He was still off his DM medications. Unfortunately no preop HOMA was performed since patient was on insulin then.

Discussion: This case illustrates first the effect of lifestyle changes on insulin sensitivity since this patient ended up needing only 1/4th of his initial insulin dose after losing only 8.9% of his body weight. Second, it demonstrates the effect of bariatric surgery on insulin resistance in the immediate postop as reflected by the dramatic improvement of his HOMA score and his null postop insulin needs. This is probably related to the known hormonal shift (GLP1, GIP, PYY stimulation) that occur after such surgery.

Conclusion: Bariatric surgery has immediate effect on insulin sensitivity. This effect seems more pronounced if associated with preop lifestyle interventions and weight loss.
Abstract #256

BASELINE CHARACTERISTICS OF PARTICIPANTS ENROLLED IN THE EMPAGLIFLOZIN CARDIOVASCULAR OUTCOME TRIAL (EMPA-REG OUTCOME™) IN PATIENTS WITH TYPE 2 DIABETES

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Objective: Although a large number of diabetes drug classes are available for the management of T2DM, the impact of different glucose-lowering therapies on cardiovascular (CV) disease remains largely unknown. The EMPA-REG OUTCOME™ trial (NCT01131676) will investigate the effect of the sodium glucose cotransporter 2 inhibitor empagliflozin 10 mg or 25 mg od compared with placebo, upon a background of optimal standard of care, on CV outcomes in patients with type 2 diabetes mellitus (T2DM) at increased CV risk.

Methods: The study is a double-blind, double-dummy and event-driven trial, powered for CV non-inferiority and superiority. The primary outcome is time-to-first occurrence of CV death, nonfatal myocardial infarction or nonfatal stroke, with all events being independently and prospectively adjudicated. 691 subjects with an event are required to provide 90% power to yield the upper limit of the adjusted 95% confidence interval for hazard ratio $<1.3$ at a one-sided $\alpha$ level of 0.025, assuming equal risks among groups. Hierarchical testing for superiority will follow for the primary and key secondary (time-to-first occurrence of CV death, nonfatal myocardial infarction, nonfatal stroke or hospitalization for unstable angina pectoris) outcomes where non-inferiority is achieved for the pooled doses vs. placebo.

Results: Between September 2010 and April 2013, 7063 patients were randomised at 594 sites. Most participants were recruited from Europe (41%), North America (20%) or Asia (19%), 29% were women, mean (SD) age was 63 (9) years (9% of patients were ≥75 years of age) and mean (SD) HbA1c was 8.1 (0.8)% (49% of patients had HbA1c <8.0%). Diabetes duration was ≤5 years in 18% of patients and >10 years in 57%. Most patients (99%) had previous CV complications. Most patients had mild (estimated glomerular filtration rate [eGFR] 60-90 ml/min/1.73m2; 52%) or moderate (eGFR 30-60 ml/min/1.73m2; 26%) renal impairment, and 40% had albuminuria.

Discussion: Baseline characteristics of participants enrolled in this trial indicate that they are at high CV risk, as anticipated. We expect the results of the EMPA-REG OUTCOME™ trial to answer the hypothesis that empagliflozin is safe or even protective from a CV standpoint, given its glucose-, weight-, and blood pressure-lowering properties.

Conclusion: This trial may further inform clinical decision-making for selecting glucose lowering therapy for patients with T2DM.

Abstract #257

INSULIN INDEPENDENCE IN A GAD-65 ANTIBODY POSITIVE PATIENT USING A PROTON-PUMP INHIBITOR

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Objective: We detail the case of a GAD-65 positive antibody (AB) patient with a BMI of 22 who, after two years of insulin therapy, became insulin independent following initiation of omeprazole.

Methods: Proton-pump inhibitors (PPI) increase gastrin levels and promote islet cell neogenesis via stimulation of the Reg receptor in exocrine pancreatic ductal cells.

Case Presentation: LC is a 56-year-old woman who presented to the ER in diabetic ketois. Two days PTA, LC was evaluated by her PMD for polydipsia and polyuria. She was started on metformin at that time but had not been on any medication for diabetes prior. Labs on hospital admission were: glucose of 774 mg/dL, pH 7.35, bicarbonate 24 mmol/L, anion gap 14, positive serum acetone, and positive urine ketones. Hemoglobin A1C was 11.1% and GAD-65 AB were 2.2 U/mL (NR: <1.0 U/mL). She was treated with an insulin drip and transitioned to basal/bolus insulin. LC was discharged on 6 units of glargine daily and 4 units of lispro with meals and correction scale (0.35 units/kg/day). At three and six months following discharge her A1Cs were 6.5% and
5.7%, respectively. After 16 months of insulin therapy, her serum C-peptide was 1.7 ng/mL (NR: 0.8-3.1 ng/mL) with a blood glucose of 87 mg/dL. Omeprazole 40 mg twice daily was begun after LC had been insulin dependent for over 2 years. Within two weeks her insulin was tapered and discontinued. In the 16 weeks since discontinuing insulin her A1C has remained ≤ 6.0% without diabetes medications. Her most recent C-peptide, 7 weeks after discontinuation of insulin was 3.12 ng/mL with a concomitant glucose of 76 mg/dL. GAD-65 AB remained elevated at 2.1 U/mL.

**Discussion:** Recent studies have documented improved glycemic control and increased beta cell mass in patients with type 2 diabetes who are treated with PPI's. This is particularly significant in light of the natural history of decreased insulin secretion in this disease process. Greater success has been seen with the use of omeprazole and pantroprazole than with esomeprazole. We hypothesize that the success of PPI therapy in our patient was dependent on adequate residual beta cell mass as reflected in her C-peptide levels.

**Conclusion:** The success seen in LC suggests that PPI's may provide a safe and novel approach for patients with type 1 and 2 diabetes. We hypothesize that early treatment with PPI while there is still enough residual beta cell mass, will contribute to greater success by enabling ongoing islet neogenesis to outpace autoimmune beta cell destruction. We also hypothesize that PPI therapy used in combination with an immune tolerance agent will lead to greater success in some patients who present with a more typical type 1 picture.

**Abstract #258**

**MENSTRUATION PROVOKING DIABETIC KETOACIDOSIS (DKA) IN A FEMALE PATIENT WITH INSULIN DEPENDENT DIABETES MELLITUS (IDDM)**

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**Objective:** To present a rare case of catamenial DKA

**Case Presentation:** A 19 year old female with history of obesity, IDDM, polycystic ovarian syndrome (PCOS), and asthma presented with nausea, vomiting, and abdominal cramps in March, 2013. Laboratory studies showed glucose 414 mg/dl, bicarbonate 13 mmol/L, anion gap 23 mmol/L and positive urine ketones. Patient was diagnosed with DKA and managed with aggressive intravenous fluids and insulin infusion, and was discharged on insulin glargine and aspart. History did not reveal any identifiable provocative factors for this episode. Retrospectively, she was treated with metformin for PCOS and hyperinsulinemia since age 9. Diabetes was diagnosed at age 17 during a hospitalization for severe hyperglycemia and ketosis. Hemoglobin A1C ranged from 10 to 12.2% due to non-compliance to both diet and medications. She was then started on insulin. She was started on microgestin (1.5mg/30mcg) for irregular menses in May, 2012. After that, she had 8 hospitalizations for DKA within 10 months, many of these were considered “unprovoked DKA’s”. During this last admission, patient reported that most of her DKA’s occurred during the week when she was menstruating. Considering this potential link between menstruation and DKA, we changed microgestin daily to depot medroxyprogesterone acetate every 3 months. She was also instructed to use a different insulin regimen (more insulin) for her perimenstrual period. She was noted to have only 3 admissions for DKA in 9 months after that. All the three DKA’s were thought to be related to upper respiratory infection.

**Discussion:** This young female has long standing poorly controlled IDDM. The regular menses induced by oral contraceptive pills (OCP) have contributed to her frequent DKA’s (almost monthly), which were mostly classified as “unprovoked” DKA’s. Decreasing the frequency of her menses by changing to prolonged hormonal contraception helped to prevent frequent DKA’s. This suggests a possible link between menstruation and DKA in this patient. Similar cases have been rarely reported in the literature, termed as ‘catamenial’ DKA. The underlying mechanism is not well understood. Some of the contributing factors include the cyclic changes of female hormones, stress level (due to perimenstrual symptoms) and behaviors (food craving). Carefully observing their glucose level and insulin needs through menstrual cycle can aid to develop a “sick day rule” management strategy.

**Conclusion:** Menstruation could be one of the provocative factors for DKA in premenopausal young female diabetic patients. Recognizing this association can help to develop specific strategy to prevent DKA in these patients.
Abstract #259

INTER-PROFESSIONAL EYE CARE COMMUNICATION AS PART OF A DIABETES COMPREHENSIVE CARE PLAN

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Objective: Management of the patient with diabetes mellitus requires a coordinated effort by various health care professionals. One of the most important, yet seldom achieved, components of this care involves an annual dilated fundus examination (DFE). The National Committee for Quality Assurance (NCQA) recognizes this as an area needing attention. The goal is for every patient over 18 with diabetes to have a dilated eye examination every year to facilitate the early detection of diabetic retinopathy.

Methods: A retrospective review of all patients with diabetes seen in the office by the endocrinologist during the continuous six month interval of June 1, 2013 through November 30, 2013 was performed to evaluate the current level of compliance, the demographics of eye care delivery in the Upstate of South Carolina, and the inter-professional communication of eye care data.

Results: The results indicate that 81.7%, 367 of the 449 patients seen had a DFE within the previous 14 months. It was possible to discern the eye care professional (ECP) seen for the DFE for 95.8% of those patients. Optometrists and ophthalmologists had similar incidences of annual DFE for the patient population at 80.7% and 83.2%, respectively. Unfortunately, we only received documentation from the ECP for approximately half of these patients. All communications were reviewed and documentation that a DFE was performed as part of the examination was confirmed in 100%. Of those patients who received a DFE within the previous 14 months, documentation of a DFE was received from 48.7% of patients seen by an optometrist and 46.8% of patients seen by an ophthalmologist.

Discussion: An annual DFE is an important part of diabetes care. The long term goal of improving eye care for patients with diabetes in the Upstate of South Carolina is ongoing. Over 80% of the patients had a timely DFE. Eye care is being provided by both optometrists and ophthalmologists with similar incidences of annual DFE, performance of a DFE, and communication. Overall documentation that a DFE was completed is still lacking. Although patient reporting of when the DFE was performed and whether pathology was noted is commonplace, it is not ideal and accurate documentation is needed.

Conclusion: While we are encouraged by the quality of eye care in our community we feel that improvement in inter-professional communication is needed to achieve optimal care for our patients with diabetes.

Abstract #260

PROFILE OF TYPE 2 DIABETES MELLITUS PATIENTS PRESENTING TO A TERTIARY CARE HOSPITAL

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Objective: The objective of the study was to see the profile of type II diabetes mellitus patients presenting to the tertiary care hospital of Karachi.

Study Design: Cross sectional study

Place and Duration: The study was conducted at the Department of Endocrinology, Liaquat National Hospital (LNH) Karachi, Pakistan from July 2013 till December 2013.

Methods: Type II diabetes mellitus patients presenting to the Outpatient Department of LNH above 18 years of age, able to understand the national language ‘Urdu’ and both gender were included in the study. Questions related to the investigation (HbA1C), use of anti diabetic medications, self monitoring blood glucose, experience of hypoglycemia with medications and follow up visits with the physicians were asked from the patients.

Results: A total of 300 patients were included in the study. There were 147 (49%) male participants. 192 (64%) patients had HbA1C of <6%. 39 (13%) patients were only using insulin, 75 (25%) were using oral hypoglycemic agents along with insulin, 30 (10%) were not taking any medication and rest were on oral hypoglycemic. Only 48 (16%) patients checked their blood glucose daily. 15 (5%) patients experienced hypoglycemia in the past. Regarding the visit to the physician, only 42 (14%) patients visited their physicians once a month, 18 (6%) did not follow any physician in the past and 15 (5%) visited the doctor once a month.

Discussion: More Patients have controlled HbA1c.

Conclusion: More than half of the patients had controlled HbA1C. Patients on anti diabetic medications should be aware of the side effects especially hypoglycemia and monitor their glucose regularly.
Abstract #261

CLINICAL EFFECTIVENESS OF LIRAGLUTIDE ACROSS BODY MASS INDEX IN TYPE 2 DIABETES IN THE US

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1. Evidera, 2. Novo Nordisk Inc

Objective: Clinical trials have shown that liraglutide effectively lowers A1C levels in adult patients with type 2 diabetes (T2D). However, no studies have evaluated the effectiveness of liraglutide for different levels of body mass index (BMI) in clinical practice. This study examined clinical effectiveness outcomes of liraglutide after 6 months in T2D patients stratified by BMI at time of liraglutide initiation.

Methods: We used the General Electric Centricity electronic medical records database to examine adult T2D patients aged >18 who initiated liraglutide without prior use of insulin anytime from January 1, 2010 through January 31, 2013 (liraglutide dose was not available). Patients were excluded if they were pregnant, had type 1 diabetes, or had polycystic ovarian syndrome without the presence of T2D at any time during the 12 months before starting liraglutide or any time after. A1C change from baseline (45 days prior to treatment initiation until 7 days after), the proportion of patients reaching A1C<7%, and weight changes (relative to baseline weight) at 6 months were examined stratified by baseline BMI categories (due to low sample in the BMI<25 category these patients were excluded).

Results: A total of 3,005 uncontrolled (A1C>7% at baseline) T2D patients initiating liraglutide were identified. Average (SD) A1C levels at baseline were 8.6% (1.4), 8.7% (1.5), 8.7% (1.4) and 8.6% (1.4) for BMI categories 25.0-29.9, 30.0-34.9, 35.0-39.9 and ≥40.0, respectively (P=0.35). After 6 months A1C decreased, on average (SD), by 0.95% (1.6), 1.02% (1.6), 0.99% (1.6) and 0.84% (1.6) for BMI categories 25.0-29.9, 30.0-34.9, 35.0-39.9 and ≥40.0, respectively (P=0.30). The proportion of patients achieving A1C<7% at 6 months were 38.1%, 37.0%, 40.9% and 41.0% for BMI categories 25.0-29.9, 30.0-34.9, 35.0-39.9 and ≥40.0, respectively (P=0.54). Patients in each BMI category also showed clinically meaningful reductions in weight (1.7-3.0% across baseline BMI).

Discussion: Our results are consistent with those of a recent meta-analysis of liraglutide clinical trials that assessed clinical across baseline BMI (Niswender, et al. Diabetes Obes Metab. 2013). An endpoint not studied by Niswender et al. was change in A1C from baseline across baseline BMI, which we included and found to be independent of BMI category.

Conclusion: We found that initiating treatment with liraglutide in adult patients with T2D is associated with clinically meaningful reductions in A1C and weight across baseline BMI groups in clinical practice.

Abstract #262

PREVALENCE OF VITAMIN D DEFICIENCY IN TYPE 2 DIABETES MELLITUS AND ITS CORRELATION WITH HBA1C IN SAUDI POPULATION

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Objective: To study the prevalence of vitamin D deficiency in type 2 diabetes mellitus and its correlation with HbA1c in Saudi population.

Methods: We tested 25OH vitamin D level, body mass index and HbA1c level in 500 Saudi type 2 diabetic patients, 30 to 60 years of age and studied prevalence of vitamin D deficiency/ insufficiency and its correlation with body weight and HbA1c in this group of population.

Results: Of the participants, 54% had severe vitamin D deficiency with 25OH vitamin D level of less than 25nmol/L, 32% had vitamin D insufficiency with level between 25 to 60 nmol/L, and only 14% had optimum vitamin D level of above 60nmol/L. Whereas, 82% of patients were overweight or obese. Moreover, 96% of patients with vitamin D deficiency or insufficiency had HbA1c greater than 7%.

Discussion: Vitamin D deficiency is a world-wide epidemic; with recent estimates indicating greater than 50% of the global population is at risk. Moreover it is highly prevalent among Saudi Population and largely attributed to obesity, poor exposure to sunlight, and poor dietary vitamin D supplementation. However, data about its prevalence in type 2 diabetes mellitus and its correlation with HbA1c is lacking.

Conclusion: There is high prevalence of vitamin D deficiency in type 2 diabetes mellitus and associated with overweight, obesity and poor glycemic control.
Abstract #263

IMPACT OF TWO INTERACTIVE WEB-BASED CME-CERTIFIED CONFERENCES ON KNOWLEDGE OF DIABETES MANAGEMENT AND INSULIN THERAPY INTENSIFICATION WITH GLP-1 RECEPTOR AGONISTS

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Objective: Based on the premise that a diabetes CME program could provide and guide clinical knowledge and to some extent, standardize choice of therapies in treating difficult diabetes cases, we developed and executed a CME-certified outcome program including 153 clinicians treating type 2 diabetes patients with insulin intensification with the goal of improving knowledge and optimizing diabetes management in this patient population.

Methods: Two interactive national web-based CME conferences were conducted by diabetes experts with slide presentation to address learning needs in diabetes treatment and management. Six months later, participating clinicians were sent a validated patient case vignette to evaluate the learning benefit and retention of the CME course.

Results: Despite multiple efforts to solicit response only 8 CME clinician participants as well as 9 Control group clinicians responded to the questionnaire. Pre-test and post-test cohort analyses were utilized for validating the questionnaire. CME and Control groups were compared after 6 months from the date the CME course was given. The results from the case study were analyzed and compared after six months comparing the CME group to a control group. A very encouraging improvement trend was observed in 4 out of 5 questions in favor of the CME group. There were no improvement in Question 1; however there were marked improvements in Questions 2 through 5 (Q2: 100% vs. 55%; Q3: 87% vs. 55%; Q4: 50% vs. 22%; Q5: 87% vs. 44%).

Discussion: Clearly lack of statistical power due to much smaller sample size than planned resulted in no statistical p-values in this case-study. However, additional power analysis showed that only 16 participants per arm would have resulted in a statically significant difference for Questions 2 and 5; and 40 participants per arms would have made the results statistically significant in all questions 2 through 5.

Conclusion: Overall these results indicate the clear benefit of the CME program in way of strong trends only suffering from lack of statistical power. Better and stronger participation of the physicians in this study would have made this CME program to stand out and establish proven benefits to physicians and patients alike.

The difference in percent of correct responses in Questions 2 to 5 of the case-study phase of the study was stunning, 30 to 45% improvement over the control group, but yet this study was not able to demonstrate statistical significance due to the length of the study and difficulty in securing the participant physicians throughout.

In light of the limited but strong results of this study, this CME program is deemed beneficial in treating type 2 diabetes patients and their management.

Abstract #264

A BLOOD GLUCOSE VISUALIZATION TOOL FACILITATED INPATIENT CONSULTATION FOR HOSPITALIZED DIABETES PATIENTS

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Objective: Hyperglycemia and hypoglycemia are significant problems which complicate the care of hospitalized patients and have been associated with adverse health outcomes. The primary medical providers for these patients request endocrinology consultation when specialized care is deemed to be beneficial, but the consultation request is often made late in the admission when the patient is near discharge and the endocrinologist has little time to impact the inpatient blood glucose (BG). In response, we created a blood glucose visualization tool (VT), where all patients in the hospital are represented on a colored grid. The cell representing each patient changes color in real time according to the category of BG value. Very high BGs (over 250 mg/dL, red) and hypoglycemia (less than 70 mg/dL blue) are highlighted. The insulin regimen, A1C, and actual BGs are displayed when the user scrolls over the cell representing the patient.

Methods: During a 4 week period, we used the VT to identify patients whose BGs were in the “red” or “blue” categories in the past 24 hours. These patients were on one specific medical-surgical care unit at a community teaching hospital. We asked their attending physicians if they would like an endocrine consultation for their patients. In a second 4 week period, we used the VT to identify patients during the month of July on the teaching service, when new internal medicine house staff begin training.

Results: During the initial 4 weeks, endocrine consultations were performed on 38 patients triggered by the VT. BG values and length of stay (LOS) were collected for...
them and for 39 patients who were cared for in the usual manner on a similar unit. In the second 4 week period, the VT triggered 23 consultations. During that time, we also collected data from 24 subjects in a control group. In the first 4-week period, the average BG was 163 mg/dL in the VT-triggered consultation group and 185 mg/dL in the matched control group. The results were not statistically significant (p=0.15). LOS was not different between the two groups (4.3 days vs. 4.0 days, p=0.8). No significant differences were seen in the second 4 week period for both mean BG or LOS.

Discussion: A blood glucose visualization tool may facilitate early endocrine consultations for patients with uncontrolled diabetes in the hospital. In this particular analysis, we were not able to show improvements in mean BG during the hospitalization or reduction in LOS.

Conclusion: Future studies are needed to see in which settings our tool would be most beneficial.

Abstract #265

DIABETES CONTROL AND FOLLOW UP PROJECT; A PROACTIVE FOLLOW UP PROGRAM EXPERIENCE IN AN OUTPATIENT PRIMARY CARE CLINIC

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Objective: To emphasize the role of proactive physician approach to improve diabetes control and follow up

Methods: 727 Patients’ charts were reviewed. Patients who had diabetes were contacted via mail or phone call for a follow up visit to measure their Hemoglobin A1C (HB A1C) during the period from September 2012 to October 2012. Follow up for 9 months was done. Patients who came for a follow up visit within 3 months, 6 months and 9 months were documented. HB A1C was measured. Number and percentage of patients who came for a follow up was documented. Level of HB A1C were measured and distributed in 3 ranges; below 5.7, 5.7 to 6.4, 6.5 to 7 and above 7 mmol/dl.

Results: 486 patients with diabetes were contacted to come for HB A1C check at Troy Internal Medicine. Of those contacted, 260 patients came for blood work, 53.49%. 13 of those who came did come in did not have HB A1C done due to insurance difficulties(5%). 16 patients were found to have a HB A1C less than or equal to 5.6(6.15%). 118 patients had a HB A1C of 5.7 to 6.4(45.38%). 64 patients had a HB A1C in the range of 6.5 to 7(24.61%). 62 patients were found to have a HBA1C more than 7(23.84%), which falls into the uncontrolled diabetes level.

Discussion: Chronic hyperglycemia has multiple microvascular and macrovascular complications. Continuous follow up for diabetes patients is mandated. The American Diabetes Association ADA guidelines1 for 2013 for diabetes follow-up are to measure HGB A1c every 3 months for patients with recent diabetes medications adjustment. In patients with controlled blood sugar, HB A1C is usually followed up every 6 months. As for HB A1c target for diabetes patients, it is recommended to have the level below 7 in non pregnant adults with long life expectancy, which showed reduced microvascular and long term macrovascular complications.

Conclusion: Proactive follow up with diabetes patients succeeded to motivate around 50% of diabetes patients to follow up on their HB A1C. Most of those patients (76%) surprisingly had controlled diabetes. Around 24% of them had uncontrolled diabetes. We had the chance to reach to uncontrolled diabetes patients in a proactive approach which will hopefully help provide better control on their blood sugar and prevent diabetic complications.

Abstract #266

DRUG INDUCED HYPERSENSITIVITY REACTION: A CASE OF SIMULTANEOUS THYROIDITIS AND FULMINANT TYPE 1 DIABETES

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Objective: We present a case of Dapsone induced hypersensitivity reaction with simultaneous thyroiditis and fulminant type 1 Diabetes.

Case Presentation: We herein present a case of a 48 year old African American man with acquired immunodeficiency syndrome (AIDS) was initially started on trimethoprim/ sulfamethoxazole then changed to Dapsone for Pneumocystis jiroveci pneumonia prophylaxis. Within a few weeks, he developed 30 pound weight loss, nausea, vomiting, exfoliative maculopapular rash, renal failure and eosinophilia 12% (normal 0-8.0%). Dapsone was discontinued and renal biopsy was consistent with acute interstitial nephritis predominately with lymphocytes and eosinophils. Patient was diagnosed with Dress Syndrome. He was also noted to have hyperthyroidism with normal thyroid-stimulating immunoglobulin and thyroid peroxidase antibodies titers. In addition, he was significantly hyperglycemic (serum glucose as high as 434 mg/dl) with prior normal glucose levels on basic metabolic panels performed one month prior. Hemoglobin
A1c was 5.9% and fructosamine level was 259umol/L (normal <285umol/L). He required almost 1 units/kg. Other laboratory work included negative glutamic acid decarboxylase and islet cell antibodies with mildly elevated insulin antibodies which was checked after receiving insulin therapy (6.5uU/mL, normal <5.0uU/mL). Patient was treated with beta blockers, tapered dose of steroid and multiple daily injections of insulin. Hyperthyroidism, acute renal failure, and rash had resolved within a few weeks. His insulin requirements decreased to 0.25units/kg.

Discussion: Drug induced hypersensitivity reaction (DRESS Syndrome) is a rare and severe drug reaction to different medications most commonly sulfonamides and antiepileptic medications. Clinical presentation includes fever, rash, eosinophilia and visceral organ involvement. While autoimmune thyroiditis has been reported uncommonly in DRESS syndrome (1), only 11 cases of de novo Fulminant Type 1 Diabetes have been reported (2).

Conclusion: To our knowledge, our case represents the first known case of simultaneous thyroiditis and fulminant type 1 Diabetes in settings of Dapsone induced hypersensitivity reaction.

Abstract #267

POST DELIVERY DETERIORATION IN GLYCEMIC CONTROL IN A TYPE 1 DIABETIC PATIENT ASSOCIATED WITH LACTATION

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Objective: To describe diabetes management during and after delivery of a pregnant type 1 diabetic patient with hyperemesis gravidarum.

Methods: We present the patient’s history, clinical findings, laboratory results, and diabetes management using a continuous subcutaneous insulin infusion (CSII) and a continuous glucose monitoring system (CGMS) during pregnancy, early post-partum period and at six month after delivery.

Case Presentation: A 27-year-old normal weight, hypothyroid pregnant type 1 diabetic patient on control with multiple insulin doses, presented hyperemesis gravidarum at 6 weeks of gestation. At that time, she suffered of recurrent hyperglycaemic and hypoglycaemic episodes, A1C before conception was 6.7% and the thyroid stimulating hormone (TSH) 4.40 uUI/ml. A CSII and CGMS were inserted during a short hospitalization period by specialized personnel to assure an optimal glycemic control. The patient gave birth to a normal child, (weight 2,700 g, height 48 cm, Apgar 9-10.) by caesarean section at the 39 weeks of gestation.

Discussion: As compared to first trimester, in the second and third trimester insulin requirements increased by 32 % and 68 % and glycemic control improved (p < 0.01). A transitory deterioration of glycemic control occurred four days and one month after delivery. Early in this period, recurrent hypoglycaemic episodes happened 10 to 15 minutes after the patient initiated lactation and were associated with rebound hyperglycaemia.

Conclusion: Optimization of glucose control in a type 1 diabetic patient with hyperemesis gravidarum was achieved using a CSII and CGMS. Sudden glucose falls and reoccurring hypoglycaemic episodes after initiation of lactation drove to a deterioration in glycemic control.

Abstract #268

ORAL GLUCOSE TOLERANCE TEST AND HEMOGLOBIN A1C FOR DIAGNOSING IMPAIRED GLUCOSE METABOLISM AMONG A HIGH METABOLIC RISK HISPANIC POPULATION

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Objective: The 75-g oral glucose tolerance test (OGTT) and the hemoglobin A1c (HbA1c) are diagnostic tests useful for identifying type 2 diabetes mellitus (T2DM) and pre-diabetes individuals. Controversies regarding their low level of concordance, its variability among different racial/ethnic groups and the cardiometabolic risk profile of subjects categorized differently by HbA1c and OGTT have been under investigation.

Methods: Data from the individuals recruited by the San Juan Obese Adult Longitudinal Study (SOALS), available for 1,377 subjects without known diabetes and aging 40-65 years, was analyzed. After inclusion and exclusion criteria were met, medical history, anthropometric measurements and blood samples results were obtained. Insulin resistance and β-cell function parameters were assessed. Pre-diabetes and diabetes were defined according to the Standards of Medical Care in Diabetes using the OGTT
and HbA1c. Categories for impaired glucose metabolism were compared with respect to cardiometabolic profile, insulin resistance and insulin secretion.

**Results:** From the 1,377 Hispanic subjects (27.8% men, mean age 50.5±6.7, mean BMI 33.4±6.3), 32.3% were diagnosed with pre-diabetes by OGTT and 53.4% by HbA1c; while 8.1% were diagnosed with T2DM by OGTT and 6.8% by HbA1c. The overall concordance among the two tests was 54.7%. A worse cardiometabolic risk profile was seen within groups identified as pre-diabetes and diabetes by HgbA1c and OGTT, when compared with individuals with normal glucose tolerance tests. In the pre-diabetes groups, those diagnosed by OGTT but not by HbA1c, had significantly higher systolic blood pressure and higher HOMA values. In the diabetes group, those diagnosed by OGTT had lower BMI and smaller waist circumference, than those subjects diagnosed by HbA1c only; this group also presented with significantly lower insulinogetic and disposition indexes. Logistic regression analyses suggested that subjects diagnosed with impaired glucose regulation by OGTT, rather than by HbA1c, had greater probability to have insulin resistance and impaired insulin secretion.

**Discussion:** In this study, low concordance was seen between HbA1c and OGTT. The HbA1c identified a higher portion as pre-diabetic individuals but a smaller number of T2DM subjects than OGTT. This discrepancy might be explained, among other factors, by the Hispanic ethnicity of the cohort.

**Conclusion:** Subjects identified by OGTT appear to be somewhat metabolically different from those classified by HgbA1c, with more chances to have insulin resistance and pancreatic β cell function impairment.

**Abstract #269**

**ACUTE ABDOMEN WITH KETOSIS/ KETOACIDOSIS IN OLDER CAUCASIAN ADULTS: ALWAYS LOOK BEYOND DIABETES**

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**Case Presentation:** Older people with diabetes other than type 1 or LADA classically present with Hyperosmolar Non-Ketotic State in response to stress or infection. Some can present with ketosis of frank ketoacidosis. Ketone body formation in this group is secondary to the precipitant rather than a primary diagnosis. In a predominantly Caucasian population as in Scotland, an underlying precipitant should not be missed. Most patients are screened for infections & cardiovascular disease but mesenteric ischaemia & pancreatic disease can present in a similar way. We present a series of four cases with interesting precipitants.

**Cases:**

4 female patients presented to the medical admission unit with hyperglycaemia & ketosis/ ketoacidosis. Two of them were above 75 years of age & the other two were about 60 of age .They either had no previous history of diabetes or history of type 2 diabetes. They were all treated as per local protocol for DKA or started on VRII. Hyperglycaemia & ketosis resolved very quickly but they all remained unwell. The older two were found to have mesenteric ischaemia but they were managed conservatively because of comorbidities. The other two patients had history of alcoholism & intercurrent infections which delayed investigations. One of them was found to have multiple collections in the abdomen & was treated with potent IV antibiotics. The other had a pancreatic abscess which eroded the intestinal wall & she required permanent colostomy.

**Discussion:** Ketoacidosis can present with abdominal symptoms and signs often associated with raised inflammatory markers. On the other hand, acute abdomen related to an occult serious pathology can precipitate ketosis/ ketoacidosis and this may get overlooked with significant morbidity and mortality. Mesenteric ischaemia can present with subtle symptoms and signs. Pancreatic disease can present in a similar fashion. History of alcohol excess may delay the diagnosis further. Mesenteric ischaemia has not been commonly reported in this context. There is only were few cases of such presentation reported in children as a complication of DKA . The largest mortality review case series over a period of 16 years revealed only one case of bowel infarction.

The main clue in our cases was an improvement in ketosis sooner than expected with minimal improvement in patients’ symptoms or general condition.

**Conclusion:** Careful history, examination & monitoring of ketone levels and other biochemical & inflammatory parameters are vital in identifying unusual cases presenting with ketosis/ ketoacidosis. Early diagnosis of these patients is vital to reduce the risks of complications and death.
Abstract #270

MUCORMYCOSIS PANSINUSITIS IN A NEWLY DIAGNOSED DIABETIC

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Objective: Mucormycosis is a fungal infection described in immunosuppressed patients with no established relationship to occupational exposure. We present a case of patient who presented with mucormycosis pansinusitis after an occupational exposure and was to have newly diagnosed uncontrolled diabetes.

Case Presentation: 53 year-old man with medical history of mild-intermittent asthma presented with nasal congestion for one month and left eye pain, swelling and diplopia for 3 days. Exam significant for a proptotic left eye with superior lid erythema. Fundoscopic exam unremarkable. Left nasal cavity contained mucopurulent discharge. Labs significant for blood sugar 450mg/dL with a hemoglobin A1C of 12.2%. CT revealed aggressive pan-sinusitis. Vancomycin, piperacillin/tazobactam and posaconazole were administered in addition to intravenous dexamethasone and long acting insulin. Initial functional endoscopic sinus surgery (FEES) with extensive debridement was performed with cultures growing MRSA in addition to insulin. A second FEES was performed with cultures growing MRSA in addition to mucormycosis, thus amphotericin was administered. Patient reported after Hurricane Sandy working on water damaged houses pulling out rotten wood and wet plaster board.

Discussion: Mucormycosis is an angioinvasive infection caused by saprophytic fungi of the Mucorales order found in decaying organic matter and/or construction activity involving many electrolyte losses, which are managed with replacement therapy. We present a case of a patient with a GS who arrived in a DKA crisis. The potential mismanagement of such a condition can lead to severe electrolyte deficiencies, severe paralysis and death.

Conclusion: Mucormycosis should be suspected in patients with uncontrolled diabetes and prolonged exposure to decaying organic matter and/or construction activity presenting with severe sino-orbital infection not responding to antibiotics. Further investigation is needed to clarify the association between mucormycosis and professional/environmental exposure to spores of the fungus.

Abstract #271

A RARE CASE OF GITLEMANS SYNDROME COMPLICATED BY DKA

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Objective: Gitlemans syndrome (GS), is a rare genetic disorder present in less than 1% of the population. It involves many electrolyte losses, which are managed with replacement therapy. We present a case of a patient with a GS who arrived in a DKA crisis. The potential mismanagement of such a condition can lead to severe electrolyte deficiencies, severe paralysis and death.

Case Presentation: A 23 year old male, diagnosed with Gitlemans, presents with complaint of thirst, lower extremity tingling, polyuria and 7 lbs weight loss over 3 months. He was tachycardic and chemistry showed serum glucose of 705(mg/dL), corrected anion gap of 18(mEq/dL), Na of 125(mEq/dl), Mg of 1.3(mEq/dL) and K of 2.8(mEq/dL) with no EKG changes. Initially managed with IV fluids, IV potassium and IV magnesium in attempt to try to increase his K prior to starting the insulin drip. His K failed to show an appropriate increase and copious amounts of Mg and K were given in an effort to start an insulin drip to correct his acidosis. Finally upon correction (K of 3.4mEq/dl), an insulin drip was started with continued aggressive replacement of electrolytes. He was managed via a modified DKA protocol and eventually bridged with lantus.

Discussion: GS involves the inactivation of the thiazide-sensitive sodium-chloride co-transporter (NCCT) in the distal convoluted tubule leading to hypokalemia, hypomagnesaemia, hypocalcaemia, metabolic alkalosis and hypereninemic hyperaldosteronism. DKA is characterized by hyperglycemia, ketonemia, metabolic acidosis and hypokalemia. GS patients are chronically hypokalemic and administering insulin worsens the condition by driving K intracellularly. Severe hypokalemia and hypomagnesemia lead to paralysis, respiratory failure and fatal cardiac arrhythmias. Finally, with the chronic loss of H+ in GS, the acidosis associated with DKA is
masked by the chronic metabolic alkalosis. This can prove fatal as initial treatment modalities aimed at severe DKA are ignored by the relatively mild acidosis. It is speculated that there is abnormal glucose metabolism and insulin secretion among patients with GS. A recent study looked at patients with GS compared to healthy controls in an oral glucose challenge test. GS patients showed a delay in their insulin secretion peak, abnormalities in insulin sensitivity, impaired fasting glucose and glucose tolerance. Thus, we conclude that patients with GS are more likely to develop Diabetes and DKA as a result of these impairments and that the cause of these abnormalities maybe secondary to hypokalemia and hypomagnesaemia.

**Conclusion:** We highlight the management of patients with GS in DKA and support a link between GS and the development of diabetes.

**Abstract #272**

**ZERO INPATIENT MORTALITY OF HYPEROSMOLAR HYPERGLYCEMIC STATE IN MEMPHIS VETERAN AFFAIRS HOSPITAL BETWEEN 2000 AND 2010**

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**Objective:** Hyperosmolar hyperglycemic state (HHS) is one of the two most serious acute complications of diabetes along with diabetic ketoacidosis (DKA). Mortality of HHS has been declining since 1980’s reportedly to 5-20% and is often due to the underlying illness and/or comorbidity. We conducted a retrospective chart review to investigate the mortality rate of HHS on patients admitted in Memphis Veteran Affairs hospital Intensive Care Unit between 2000 and 2010.

**Methods:** ICU admissions which met the following criteria were selected:
1. Diabetes Mellitus
2. Blood glucose >=600 mg/dL
3. Calculated osmolality (2*Na + Glucose/18 + BUN/2.8) >= 320 mosmol/kg
4. Maintained full resuscitation code during their hospitalization

Demographics, basic metabolic profiles, vital signs, mental status, comorbidities, length of hospital stay, body mass index, glycosylated hemoglobin, home medications and outcome were studied.

**Results:** Thirty-six hospitalizations of twenty-one patients met the above definition. Two homeless patients contributed 12 recurrent hospitalizations. The precipitating factors include medication non-compliance due to lack of financial or social support, psychiatric disorder or seizure, infection, gastroenteropathy, substance abuse, pancreatitis, uremia. Among the twenty-one patients, one patient (4.7%) was female, and nineteen patients (90.47%) were African American. Thirty-two cases (88.89%) were using insulin prior to admission. Average age of patients was 52.97+5.32 years old. Average serum glucose level was 1088.81+360.49 mg/dL and average osmolality was 346.64+23.62 mosmol/kg. Average glycosylated hemoglobin level was 12.46+3.05%. Average hospital stay was 7.06+5.39 days. No inpatient mortality occurred during their stay.

Twenty-one cases (58%) had combined DKA and HHS. Glucose level and the osmolality were compared, and no significant difference was noted with P value 0.85 and 0.44 respectively. Bicarbonate (7.16+2.51 vs. 20.67+6.44mmol/L, P value 4.46E-10), ketone (20>moderate vs. 2 > moderate, p value 8.73E-08) and anion gap (35.84+5.97 vs. 19.14+7.45, P value 1.15E-08) were significantly different between the Combined group and HHS only group.

**Discussion:** Memphis VA hospital has Implemented HHS treating protocol since 1995. It is encouraging to see that there was no mortality occurred during the period of 2000 and 2010. However there is limited data on female and Caucasian in this study.

**Conclusion:** HHS mortality continues to fall and could be avoided with aggressive intervention. Clinically HHS is underdiagnosed due to the coexistence of DKA. Social support to gain medicine access will prevent recurrent hospitalizations.

**Abstract #273**

**POORLY CONTROLLED DIABETES MELLITUS AS AN EARLY FEATURE OF PANCREATIC CANCER**

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**Objective:** Pancreatic cancer is an aggressive malignancy often presenting in an advanced stage that is amenable only to palliative measures. Diabetes mellitus (DM) is associated with this cancer but the link is poorly understood. Here we describe a patient with worsening hyperglycemia 5-6 months preceding the diagnosis of pancreatic cancer.

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

**Case Presentation:** A 58 year old man was diagnosed with DM that was well managed with lifestyle modification and metformin for several years. Suddenly he developed progressive polyuria and polydipsia due to worsening hyperglycemia that was stabilized only with escalating doses of insulin. He had intensified his diet losing 35
pounds over a few months. Five months after starting insulin abdominal pain led to imaging revealing a hypodense pancreatic mass with mixed cystic and solid components with arterial encasement and splenic vein thrombosis.

**Discussion:** Pancreatic cancer is known to be associated with new-onset diabetes mellitus. Epidemiologic studies state that about one third of pancreatic cancer patients have new onset diabetes (defined as DM diagnosed 24 months prior to cancer diagnosis) in the preclinical or early stages of cancer evolution. This association is deemed to be causal by studies that reported resolution of DM in >50% following resection of cancer. Intuitively prevalence of pancreatic CA in new onset DM is <1%1. Various clinical features that have been associated with pancreatic CA related DM include, age at onset >65, female gender, active smoking, negative family history of DM, positive family history of cancer, lower BMI and greater weight loss.2-4 It is important to note that our patient had stable DM for several years until 5-6 months prior to cancer diagnosis. Recent insulin therapy, increasing insulin requirements and worsening hyperglycemia have also been described as early features of pancreatic CA.5 Proposed mechanisms include cancer related insulin resistance, beta cell dysfunction and insulin receptor signaling defects. Despite this well known association no consensus is currently available on the approach to considering pancreatic CA in newly diagnosed or worsening DM.

**Conclusion:** We report a patient with difficult to manage DM a few months preceding the diagnosis of pancreatic CA. Prospective studies are needed to elucidate the differentiating characteristics of pancreatic CA related DM. Further research is required before any screening recommendations can be made for pancreatic CA in newly-onset/worsening DM.

**Abstract #274**

**METABOLIC MEMORY AND DIABETIC COMPLICATIONS: GLYCAEMIC CONTROL AND DIABETES NEPHROPATHY**

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**Objective:** Diabetic nephropathy (DN) is the one of the most serious microvascular diabetic complications which leading cause of chronic kidney disease and kidney replacement therapy. Poor understanding about aetiology of diabetic complications causes prevention and control strategies of diabetic complications are not efficient enough. Metabolic memory and epigenetic hypothesis in aetiology of diabetic complications coming of long term deleterious effects of mediator factors linked to long term hyperglycaemia.

The aim of this study was to investigate the role of glycaemic control and diabetic risk factors on development of diabetic nephropathy in type 2 diabetic patients.

**Methods:** A historical cohort study was designed by recruiting 1228 type 2 diabetic patients from a diabetes referral clinic over a six-month period (from July to December, 2012). Diabetes risk factors, complications, laboratory results have been recorded.

**Results:** Of the 1228 diabetic patients (54% women, mean age 58.48±9.94 years), 1137 patients had clinical and laboratory available data for nephropathy analyses. The prevalence of diabetes nephropathy was 9.6%. Among patients with nephropathy, the prevalence of retinopathy and hypertension was 53.3%, and 90.7%, respectively. Diabetic nephropathy was about 1.8 times more common among men than women (64.2% vs. 44.8%) (OR=2.20, 95% CI: 1.46, 3.32). Patients with nephropathy were tended to be older, with a longer duration of diabetes and higher HbA1c. Although patients with DN had higher HbA1c levels, we observed no association between DN and poor glycaemic control (HbA1c ≥7) (p=0.13).

Related to micro-albuminuria, as a clinical symptom of early stages of DN, there were significant differences in HbA1c levels (p = 0.009, F= 7.76) and we did observe an increasing HbA1c levels in terms of albuminuria severity. In a multiple logistic regression model after adjusting for age and sex; hypertension and obesity were independent predictors of nephropathy. In this model, there were not significant relationships between DN and glycemic control, duration of diabetes, age and age at onset of diabetes, dyslipidemia, smoking and family history of diabetes.

**Conclusion:** In conclusion based on our findings, glycaemic control is not associated with DN development. It is verifying the metabolic memory effect of hyperglycaemia in early stage of etiological process that leads to type 2 diabetes and its complications.
Abstract #275

FREQUENCY OF NON-ALCOHOLIC FATTY LIVER DISEASE AMONG PATIENTS WITH TYPE 2 DIABETES MELLITUS AND ITS RELATIONSHIP TO GLYCAEMIC CONTROL

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Objective: To determine frequency of NAFLD and assess its impact on the glycaemic control of patients with T2DM attending the Diabetes Clinic of the University College Hospital, Ibadan.

Methods: A total of 147 subjects living with T2DM were recruited between September and October, 2012. Participants were interviewed with a questionnaire containing information about history and risk factors for NAFLD. Anthropometric measurements were taken and blood samples collected for: FBG, HbA1C, fasting lipid profile, ALT, AST, ALP, GGT, albumin and creatinine. Hepatic ultrasonography was done by an experienced sonologist to diagnose NAFLD. Appropriate univariate and multivariate analysis were performed to determine frequency of NAFLD among subjects and compare glycaemic control between those with and without NAFLD.

Results: Among 139 subjects who underwent ultrasonography, 64 (or 46%) had fatty liver with higher female preponderance. Type 2 DM subjects with NAFLD had significantly higher HbA1C compared to those without NAFLD (mean SD=7.7 (1.9) versus 7.0 (1.9) p=0.033). Waist circumference, BMI, HbA1C, ALP, albumin and creatinine were independently associated with occurrence of NAFLD. Subjects with high waist circumference were 5 times more likely than those with normal to have NAFLD. The odds of NAFLD were higher with increasing ALP, albumin and HbA1C (1.04, 3.44 and 1.4 respectively).

Discussion: The relationship between obesity and type 2 diabetes has led to an increase in insulin resistance and insulin requirements for effective treatment. Severe or clinical insulin resistance occurs when a patient requires greater than a total daily dose of 200 units of insulin for greater than 2 days. Doses of more than 1 ml of insulin are known to have an attenuated response making U500 insulin an alternative treatment. U500 insulin offers an effective form of treatment in patients with severe insulin resistance due to administration of large amounts of insulin in a lesser volume and/or fewer injections. Compared with U100 insulin, U500 regular insulin has both a bolus effect with similar onset and slightly delayed peak effect, and a basal effect with duration of action between 6 to 12 hours. Studies have proven the efficacy of U500 insulin in attaining glycemic control; however, with the consequence of weight gain. This increase in weight has the potential to further increase insulin resistance, initiating a cycle of increased weight leading to increased insulin resistance, leading to increased insulin requirements, leading to increased weight. Although, clinical studies have shown

Abstract #276

CLINICAL EXPERIENCE WITH THE USE OF U500 INSULIN IN AN OBESE, SEVERE INSULIN-RESISTANT TYPE 2 PATIENT.

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Case Presentation: TE is a 50 year-old African-American female presenting to the ED with abdominal pain, chest pain and back pain. Her past medical history is significant for obesity, uncontrolled type 2 diabetes, hypertension, dyslipidemia, and pain disorder. Her diabetic regimen on presentation to the ED consisted of insulin levemir 120 units at bedtime and insulin aspart 35 units before meals. Abnormal laboratory values on admission included hemoglobin A1c 9.9% and random blood glucose 366 mg/dL. Upon admission to the hospital, the patient was switched from insulin levemir/insulin aspart to U500 regular insulin 25 units subcutaneously with breakfast, 20 units with lunch and 15 units at dinner. Fasting blood glucose for the next two consecutive mornings were recorded as 102 mg/dL and 123 mg/dL.
that weight gain is associated with titration in dose and stabilizes within a year.

**Conclusion:** After three months of treatment with U500 insulin, TE experienced a decrease in A1c by 0.8% with an increase in insulin dose to 30 units subcutaneously before breakfast, 25 units with lunch and 20 units with dinner. Due to the pharmacodynamics of U500 insulin, doses were adjusted based on weekly trends in blood glucose rather than levels with each dose. The patient did experience a 2 kg weight gain during this period of time, and an increase in the number of non-severe hypoglycemic episodes. The patient received counseling on diet, exercise and treatment of hypoglycemia.

**Abstract #277**

**CLINICAL OUTCOMES OF SLEEVE GASTRECTOMY IN VETERANS WITH TYPE 2 DIABETES**

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**Objective:** The link between obesity and type 2 diabetes is clearly established with weight loss resulting in improvement in insulin sensitivity and glycemic control. Laparoscopic sleeve gastrectomy involves the removal of the greater curvature of the stomach, and is now a common low-morbidity surgical technique for weight loss. Previous cohort studies have shown improvement in obesity in patients undergoing sleeve gastrectomy. However, there have been no studies comparing long term diabetes outcomes in patients undergoing surgical intervention as compared to controls who are on nonsurgical diabetes care.

Research question: To compare long term diabetes outcomes in patients undergoing sleeve gastrectomy as compared to controls who undergo nonsurgical diabetes care.

**Methods:** We reviewed medical records of veterans between 18 and 80 years of age with type 2 diabetes undergoing sleeve gastrectomy at a VA medical center in a major metropolitan area. Primary study outcomes included measures of diabetes control including HbA1c and BMI. Secondary outcomes such as total and LDL cholesterol, hospitalizations and mortality were also assessed. Data from surgery patients were compared to data from diabetic controls that did not undergo surgery using descriptive analyses, t-tests, and repeated measures ANOVA.

**Results:** Data from charts of 30 surgery patients and 23 controls were analyzed from 2010 to 2013. Most of the subjects enrolled were males (96%) with an average age of 57 years (range 29-80 years). The median BMI at baseline was 41 (range 36-60) kg/m\(^2\) and median HbA1c was 7.3. There was a significant improvement in BMI and HbA1c in surgery patients over one year follow up; improvements were sustained through the end of two years after surgery. Mean BMI decreased from 41 to 34 over two years (P<0.001) and mean HbA1c decreased from 7.25 to 5.98 (P<0.001). Similar outcomes were not seen in controls during the study period. Differences in these outcomes between surgery patients and controls were significant over short term and long term follow up (P<0.001). No changes were seen in total cholesterol or LDL cholesterol for surgery patients. However, it was noted that the changes in outcomes plateau after the first year of surgery.

**Discussion:** It is interesting to note that sleeve gastrectomy may offer better diabetes control and improved outcomes compared to patients who follow medical care only. However, the improvement in outcomes in surgery patients may not be a permanent solution for diabetes outcomes.

**Conclusion:** Sleeve gastrectomy is effective in improving diabetes outcomes in veterans as compared to those receiving nonsurgical diabetes care.

**Abstract #278**

**INITIATING MORE THAN ONE V-GO® IN PATIENTS WITH TYPE 2 DIABETES**

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**Objective:** V-Go® is a disposable 24-hour device that delivers a continuous basal rate of insulin and provides on-demand bolus dosing. Patients who have long-standing diabetes and receive high insulin doses are often the most complicated patients to treat when A1C’s remain elevated. More than one V-Go is sometimes initiated in these patients due to high baseline insulin doses. The purpose of this analysis is to report on changes in insulin dose and A1C in patients (pts) initiating more than one V-Go.

**Methods:** SIMPLE is an ongoing prospective, open-label, multicenter study being conducted in pts with type 2 diabetes previously treated with any of the following: oral antidiabetic medications alone (OADs); OADs + incretins; intermediate or long-acting insulin (LAI) ± OADs; premixed insulin (PM) ± OADs; multiple daily insulin injections (MDI) ± OADs. After switching to V-Go, pts
POORLY CONTROLLED DIABETES IN PATIENTS UNDERGOING ELECTIVE SURGERY: IMPROVING HBA1C TESTING IN THE PRE-OPERATIVE PERIOD

**Objective:** Previous studies have demonstrated poor clinical outcomes in patients with poorly controlled diabetes (HbA1c >8%) undergoing surgery. We developed a strategy to increase identification of individuals with HbA1c >8% undergoing elective surgery and to increase their access to diabetes specialist services before the day of surgery.

**Methods:** A diabetes management team worked collaboratively with anesthesiologists, surgeons, and pre-operative nurse practitioners to develop an algorithm to ensure that HbA1c measurements were obtained in all patients with diabetes on the day of their preoperative evaluation. Those with HbA1c >8% were referred to a diabetes specialist on an urgent basis. Historic data were used as control group to evaluate the effectiveness of this effort.

**Results:** From January 1, 2011 to December 31, 2012 (control group), HbA1c testing was recorded in 854/2335 (37%) of the patients with diabetes. After implementation of the algorithm in February 2013 to October 1 2013, HbA1c testing occurred in 717 out of 774 (93%) patients with diabetes (p<0.0001). Out of the 717 individuals with HbA1c testing, 172 (24%) were considered high risk with HbA1c >8% and 156 received pre-operative endocrine consultation. Within the high risk group that received the pre-operative consultation 80% (124/154) achieved goal blood glucose (<200mg/dl) on the morning of surgery.

**Discussion:** The development of a diabetes management team in the pre-operative setting resulted in an increase in the identification of individuals with poorly controlled diabetes undergoing elective surgery.

**Conclusion:** A strategy to improve HbA1c testing resulted in substantial improvements in providing access to care for individuals with poorly diabetes control before elective surgery. Further studies are needed to evaluate whether this strategy results in improved clinical outcomes.

**Abstract #279**

**INTENTIONAL SULFONYLUREA OVERDOSE: OCTREOTIDE’S ROLE IN MANAGING THE PROPERTIES OF SOMATOSTATIN**

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**Objective:** Sulfonylurea agents are a common form of pharmacotherapy utilized in the treatment of type 2 diabetes. Sulfonamide antibacterial agents were first noted to exert hypoglycemic effects in the 1940s [1]. Excess sulfonylureas cause severe hypoglycemia, with onset delayed up to 12 hours, and prolonged effect up to several days post-exposure. Review of national poison center data by Doughtery and Klein-Schwartz revealed 14 sulfonylurea-associated fatalities reported between 1992 and 1996 in adults between the ages of 18 to 79 years. Octreotide is a long-acting synthetic analog of somatostatin that can be utilized to counteract the insulin-releasing properties of sulfonylureas [3]. We report a case involving a patient who intentionally overdosed on his home meds which included a sulfonylurea, and the use of octreotide to address his persistent, difficult to control hypoglycemia.

**Case Presentation:** 61-year-old male with 10 year history of type 2 diabetes, laryngeal carcinoma post chemoradiation, and major depressive disorder, presented to the JAHVA ER after ingesting approximately 20 tablets of various home meds, including glipizide, in an
intentional overdose. Blood glucose on arrival to ER was 24 mg/dL, BP 52/29 mm Hg. Initially, patient bolused with 2 liters normal saline, 2 amps 50% dextrose IV, and given 260 mg charcoal via his feeding tube. Toxicology screen was positive for cannabinoids. Patient transferred to unit for further management. Three days after presentation to ER, first dose of subcutaneous octreotide 50 mcg given due to persistent hypoglycemia. Dextrose 10% infusion at 50 mL/hr also started. His glucose rose from 60 mg/dL 1 hour after injection to 119 mg/dL 1 hour after injection. His sugars ranged from 180-230 mg/dL, but began to drop again 12 hours after octreotide injection. Therefore, another 50 mcg dose of octreotide was administered, and repeated every 6 hours for 24 hours. Once sugars trended into 200-300 mg/dL ranges, dextrose fluids were discontinued and euglycemia maintained through oral/feeding tube intake alone. Patient stabilized and transferred to in-hospital psychiatric ward for further management without residual effects.

Discussion: Sulfonylureas are drugs which can also lead to severe, persistent hypoglycemia especially in those consuming excess amounts to achieve self-harm. When given subcutaneously, octreotide is quickly and completely absorbed, reaching 100% bioavailability in as little as 30 minutes [4]. Adverse effects related to short-term use of octreotide are minimal and may include gastrointestinal upset and diarrhea [3,5].

Conclusion: Thus Octreotide could be used in managing intentional sulfonylurea overdose.

Abstract #281

SUDOSCAN: AN ALTERNATIVE TOOL IN THE UNDERSTANDING OF THE MICROVASCULAR COMPLICATIONS OF DIABETES

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Objective: Microvascular complications (MVC) of diabetes mellitus (DM), including peripheral neuropathy (DPN), nephropathy (DKD) and retinopathy lead to significant morbidity; yet few non-invasive, practical, and reliable tools are available for early detection, prevention, or follow-up. We report the findings of 3 studies using SUDOSCAN® and how these may impact the management of DM by clinicians. SUDOSCAN measures sweat gland function via reverse iontophoresis & chronoamperometry; results are reported as electrochemical skin conductances (ESC) and reflex the function of small and autonomic peripheral nerves.

Methods: 3 investigators at 3 American academic centers completed SUDOSCAN tests on healthy controls (HC), patients with type 1 (T1D) or 2 DM (T2D), or patients with suspected neuropathy (SN). Results were adjusted for covariates in each study individually.

Results: Among 83 T1D and T2D patients and 210 HC, foot ESC scores had a sensitivity of 78% and a specificity of 92% to detect DPN defined by the Toronto convention.

DM patients with DPN had significantly worse ESC of both feet and hands than patients without DPN (56.3±3 vs 75.9±5.5, p<0.005 for feet, and 51.9±2.4 vs 67.5±4.3, p<0.005 for hands). DM patients with painful DPN had significantly worse feet ESC than patients with non-painful DPN (52.8±3.6 vs 68±6.6, p<0.05).

Among 37 patients with SN, 15 with DM, neuropathy was confirmed in 30 using Utah Early Neuropathy Score, while SUDOSCAN had a diagnostic performance similar to intraepidermal nerve fiber density and quantitative sudomotor axon reflex testing (area under the curve 0.73, 0.80, and 0.77 respectively). Feet and hand ESC in patients with SN correlated with symptoms on the Michigan Neuropathy Screening Instrument (-0.420, 0<0.015 and -0.469, p<0.006 respectively).

In African American (AA) T2D patients with minimal DKD, there was a positive association between ESC and estimated glomerular filtration rate (eGFR) (parameter estimate 3.38, standard error 1.2; p=5.2E-3). These results are being investigated further in Caucasian and AA DM patients with eGFR<60ml/min/1.73 m2.

Both HC and T2D AA have lower hands and feet ESC than Caucasians (p<0.0001).

Discussion: ESC correlated closely with the MVC of DPN and DKD, and has proven utility in Caucasian and AA populations.

Conclusion: SUDOSCAN is a 3-minute painless and reproducible test that may allow every clinician caring for DM patients to objectively detect DPN and DKD, select at risk patients for aggressive therapeutic intervention, and easily follow the patients’ clinical progress. Further studies are needed to assess SUDOSCAN’s ability to measure a patient’s response to intervention for DPN and to detect MVC in pre-diabetic conditions.
Abstract #282

IMPLEMENTATION OF A CONTINUOUS SUBCUTANEOUS INSULIN INFUSION PROTOCOL IN AN INPATIENT SETTING AND THE EFFECTS ON HYPOGLYCEMIC EVENTS

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NSLIJHS

Objective: To assess the rates of hypoglycemia in persons with Diabetes Mellitus (DM) in an inpatient setting 6 months pre and post implementation of a continuous subcutaneous insulin infusion (CSII) protocol.

Methods: In this quality improvement project, access to records of patients with an “insulin pump” order within the electronic medical record from 9/2012-9/2013 was provided by the analytic department. By utilizing the electronic medical record, a review of the bedside capillary blood glucose (CBG) levels was performed for 120 patients, ages 18-75, admitted to the hospital with a continuous subcutaneous insulin infusion 6 months before and 6 months after the implementation of a CSII. Patients were subsequently divided into two groups, pre and post intervention to further assess the rates of hypoglycemia, capillary blood glucose <70 mg/dL, in both groups.

Results: Data analysis revealed that 49.2% (30/61) of patients in the pre-intervention period had one or more hypoglycemic event, and 39.740% (23/58) of patients in the post-intervention group had one or more event, however, this difference was not statistically significant (chi-square test). Interestingly, of the 30 patients in the pre-intervention group who had at least one hypoglycemic event, 56.7% (17) had a recurrent event, whereas, of the 23 patients in the post-intervention period who had at least one hypoglycemic event, 52.2% (12) had a recurrent event.

Discussion: Guidelines have been proposed for the use of CSII in the inpatient setting suggesting that a standardized CSII policy should be used. At NSUH we implemented such a policy and provided education to nurses, mid-level providers, and physicians. In addition, all patients are required to have a certified diabetes educator and endocrinology consult to evaluate patient’s knowledge of their pump as well as the appropriateness of their settings. Despite these efforts hospitalized patients often have conditions that can predispose them to hypoglycemia such as infection, reduced enteral nutrition or worsening renal function.

Conclusion: Implementing a continuous subcutaneous insulin infusion protocol not only standardizes delivery of care being provided to a sensitive patient population, but may also improve the care by limiting recurrent episodes of hypoglycemia.

Abstract #283

DIABETIC KETOACIDOSIS: CHARACTERISTICS AND OUTCOMES IN AN URBAN AFRICAN AMERICAN POPULATION.

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Objective: To study the clinical, biochemical characteristics and outcomes of African American (AA) patients admitted to our institution for management of diabetic ketoacidosis (DKA).

Methods: A retrospective study was conducted on patients who were admitted with hyperglycemic crisis to our institution from July 2012 through June 2013. We analyzed 130 charts with a final discharge diagnosis of hyperglycemic crisis (250.12, 250.13) and included only AA (self reported) patients who satisfied all of the following criteria for DKA: serum glucose >250mg/dl, serum bicarbonate <18mmol/l, arterial pH <7.30 and serum ketones >/= 2 fold above normal. Both type 1 and 2 diabetes mellitus (DM) patients were included in the study. Patients with hyperglycemic hyperosmolar state, mixed acid-base disorders and incomplete lab data were excluded. Results: Thirty three patients met our criteria with 42% females, 54% had type 1 DM. Altered mental status was evident in 24% of cases. The mean glucose was 659 ± 222 mg/dl, sodium was 132±5 mEq/dl, potassium was 5.5±0.89 mEq/dl, bicarbonate was 10±4 mEq/dl, anion gap of 25±6, pH was 7.14± 0.09, serum osmolality was 301±15 and serum ketones was 84± 38mg/dl. Seventy nine percent were admitted with moderate DKA based on arterial pH of 7.00 to < 7.24 on admission (based on American Diabetes Association DKA classification). Mean Glycated hemoglobin was 11.9% Seventy five percent of cases were secondary to non-compliance with medications. Almost 91% of the patients were admitted to medical intensive care (MICU) unit for management. A standardized DKA treatment protocol was used in all 100% cases. About 48% of patients were discharged within 3 days and about 15% stayed for longer than 7 days due to other co-morbidities. Total in-hospital mortality was 0%.

Discussion: DKA is one of the most common acute complication of DM that is associated with increased morbidity, mortality and healthcare expenditure. Mortality rates between 2-5% have been reported. Prompt diagnosis, early initiation of therapy using a standardized treatment
protocol and diligent search for the precipitating factors lead to successful outcomes.

**Conclusion:** DKA was a common cause for admission to our MICU with 0% in-hospital mortality. There was no difference in clinical, biochemical characteristics or outcomes observed between type 1 and 2 DM or between the genders. Most of our patients were stabilized and discharged within 3 days, compared to a national average of 2.6 - 5.5 days based on the presence or absence of co-morbid or major co-morbid conditions. Easy access to physicians/ endocrinologists and regular follow up with serial reminders on medication compliance might help reduce incidence of DKA.

**Abstract #284**

**U-500 INSULIN: POSSIBLE TREATMENT STRATEGY FOR PATIENTS WITH ANTI-INSULIN ANTIBODY MEDIATED INSULIN RESISTANCE**

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**Objective:** Severe insulin resistance secondary to anti-insulin antibodies is well documented. The prevalence of this phenomenon was higher with older animal insulin preparations, and with the advent of recombinant and semisynthetic human insulin preparations this is a rare occurrence. We present a case report of a patient with severe insulin resistance and positive anti-insulin antibody treated with U-500 insulin.

**Case Presentation:** 70 years old male with type 2 diabetes (for 13 years), hypertension, hypothyroidism, chronic kidney disease, congestive heart failure, and morbid obesity (BMI 53) was evaluated in the endocrine clinic for uncontrolled diabetes complicated by nephropathy and neuropathy. His most recent HbA1C was 9.3% and he had been on insulin for 3 years. His insulin requirement had been progressively increasing, and at the time of his evaluation he was on a total insulin dose of 604 U/day (140 U of glargine BID and 108 U of aspart with meals). In spite of this very high total daily insulin dose, his blood sugars remained elevated (300-400 mg/dL). He was evaluated for Cushing’s syndrome and the presence of insulin autoantibodies. Insulin autoantibody level was 33.9 (normal <0.4 U/ml). Salivary cortisol levels were normal. Insulin auto-antibody was thought to be contributing to his insulin resistance. Because of his elevated creatinine and history of heart failure, metformin and pioglitazone were not considered for treatment. He was started on U-500 insulin, initially 36 U TID premeals and subsequently increased to 50/54/36 U with breakfast/lunch/dinner respectively. His blood sugar levels have improved significantly and currently range from 100-200 mg/dL. The patient has reported improved energy and sense of wellbeing with no episodes of hypoglycemia in the past three months while using U-500 insulin.

**Discussion:** Anecdotal reports describe patients with anti-insulin antibody mediated insulin resistance receiving treatment with steroids, insulin analogues, plasmapheresis and immunosuppressants. There have been few case reports describing the use of U-500 insulin in patients with severe insulin resistance. It allows high doses of insulin to be administered in smaller injection volumes. Studies have shown that use of U-500 insulin decreases the daily insulin dose requirement and improves glycemic control by decreasing the HBA1c by >1%. Possible mechanisms by which glycemia may improve include a longer duration of action, an altered release rate of U-500 insulin from subcutaneous sites or an altered affinity of the insulin receptor for U-500 insulin.

**Conclusion:** Therefore, we demonstrate that U-500 insulin may be considered as an alternative treatment modality for antibody induced insulin resistance.

**Abstract #285**

**THE EFFECT OF PAYOR SOURCE ON ACHIEVING DIABETES METRICS IN AN ENDOCRINOLOGY CLINIC**

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**Objective:** The rate of achieving diabetes management goals of hemoglobin A1c (HbA1c) <7.0%, blood pressure (BP) <140/80 mmHg, and LDL-cholesterol (LDL-C) <100 mg/dL as recommended by the American Diabetes Association (ADA) in clinical practice is suboptimal. The aim of this study was to determine if a payor source could influence meeting of diabetes care goals.

**Methods:** We performed a retrospective chart review of patients with diagnosis of diabetes mellitus that attended endocrinology clinic for 24 months under the care of a single endocrinologist in an academic medical center (n=93). We analyzed HbA1c, systolic BP, LDL-C, body mass index (BMI) and type of anti-diabetic agents used in patients having commercial insurance (n=33), Medicaid (n=13), and Medicare (n=47).

**Results:** Subjects in the Medicare group were older (63.6±12.9 yrs) compared with the commercial and Medicaid groups (50.6±11.6 and 48.3±13.4, respectively) (P<0.05). BMI was similar among all groups with an average
A 51-year-old Caucasian woman programs across the United States about their experience in
residency. After 24 months of continuous clinical care, 50% of the patients in the commercial group, 25% in the Medicaid and 62% in the Medicare group achieved diabetic metrics as recommended by the ADA. Individual goals over the two year in the patients with commercial insurance, Medicaid and Medicare were achieved in 55%, 32%, and 72% for HbA1c, in 80%, 83%, 83% for systolic BP, and in 88%, 42%, 89% for LDL-C, respectively. BMI has not significantly changed in all three patient groups during the treatment. There was no statistically significant difference in age, BMI, insulin use, and incretin mimetic use between patients who achieved and did not achieve combined diabetes targets in either group. Additional evaluations were performed among individuals who only completed 12 months of continuous clinical care and were comparable to those who completed 24 months of continuous clinical care.

Discussion: Patients in the commercial insurance group and Medicare group can achieve substantial improvement in diabetes care metrics while receiving care in subspecialty clinic. We also found that glycemic goals are more difficult to achieve than control of BP or LDL-C.

Conclusion: Other clinical and potentially therapeutic approaches must be used in patients who are not able to meet the ADA performance measures targets.

Abstract #286

THE IMPACT OF TRAINING IN THE DIABETIC MONOFILAMENT EXAMINATION PRIOR TO RESIDENCY

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Objective: Little is known about training of International Medical Graduates (IMGs) in the diabetic foot examination (DFE). We hypothesized that IMGs had less formal training in the DFE and this would translate into less frequent performance of the DFE.

Methods: We surveyed U.S. Medical School Graduates (USMGs) and IMGs in internal medicine residency programs across the United States about their experience in the DFE. Our survey assessed their prior training, current use of monofilament, and barriers to performing the test. All data was collected using a third-party survey tool (www.surveymonkey.com) and analyzed in SPSS (version 17.0) and Microsoft Excel software. We compared groups using chi-squared and student t-tests as appropriate.

Results: A total of 185/298 (62%) internal medicine residents responded to the survey. 108 (58.3%) of them were USMGs (allopathic or osteopathic) while 77 (41.6%) were IMGs. 77.8% of USMGs reported training in the monofilament examination during medical school compared to 44.2% of IMGs (p < .001). Despite training, only 41.1% performed the monofilament test on more than 25% of their patients. No difference was found comparing IMGs to USMGs. Residents reported lack of time (45.4%), unavailability of monofilament (41.6%), and someone else’s job (25.9%) as their main barriers to performing the monofilament examination.

Discussion: IMGs are less likely to have received formal training in performing the monofilament test during medical school than USMGs. However, this did not impact their self-reported usage of this examination. Majority of residents self-reported performing monofilament examination on less than ¼ of their diabetic patients in their continuity clinic.

Conclusion: Residency programs may need to focus training efforts for IMGs early during residency. However, the lack of correlation between prior training and current performance in the monofilament examination suggests that education in this skill alone is insufficient to increase its performance. Other system’s changes, including more availability, reminders, delegation of this task to other members of the health care team, and chart reviews may be needed to improve performance. To our knowledge this is the first study on health care providers regarding their monofilament examination training and usage.

Abstract #287

GLYCEMIC CONTROL IN A PATIENT WITH TYPE 1 DIABETES AND PERITONEAL DIALYSIS

Nadir Khir, MD, Stephen Brietzke, MD

Case Presentation: A 51-year-old Caucasian woman with past medical history of diabetes mellitus type 1, complicated by end-stage renal disease on maintenance automated peritoneal dialysis, admitted to the hospital with increasingly labile glycemia became increasingly frequent over a one-year period, roughly coinciding with a change in her peritoneal dialysate to icodextrin. Her insulin regimen included glargine 10 units each morning and NPH insulin 8 units at the start of peritoneal dialysis exchanges each night. Mealtime insulin boluses were
aspart 1 unit per 10 grams of carbohydrate. Her most recent HbA1c was 7.5%. Physical examination was significant for legally blind and BMI 25. Initial assessment was falsely elevated home blood sugars due to analytical interference of point-of-care testing glucometer by maltose or other metabolites of icodextrin. Initial action was to use a Novastat glucometer, which uses glucose oxidase methodology, increase glargine dose to 14 units each evening, and eliminate the NPH component of her previous “double basal” insulin regime. Initially, the response to regimen adjustments was poor, with extreme morning hyperglycemia associated with nausea. High blood sugars were confirmed by venous blood samples. Patient responded well to treatment with insulin correction with no hypoglycemia. Upon further evaluation of her dialysis routine, patient was found to be using 2.5% dextrose solution with fill volume of 2L in a total of 6 cycles over 9 hours at night time. Last bag fill with icodextrin 1L. At that point, true hyperglycemia, secondary to absorption of dextrose, was assumed. We adjusted her insulin regimen to glargine 14 units each morning plus NPH 6 units and regular insulin 10 units prior to peritoneal dialysis exchange. A fasting glucose of mid-100 mg/dL was attained, without limiting nocturnal hypoglycemia. She was discharged on above regimen and a blood glucose meter/test strip system utilizing glucose oxidase methodology. Subsequent outpatient follow up has documented narrower glycemic excursions and less hypoglycemia.

Discussion: Patients using icodextrin peritoneal dialysis solution may have incorrect blood glucose results when using particular blood glucose monitors or test strips. Absorption of dialysate would cause loss of osmotic gradient and the potential for suboptimal ultrafiltration and clearance. Such patients would benefit from a peritoneal equilibration test.

Conclusion: To avoid interference by maltose or other metabolites of icodextrin, only glucose monitors and test strips that are glucose-specific should be used. True hyperglycemia following peritoneal dialysis exchanges could be an early sign of rapid transporter state.

Abstract #288

USE OF YALE INSULIN INFUSION PROTOCOL IN THE MANAGEMENT OF DIABETIC KETOACIDOSIS

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Objective: There is lack of data on the use of Yale Insulin Infusion Protocol (IIP) in the management of Diabetic Ketoacidosis (DKA). Yale IIP is a validated protocol for managing hyperglycemia. The Yale IIP that we use at our institution targets blood glucose (BG) 100 to 139 mg/dL. In this study we describe the use of this Yale IIP in the management of DKA.

Methods: This retrospective study was performed at a university-based tertiary care hospital. Data was obtained on patients discharged from the hospital between 1/1/2010 and 12/31/2011 with discharge diagnosis of Diabetic Ketoadacidosis (identified with diagnosis code of 250.30 - 250.33 or 250.1 - 250.13) and the presence of the following inclusion criteria: age > 18 years, BG on admission > 500 mg/dL and received intravenous (IV) insulin infusion. Information was obtained on the values of BG and anion gap (AG) over the initial 48 hours.

Results: A total of 58 patients were identified using the above inclusion criteria. In 15/58 patients Yale IIP was started within 4 hours of recording BG > 500 mg/dL, it took more than 4 hours in the remaining patients. On average it took about 8 hours for BG to drop below 250 mg/dL, and BG stayed between 200 mg/dL and 250 mg/dL for next 26 hours, after which the BG was maintained between 150 mg/dL and 200 mg/dL until the end of initial 48 hours of admission. On average it took about 10 hours for anion gap to fall below 12.

Discussion: There is paucity of data on validated protocols for management of DKA and on the use of Yale IIP in the treatment of DKA. It has been shown that adherence to a protocol during management of DKA improves outcomes. In this study we describe the effectiveness of Yale IIP in the management of DKA.

Conclusion: We have now established a protocol for treatment of DKA, which includes the fluid and electrolyte management in addition to Yale IIP. We will subsequently compare the pre-DKA protocol data with the post-DKA protocol data to review the effect of this DKA protocol on outcomes in the management of DKA.

Conclusion: In the absence of a specific DKA management protocol, the Yale IIP is effective in the management of DKA.

Abstract #289

DISCORDANT REGIONAL CHANGES IN ACANTHOSIS NIGRICANS FOLLOWING METFORMIN TREATMENT

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Objective: Acanthosis nigricans (AN) is a common skin condition seen in patients with obesity and hyperglycemia. Though AN is likely a result of insulin resistance and hyperinsulinemia, there are few reports in the literature
regarding its treatment with anti-diabetic medications. We report a patient with AN who had body region-specific responses to metformin therapy.

**Case Presentation:** An obese 35-year-old African American woman was seen in clinic for evaluation of acanthosis nigricans. She had noted skin darkening involving her face, neck, arms and legs starting at age sixteen. She did not have a personal or family history of diabetes, had no known malignancy, and was not taking any medications associated with AN. On physical examination she had a body mass index of 33.7 kg/m², and had hyperpigmented, velvety-appearing skin lesions over the sides of her face, chin, posterior neck, antecubital fossae, axillae, inner thighs, and the extensor surfaces of each elbow. Laboratory evaluation revealed a hemoglobin A1c of 5.9%, fasting blood glucose of 89 mg/dL, and an elevated fasting serum insulin concentration of 28.5 μIU/mL (ref. 2.6-24.9 μIU/mL). An oral glucose tolerance test revealed a normal 2-hour glucose of 101 mg/dL, but a significantly elevated insulin concentration of 374.6 μIU/mL. The patient was started on metformin 1,000 mg daily, which was increased to 2,000 mg daily after 4 months. After two years there was significant improvement in the AN involving her neck, but her axillary involvement worsened. Her serum insulin concentration decreased to 8.1 μIU/mL.

**Discussion:** Acanthosis nigricans is common in patients with obesity and hyperglycemia. AN is felt to be related to underlying insulin resistance, hyperinsulinemia, and subsequent activation of insulin-like growth factor receptors. This receptor stimulation leads to the proliferation of keratinocytes and fibroblasts. Metformin, a biguanide with insulin-sensitizing effects, has been used to treat AN, though its efficacy is not well documented. A decline in circulating insulin concentration, as was seen in our patient, likely plays a significant role in metformin’s mechanism of action for treating AN. Our patient had only regional improvement, rather than widespread improvement of her AN. The reasons for this variation are unclear.

**Conclusion:** We describe a patient that demonstrated regional improvement of AN after two years of therapy with the insulin-sensitizing agent metformin. Further exploration into the mechanism for metformin efficacy in treating AN is needed.

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**Abstract #290**

**MANAGEMENT OF PATIENTS WITH TYPE 1 DIABETES AND SUICIDAL IDEATION TREATED WITH CONTINUOUS SUBCUTANEOUS INSULIN INFUSION (CSII)**

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**Objective:** These cases detail the difficulty of managing patients with Type 1 Diabetes (T1DM) and suicidality. The prevalence of lifetime suicide attempts in the US population is about 5%, and is slightly increased in those with chronic medical conditions.

**Case Presentation:** Case 1: 51 yo woman with uncontrolled T1DM with complications and bipolar I disorder presented with one day of hyperglycemia. On exam, she was afebrile, normotensive, with a labile mood. Labs were consistent with DKA. The patient was initiated on an insulin infusion, and her CSII was removed. Her acidosis resolved, and she was transitioned to SQ insulin and then CSII. Upon transfer to the medical floors, she expressed persistent thoughts of death, and requested DNR status. Psychiatry consultation was obtained to assess her capacity to elect DNR status. During the evaluation, the patient reported three prior suicide attempts, one involving an insulin overdose. Given these safety concerns, the consultant opined that risks outweighed benefits for continued CSII treatment. Her CSII was removed, and she was transitioned to SQ insulin. After further evaluation and management of mood instability, she was discharged on CSII.

Case 2: 20 yo woman with T1DM, depression, ADHD, and polysubstance abuse presented with mental status changes after an intentional ingestion of 15 mg of alprazolam. On exam, vitals were stable and labs were normal, resulting in clearance for admission to the psychiatry unit. The patient denied ongoing suicidal thinking, but a relative remained concerned about continued risk for harm. Initially, the patient was maintained on her CSII with 1:1 supervision but after consultation with endocrinology she was transitioned to SQ insulin. The patient’s mood, insight and judgment improved and CSII was retained upon discharge.

**Discussion:** CSII is an alternative method for managing inpatient T1DM. Proposed contraindications to CSII therapy include patients at risk for suicide. Thus, patients with T1DM and co-morbid mood disorders must be screened for suicidality both on admission and during hospitalization.
Conclusion: These cases illustrate challenges in managing patients with T1DM and past or emergent suicidality. The CSII provides a mechanism by which patients who intend to kill themselves might rapidly effect their plans. Risk stratification at the outset of CSII placement, utilizing standardized evidence-based assessments that do not require mental health expertise, may improve outcomes and safety for this patient population. For inpatients in crisis, multidisciplinary communication and early psychiatric consultation are vital to minimize risk in these patients, and to decide whether to continue CSII therapy upon discharge.

Abstract #291

HYPOTHYROIDISM AND TYPE 2 DIABETES

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Objective: To study the prevalence of Hypothyroidism and Thyroid autoimmunity in Type 2 Diabetic patients in a Tertiary care Endocrine center in India

Methods: 866 patients with type 2 diabetes were screened for thyroid abnormality from 2011 to 2013. T3, T4, TSH and Anti-TPO antibody tests were performed in all subjects. Iodine Intake was also studied by diet recall and urinary iodine.

Results: 181 patients had overt hypothyroidism and 340 patients tested positive for thyroid autoimmunity out of the 866 Type 2 diabetic patients. Family history of hypothyroidism was found in 59 out of 181 hypothyroid patients. 106 cases with positive Anti-TPO antibody test had family history of hypothyroidism. Iodine Intake did not correlate with hypothyroidism; but correlation between iodine status (replete) and thyroid autoimmunity was observed.

Discussion: This study shows that there is a high prevalence of hypothyroidism and thyroid autoimmunity among patients with Type 2 diabetes in India. Patients with positive family history of hypothyroidism and positive Anti-TPO antibody test should be considered for screening with TSH testing more frequently. Positive correlation between iodine replete status and thyroid autoimmunity may be presumably due to the peak of iodinisation in India. Iodine replete state, possibly may be a trigger for autoimmunity in India which merits for the investigation.

Conclusion: All Asian Indians with Type 2 diabetes must be screened for Hypothyroidism and Thyroid autoimmunity, because of the high prevalence. There may be a correlation between iodine repletion and thyroid autoimmunity.

Abstract #292

IMPLEMENTATION OF A HOSPITAL POLICY REQUIRING DIABETES TEAM EVALUATION FOR INSULIN PUMP USE AS AN INPATIENT

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Objective: Insulin pump therapy (CSII) is rapidly increasing in patients with type 1 and type 2 diabetes. Options for insulin use in the pump include Regular insulin, rapid acting analogues and U-500 Regular insulin. The epidemic of cardiovascular disease in patients with diabetes has led to an increasing number of patients being admitted to the hospital with instructions to stop their insulin pump on arrival to the hospital, which can lead to uncontrolled hyperglycemia and, possibly, to DKA. We proposed a hospital wide policy to require diabetes team evaluation to determine if the patient may continue their pump therapy and, if not, to facilitate transition for a basal-bolus regimen. The goals of this retrospective study were to determine how many patients presented with established CSII, how many continued on the CSII and what were the reasons to transition to basal-bolus or insulin infusion therapy.

Methods: Pharmacy records were reviewed to identify insulin pump orders entered by Diabetes team members for the two years prior (2010-2012) and the first 6 months subsequent (2012-2013) to implementation of the insulin pump policy. Hospital charts were reviewed for actual insulin pump use during that admission.

Results: There was a significant increase in the number of patients utilizing insulin pumps in the first 6 months after implementing the policy, as compared to the total number identified in the 2 years prior. Insulin pumps were continued during admission except for during surgery lasting more than 2 hours, admissions for DKA or if no supplies were available for that pump.

Discussion: We found a significant number of patients admitted with CSII who we believe had previously been undetected either due to lack of documentation and/or handwritten orders specifying “continue home pump settings”. The lack of documentation of their CSII therapy presents a potential hazard as insulin is a high risk medication with CSII as a potentially unrecognized cause...
of in-hospital hypoglycemia, hyperglycemia or even DKA. **Conclusion:** Our study has led to the recognition of hidden insulin pumps in the hospital. We recommend that all institutions implement specific policies to identify these patients and document their settings. We have designed a specific order set to capture the information regarding insulin pump use in the hospital in greater detail.

**Abstract #293**

**CHANGING PROFILE OF GAD AND IA2 POSITIVITY IN CHILDREN WITH TYPE 1 DIABETES IN INDIA**

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**Objective:** We wanted to see the number of newly diagnosed patients with type 1 diabetes who were antibody positive at presentation and the change in antibody status over time.

**Methods:** All newly diagnosed type 1 patients had GAD and IA-2 antibodies measured by a standard method between 2007 and 2012. Antibody positivity was defined as positivity of any antibody. The patients were segregated into two cohorts, one between the year 2007 and 2009 and other between the year 2010 and 2012.

**Results:** A total of 124 patients with type 1 diabetes under the age of 21 years were studied. Overall prevalence of GAD and IA-2 antibody was 33.33% between 2007 and 2009 which raised to 43.33% between 2010 and 2012. GAD antibody prevalence was 2.18 times significantly higher in the 2010-2012 cohort than 2007 and 2009, (OR=2.18 with a 95% confidence interval of [1.308-3.63] and p=0.003). No significant difference between the two cohorts with respect to IA2 antibody positivity rate (OR=1.5 with a 95% confidence interval of [0.517-4.356] and p=0.456) or dual antibody (GAD + IA2) positivity rate, (OR=1.305 with a 95% confidence interval of [0.694-2.453].

**Discussion:** The overall prevalence of GAD and IA-2 antibody was 29.8% and 4.79% respectively. Prevalence of mono GAD antibody positivity was found to be 8.62% in the cohort between 2007-2009 which increased to 21.23% in the 2010-2012 cohort. Prevalence of mono IA-2 antibody positivity increased from 1.41% to 3.38% and dual (GAD and IA-2) antibody positivity also increased from 6.19% to 11%, but non-significantly. Wide spread polio immunization may have led to alteration of antibody positivity. Tandon et al. had found overall GAD65 and IA-2 antibodies to be present in approximately 26% of cases of type 1 diabetes in northern India. Prevalence of GAD and IA-2 was found to be 13.9% and 14.9% respectively in type 1 diabetes.

**Conclusion:** Significant increase in antibody positivity in type 1 diabetes was noted in our study overtime. The major public health change that took place in India at this time was universal usage of oral polio vaccine. It is possible that oral polio vaccination resulted in higher antibody positivity.

**Abstract #294**

**CARDIOMETABOLIC RISK FACTORS IN PATIENT WITH 1- HOUR ELEVATED GLUCOSE POST GLUCOSE TOLERANCE TEST**

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**Objective:** To describe Cardiometabolic Risk factors in patient with an elevated glucose one hour (> 155 mg/dl) post 75 gr Oral Glucose Tolerance Test (OGTT), with previous Impaired Fasting Glucose (IFG) at the Endocrinology Department of Central Air Force Hospital in Lima -Perú

**Methods:** We evaluated patients who had a fasting glucose over 100mg/dl in a descriptive study. Exclusion criteria: Diabetes mellitus diagnosis, thyroid or cardiovascular disease, use of metformin, statins and antipsychotics drugs. A total of 91 consecutive subjects were evaluated with a 75 gr OGTT. We measured lipid profile, liver enzymes (aspartate transaminase or AST and alanine transaminase or ALT), uric acid and obtained anthropometrics measurements such as body mass index and abdominal circumferences.

**Results:** We found 1-hour OGTT > 155mg/dl in 28.5% and 40.5% =< 155mg/dl, both with No Impaired Glucose Tolerance (NIGT). 21% of subjects were with IGT and 10% had newly diagnostic of diabetes. Among subjects with no IGT (N=63), the group with one hour OGTT glucose > 155mg/dl had higher control or measure in the media of total cholesterol (207.96 vs. 196.08), low density lipoprotein cholesterol (121.27 vs.115.79), triglycerides (211.46 vs.184.73), ALT (50.69 vs. 43.66), uric acid (5.27 vs.4.70) than the group with =< 155mg/dl and we found significant differences in abdominal perimeter and basal glucose with P=0.003 and P=0.001 respectively between both groups.
**Discussion:** In subjects with normal glucose tolerance, but with one 1-hour > 155mg/dl in the Oral Glucose Tolerance Test (OGTT) predicts type 2 diabetes and is associated with subclinical atherosclerosis, were found in different reports. We described the cardiometabolic profile in subjects who were evaluated with OGTT. We found higher levels of cardiometabolic risk factor in subjects with 1-hour OGTT glucose > 155mg/dl in the group with No Impaired Glucose Tolerance.

**Conclusion:** In subject with IFG who were evaluated with a 75 gr OGTT, those with glucose >155mg/dl at the first hour had worse Cardiometabolic risk profile among the group with NIGT.

**Abstract #295**

LIRAGLUTIDE AS ADDITIONAL TREATMENT TO INSULIN IN PATIENTS WITH TYPE 1 DIABETES MELLITUS: A RANDOMIZED CLINICAL TRIAL

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**Objective:** We have previously demonstrated that the addition of liraglutide to insulin therapy in patients with type 1 diabetes(T1D) results in an improvement in glycemic control, weight loss and a reduction in systolic blood pressure(SBP). We have now conducted the first prospectively randomized study investigating effects of liraglutide in patients with T1DM.

**Methods:** We present an interim analysis of 47 patients that have completed the study (Placebo=14; Liraglutide =33). All patients had T1D for at least one year, on insulin therapy and had no detectable c-peptide in plasma (mean BMI: 29±1, mean A1c: 7.55±0.10%, mean age: 46±2 years, mean age of T1D diagnosis: 20±2). They were randomized to receive placebo, 0.6 , 1.2 and 1.8mg of liraglutide daily for 12 weeks. The number of patients receiving 0.6, 1.2 and 1.8mg doses was 10, 13 and 10 respectively (For purposes of this interim analysis, we have combined data on all 23 patients who received 1.2 and 1.8 mg).

**Results:** In combined group (1.2 and 1.8mg), HbA1c fell by 0.5% from 7.62±0.12% to 7.12±0.11%(p<0.0001, p=0.03 vs placebo). Daily average blood glucose fell from 174±4 to 164±6mg/dl (p=0.08, p=0.05 vs placebo). Percent time spent between 70 to 160 mg/dl increased from 42±2 to 49±3%(p=0.05) and that between 160-400 mg/dl decreased from 52±2 to 45±3%(p=0.03) with no additional hypoglycemia. The dose of insulin did not alter. There was a reduction in body weight (194±8.5lbs to 184±8.9lbs,p<0.0001 in combined 1.2 and 1.8 mg groups and 165±8 to 158±8, p=0.0006 in 0.6 mg group) and daily carbohydrate intake (163±14g vs 123±15g,p<0.0002 in higher dose groups) over 12 weeks. SBP in 1.8 mg group fell by 9 mm (118±2.8 to 109±3,p=0.03). CRP fell by 18±7%. There was no change in any of these indices in patients treated with the placebo and 0.6 mg liraglutide.

**Discussion:** This is the first prospective study to show that the addition of liraglutide 1.2 and 1.8mg to insulin significantly reduces HbA1c, mean blood glucose, blood pressure, body weight, carbohydrate intake and CRP in subjects with type 1 diabetes over a period of 12 weeks. Long term studies are needed to establish the durability of the effects. Our findings have significant implications for the future treatment of type 1 diabetes.

**Conclusion:** We conclude that the addition of 1.2 and 1.8 mg of liraglutide to insulin significantly reduced HbA1c, mean blood glucose, blood pressure, body weight, carbohydrate intake and CRP in patients with type 1 diabetes.

**Abstract #296**

COMPARATIVE ACCURACY OF INSULIN DOSING BASED ON RESULTS FROM THREE BLOOD GLUCOSE MONITORING SYSTEMS

Brian Pflug, PharmD, Scott Pardo, PhD, PStat®, Holly Schachner, MD

**Objective:** Self-monitoring of blood glucose (SMBG) is often used as part of a diabetes management plan. The accuracy of blood glucose monitoring systems (BGMSs) is particularly important for people with diabetes who use insulin therapy and adjust their insulin dose based on SMBG results. Previously, unmodified fingertip capillary blood samples from 111 subjects were evaluated using 3 different BGMSs that can communicate wirelessly with an insulin pump (CONTOUR® NEXT LINK, OneTouch® UltraLink®, and Nova Max Link™). Samples were also tested in parallel on a YSI 2300 STAT Plus™ reference analyzer to obtain reference values. In this analysis, blood glucose measurements from the previous study using the 3 BGMSs were used to calculate insulin dosing; error in insulin dose was compared across the meters.

**Methods:** Blood glucose measurements were used to determine an appropriate pre-meal bolus insulin dose assuming a meal containing 60 g of carbohydrates and a
target glucose level of 100 mg/dL. Two methods were used to calculate insulin dose: an insulin dosing application and a computer model. The application assumed an insulin sensitivity of 1/25 and an insulin:carbohydrate ratio of 1:15; these values were adjusted in the computer model to account for the error of meter results in comparison with YSI readings. For each method, the insulin dose error was calculated as the difference in the dose determined using the meter result and the dose determined using the YSI result.

Results: The 95% dose error ranges for the meter systems (in units of insulin) using the application were as follows: CONTOUR® NEXT LINK, -0.49 to 0.20; OneTouch® UltraLink®, -1.40 to 0.96; and Nova Max Link™, -0.65 to 1.05 (negative dose error represents underdosing, while positive dose error represents overdosing). The dose error associated with the CONTOUR® NEXT LINK was statistically significantly less than that of the OneTouch® UltraLink® and the Nova Max Link™ (P = 0.0387 and P <0.0001, respectively). Using the computer model, the CONTOUR® NEXT LINK was also associated with a smaller dose error range (-0.94 to 0.30) than the OneTouch® UltraLink® (-2.80 to 1.64) and the Nova Max Link™ (-1.30 to 1.74), and these differences were statistically significant (P = 0.0072 and P <0.0001, respectively).

Conclusion: Thus, calculations using both methods predicted that 95% of insulin dose errors with the CONTOUR® NEXT LINK BGMS will be within a relatively narrow range, compared with dose errors with the OneTouch® UltraLink® and Nova Max Link™ BGMSs. More broadly, while various BGMSs may meet specific accuracy criteria, differences in accuracy could result in clinically important differences in insulin dosing.

Abstract #297

STRATIFICATION OF DIABETES RISK USING AN INDEX COMPRISED OF PLASMA MARKERS OF INSULIN RESISTANCE, INFLAMMATION AND β-CELL FUNCTION

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Objective: Although progression to Type 2 diabetes (T2DM) generally increases with glucose levels, the risk of individual progression varies widely at a given glucose value, particularly among individuals with moderately elevated fasting glucose levels in the range of 90-110 mg/dL. To better identify the highest-risk patients who would benefit most from lifestyle or pharmacologic intervention, a Diabetes Risk Index (DRI) was developed.

Methods: The DRI score (1-10) was designed to use information derived from a single nuclear magnetic resonance (NMR) spectrum of a fasting plasma sample: 1) lipoprotein subclass/size parameters, 2) the branched-chain amino acid valine and 3) an inflammatory signal that arises largely from glycosylated acute phase proteins. These markers were selected based on the literature and preliminary data linking them to insulin resistance, inflammation, β-cell function, and diabetes risk. Baseline samples from the Multi-Ethnic Study of Atherosclerosis (MESA) and Insulin Resistance Atherosclerosis Study (IRAS) participants were used to develop the DRI assay. The MESA dataset consisted of 4,985 non-diabetic participants, 411 of whom developed diabetes and the IRAS study consisted of 982 pre-diabetic subjects, 134 of whom developed diabetes during 5 years of follow-up.

Results: The DRI score added significantly to a logistic regression model (adjusted for age, gender, race, glucose) in MESA subjects with glucose levels 90-110 mg/dl, improving both the χ² value (183.8 vs 140.6) and the c-statistic (0.765 vs 0.725), suggesting that the DRI score can add predictive power independently of glucose. DRI scores determined for MESA and IRAS subjects with glucose levels 90-100 mg/dL predicted substantial heterogeneity of diabetes risk. For example, in IRAS subjects with a glucose level of 110 mg/dL and a DRI score of 10, the 5-year probability of diabetes conversion was 40%, but <10% when the DRI score was 1. The DRI score added significant predictive power above glucose in all subjects, including those whose BMI was normal (p<0.0001) suggesting that the DRI score is capable of stratifying diabetes risk even in patients who are not overweight or obese.

Discussion: The DRI assay uses information regarding insulin resistance, inflammation and metabolic derangement all of which impact pancreatic β-cell function and lead to T2DM. The DRI score gives visibility to a patient’s relative risk at any given glucose level.

Conclusion: The DRI score can be used in conjunction with clinical evaluation to stratify patients with fasting glucose between 90-110 mg/dL and identify those at highest risk for developing T2DM within 5 years.
Abstract #298

**VITAMIN-D SUPPLEMENTATION THROUGH MODULATION OF INSULIN RESISTANCE AND SYSTEMIC INFLAMMATION REDUCES PROGRESSION OF PREDIABETES TO DIABETES: AN OPEN LABEL RANDOMIZED CONTROLLED STUDY FROM EASTERN INDIA**

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**Objective:** Indian individuals with prediabetes (IPD) have higher progression (≈18% per year) to type2 diabetes (T2DM). Since vitamin-D deficiency has been linked to prediabetes, we aimed to evaluate role of vitamin-D on progression to T2DM and reversal to normoglycemia in IPD.

**Methods:** IPD with persistent impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) over 2 oral glucose tolerance test (OGTT), without any severe co-morbid state or drug intake, having serum 25-OH-vitamin-D (25OHD) ≤30ng/ml were randomized into Group-A [n=66; received vitamin-D (cholecalciferol 60,000 U once weekly for 8 weeks then monthly) and calcium (1250mg of calcium carbonate/day equivalent to elemental calcium 500mg)] and Group-B (n=61; received calcium only). IPD with serum 25OHD>30ng/ml (n=43) were also followed with calcium supplementation (Group-C). All received therapeutic lifestyle modification. OGTT, insulin, 25OHD, lipids, interleukin-6 (IL6), tumor necrosis factor-α (TNFα) and hsCRP were done at baseline and annually. Data from IPD with at least 1-year follow up were analyzed. The trial is registered with clinical trial registry of India (CTRI/2011/091/000192).

**Results:** 1946 individuals were initially screened, 498 underwent OGTT1 and 301 underwent OGTT2. 125 out of 170 finally included IPD (73.52%) had 25OHD ≤30ng/ml. Mean follow-up in Group-A (n=55), B (n=49) and C (n=32) was 28.2±8.83, 29.15±7.69 and 27.51±7.8 months respectively. 25OHD had significant correlation with HOMA2-IR (r=-0.42; P=0.004), TNFα (r=-0.31; P=0.03) and hsCRP (r=-0.31; P=0.03), after adjusting for BMI. At study end, Group-A IPD had significantly higher 25OHD (35.47±10.1 ng/ml; p<0.001), lower FBG (104.8±17.6; p=0.023), 2hPGBG (144.5±34.3; p=0.001), TNFα (44.1±25.59 pg/ml; p=0.002) and IL-6 (3.61±2.82; p=0.0005) as compared to Group-B and C. Group-A IPD as compared to Group-B had significantly lower progression to diabetes (6/55 vs. 13/49; P=0.04), and higher reversal to normoglycemia (23/55 vs. 10/49; P=0.02). Cox regression revealed baseline 25OHD [Exp(B)=0.921; P=0.049] and 2hPGBG [Exp(B)=1.033; P=0.014] independently predicted progression to diabetes. Hypertension [Exp(B)=0.416; P=0.043] and baseline 25OHD [Exp(B)=1.054; P=0.046] predicted reversal to normoglycemia.

**Discussion:** The relative and absolute risk reduction of vitamin-D on progression to diabetes was 58.83% and 15.59% respectively. This higher risk reduction is perhaps due to increased progression to diabetes in Group-B. This evaluation achieved 76.49% statistical power with 5% type-I error at 2.8 odds ratio.

**Conclusion:** Vitamin-D supplementation reduces prediabetes progression to diabetes and increases reversal to normoglycemia.

Abstract #299

**INSULIN RESISTANCE BY HOMEOSTASIS MODEL ASSESSMENT IN HIV-PATIENTS ON HIGHLY ACTIVE ANTIRETROVIRAL THERAPY: A CROSS-SECTIONAL STUDY**

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**Objective:** To determine the prevalence of insulin resistance in a cohort of HIV-patients on highly active antiretroviral therapy (HAART) and to investigate the potentially associated factors.

**Methods:** We conducted a cross-sectional study including 219 adult patients with HIV on HAART. Insulin resistance (IR) was determined through the HOMA-IR mathematical model, using fasting plasma glucose (FPG) and insulin. Bivariate and multivariate analyses were performed to assess the association between demographic information, clinical characteristics and laboratory results, and insulin resistance.

**Results:** 75 (34.2%) (95% CI 28.9 - 40.9) HIV-patients on HAART showed insulin resistance. 61 (81%) of these patients were more than one year on HAART regimen, which was mainly composed by non-protease inhibitors drugs (88%). Metabolic syndrome was found in 59 (26.9%) subjects. In the multivariate analysis, the factors associated with IR were age ≥ 46 years (PR = 1.956, 95% CI 1.470 to 2.601), greater body mass index (PR = 1.054, 95% CI 1.023 to 1.085) and greater fasting serum insulin level (PR = 1.036, 95% CI 1.030 to 1.042).

**Discussion:** In our study, the prevalence of IR was two times higher than that of the non-HIV-infected population.
The reported prevalence rates of IR among HIV-infected patients on HAART are highly variable, ranging from 13% to 45.7%. We did not find a significant association between IR and the use of protease inhibitors (PI) in contrast to other reports which may be explained by the small number of patients [20 (9%)] using PI as part of their HAART regimen included in our study.

In the multivariate analysis, we found a 3% increased risk of IR for each additional year of life. Similarly, we found an increased risk of IR with higher body mass index and higher levels of basal insulin.

The prevalence of metabolic syndrome (MS) in our series was 27%, similar to the prevalence reported in American and Latin American series. Dyslipidemia and hyperglycemia were the predominant components, which differs from reports of MS in the general population. The prevalence of hyperglycemia was 43%; higher than that in other studies of HIV patients on HAART. This suggests that HIV treatment is an important factor in the development of IR and other metabolic disorders such as impaired glucose tolerance and type 2 diabetes mellitus.

**Conclusion:** The prevalence of IR was 34.2%. Factors associated with insulin resistance were age, body mass index and insulin levels. We did not find any significant association between insulin resistance and protease inhibitors.

**Abstract #300**

PREVALENCE OF GLUCOSE INTOLERANCE AT 6 WEEKS POSTPARTUM IN PATIENTS OF GESTATIONAL DIABETES MELLITUS

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**Objective:** To study the prevalence of glucose intolerance at 6 weeks postpartum in patients of Gestational Diabetes Mellitus (GDM) diagnosed according to ADA criteria.

**Methods:** The study included pregnant females aged > 18 years diagnosed as GDM, who were referred to the Endocrine Department. Pregnant females with type 1 diabetes, pre-existing type 2 diabetes (T2D), secondary diabetes, and those with acute metabolic decompensation were excluded from the study.

The patients were educated about the risk of future T2D. They were counselled about the need for Oral Glucose Tolerance Test (OGTT) at 6 weeks postpartum and telephonic reminders were given to the women during the postpartum period. OGTT with 75 gram of glucose was performed at 6 weeks (upto +7 days) postpartum.

**Results:** Out of the 75 women who had GDM and were recommended an OGTT at 6 weeks postpartum, 13 (17.33%) did not return for the test. Out of 62 women, 43 (69.35%) were more than thirty years old; while 19 (30.64%) were less than thirty years old. About one-third (33.88%) of study population developed an abnormal OGTT at 6 weeks postpartum, while 66.12% had reverted to normal glucose tolerance. Impaired Fasting Glucose (IFG) was seen in 14.51%, 4.83% had Impaired Glucose Tolerance (IGT), 8.06% had both IFG and IGT, and 6.45% had overt T2D.

As compared to the women who reverted to normal glucose tolerance postpartum, the women in whom dysglycemia persisted at 6 weeks postpartum were younger in age (31 ± 3.50 vs. 32.24 ± 3.60 years), had an earlier diagnosis of GDM, had a higher pre-pregnancy Body Mass Index (26.73 ± 4.44 vs. 25.48 ± 3.40 kg/m2), and had a greater insulin requirement during pregnancy (36.62 ± 25.21 vs. 25.55 ± 23.69 IU/day). Also, the levels of glycemia in the OGTT done during pregnancy were higher in women in whom an abnormal glucose tolerance persisted at 6 weeks postpartum.

**Discussion:** In our part of the world, there is a general lack of awareness regarding the importance of postpartum follow up after GDM. Prevalence of an abnormal OGTT in one-third of the study population may be due to the socio-cultural factors like mothers being fed calorie dense food and being confined to their homes in the early post-partum period. Also, mothers get so busy taking care of their babies and adjusting to this new phase in their lives, that they do not pay attention to their own health.

**Conclusion:** Our study emphasizes the need for compulsory follow up OGTT for women with GDM in our part of the world in view of ethnicity and prevailing socio-cultural factors.

**Abstract #301**

INSULIN INFUSION AND GLUCOSE SENSING BY MINIMED DUO, A NEW COMBINATION DEVICE

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**Objective:** Sensor-augmented pump therapy currently requires separate insertion procedures for the insulin infusion catheter and the subcutaneous glucose sensor. MiniMed Duo is a device that combines an insulin infusion catheter and a glucose sensor, and is intended to simplify device insertion and reduce patient burden.

**Methods:** This was a multi-center, nonrandomized, proof-
of-concept study of MiniMed Duo used in conjunction with the Veo insulin pump. Forty-five subjects with type 1 diabetes and previous use of sensor augmented pump therapy (age 45.3±11.0 years, 24 male, 21 female, all Caucasians) wore the devices for 15 days. Each subject was to wear 5 devices over that period, each for 3 days, and to test capillary blood glucose at least 7 times per day. The primary endpoint was the percentage of sensor data points within ±20% of paired SMBG data points. Subject experiences were assessed via questionnaires.

**Results:** Overall, 74.81% of the sensor-SMBG paired points were within 20% of one another, meeting the primary endpoint. Consensus and Clarke error grid analysis showed that >90% of points were within the A+B zones, thus exceeding the clinical accuracy threshold. The mean absolute relative difference was 15.5±17.1%. The functional survival of the device entering day 3 was 90.5%. Performance characteristics of threshold and 30 min predictive alerts for hypoglycemia and hyperglycemia were evaluated. For hypoglycemia (≤70 mg/dL), the true and false alert rates were 92.4% and 56.5%, respectively. For hyperglycemia (≥250 mg/dL), the true and false alert rates were 87.2% and 32.2%, respectively. Forty-four adverse events occurred in 26 subjects - none were serious, 1 was moderate, and 43 were mild; 97.7% of the adverse events were skin-related (such as bruising or bleeding). There were no device related complaints or deficiencies that could have potentially resulted in a serious adverse event. Questionnaire results indicated an overall high degree of satisfaction with the device. The median responses for “Pain at time of insertion” and “Pain level at removal” were both 0 (no pain). A total of 95.7% of the subjects agreed that setting up the device for insertion was easy, and 82.9% agreed that their overall experience with the device was acceptable.

**Discussion:** MiniMed Duo provides continuous glucose sensing and concomitant insulin infusion in a single device, which is safe to wear and perceived positively by patients.

**Conclusion:** The device provides accurate and reliable glucose readings, and is projected to simplify sensor-augmented insulin pump therapy and improve patient satisfaction.

**Abstract #302**

**CARDIOVASCULAR SAFETY OF SAXAGLIPTIN IN PATIENTS WITH TYPE 2 DIABETES: POOLED ANALYSIS OF 20 CLINICAL TRIALS**

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**Objective:** A large outcome trial of saxagliptin (SAXA) in patients with prior cardiovascular (CV) disease or multiple CV risk factors (SA VOR) was recently published. In contrast to SAVOR, this analysis evaluated major adverse CV events (MACE), including component events of CV death, myocardial infarction (MI), and stroke; and heart failure (HF) in a general population of patients with type 2 diabetes (T2D) at lower risk for CV events enrolled in SAXA clinical trials.

**Methods:** Pooled analyses were performed on 20 randomized controlled trials of SAXA as monotherapy or add-on therapy in 9156 patients with T2D and a subset of 11 SAXA add-on to metformin trials (N=5171). Adjudicated MACE and investigator-reported HF were assessed. Weighted incidence rates (IRs; events/100 person-years) and IR ratios (IRRs; SAXA/control [CTL]) were calculated (Mantel-Haenszel). IRR confidence intervals were calculated using an exact method.

**Results:** MACE composite: In the 20-study pool, exposure time to first MACE or censoring was 6039 patient-years in the SAXA group vs 2864 patient-years in the CTL group. 43 patients in the SAXA group and 31 in the CTL group had MACE. IRs per 100 patients-years (SE) were 0.85 (0.14) for SAXA and 1.12 (0.20) for CTL, with an IRR (95% CI) of 0.74 (0.45, 1.25). The Cox proportional hazard ratio (HR; 95% CI) was 0.75 (0.46, 1.21), suggesting no increased risk of MACE. In the 11-study SAXA add-on to metformin pool, exposure time was 3287 patient-years with SAXA vs 1783 patient-years with CTL. The IR was similar for SAXA (0.79 [0.17]) and CTL (0.85 [0.23]), with an IRR of 0.93 (0.44, 1.99).

Components of MACE: In the 20-study pool, patients with events for SAXA and CTL and the IRs (95% CI) for the individual components of MACE were 17 and 15, 0.61 (0.28, 1.36) for CV death; 19 and 12, 0.87 (0.39, 2.02) for MI; and 16 and 10, 0.75 (0.31, 1.90) for stroke. In the 11-study SAXA add-on to metformin pool, patients with events and IRs (95% CI) were 8 and 8, 0.51 (0.16, 1.63) for CV death; 12 and 5, 1.49 (0.47, 5.57) for MI; and 7 and 4, 0.96 (0.23, 4.66) for stroke.

Heart failure: 21 SAXA and 18 CTL patients had HF (20-study pool only), with an IRR of 0.55 (0.27, 1.12).

**Discussion:** Patients with T2D are at an increased risk for adverse CV events. Consistent with SAVOR, which analyzed MACE in patients with T2D and CV disease or multiple CV risk factors, this 20-trial pooled analysis of patients from the general T2D population found that SAXA was not associated with an increased risk of MACE or its components.

**Conclusion:** Saxagliptin was not associated with an increased risk of MACE or HF in this general population of patients with T2D.
Abstract #303

TESTOSTERONE RESTORES INSULIN SENSITIVITY AND IMPROVES INSULIN SIGNAL TRANSDUCTION IN PATIENTS WITH DIABETES AND HYPOGONADOTROPIC HYPOGONADISM

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Objective: 1) To investigate whether insulin resistance is increased and insulin signaling mediators are decreased in patients with Hypogonadotropic Hypogonadism (HH) and Type2 DM
2) To investigate effects of testosterone supplementation on insulin sensitivity and on mediators of insulin signaling. 

Methods: Twenty six patients with HH and T2DM were compared with 24 eugonadal patients with T2DM. Patients with HH were treated with testosterone 200mg or placebo every 2 weeks injected intramuscularly for 6 months. Fasting blood samples, fat biopsies and Hyperinsulinemic euglycemic clamps were done at baseline and at 6 months. 12 patients randomized to testosterone and 10 to placebo have completed the study so far.

Results: Using hyperinsulinemic euglycemic clamps, we demonstrated that patients with HH have 28% lower glucose infusion rates (GIR) for a given rate of insulin infusion compared to eugonadal patients. Following testosterone treatment, there was an increase in GIR by 30%, consistent with a reversal of insulin resistance. Basal expression of mediators of Insulin signaling including IR, IRS-1 and GLUT-4 was lower by 32%, 35% and 27% (p<0.05), respectively, in HH adipose tissue (AT) compared to eugonadal. Following testosterone, the AT expression of IR, IRS-1 and GLUT-4 increased significantly by 63±15%, 54±17% and 59±14%, respectively, while there was a decrease in the expression of PTP-1B by 23±8% and TLR-4 by 21±11%, both of which interfere with insulin signaling. There was a significant fall in circulating mononuclear cells expression of SOCS-3 by 27±8% and IKKβ by 23±11%, both known to interfere with insulin signaling. Additionally, plasma concentrations of FFA, TNFα and CRP, all of which interfere with insulin signaling, fell by 35%, 18% and 26%, (p<0.05) respectively. There were no changes in the insulin sensitivity or insulin signaling mediators in the placebo group.

Discussion: Hypogonadotropic Hypogonadism is associated with insulin resistance and lower expression of mediators of insulin signaling in adipose tissue as compared with eugonadal patients. Following Testosterone replacement the expression of mediators of insulin signaling increases and there is reduction in expression of markers interfering with insulin signaling leading to improved insulin sensitivity.

Conclusion: Testosterone supplementation has an insulin sensitizing effect in HH patients at various levels involving an increase in the expression of mediators of insulin signaling and a reduction in factors that interfere with insulin signaling.

Abstract #304

HYPERINSULINEMIA AND INSULIN RESISTANCE IN NAFLD PATIENTS WITHOUT DIABETES

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Objective: Non-alcoholic fatty liver disease (NAFLD) is now described as the hepatic component of the Metabolic Syndrome. The global epidemic of NAFLD has led to the recognition of the associated complications that include not only liver failure and/or hepatocellular carcinoma related to the nonalcoholic steatohepatitis (NASH) but also diabetes and cardiovascular disease. Recent reports of the high prevalence of NAFLD and NASH in people with diabetes led us to hypothesize that NAFLD patients without diabetes were likely to have prediabetes and thus would represent a target population for strategies to prevent diabetes. We characterized sequential patients referred to our Metabolic Liver Clinic with evaluation of metabolic parameters and steatosis, as measured by NASH FibroSURE®.

Methods: Charts were reviewed from consecutive NAFLD patients. Glucoregulatory status was assessed by A1c and by OGTT with glucose & insulin measured at 0, 30, 60, 90 & 120 minutes plus c-peptide & proinsulin measured at 0 & 30 minutes. After excluding known diabetes and incomplete metabolic data, we assessed correlations of metabolic parameters and steatosis. Spearman correlation coefficient was used to measure the association between metabolic parameters and NASH FibroSURE® scores.
Results: The most significant association was Steatosis Score vs. BMI with a p-value < 0.0001. Additional significant associations included insulin resistance, as measured by HOMA-IR, vs. BMI, beta-cell function, as measured by HOMA-B, vs. BMI, and glucose level as measured by A1C vs. Steatosis Score. Multivariate analysis revealed that the only significant correlation in women was A1C vs Steatosis Score.

Discussion: We found that hyperinsulinemia and insulin resistance are highly prevalent in patients with NAFLD who did not yet have diabetes. The primary risk factor for all of the associations was male gender. The magnitude of the hyperinsulinemia suggested that the prediabetes was still in an early and potentially reversible stage. However, the level of hyperproinsulinemia suggested that significant beta-cell dysfunction was already present.

Conclusion: Patients with NAFLD who do not have diabetes represent a population that may benefit from diabetes prevention strategies such as weight loss and pioglitazone to prevent progression to diabetes and its complications while also improving the steatosis.
HYPOGLYCEMIA

Abstract #400

HYPOGLYCEMIA AS A PREDICTOR OF ACUTE LIVER FAILURE OUTCOMES

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Objective: Acute liver failure (ALF) is a disease with high morbidity and mortality. The liver plays critical roles in glycemia homeostasis. However, the role of blood glucose (BG) values as a predictor of ALF outcomes has never been studied. The objective of this study is to determine the role of hypoglycemia as a prognostic factor in ALF outcomes.

Methods: We conducted a retrospective study on all ALF patients admitted to a large liver transplant center between January 1, 2005 and December 31st, 2012. ALF was defined as (1) hepatic encephalopathy, (2) increased prothrombin time (>3 seconds prolonged) or international normalized ratio (INR >1.5), and (3) time of onset within 26 weeks. BG by serum blood test or finger stick at any time during the hospital stay less than 70mg/dL was defined as hypoglycemia and less than 50mg/dL as severe hypoglycemia. Subjects with decompensated pre-existing liver disease, shock liver and severe sepsis were excluded. Patient's demographic, clinical and laboratory parameters were assessed. Prognostic scoring systems including Model for End Stage Liver Disease (MELD) score and Acute Physiology and Chronic Health Evaluation (APACHE) II score were reviewed. Outcomes of interest were ICU length of stay (LOS), hospital LOS, mortality and transplant.

Results: 80 patients were included in our analysis. The median age was 45 years (19-85). Sixty-four percent were female and 59% Caucasian. The most common cause of ALF was Acetaminophen induced toxicity (43%). The median MELD score for the group was 32 (8-57) and 93% patient had a MELD score >=15. The proportion of patients with hypoglycemia and severe hypoglycemia were 55% and 24%, respectively. Mean lowest BG was 63.2 (SD=3) mg/dL. Mean ICU LOS was 6 (SD=5.1) days. Mean hospital LOS was 9 (SD=7) days. Forty-six percent of patient died during their hospitalization while only 4 % received liver transplantation. On univariate analysis, MELD score >=15, APACHE II score, hypoglycemia, severe hypoglycemia and values of lowest BG were significantly associated with in hospital death. Both hypoglycemia and severe hypoglycemia were also associated with longer ICU LOS (p=0.024 and 0.036, respectively) but not hospital LOS. On multivariate analysis, severe hypoglycemia and values of lowest BG were associated with increased ICU LOS (p=0.03 and 0.01, respectively).

Discussion: Further studies are warranted to investigate if value of blood glucose and the presence of hypoglycemia should be considered as an important part of scoring systems for ALF prognosis and liver transplant evaluation.

Conclusion: Hypoglycemia is a poor prognostic factor in patients with ALF.

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Abstract #401

DO ORDER SETS IMPROVE MANAGEMENT OF INPATIENT HYPOGLYCEMIA?

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Objective: Hypoglycemia in the hospital setting is a patient safety concern as we target for improved inpatient glycemic control. Hospitals are increasingly adopting hypoglycemia management protocols and order-sets(OS) to treat hypoglycemia more efficiently. We evaluated the use of OS and its influence on the management of hypoglycemic events (HE) at a community hospital.

Methods: A retrospective chart review was conducted on 150 diabetic patients on general medical floors who had HE (blood glucose[BG]<70 mg/dl). The data consisted of patients’ demographics, medication regimen, co-morbid conditions, and HE details (severity, treatment and outcomes). Standard statistical analyses including multivariate analysis were performed. A follow-up survey was conducted on 100 random physicians and nurses to assess utilization of OS.

Results: OS were instituted in 94/150(63%) of the patients upon admission. Baseline demographics did not vary between the two groups. Patients with and without OS did not differ significantly in treatment of their HE, initiation of intervention (56.5% vs. 53.2%), intervention within 30 minutes (20.2% vs. 14.3%), repeat BG within 30 minutes (23.4% vs. 14.3%), and change in management post-HE (26.6% vs. 26.8%). Comparison of severe HE (BG <55mg/dl) vs. mild HE (BG 56-69mg/dl) revealed significant differences in management of HE, initiation of intervention (74.4% vs. 47.7%), repeat BG within 30 minutes (34.9% vs. 14%), intervention within 30 minutes (27.9% vs. 14%) and change of management post-HE (48.8% vs. 17.8%).

Discussion: Currently, the ADA recommends the implementation of inpatient hypoglycemia management protocols. Our findings indicated that OS were not initiated in 37% of patients in our hospital. There were no identifiable patient-related characteristics to explain this. OS did not influence management in our study, except when the patient had severe hypoglycemia. Another alarming issue was the lack of change in medical therapy after HE. A post-analysis survey revealed that many physicians fail to remember to order the OS, whereas nursing failed to comply with OS due to asymptomatic hypoglycemia. Further education of physicians and nursing staff may improve utilization of OS. Possible resolutions may include pop-up OS when a patient...
is diabetic, along with mandatory algorithms documenting the management of HE.

**Conclusion:** Our study showed that order sets did not influence the management of acute hypoglycemia or affect medical management after a hypoglycemic event. Although current emphasis is placed on hypoglycemia management protocols, further investigation for alternative methods may be more effective.

**Abstract #402**

**A RARE CASE OF NON ISLET CELL TUMOR HYPOGLYCEMIA ASSOCIATED WITH ADVANCED GASTROINTESTINAL STROMAL TUMOR**

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**Objective:** We report a rare case of symptomatic hypoglycemia in a patient with advanced gastrointestinal stromal tumor (GIST).

**Case Presentation:** 77 year old female with history of type 2 diabetes mellitus and advanced GIST presented with complaints of lightheadedness and weakness. Symptoms improved after administration of IV dextrose by the EMS. She did not lose consciousness or have involuntary movements. She denied chest pain, palpitations, sweating, urinary or fecal incontinence during the episode. Glyburide had been discontinued in view of hypoglycemic episode 4 months back. She had undergone tumor resection 3 years prior, and was on Imatinib for liver metastasis. Initial physical exam was remarkable for BP 149/97mmHg, HR 87/min, RR 18/min, Temp 97.9F. Patient appeared frail. Rest of the systemic exam was unremarkable except for a healed vertical midline abdominal scar. Initial fingerstick glucose was 87mg/dL. Subsequently, patient had multiple hypoglycemic episodes, lowest fingerstick glucose being 27mg/dL. Patient was given IV dextrose, and was noted to have a good appetite. Labs revealed elevated liver enzymes, HbA1C of 5.5% and a normal CBC except for microcytosis and elevated RDW. Additional investigations revealed an early morning serum cortisol of 20.79ug/dL; serum insulin and C-peptide levels were 0.32 mU/L and 0.30 ng/mL respectively. Serum IGF-I and IGF-II levels were 28ng/ml and 264ng/mL. Insulin autoantibody was <0.4U/mL. Thyroid function tests were normal. Sulfonylurea screen was negative. Hypoglycemia resolved after initiation of subcutaneous octreotide.

**Discussion:** Gastrointestinal stromal tumors are uncommon neoplasms of the intestinal tract. Historically, it has been a challenging diagnosis due to overlap with other smooth muscle tumors. They can now be classified more definitively as a result of discovery of the kit mutation and recognition of CD34 antigen expression. Hypoglycemia associated with GIST is extremely rare. The mechanism of hypoglycemia is due to release of pro-IGF II or “big” IGF II. “Big” IGF II is improperly processed pro-IGF II. The protein is not cleaved in the manner that it would normally be, leading to a pro-IGF that is larger than the normal factor but can still bind receptors. This protein is aberrantly released from the tumor cells without any feedback, leading to hypoglycemia.

**Conclusion:** New onset hypoglycemia may suggest a paraneoplastic syndrome. Therefore, after excluding common causes of hypoglycemia, such as exogenous insulin, adrenal insufficiency, thyroid insufficiency and poor oral intake, as in our case, it is important to rule out hormonally active neoplasms. Though extremely rare, it is important to recognize hypoglycemia associated with GIST.

**Abstract #403**

**HYPOGLYCEMIA IN THE SETTING OF ENDOGENOUS INSULIN PRODUCTION**

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**Case Presentation:** Insulinomas are rare cause of hypoglycemia and represent neuroendocrine tumors. We present a case of previously healthy male who presented with confusion and hypoglycemia.

A 30 year old man with no significant past medical history presented with altered mental status at a foot ball game. He had a big breakfast before the game. After first half he was confused and was not responding to commands. He was escorted to ED and POC glucose check was 21. He received D50 with resolution of symptoms. He had similar symptoms since last 5 years which tend to resolve with snack. Differential considered were exogenous insulin use, insulinoma, insulin autoimmune hypoglycemia or NIPHS. He underwent 72-hour fasting test. Patient developed symptomatic hypoglycemia 20 hours post meal. His BG was noted to be 37. Symptoms improved with glucagon injection. At the end of test, insulin (66.7 uU/ml) and c-peptide (7.1 ng/ml) were high. Gastrin, Prolactin and PTH levels were normal.

CT abdomen showed ovoid, hyper-dense focus in the uncinate process of the pancreas, which measured about 1.7 x 1.2 cm. No metastatic disease. CT scan patient underwent EUS, which showed mass at the uncinate process of pancreas. FNA was performed. Pathology results showed plasmacytoid cells with uniform round nuclei and moderate amount of eosinophilic
cytoplasm. Cells were positive for chromogranin and synaptophysin. Patient underwent surgery with resolution of symptoms.

Discussion: Insulinomas are islet-cell tumors arising from acinar system of pancreas. Apart from insulin they may secrete hormones like ACTH, glucagon and somatostatin. Clinical feature is fasting hypoglycemia (73%). Insulinomas are characterized by Whipple’s triad (presence of symptoms of hypoglycemia, low sugars at the time symptoms and reversal of symptoms with administration of glucose). Insulinomas can be single (87%) or multiple, and benign or malignant. MEN syndromes are usually associated with multiple insulinomas. Diagnosis is based on high insulin levels during 72-hour fasting period. Tumor can be located with trans abdominal ultrasound, CT of abdomen, pentetreotide scintigraphy, endoscopic ultrasonography or SACST with hepatic venous sampling. Presence of MEN syndrome must be evaluated with parathyroid, prolactin and gastrin levels. Surgical resection has high cure rate (90%) and is the treatment of choice. Consider medical therapy (diazoxide or somatostatin) in patients who are not surgical candidates.

Conclusion: Consider the possibility of insulinoma after ruling out exogenous use of insulin in the setting of hypoglycemia. 72-hour fasting test with monitoring of insulin levels helps with diagnosis. Surgery remains the treatment option.

Abstract #404

HYPOGLYCEMIA ASSOCIATED WITH TPN DISCONTINUATION

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Cleveland Clinic Foundation

Objective: Hypoglycemia is a rare side effect of total parenteral nutrition (TPN) and may occur on abrupt discontinuation. Such hypoglycemia is believed to result from unopposed endogenous hyperinsulinemia, has been most commonly reported in children, but rarely in adults. We describe an adult case of hypoglycemia shortly after TPN discontinuation and propose possible mechanisms for this uncommon side effect of TPN.

Case Presentation: A 50-year-old man with history of small bowel ischemia and extensive abdominal surgeries was admitted for intra-abdominal abscess and enterocutaneous fistula. The patient had been on 12-hr-cycling TPN with added lipids for a year. The cycle was temporarily increased to 24 hrs during the 1-month hospitalization. Enteral feeding was impossible due to high fistula output. Due to a nationwide shortage of lipid emulsions, the TPN was made fat-free. After the resolution of the infection, it was decided to resume the 16-hr-cycling TPN prior to discharge. When the 16-hr-cycling TPN was restarted in the hospital, the patient experienced episodes of sweating and shakiness with concurrent blood sugar readings from 42-69 mg/dL within 1 hr of discontinuing TPN. The symptoms occurred despite elimination of insulin from TPN. Physical exam revealed a BMI of 21.41 kg/m2 (lost 5 lbs. in the past month), moderate to severe subcutaneous fat loss and muscle wasting, a percutaneous gastrostomy tube and active draining from the surgical drainage site. Lab tests showed an albumin of 2.7 g/dL, alkaline phosphatase of 200 units/L and creatinine of 1.5 mg/dL. The fat-free TPN was gradually tapered over 3 hrs but the hypoglycemic episodes continued. He was finally discharged with 24-hr-cycling TPN.

Discussion: Several co-existing conditions likely increased the hypoglycemic risk in this patient. Fat-free TPN has been shown to cause more hyperinsulinemia when compared to lipid-added TPN. The lack of essential fatty acids in the TPN also aggravates hepatic steatosis and liver dysfunction. Carnitine deficiency may develop after hepatic dysfunction and diet restriction and lead to impaired fatty acid oxidation and diminished hepatic gluconeogenesis. A combination of hyperinsulinemia, liver dysfunction, and substrate deficiency from malnutrition likely contributes to impaired endogenous glucose production in such patients and results in hypoglycemia post TPN discontinuation.

Conclusion: Hypoglycemia after TPN cessation is uncommon in adults but can occur on abrupt discontinuation of high carbohydrate loaded TPN due to stimulated hyperinsulinemia, poor nutritional status, hepatic dysfunction and the lack of free fatty acids suppression of insulin secretion.

Abstract #405

ABSTRACT WITHDRAWN

Abstract #406

CASE OF SEVERE HYPOGLYCEMIA DUE TO METASTATIC INSULINOMA

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Objective: Insulinomas are the most common functioning endocrine neoplasm of the pancreas, however the incidence of metastatic insulinomas is rare. We present a case of severe hypoglycemia due to metastatic insulinoma.

Case Presentation: A 55-year old woman presented for...
A 48 year old female presented to the hospital in an unresponsive state, and found to have a blood glucose (BG) level <30mg/dL. For four months prior, she recalled having symptoms of sleepiness, perioral paresthesia, “feeling drugged”, confusion and “spotty vision” with prolonged fasting. Her symptoms resolved with food and normalization of her BG, confirming Whipple’s Triad. During her hospitalization, she had confirmed low BG with inappropriately elevated insulin and C-peptide levels. An MRI with multiplanar imaging showed no evidence of a pancreatic mass or inflammation. An abdominal CT scan with and without contrast was also negative for any pancreatic abnormalities. Her pituitary, thyroid, and adrenal function were all normal. When she presented to me, low BG in the setting of elevated insulin and C-peptide levels were again confirmed as an outpatient, after an overnight fast. Her Beta-Hydroxybutyrate level was normal at 0.06mmol/L (reference 0.28 or less) during an episode of hypoglycemia. Her insulin antibody level and sulfonylurea screen were both negative. Her proinsulin level was elevated at 99.7pmol/L (reference 18.8 or less). She finally had an endoscopic ultrasound, which was suspicious for a 10mm x 8mm lesion at the head of the pancreas near the bile duct; four fine-needle aspiration biopsies showed results consistent with a neuroendocrine tumor, which stained positive for chromogranin and synaptophysin. Calcium and prolactin levels were normal, making MEN type 1 less likely. Her symptoms were controlled with conservative dietary measures and Diazoxide. She underwent a laparoscopic enucleation of a solitary 1.5cm x 1.4cm x 0.9cm ovoid insulinoma, confined to the pancreas and without metastases. The pathology confirmed a benign, well-differentiated, grade 1 neuroendocrine tumor (Ki-67 labeling index <2%). One month postoperatively, she had complete resolution of her hypoglycemia, with an average BG of 93mg/dL (range 78-119mg/dL). 

Discussion: Insulinomas represent a rare subtype of pancreatic neuroendocrine tumors, with a reported incidence of 4 cases per 1 million patient-years. The average age of diagnosis is 47 years, with women accounting for 59% of the cases. Surgical excision is the treatment of choice, and usually curative when sporadic.

Conclusion: We report a case of a 48 year old female with a benign well-differentiated insulinoma at the head of the pancreas. She presented with classic neuroglycopenic symptoms, and treated conservatively with diet and Diazoxide. The insulinoma was discovered by endoscopic ultrasound, and symptoms resolved after enucleation of the mass. Microscopic pathology was consistent with a well-differentiated neuroendocrine tumor.

Abstract #407

CASE REPORT OF AN INSULINOMA IN A 48 YEAR-OLD FEMALE

Ashley Thorsell, MD, Matthew Levine, MD, FACE

Scripps Clinic

Case Presentation: A 48 year old female presented to the hospital in an unresponsive state, and found to have a blood glucose (BG) level <30mg/dL. For four months prior, she recalled having symptoms of sleepiness, perioral
Abstract #408

HYPOGLYCEMIA ASSOCIATED WITH TIGECYCLINE USE IN A PATIENT WITH TYPE 1 DIABETES

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Case Presentation: A 65 year-old man with type 1 diabetes (T1DM) for 48 years was admitted for rectal bleeding. Subcutaneous insulin infusion via insulin pump kept glucose levels generally well-controlled with occasional hyperglycemia, but only rare hypoglycemia, and a HbA1c of 6.8% prior to admission. Basal insulin requirements were 19.2 units/day. The hospital course was complicated by bacteremia requiring tigecycline (TIG) therapy. Starting on day 2 of TIG therapy, daily hypoglycemia (39-62 mg/dl) occurred without a change in pump settings. Hypoglycemia continued for the duration of TIG therapy (6 days). As a consequence, the insulin pump was discontinued and basal insulin dose was changed to 14 units/day of glargine. After TIG was discontinued glucose control worsened, with multiple finger stick glucose readings in the 200-400 mg/dl range, requiring resumption of the insulin pump and increase in basal insulin back to 19.2 units/day. During the rest of the hospital stay, no further hypoglycemic events were noted and glucose levels remained controlled with occasional hyperglycemic excursions.

Discussion: This is the second case of potential TIG-induced hypoglycemia in a patient with T1DM that has been reported by our group. TIG has structural resemblance to tetracycline-class antibiotics and hypoglycemia has been reported with several members of the tetracycline group. Hypoglycemia was not a common adverse event associated with TIG use in phase II and III studies. The package insert from the manufacturer, however, reports hypoglycemia to be a rare occurrence in patients treated with TIG. Moreover, 11 co-occurrences of hypoglycemia associated with TIG were reported in FDA Adverse Event Reporting System from 2004-2009, although this does not necessarily prove a causal relationship.

Conclusion: Even though hypoglycemia is a rare complication associated with TIG, its prevalence may be higher in patients with T1DM receiving the drug. Patients with T1DM treated with TIG should be closely monitored for hypoglycemia.

Abstract #409

CONSERVATIVE MANAGEMENT IN PERSISTENT HYPOGLYCEMIA: A COST EFFECTIVE OPTION.

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SUNY Upstate Medical University

Objective: Obesity rates have reached pandemic proportions worldwide and currently affects nearly 40% of the adult US population. Consequently to this rise, 200,000 bariatric surgeries are performed in this country annually. Concern for post-gastric bypass surgery (PGBS) hypoglycemia is increasing, with uncertainty as to the pathophysiological mechanisms. An estimate of <1% of PGBS population develops severe hypoglycemia. This complication can be devastating, and an optimal management strategy is required.

Case Presentation: A 50 year old Caucasian female was found unconscious at home. She had lightheadedness after having her breakfast that morning. The EMS reported blood glucose (BG) of 40 mg/dL. She was resuscitated and monitored intensively in ICU and her BG persisted between 50-110 mg/dl for 15 days despite continuous D5-D10 infusion and octreotide. She continued to feel weak, fatigued, with episodic dizziness and sweating. She had a gastric bypass surgery one year ago, with no diabetes mellitus or previous syncopal episodes. Her physical examination, preliminary labs and CT head were unremarkable except low BG on BMP. A 72 hour fasting test was discontinued in 2 hours due to symptomatic hypoglycemia with BG 47 mg/dL, and simultaneous blood work showed normal insulin (8.4 uU/mL), proinsulin (6.0 pmol/L) and C peptide levels (3.0 ng/mL) with low beta-hydroxybutyrate (0.03 mmol/L), consistent with Insulinoma vs noninsulinoma pancreatogenous hypoglycemia syndrome (NIPHS). CT abdomen and an octreotide scan were normal. The patient elected not to undergo invasive testing with selective arterial calcium stimulation test (SACST) or diagnostic and therapeutic laparotomies. She agreed to initiate conservative management with frequent small meals of high protein content without large carbohydrate loads. Since then, her BG has been well maintained with no new syncopal episodes.

Discussion: This unique case of persistent hypoglycemia despite continuous D10 infusion supports the hypothesis of increased stimulation of insulin release in NIPHS. CT abdomen and an octreotide scan were normal. The patient elected not to undergo invasive testing with selective arterial calcium stimulation test (SACST) or endoscopic US. She agreed to initiate conservative management with frequent small meals of high protein content without large carbohydrate loads. Since then, her BG has been well maintained with no new syncopal episodes.
Conclusion: Hypoglycemia following gastric bypass can be a serious complication. We expect that the incidence of this will increase, with increasing rates of gastric bypass procedures. Raising awareness of an effective conservative approach with dietary modification is helpful for successful and safe management. Avoiding expensive and invasive studies can reduce patient morbidity, utilize less hospital resources and maintain a good quality of life.

Abstract #410

A RARE CASE OF NON ISLET CELL TUMOR HYPOGLYCEMIA (NICTH)

Brij Makkar, MD, Ajay Gainda, MD, Deepak Gupta, MD

Case Presentation: We are reporting an extremely rare case of Non Islet Cell Tumor Hypoglycemia (NICTH). This 62 years male patient presented with altered sensorium since 2 hours. Patient had adenocarcinoma of prostate in past, for which he had bilateral orchidectomy with prostate resection 7 years prior to admission. He was on fosfestrol since then. He did not have any other illness, and was not on any drugs which could have possibly caused hypoglycemia. At time of admission he was afebrile and his pulse, BP and respiration were normal. His blood glucose was 48 mg/dl, which increased to 132 mg/dl after glucose infusion. Patient regained consciousness and was admitted for investigations & management. His hemogram, liver, kidney and thyroid functions were normal. Serum PSA (184) was increased. He continued to have recurrent hypoglycemia during hospital stay of 2 weeks. Further investigations - ultrasonography revealed multiple lymph nodes in abdomen, NCCT of head showed cerebral atrophy, and MRI brain was inconclusive. PET-CT scan showed local residual disease with bilateral lung, bone and lymph nodes (pelvic and mediastinal) metastases. Serum insulin, c-peptide, and cortisol levels were normal, and IGF-1 levels were low (<25U/ml, normal 55-125). Finally a diagnosis of NICTH was made.

Discussion: Tumor associated hypoglycemia is a rare clinical entity which may be caused by insulin producing islet cell tumors, or may be a paraneoplastic manifestation of extra-pancreatic tumors, termed as NICTH. NICTH is extremely rare, typically affects elderly patients with advanced cancers, and presents with constant/recurrent hypoglycemia with glucose levels going as low as 20mg/dl. Occasionally, hypoglycemia may predate the diagnosis of underlying tumor. Almost half cases are linked to large pleural or abdominal mesenchymal tumors, classical prototype being retroperitoneal fibrosarcoma. Other reported associations include hepatocarcinomas, adrenal carcinomas, and rarely gastrointestinal and genitor-urinary tumors, and lymphomas. Hypoglycemia associated with prostate cancer is extremely rare and only 3 such cases have been described, and the possible cause is increased IGF2 activity. Mechanisms responsible for hypoglycemia in NICTH may be insulin like activity of IGF2, low levels of GH and IGF1, increased ratio of IGF2:IGF1, a decreased hepatic glucose output, excessive glucose consumption by a large tumor, and inadequate production of counter-regulatory. Management involves treatment of underlying tumor, and use of glucocorticoids, glucagon, GH or Somatostatin analogues for recurrent/chronic hypoglycemia.

Conclusion: This patient improved with oral prednisolone, and blood glucose at discharge was 132mg/dl.

Abstract #411

A CASE OF INSULINOMA ILLUSTRATING THE SIGNIFICANCE OF NEUROGLYCOPENIA IN THE DIAGNOSTIC EVALUATION OF PATIENTS WITH SUSPECTED HYPOGLYCEMIA

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SAMMC

Case Presentation: A 21-year old man was referred for endocrine evaluation by his PCM; he had presented with history of two episodes of syncope concerning for hypoglycemia. On the day of first fainting episode, 6 months ago, he ate little food in the morning and then participated in a group exercise, subsequently he felt he needed some food; became dizzy and then passed out while waiting in line in a restaurant. BG obtained by EMS was 38 mg/dl. For the more recent second episode, he woke up feeling weird and the next thing he could recall was waking up in a hospital. Per records, patient responded to IV D50 with improved mental alertness, then became more combative when dropping his blood sugar again; responded to additional D50, diazepam and haloperidol. The endocrinologist who saw him at that time noted fasting glucose in the 40-50’s mg/dl, felt this was normal, and that hypoglycemia and syncope could have been due to prolonged fasting and strenuous activities; concluded that an extended workup for hypoglycemia would be premature. Patient was healthy until 6 months ago; wakes up in the morning feeling “yucky” with trouble comprehending; obtains relief by drinking juice. There has been gradual weight gain, 17 lbs over 9 months. On exam: Conscious, alert and oriented X3, no focal neurological deficit; BP 125/78, HR 65, Wt 211 lbs, BMI 26.2 kg/m2. Impression: Neuroglycopenia, requires diagnostic workup for hypoglycemia. He was admitted for a prolonged fast; within 24 hrs became symptomatic, had lightheadedness...
and confusion; BG values 30’s - 40’s mg/dl; he responded promptly to D50. His insulin levels ranged from 57.8 to 94 mcIU/ml; C-peptide 5.8 to 6.1 ng/ml, and proinsulin levels were persistently above 800 pmol/L; Beta(OH) butyrate 0.39 to 0.55 mmol/L; BG rose by more than 25 mg/dl after glucagon injection. Sulfonylurea screening and insulin antibody testing were negative. The findings were consistent with hypoglycemia from endogenous hyperinsulinism, most likely an insulinoma. Abd CT scan with pancreatic protocol was negative. EUS revealed 2 pancreatic lesions in the body and uncinate process. FNA cytology of larger 1.5 cm lesion was consistent with a neuroendocrine neoplasm. He underwent a Whipple resection. Histopathology showed a unifocal 1.8 cm tumor with an immunohistochemical staining pattern characteristic of an insulinoma.

Discussion: The two episodes of neuroglycopenia in this patient suspected to have hypoglycemia warrant a diagnostic evaluation.

Conclusion: Most patients presenting with only neurogenic symptoms with no documented low BG are unlikely to have a hypoglycemic disorder; however, one episode of neuroglycopenia should prompt a diagnostic evaluation for hypoglycemia.

Abstract #412

SPONTANEOUS RESOLUTION OF TYPE B INSULIN RESISTANCE SYNDROME

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Objective: To present a case of Type B insulin resistance syndrome presenting with hypoglycemia.

Case Presentation: A 32 year old female with a 3 year history of Type B insulin resistance syndrome (proven by presence of antibodies to insulin receptor done by NIH research laboratory) and requiring high doses of insulin (1ml of U-500 human regular insulin four times a day) was admitted with altered mental status. Last insulin dose was 24 hours prior to presentation. Family reported that the patient was in good glycemic control but had been frequently hypoglycemic in last few days. Physical exam showed a thin woman with acanthosis nigricans, blood pressure-114/61 mm Hg, pulse rate-118, temperature-102.6 F, weight 97 pounds and BMI of 17 kg/m2. Point of care capillary finger stick glucose was <40 g/dL. Dextrose and glucagon were administered. Urine showed pyuria and grew Pseudomonas aeruginosa which was treated with antibiotics. Initially hypoglycemia was felt to be a result of high doses of insulin in the setting of sepsis and inadequate nutrition. Labs performed 48 hours after her last insulin dose: Glucose 239 mg/dl; c-peptide 7 ng/ml (normal 0.8-3.5); Total insulin 532 µIU/ml (3-19); Pro-insulin 46 pmol/L (<26.8); Insulin antibodies <0.4 U/mL (<0.4) and Hemoglobin A1c 6.2%. Adrenal insufficiency was ruled out with appropriate response to ACTH stimulation test: (cortisol increased from 9 mcg/dl to 22.3 mcg/dl after 60 minutes). Hypoglycemia resolved upon complete cessation of insulin. The patient’s blood sugars were subsequently stabilized with a small dose of insulin glargine 5 units at bedtime and she was discharged home on this regimen (prior to hospitalization she required 2000 units of insulin/day).

Discussion: Type B insulin resistance results from auto antibodies against insulin receptors that act as antagonists causing severe insulin resistance. Caution must be exercised as during the disease course the antibodies may disappear making subjects susceptible to hypoglycemia from exogenous insulin. This is the likely scenario in our case. Lack of a commercially available universal assay for the receptor antibodies makes the diagnosis a challenge. Insulin receptor auto- antibodies can also act as partial agonists and cause intermittent hypoglycemia. However, the hypoglycemia in the patient did not recur after the resolution of sepsis and cessation of high dose insulin. This argues against the patient’s antibodies having an agonistic action.

Conclusion: We conclude that this patient had spontaneous resolution of type B insulin resistance syndrome.

Abstract #413

ACUTE HYPOGLYCEMIC UNAWARENESS ASSOCIATED WITH LACTATE EXCESS

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Objective: Hypoglycemia with elevated serum lactate is a reported complication of hematologic malignancies. This association is a consequence of the Warburg effect with increased glycolytic flux. We report a case of asymptomatic acute hypoglycemia in a patient with diffuse large B-cell lymphoma.

Case Presentation: A 73-year-old male with chronic lymphocytic leukemia presents to our institution with fever, nausea and pleural effusion. One year prior a biopsy of an abdominal mass revealed diffuse large B-cell lymphoma. Six cycles of R-CHOP chemotherapy
induced remission. Three months prior to presentation he noted a mandibular mass, which was found to be a recurrence of lymphoma. He failed therapy with a PI3 kinase inhibitor, bendamustine and lenalidomide. He did not receive glucocorticoid therapy. Physical examination demonstrated a 5x10 cm palpable mandibular mass, hepatosplenomegaly, and diffuse muscle wasting. The admission glucose was 93 mg/dL, but on hospital day 8 a random glucose of 47 mg/dL, was reported by the lab. He remained asymptomatic. Diagnostic evaluation demonstrated insulin < 1.0 uIU/mL and C-peptide 0.7 pg/mL with glucose 58 mg/dL. Continuous intravenous dextrose infusion titrated to 7 g/hr was administered along with intermittent D50W boluses. The glucose remained <60 mg/dL. Lactic acid concentration rose from 3.5 to 13.8 mmol/L during the glucose infusions. There was no evidence of sepsis or significant impairment of liver or kidney function. Dynamic tests confirmed an intact adrenal axis. The patient and his family refused further intensive care therapy. Further laboratory testing was discontinued. He expired on hospital day 12.

Discussion: Hypoglycemia with elevated lactate can be seen with hematologic malignancies. A possible explanation is excessive consumption of glucose with subsequent lactate production caused by the tumor’s shift to a glycolytic state, a phenomenon called the Warburg effect. The mechanism of hypoglycemia in this case was independent of the actions of insulin. It resulted from accelerated glucose utilization through aerobic glycolysis that exceeded glucose delivery into the circulation from hepatic and renal sources.

Conclusion: Hypoglycemia with acute unawareness is an uncommon phenomenon. In our case, we hypothesize that lactate served as a fuel to the CNS and blocked the adrenergic and neuroglycopenic symptoms of hypoglycemia. For the practicing endocrinologist confronted with an asymptomatic patient with hypoglycemia, we recommend measuring lactate levels. If elevated, suspect the presence of malignancy and a Warburg effect.

Abstract #414

PSYCHOMETRIC VALIDATION OF THE FEAR OF HYPOGLYCEMIA SURVEY-II IN SINGAPORE

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Objective: To validate the Fear of Hypoglycemia Survey-II (FoH-II), originally developed and validated in the US, in Singapore.

Methods: Patients with Type I or Type II diabetes who had been on insulin treatment for at least one year at the time of the survey and were on active follow-up in the Diabetes Center at the Singapore General Hospital during their follow-up visits at the Center from September to December 2013. Eligible patients must be literate in English or Chinese, and the survey was self-administered in either of the two languages of patient’s choice. The instrument was culturally adapted with permission from its developer before it was adopted in this survey. Traditional psychometric analysis was performed to assess the reliability and validity of the instrument using SPSS 17.0.

Results: 150 eligible patients were recruited for the study (50% females, mean(SD) age 45.21(14.02) years, 63% Chinese, 12% Malays, 20% Indians, and 5% others). Mean (SD) duration of diabetes and duration of insulin treatment were 14.74(8.60) and 9.24(7.87) years respectively. 31% of the patients had at least one episode of severe hypoglycemia in the 12 months prior to the survey; 51% had at least one episode of moderate hypoglycemia in the six months before the survey; and 56% had at least one episode of mild hypoglycemia in the one month before the survey. The Chronbach’s alpha for the worry subscale of the instrument was .946 and that for the behavior subscale was .838. The worry subscale has significant floor effect (16% scoring 0). No floor effect was found in the behavior subscale (8% scoring 0) or ceiling effect in either subscale. In contrast to the two-factor structure in the original instrument, exploratory factor analysis of our data suggests a five-factor solution with the original worry subscale splitting into two factors, and the original behavior subscale splitting into three. These five factors explained 55% of the total variance.

Discussion: Although five factors have emerged from our data, they are nested under the original two subscales—worry and behavior—and are specific types of them. Therefore, our findings confirm rather than contradict the conception of fear of hypoglycemia as consisting of two broadly defined components—worry and behavior. The fact that there was no cross-loading between the original worry items and behavior items in our five-factor solution lends further evidence to this interpretation.

Conclusion: Our data shows that FoH Survey-II is a reliable and valid instrument to measure the fear of hypoglycemia for diabetic patients on insulin treatment in Singapore, but a five-factor structure seems more informative than the original two-factor structure in our local context.
GLYCEROL KINASE DEFICIENCY IN A MAN CAUSING PSEUDOHYPERTRIGLYCEREMIA

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SAVAHCS

Objective: Glycerol kinase deficiency (GKD) is a rare X-linked disorder characterized by elevated plasma and urine glycerol, affecting fewer than 200,000 people in the United States. Three forms have been recognized; infantile, juvenile, and adult. It may occur in isolation (juvenile and adult) caused by mutation of the glycerol kinase (GK) gene, or as part of a contiguous gene syndrome (infantile) involving the DAX1 and DMD genes on Xp21.3. The presentation of isolated GKD is varied, ranging from asymptomatic individuals to those who experience episodes of vomiting, acidosis and lethargy, even progressing to coma. Asymptomatic patients are often misdiagnosed with hypertriglyceridemia as elevated glycerol levels are erroneously interpreted by most assay systems to reflect high triglycerides.

Case Presentation: A 71 year old man with a long standing diagnosis of hypertriglyceridemia (>1000 mg/dl) was treated with fibric acid derivatives, statins, niacin and omega-3 fatty acids without significant effect. He was referred to endocrinology clinic at which time it was learned that his brother had been diagnosed with GKD.

Discussion: Initial testing by lipoprotein electrophoresis was consistent with Type IV hyperlipoproteinemia. However, due to a high suspicion of GKD, “glycerol-blanked” triglyceride measurements were performed revealing only a modest elevation in serum triglycerides to 150 mg/dl (<140 mg/dl). Moreover, it was noted that the patient’s serum was clear rather than lipemic or cloudy as would be expected with actual hypertriglyceridemia. Subsequent FISH analysis (Medical Genetics Lab, BCM, Houston, TX) detected the GK gene at Xp21 (GK x1) with no evidence of deletion or duplication in the glycerol kinase critical region. Since FISH analysis cannot detect a balanced translocation or a point mutation additional gene sequence analysis was performed (Gene Dx, Gaithersberg, MD). This analysis was positive for a variant of the A305V missense mutation in the GK gene, which has been associated with GKD.

Conclusion: GKD was confirmed in our patient by detection of a variant gene missense mutation in the GK gene. While the patient remained asymptomatic, the resulting hyperglycerolemia was mistaken for refractory hypertriglyceridemia (pseudohypertriglyceridemia) for many years which is often the case for patients with isolated GKD detected in adulthood. Glycerol kinase deficiency should be considered when persistent elevations in triglycerides do not respond to aggressive pharmacological and dietary intervention.

Abstract #501

DISCORDANCE BETWEEN LDL CHOLESTEROL (LDL-C) AND LDL PARTICLE NUMBER (LDL-P) IN YOUTH

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Objective: The increased prevalence of obesity among children has led to a rise in the number of youth referred to endocrinologists with lipid abnormalities. Elevations in plasma triglycerides (TG) are commonly seen however, LDL cholesterol (LDL-C) levels are often within recommended levels. LDL particle number (LDL-P) provides an alternate measure of LDL that correlates more strongly with cardiovascular events than LDL-C, particularly in adult patients with metabolic disease and high TG. The ability to identify children at risk for developing premature atherosclerosis is of clinical importance. The objective of this study was to evaluate discordance between measures of LDL in a cohort of youth.

Methods: Data were derived from a single laboratory database (Cook Children’s Medical Center). Serum samples from patients referred to the medical center for endocrine disorders between January 2012 and October 2013 were analyzed for lipids using standard automated methods and for lipoprotein particle concentrations using nuclear magnetic resonance spectroscopy (NMR).

Results: Among the 799 patients identified, 53% were male and the mean age was 11.7 + 3.2 years. Mean LDL-C was 95 + 32 mg/dL, LDL-P was 1392 + 482 nmol/L, and TG were 123 + 74 mg/dL. These values were not significantly different between boys and girls however LDL-C and LDL-P levels tended to decrease in boys and increase in girls during the teen years, presumably related to the onset of puberty. Overall, 88% of children had LDL-C levels <130 mg/dL and 61% had levels <100 mg/dL. In contrast, only 47% had comparable LDL-P levels <1300 nmol/L while 21% had LDL-P levels <1000 nmol/L. Among children with LDL-C levels <100 mg/dL, 68% had discordantly high LDL-P levels (>1000 nmol/L) whereas 47% with LDL-C levels <130 mg/dL had discordantly high LDL-P levels (>1300 nmol/L). TG were elevated (>150 mg/dL) in 30% of children and those
with elevated TG levels had lower LDL-C levels (90 vs. 97 mg/dL, p<0.01) but higher LDL-P levels (1711 vs. 1256 nmol/L, p<0.0001) compared to children whose TG were <150 mg/dL.

**Discussion:** Considerable discordance between LDL measures (LDL-C and LDL-P) was observed in youth, particularly in those with elevated TG levels.

**Conclusion:** The presence of discordance in children may predispose them to previously unrecognized atherogenic burden leading to considerable LDL-attributable cardiovascular risk as adults.

**Abstract #502**

**REFRACTORY HYPERTENSION CAUSED BY CO-EXISTING RENOVASCULAR DISEASE AND CONN’S SYNDROME**

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**Case Presentation:** Renovascular disease (RVD) and primary hyperaldosteronism (PHA) are two common etiologies of secondary blood pressure elevation in patients with refractory hypertension. However, little is published in the peer reviewed literature regarding the co-occurrence of RVD and PHA. We present a case of persistent hypertension and hypokalemia after successful bilateral percutaneous renal angioplasty (PTRA) that was due to Conn’s syndrome.

A 54-year-old female with resistant hypertension of approximately 30 years duration underwent renal artery angiography as part of screening for a selective renal sympathectomy study protocol and was diagnosed with bilateral renal artery fibromuscular dysplasia. Bilateral PTRA was performed with restoration of normal blood flow in both renal arteries. However, severe hypertension and hypokalemia persisted after the procedure, prompting endocrinology referral. Simultaneous morning measurements of plasma aldosterone (PA) and plasma renin activity (PRA) were 25 ng/dL and 0.09 ng/mL/hr, respectively, and PA/PRA ratio was 278. Urine 24 hr aldosterone was elevated at 15.3 μg (normal < 12 μg/d). Contrast enhanced computed tomography (CT) of the abdomen revealed a 5 mm left adrenal nodule. Adrenal vein sampling was subsequently performed, and the left:right ratio of aldosterone/cortisol ratios was 7.96, indicating a diagnosis of Conn’s syndrome with left adrenal aldosteronoma. Spironolactone was then added to the patient’s antihypertensive regimen. The patient elected to undergo laparoscopic left adrenalectomy, and aldosteronoma was confirmed on post-surgical histopathological evaluation. After surgery, hypokalemia completely resolved. The patient was taking five antihypertensive medications (spironolactone, clonidine, olmesartan, amlodipine, and hydralazine) before surgery, and all but clonidine have been stopped, with clonidine being carefully tapered.

**Discussion:** Significant residual hypertension may persist in close to half of patients with RVD after technically successful PTRA that restores normal renal artery blood flow. Given high prevalence (10-20%) in patients with refractory hypertension, PHA is an important consideration in the differential diagnosis of PTRA patients who fail to experience significant improvement in blood pressure after the procedure. The only patient series found on search of the peer reviewed literature documented a 29% (7/24) prevalence of PHA in patients with residual hypertension after PTRA.

**Conclusion:** This case demonstrates that RVD and PHA may occur together in patients with refractory hypertension and that PHA may be the etiology of persistent hypertension in RVD patients who fail to respond to PTRA.

**Abstract #503**

**CIPROFLOXACIN INDUCED POLYMORPHIC VENTRICULAR TACHYCARDIA IN HYPOPARATHYROIDISM**

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**Case Presentation:** A 38-year-old female presented to the emergency room with acute intractable vomiting associated with diffuse abdominal pain. Her history was pertinent for hypoparathyroidism related to parathyroid removal during thyroidectomy twenty years earlier. Laboratory testing revealed a potassium of 2.8 mEq/L (3.5-5.5), magnesium 2.1 mg/dL (1.8-2.4), calcium 9.3 mg/dL (8.8-10.3), WBC 15.7 K/UL (3.6-11.0), lactic acid 2.5 mmol/L (0.4-2.0), phosphorous 4.9 mg/dL (2.3-5.0), albumin 5.1 g/dL (3.2-5) and pyuria. Electrocardiogram revealed sinus tachycardia with a heart rate of 102 bpm (70-90) and premature ventricular complexes with a QT interval of 516 ms (451-470). CT scan of the abdomen demonstrated a partial small bowel obstruction and findings suspicious for infectious enteritis. Subsequently she was treated with intravenous ciprofloxacin and potassium. A previous electrocardiogram showed sinus rhythm with incomplete right bundle branch block, with a QT interval of 422 ms. Even with aggressive replacement the patient’s potassium dropped to 2.4 mEq/L, magnesium to 1.7 mg/dL and calcium to 7.2 mg/dL, albumin to 3.6 g/dL and WBC rose to 17.3 K/UL. Telemetry demonstrated polymorphic ventricular tachycardia with a QT interval...
of 570 ms. She was asymptomatic and was treated with amiodarone and magnesium sulfate. Ciprofloxacin was discontinued and replaced with piperacillin-tazobactam. Her symptoms of abdominal pain and vomiting improved, and with aggressive electrolyte replacement, her subsequent electrocardiogram showed resolution of polymorphic ventricular tachycardia with QT interval of 472 ms.

Discussion: Hypoparathyroidism is a potential complication after total thyroidectomy. Patients are at risk of developing muscle spasms, neuromuscular instability, seizures and hypocalcemia-induced Torsades de Pointes from prolonged QT interval. Hypocalcemia prolongs phase two of the action potential, resulting in prolongation of QT interval which is associated with early after-repolarizations and induces dysrhythmias. Torsades de Pointes can also be triggered by hypokalemia or hypomagnesaemia but less commonly by ciprofloxacin, which is commonly used antibiotic. This case highlights a rare but potentially fatal complication of this antibiotic in the setting of hypoparathyroidism. Ciprofloxacin may have triggered the polymorphic ventricular arrhythmia in our patient who was already at risk for a significant dysrhythmia due to hypokalemia and hypocalcemia.

Conclusion: Ciprofloxacin should be avoided in patients with severe electrolyte abnormalities, including patients with hypoparathyroidism to prevent dysrhythmias. Immediate electrolyte repletion and cardiac monitoring is essential in these patients.

Abstract #504

A CASE OF SECONDARY HYPERTENSION DUE TO UNILATERAL RENAL ARTERY STENOSIS SUCCESSFULLY TREATED WITH RENAL ARTERY ANGIOPLASTY

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Case Presentation: Approximately 5 to 10 percent of adults with hypertension have a secondary cause. In young adults, especially women, renal artery stenosis caused by fibromuscular dysplasia (FMD) is one of the most common etiologies of secondary hypertension. A 36-year-old Caucasian female was referred for evaluation of recent onset hypertension and hypokalemia. Symptoms included fatigue, profuse sweating, muscle cramps, palpitations, dizziness, and near syncope spells. Antihypertensive medications included carvedilol, amlodipine and hydrochlorothiazide (HCTZ). Serum potassium level was very low (2.8 mM), prompting HCTZ to be stopped and supplemental potassium to be started. The patient required 120 mEq/d potassium to achieve eukalemia. Additional evaluation was notable for significant elevations of both renin activity (9.4 ng/mL/hr, 1.32-3.95) and aldosterone (120 ng/dL), indicating secondary hyperaldosteronism. Computed tomography (CT) angiogram of the renal arteries showed a focal area of severe stenosis in the left renal artery and small left kidney with diffuse cortical thinning. Age, gender, and absence of risk factors for atherosclerosis were most consistent with unilateral renal artery stenosis due to fibromuscular dysplasia. The patient decided to proceed with left percutaneous renal angioplasty (PTRA). After the procedure, she became normotensive off all blood pressure lowering medications, supplemental potassium requirement fell to 60 mEq/d, and symptoms present before treatment resolved. Repeat laboratory screening four months later showed moderate persistent secondary hyperaldosteronism, with aldosterone 43.8 ng/dL and renin activity 2.24 ng/mL/hr. At six months clinical follow up, the patient remained normotensive but continued to require supplemental potassium (60 mEq/d) to prevent hypokalemia.

Discussion: FMD accounts for about 10% of all cases of renal artery stenosis, with the majority of cases diagnosed in women. Though historically considered a disease of young adults, the mean age at presentation in the United States Registry for Fibromuscular Dysplasia is 55 years. FMD is one of the most common treatable forms of hypertension and should be considered in new onset hypertension in young adults. The primary treatment objective is adequate control of blood pressure to prevent complications of long-standing poorly controlled hypertension.

Conclusion: PTRA is the preferred choice of treatment for symptomatic renal FMD. However, even after a technically successful procedure that restores renal artery blood flow, patients need prospective follow up to carefully monitor for resolution of hypertension and hypokalemia.

Abstract #505

THE EFFECT OF INSULIN ON CIRCULATING PCSK9 IN POSTMENOPAUSAL OBESE WOMEN

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Objective: The purpose of this study was to investigate the effects of chronic and acute hyperinsulinemia on PCSK9 in a large cohort of human subjects as well as at a cellular level.

Methods: The in vivo effect of hyperinsulinemia on plasma PCSK9 concentration was studied using EHC
(euglycemic-hyperinsulinemic clamps) in 82 non diabetic post menopausal obese patients. We studied the in vitro effects of insulin stimulation on PCSK9 mRNA as well as on protein expression and secretion in HepG2 and Huh7 cells. Results: Analysis of the pre and post-clamp data revealed a 15.4% (p<0.001) lowering of plasma PCSK9 concentration by insulin. Cellular studies showed that after insulin stimulation, levels of PCSK9 mRNA were 25% lower in HepG2 cells (p<0.027) and 59% lower in Huh7 cells (p<0.01). Intracellular concentration of PCSK9 were 10% lower in HepG2 cells (p<0.05) and 35% lower in Huh7 cells (p<0.05).

Discussion: PCSK9 (Proprotein convertase subtilisin/kexin type 9) promotes the degradation of the LDLR (LDL receptor) in hepatocytes, leading to an increase in plasma LDL-C (LDL cholesterol). Previous animal studies have shown that insulin stimulates PCSK9 transcription and observational human studies showed a positive correlation between plasma PCSK9 concentration and fasting insulinemia.

Conclusion: Our results show an inhibitory effect of acute hyperinsulinemia on PCSK9 in humans both in vitro and in vivo. This data may assist in evaluating PCSK9 levels in individuals on insulin therapy.

Abstract #506

THE EFFECT OF STATIN USE IN SEVERITY OF PANCREATITIS

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Objective: The aim of this study was to examine the effect of statin use on the severity of acute pancreatitis.

Methods: A total of 135 patients with the diagnosis of acute pancreatitis were included in this retrospective study. Relevant clinical data were collected. Patients were divided into two groups according to statin use or non-use and the severity of acute pancreatitis was compared. Severe pancreatitis was defined as a Ranson score at any time ≥ 3. Appropriate descriptive statistics and statistical tests were performed. Statistical significance was defined as a p value < 0.05.

Results: The cohort consisted of 58% (78 of 135) men with a mean (SD) age of 50 (18) years. Of the 135 patients, 4 (2.96%) had gallstone pancreatitis, 4 (2.96%) had alcoholic pancreatitis, and 127 (94.07%) had pancreatitis of unknown etiology. Median (interquartile range) Ranson score on admission and 48 hours afterwards were 2 (1,3) and 1 (0,2), respectively. On admission, there was no statistically significant difference in statin user group and non-statin user group between the mild-to-moderate acute pancreatitis group and the severe acute pancreatitis group.

Likewise, at 48 hours after admission, the percentage of patients with statin use was not statistically different (p = 0.415) between the two severity groups. Multivariable regression analysis showed that female gender was the only independent variable associated with a higher severity of pancreatitis (p = 0.046).

Discussion: Acute pancreatitis is a common gastrointestinal disease often seen in daily practice. Although the precise mechanism of pancreatitis is still not fully understood, it is believed that the inflammatory response via phospholipase A2, cyclohexanone, and neutrophils plays a role. Statin drugs have previously been shown to very significantly reduce cardiovascular disease events and become frontline therapy for diabetes mellitus, hypertension, and other known cardiovascular disease risk factors. Recent study showed that statin has the potential effect in decreasing inflammation. This pilot study demonstrates that statin use has no effect on decreasing the severity of acute pancreatitis. Female gender was associated with a higher severity of acute pancreatitis in the first 48 hours after admission.

Conclusion: This pilot study demonstrates that statin use has no effect on decreasing the severity of acute pancreatitis. Female gender was associated with a higher severity of acute pancreatitis in the first 48 hours after admission.

Abstract #507

EFFICACY AND SAFETY OF LONGER-TERM, MONTHLY ADMINISTRATION OF THE PCSK9 INHIBITOR EVOLOCUMAB IN SUBJECTS WITH DYSGLYCEMIA OR METABOLIC SYNDROME

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Objective: Patients with dysglycemia receive significant clinical benefits from aggressive lipid lowering with statins; however, high-intensity statins have been associated with worsening glucose metabolism. We
investigated the effects of evolocumab (AMG 145, a fully human monoclonal antibody to PCSK9) on lipid parameters, fasting plasma glucose (FPG), and HbA1C.

Methods: In the Open-Label Study of Long-term Evaluation Against LDL-C (OSLER), 1104 patients that participated in a parent phase 2 study were randomized 2:1 to open-label subcutaneous evolocumab 420 mg monthly with standard of care (SOC) or SOC alone for 1 year. Of the subjects with a history of type 2 diabetes mellitus (T2DM, recorded at baseline; n = 109), impaired fasting glucose (IFG, FPG 110-126 and no T2DM; n = 134), or metabolic syndrome (MetS, ≥3 risk factors, no T2DM; n = 425) from OSLER, 90, 112, and 337, respectively, had an observed week 48 LDL-C value.

Results: T2DM, IFG, and MetS patients on evolocumab + SOC in OSLER had mean LDL-C changes from parent-study baseline (SE) at week 48 of -46.1(3.3)%, -51.2(2.5)%, and -53.6(1.4)%, respectively. In subjects that received SOC alone, changes were: -4.8(4.2)% (T2DM); 1.6(3.6)% (IFG); and -2.6(2.0)% (MetS). Adverse event (AE) rates observed in OSLER among patients with T2DM, IFG, or MetS were 76% (evolocumab + SOC) and 71% (SOC alone); serious AEs occurred in 8% and 7% of patients, respectively. Patients that received evolocumab + SOC did not demonstrate significant changes in FPG (median change in mg/dL [Q1, Q3] EvoMab + SOC: 8 [-3, 24] T2DM; -4 [-12, 4] IFG; 1 [-6, 8] MetS) or (when obtained at parent-study baseline visit) in HbA1C (median change in percentage [Q1, Q3] EvoMab + SOC: 0.2 [-0.2, 0.6] T2DM; 0.0 [-0.1, 0.2] IFG; 0.0 [-0.1, 0.2] MetS) from parent-study baseline to week 48.

Discussion: Patients with dysglycemia and metabolic syndrome are at higher risk for cardiovascular events, and benefit from LDL-C reduction. When assessing these patients in OSLER, treatment with evolocumab resulted in an incremental LDL-C reduction of approximately 50% compared to parent-study baseline without associated changes in glucose metabolism. Based on these findings, evolocumab may be a therapeutic option to effectively lower LDL-C in patients with dysglycemia or metabolic syndrome.

Conclusion: Monthly evolocumab treatment resulted in comparable LDL-C reductions among subjects with T2DM, IFG, or MetS at 48 weeks with no notable changes in glycemic control, and was well tolerated.

Abstract #508
SUCCESSFUL TREATMENT OF AN ACUTE HYPERTRIGLYCERIDEMIA-INDUCED PANCREATITIS USING INSULIN AND HEPARIN INFUSION

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Objective: Hypertriglyceridemia over 1,000 mg/dl can provoke acute pancreatitis and its persistence can worsen the clinical outcome. There are no clinical guidelines to severe hypertriglyceridemia, but therapy with insulin, heparin, a combination of both, plasmapheresis, or octreotide have been tested successfully.

Methods: We report a case of a 43-year-old female with clinical acute pancreatitis along with incidental finding of an severe hypertriglyceridemia, who had a good outcome after treatment with insulin, and heparin intravenous infusion.

Case Presentation: A 43-year-old female with previous history of acute pancreatitis, was admitted to Intensive Care Unit (ICU) because of severe abdominal pain, anorexia, vomiting, and hyperventilation. She was diagnosed with acute pancreatitis. Her laboratory tests revealed: Amylase: 1740 (25-125 IU/L), Lipase: 536 (0.0-6 IU/L), Anion Gap: 10 (10-20 mmol/l), Glucose: 110 mg/dl, normal liver function panel, HbA1c: 5.2% (<5.7). Ultrasound showed evidence of pancreas edema consistent with acute pancreatitis, there was no evidence of cholelithiasis, common bile duct dilatation, or cholecystitis. Patient was diagnosed with acute pancreatitis. Her laboratory tests revealed: Amylase: 1740 (25-125 IU/L), Lipase: 536 (0.0-6 IU/L), Anion Gap: 10 (10-20 mmol/l), Glucose: 110 mg/dl, normal liver function panel, HbA1c: 5.2% (<5.7). Ultrasound showed evidence of pancreas edema consistent with acute pancreatitis, there was no evidence of cholelithiasis, common bile duct dilatation, or cholecystitis. Patient was diagnosed with acute pancreatitis. Treatment was initiated with fasting, gastric decompression by nasogastric tube, normal saline infusion with rate of 125 cc/h, and analgesia with morphine. Her fasting lipid profile the next day revealed: Triglyceride: 18000 mg/dl, and total cholesterol: 970 mg/dl. Patient was started on insulin and heparin drip, and dextrose 5% infusion. Triglyceride levels decreased progressively so insulin infusion remained at 0.5 to 1iu/kg/h. At 48 hours, TGC levels dropped to 6174, and decreased to 476 at 96 hours during her stay in ICU, there were no neurological disorders, respiratory or kidney problems, and she did not experience abdominal pain after discontinuation of analgesia within 24 hours after admission. There were no bleeding and no clinical or laboratory signs of infection.. She was discharged from the ICU after 72 hours, following clinical stabilization, and remained stable on floor where she remained hospitalized for 1 week. She was discharged with prescription of gemfibrozil 600 mg twice daily.

Discussion: In this case report, the triglyceride levels
of 18000 was successfully treated with combination of insulin and heparin drip. Both activate the lipoprotein lipase enzyme (LPL) bound to endothelium. In addition, heparin mobilizes and releases the enzyme of the endothelium to plasma. Insulin promotes the synthesis of LPL and stimulates the uptake of fatty acids released from triglyceride hydrolysis by LPL itself.

**Conclusion:** Heparin and insulin can be considered a safe treatment modality for rapidly reducing triglyceride levels.

**Abstract #509**

A STORY BEHIND THE UNUSUAL RASH

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**Case Presentation:** A 28 year old, non-smoker, morbidly obese male presented to the emergency with the complaints of severe upper abdominal pain, nausea and vomiting for a week. Detailed physical examination beside diffuse upper abdominal tenderness also revealed 3 to 5mm yellowish papules with erythematous borders and central lobulation that were distributed across the elbows, knees, truck, and buttocks and were too numerous to count. Palms and soles were spared. These rashes were pruritic, started few months back, had been getting worse over time, diagnosed as psoriasis and treated without improvement. Family history was significant for similar rash in his father, again as psoriasis and treated without improvement. His history was significant for diabetes at young age and insulin resistance, obesity, and increased coronary risk. Our patient’s genetically elevated triglyceride got worse with the new untreated diabetes resulting into acute pancreatitis. If the rash were identified appropriately and treated; and patient evaluated for associated metabolic abnormalities the pancreatitis could have been potentially avoided.

**Conclusion:** This case emphasizes the need for health care providers to be aware of the dermatologic manifestation of hyperlipidemia so that diagnosis is not missed; patient is evaluated for associated metabolic abnormalities and appropriate management initiated promptly to avoid potential complication.

**Abstract #510**

ELUCIDATION OF HYDROXYL RADICAL ROLE IN AUGMENTED RESPONSE OF ENDOTHELIN-1 IN HYPERTENSIVE RAT

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**Objective:** To evaluate role of hydroxyl radical in endothelin 1 induced hypertension in rat.

**Methods:** Endothelin 1 (ET-1) is peptides produced primarily in the endothelium and constrict blood vessels and raise blood pressure. Potentiation of responses of ET-1 by Ang-II may be due to activation of NAD(P)H oxidase, I have used Edarevone (3 mg/kg, i.p ) (Hydroxyl radical scavenger) as a tool to study the role of hydroxyl radical in the enhanced response to ET-1 in hypertensive rat and ascorbic acid (100 mg/kg,orally) as a standard drug. Hypertension was induced with the help of Ang- II infusion (10-7M) upto 2 weeks in male Sprague Dawley rats. Different parameters were evaluated. Systolic Blood Pressure was measured by Tail Cuff Method.

**Results:** Edarevone treated animals showed significantly decreases level of insulin and lipid profile. hydroxyl radical and hydrogen peroxide have been shown to induce vascular contraction. In vitro incubation of edaravone at different concentrations in Ang-II induced hypertensive rat aorta showed there was significant inhibition in pD2 value and Emax of ET-1 responses at 10-5M edaravone. This indicates that hydroxyl radical may be responsible for augmented responses of ET-1 in hypertensive rat aorta. In support to this, aorta isolated from edaravone treated rats also showed significant inhibition in pD2 value and Emax of ET-1 responses. This treatment also significantly reduces blood pressure as compared to hypertensive control rats. Ascorbic acid treatment also showed same
results as edaravone treatment. Significant decrease in SOD and catalase while significant increase in lipid peroxidation was observed in angiotensin-II administered animals compared to normal animals.

**Discussion:** These all data shows the production of oxidative stress due to angiotensin-II administration, which may have correlation with elevated blood pressure. These data confirm that hydroxyl radical generation may be responsible for augmented responses of ET-1 and increase in blood pressure in hypertensive rats. Hydroxyl radical as a key mediator for the reactive oxygen species and hypertension potentiated augmented response of endothelium-1 in thoracic aorta. Edaravone treatment attenuates the enhanced vasocontractile response.

**Conclusion:** Hydroxyl radical may involve in augmented response of endothelin-1. Thus, anti-oxidant therapy serves as adjuvant therapy for vascular complication of hypertension.

**Abstract #511**

**INHIBITION OF ENDOPLASMIC RETICULUM STRESS AND OXIDATIVE STRESS BY VITAMIN-D IN ENDOTHELIAL CELLS.**

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**Methods:** ER stress was measured using the placental secreted alkaline phosphatase (ES-TRAP) assay and oxidative stress was measured by hydroethidine fluorescence. Expression of ER stress markers, including glucose-regulated protein 78 (GRP 78), c-jun N-terminal kinase 1 (JNK1) phosphorylation, and eukaryotic initiation factor 2α (eIF2α) phosphorylation, as well as X-box binding protein-1 (XBP-1) splicing were measured in tunicamycin (TM)-treated human umbilical endothelial cells (HUVEC) treated with 1,25-dihydroxyvitamin D (1,25-(OH)2D3) and other vitamin D analogs and metabolites.

**Results:** When TM and 1,25-(OH)2D3 were added simultaneously, 1,25-(OH)2D3 prevented ER stress. However, the effect was much stronger when cells were pre-treated with 1,25-(OH)2D3 for 24-hours. Endoplasmic reticulum stress was not inhibited by 25-OH vitamin D3 (25-OHD3) or the non-calcemic vitamin D analog EB1089. However both ZK191784 and the vitamin D metabolite 24,25-dihydroxyvitamin D3 were as effective as 1,25-(OH)2D3 in preventing ER stress. Similar effects were observed when ER stress was induced by hyperglycemia (27.5 mM dextrose). All of the compounds tested, except for 25-OHD3, inhibited dextrose-induced oxidative stress.

**Discussion:** Background. Endoplasmic reticulum (ER) stress and oxidative stress promote endothelial dysfunction and atherosclerosis. Since vitamin D has been shown in several studies to lower the risk of cardiovascular disease, we examined the effects of vitamin D on endothelial cell ER stress and oxidative stress in endothelial cells.

**Conclusion:** These results suggest that vitamin D has a protective effect on vascular endothelial cells.

**Abstract #512**

**INSULIN DRIP IN SEVERE HYPERTRIGLYCERIDEMIA: RECIPE FOR BETTER PATIENT OUTCOMES & REDUCED LENGTH OF HOSPITAL STAY**

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**Objective:** To highlight the importance continuous insulin drip in managing severe Hypertriglyceridemia in reducing length of stay in hospital.

**Case Presentation:** 34 year-old healthy junk food addict was transferred to the ICU with severe ARDS from severe pancreatitis. his presenting complaints were abdominal pain, nausea, and vomiting. Patient had a special liking for junk food. His triglyceride level was >27,000 at the time of presentation. He Patient subsequently developed respiratory failure requiring mechanical ventilation. He underwent one cycle of therapeutic apheresis that brought down triglyceride levels significantly. At this point we decided to put the patient on insulin drip. Constant close monitoring with insulin drip of about 1 unit/hour resulted in triglyceride levels normalizing within 48 hours of ICU stay. Pancreatitis resolved and the patient was taken off the mechanical ventilation. He was discharged home in 4 days with outpatient endocrine follow up.

**Discussion:** Hypertriglyceridemia is associated with a number of severe diseases such as acute pancreatitis and coronary artery disease. In severe hypertriglyceridemia (SHTG, triglycerides >1000 mg/dl), rapid lowering of plasma triglycerides (TG) has to be achieved. Treatment regimes include nutritional intervention, the use of antihyperlipidemic drugs, therapeutic apheresis and continuous insulin infusion. Even though insulin drip use is commonly done in the ICU, its use in hyper triglyceridemia needs nursing awareness and co-ordination about monitoring finger stick glucose. Outcomes are definitely better and patient care much improved.

**Conclusion:** Continuous insulin infusion in severe triglyceridemia results in better patient outcomes. However its use in the inpatient setting needs co-ordination between the nursing staff and the physicians.
Abstract #513

EARTHING (GROUNDING) THE HUMAN BODY REDUCES BLOOD VISCOSITY—A MAJOR FACTOR IN CARDIOVASCULAR DISEASES

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Objective: Emerging research is revealing that direct physical contact of the human body with the surface of the earth (grounding or earthing) has intriguing effects on human physiology and health, including beneficial effects on various cardiovascular risk factors. This study examined effects of 2 hours of grounding on the electrical charge (zeta potential) on red blood cells (RBCs) and the effects on the extent of RBC clumping.

Methods: Subjects were grounded with conductive patches on the soles of their feet and palms of their hands. Wires connected the patches to a stainless-steel rod inserted in the earth outdoors. Small fingertip pinprick blood samples were placed on microscope slides and an electric field was applied to them. Electrophoretic mobility of the RBCs was determined by measuring terminal velocities of the cells in video recordings taken through a microscope. RBC aggregation was measured by counting the numbers of clustered cells in each sample.

Case Presentation: Earthing or grounding increased zeta potentials in all samples by an average of 2.70 and significantly reduced RBC aggregation.

Conclusions: Grounding increases the surface charge on RBCs and thereby reduces blood viscosity and clumping. Grounding appears to be one of the simplest and yet most profound interventions for helping reduce cardiovascular risk and cardiovascular events.

Discussion: A number of clinical studies on the physiologic effects of grounding the human body have indicated improvements in various cardiovascular and heart-related parameters. One of the first investigations reported normalization of the day-night cortisol rhythms in subjects who were grounded by sleeping on a conductive mattress pad connected via a wire to a rod inserted into soil. It is known that chronic elevation of cortisol can result in disruption of circadian rhythms and chronic activation of the sympathetic nervous system.

Conclusion: Grounding or earthing the body is virtually harmless. To date, there has been no systematic study of the effects of grounding on BP. However, there are anecdotal reports that patients using blood-thinning drugs, such as warfarin (Coumadin®), need to have their clotting time monitored when they begin to make more frequent conductive contact with the earth. When physicians recommend evidence-based, harmless, and simple natural interventions, alleviation of human suffering and improved quality of life can be realized.

Abstract #514

THE EFFECT OF BLACK SEED (NIGELLA SATIVA) EXTRACT ON FOXO3 EXPRESSION IN HEPG2 CELLS

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Objective: Extracts prepared from black seed (Nigella sativa) have been shown to have insulinotropic properties, but their effects on intracellular signaling pathways have not been investigated. Since Forkhead box transcription factor 3 (FOXO3) has a significant role in regulating cellular metabolism in response to insulin, we investigated the effects of lipid extracts of black seed on FOXO3 levels and AKT and 5-AMP activated protein kinase (AMPK) in HepG2 hepatoma cells.

Methods: FOXO3 levels, phosphorylation, and nuclear exclusion were measured by Western blot, as were AKT and AMPK expression and activity using phosphorylation-specific antibodies. Apolipoprotein A-I expression, a black seed-responsive gene, was measured by Western blot.

Results: Treatment with black seed extract increased FOXO3 phosphorylation and decreased its expression. In contrast to control cells where FOXO3 was located primarily in the nucleus, in black seed-treated HepG2 cells, FOXO3 was localized primarily to the cytoplasm. These changes in FOXO3 phosphorylation, expression, and localization were accompanied by increased AKT activity. Black seed also decreased AMPK activity but increased AMPK expression.

Conclusion: These results suggest that lipid extracts from black seeds behave similar to insulin by inhibiting FOXO3 activity and modulating the expression of FOXO3-dependent genes. Further research is needed to investigate whether or not black seed extract induces insulin receptor activity or if it acts as insulin sensitizers.
Abstract #515

HYPERTENSION IN SURULERE: A COMMUNITY SURVEY

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Objective: The cure for hypertension remains a global challenge. In the past numerous surveys had been conducted to determine the prevalence of hypertension in different settings but unfortunately these surveys are mostly done in developed countries. The present pilot study evaluated the prevalence of hypertension in an urban area in patients living in a resource poor country in Africa.

Methods: The blood pressure of 72 participants was measured using a mercurial sphygmomanometer at heart level in the community setting. The study location was Surulere in Lagos Nigeria in a small community with access to health care delivery at primary, secondary and tertiary level.

Results: A total of 72 participants were screened in our pilot study. The age range was from 18-88 years. 51.39% (37 participants) were hypertensive. 24.32% of the hypertensive were male while 75.67% were females. Hence the male to female ratio (M:F) amongst hypertensive patients was 1:3. In this study population the age range of the hypertensive patient that are male was 37-70 years with mean age of 57.55 years, the age range of hypertensive patients that are females was 30-81 years with mean age of 51 years.

Discussion: The findings in this paper suggest that hypertension occurs at earlier age in females than males. Furthermore a high prevalence is noted in our study population. There were more females who are hypertensive in the fourth decade of life than males that are in Surulere community.

Conclusion: The prevalence of hypertension in Surulere is 51.39% with a female preponderance. Although our sample size is very small hypertension is very prevalent in Surulere and proper education of medical providers and patients is of paramount importance. Universal screening of population is urgently needed.

Abstract #516

GENDER DISPARITIES IN RANDOMIZED CONTROLLED TRIALS OF STATINS: THE IMPACT OF AWARENESS EFFORTS

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Objective: To systematically explore the gender disparities in participants of RCTs on statins.

Methods: This review focused on RCTs on statins that reported participants’ numbers by sex/gender. Studies were identified from an initial PubMed and EMBASE search using several combinations of MESH terms. The search was limited to the RCTs on adult human beings in English-language publications. The date for search was set between January 1, 1990 and December 31, 2010.

Results: The ratio of male to female in participants of RCTs on statins illustrated two chronological distinctive patterns. The RCTs on statins in the 1990s mostly included men [mean (SD)] compared to women [82% (12%) males versus 18% (13%) females, P-value less than 0.0001]. This pattern was observed both for primary and secondary prevention trials. After the year of 2000, this gap has been reduced significantly. RCTs on statins that have been conducted after year the 2000 on average included 64% (15%) males versus 36% (14%) females.

Discussion: Studies demonstrated gender differences in the burden of cardiovascular outcomes for patients with dyslipidemia. Progress in the sex composition of Randomized Controlled trials (RCTs) is crucial for understanding the distribution of therapeutics effectiveness in the population according to sex/gender. This result illustrated a significant increase in recruitment of the women for RCTs on statins (p-value less than 0.001).

Conclusion: This study demonstrated a significant progress in the inclusion of women in RCTs on statins. This finding can reflect the efforts of different agencies and groups to increase the representation of women in clinical trials.
Abstract #517

ACQUIRED GENERALIZED LIPODYSTROPHY AND SEVERE INSULIN RESISTANCE (LAWRENCE SYNDROME), A CASE REPORT AND LITERATURE REVIEW

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Objective: To highlight rare causes of severe insulin resistance and other metabolic complications.

Methods: We discussed a case of severe generalised lipodystrophy. In this context we reviewed the literature using Pubmed, Embase, and Medline by using following terminologies:” Generalized lipodystrophy “Seip Berardinelli syndrome”, “Lawrence syndrome”, “Leptin therapy”.

Case Presentation: We present a case report of 19 year old male with sudden onset of severe GL with severe loss of adipose tissue, acanthosis nigricans, severe insulin resistance with difficult to control diabetes, hypertriglyceridemia, hemolytic anemia, hepatomegaly with autoimmune hepatitis with rapid progression to liver cirrhosis. We reviewed literature about pathophysiology and treatment options.

Discussion: Generalized lipodystrophy (GL) is a rare condition, congenital or acquired. The congenital (CGL) form also called Seip Berardinelli syndrome) presents early with autosomal recessive pattern. Whereas, acquired GL (Lawrence syndrome) develops in previously healthy child or adult over period of weeks or months. Only few case reports are published. These patients tend to have severe fat loss, severe insulin resistance, diabetes mellitus, hepatic steatosis. Mechanism remains unclear, however adipokines play important role in associated metabolic complications. Therefore, replacement of leptin can reduce their plasma insulin and glucose level besides correcting associated hypertriglyceridemia, liver steatosis and hormonal imbalance.

Conclusion: Therefore we presented a case report with evidence based literature review to highlight the rare metabolic disorder requiring specific treatment.

Abstract #518

DOWNGRADE OF STATIN THERAPY WHEN TRANSLATING THE 2013 ACC/AHA LIPID GUIDELINES INTO CLINICAL PRACTICE IN A LOS ANGELES COUNTY SAFETY NET DIABETES CLINIC

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Objective: The new ACC/AHA 2013 guidelines on the treatment of blood cholesterol recommend a significant change in the way that physicians currently manage cholesterol in patients, especially in diabetic patients. The new guidelines shift away from using LDL and non-HDL targets as treatment goals of therapy. Instead, the new guidelines propose using a calculated 10 year atherosclerotic cardiovascular disease (ASCVD) risk score to guide statin therapy in many patients. Our objective was to evaluate diabetic patients who would need a downgrade in their statin therapy based on the new ACC/AHA guidelines.

Methods: We performed a retrospective chart review of consecutive patients within a diabetes clinic at the LAC+USC Medical Center. Diabetic patients age 40-75 were analyzed based on the ACC/AHA guideline age recommendations. In order to focus specifically on the guideline’s effect on diabetic patients, those diabetic patients also meeting criteria for the other statin benefit groups (LDL > 190 and clinical ASCVD) were eliminated. The patient’s 10 year ASCVD risk score was calculated using the ACC/AHA cardiovascular risk calculator, and the risk score was used to determine recommended change in statin therapy per the new guidelines. 100 consecutive diabetic patients, selected based on the inclusion criteria, were analyzed using the new guidelines to determine the percentage of patients who would require changes to their current statin therapy. From this cohort, we evaluated the percentage of patients who needed a reduction of statin therapy using these guidelines.

Results: 60% of patients in the study group required changes to their statin therapy based on the new guidelines. Of those patients requiring changes to their statin therapy, 23% required a downgrade from high to moderate intensity statins, as they had 10 year ASCVD risk scores < 7.5%.

Discussion: From our preliminary evaluation, the implementation of the new ACC/AHA guidelines will require significant adjustment of lipid agents for a standard diabetes cohort. Additionally, the new guidelines recommend a downgrade of statin intensity for many
Background: To evaluate the value of criteria published in ATP - IV and HbA1c, presence of CAD and relates vessels number in diabetic patients involved in the Regional Hospital of Temuco. The analysis was performed using Stata 11.1 (Chi 2, T Student, ANOVA and stratified analysis). Statistical significance p < 0.05 were considered. The results were expressed as mean and SD.

Methods: 147 diabetic patients who underwent elective coronary angiography for anginal syndrome, malignant arrhythmias or diabetic patients involved in the Coronary Unit of the Regional Hospital of Temuco. The prevalence of CAD was 64.5 % (n 95). We divided patients in group HbA1C<7 and a control group with HbA1C<7. The prevalence of men and women in the group of HbA1C<7 was 34.6 and 65.3 % vs 52.1 and 47.8 % for HbA1C>7, respectively (p 0.03), with an OR 2.05 for males and elevated HbA1C (CI 1.01 - 4.2) p 0.03. Average BMI was 28.4 ± 4.3 (range 19.7 - 45.6), without difference between groups, with 33.3 and 28.3 % obesity in HbA1C<7. Mean arterial pressure in both samples was 133.8 ± 24.1 and 76 ± 8.4 for systolic and diastolic respectively. There was no difference between the number of vessels involved and A1C or dyslipidemia. Presence of CAD for HbA1c levels greater than 7, 7.5, 8 and 8.5 no significant correlation observed in each of the groups were observed. The cutoff values of LDL > 70 (p 0.2), 100(p 0.7) and 130 (p 0.3) were not associated with increased prevalence of coronary heart disease. According to the ATP IV criteria was considered as a variable patients between 40-75 years LDL between 70-189 without encountering greater presence of coronary artery disease (p 0.4).

Discussion: In this study 64.5 % presented CAD. Males had increased risk (OR: 2.05). The group with HbA1c> 7 present more risk DLP (OR 2.03). The presence of CD was not related to the value of LDL independent cutoff. There is no difference between the number of vessels involved and A1C or dyslipidemia.

Conclusion: Metabolic control (HbA1c) was not related to the presence of CAD. In this study by variables used in ATP IV, the association between older age and elevated LDL was not associated with increased prevalence of coronary heart disease in diabetics.

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Discussion: Saturated fat was thought to be associated with ASCVD due to known LDL-C and apoB increasing effects but recent data suggests no such direct link. Evidence suggests that dietary fat via mono-unsaturated fats, poly-unsaturated fats and potentially MCT saturated fatty acids (SFAs) have favorable lipoprotein effects and CVD outcomes when replacing long-chain (LCT) SFA and carbohydrates. It is unknown if adding MCT oil +/- LCT-SFA with an isocaloric diet improves or adversely affects the lipoprotein profile and, thus, atherogenic risk. Dairy food has evidence to support its benefits for risk of CVD and DM, but not butter or cream, and the effects of MCT oil regarding lipids are unclear. There may be improved energy and caloric deficit from improved satiety when MCTs isocalorically replace LCTs, but studies of the effects of MCT/coconut oil on lipoproteins are mixed.

Conclusion: While the purported benefits of dairy fat and MCTs have some merit when derived from their whole food sources, there have been anecdotally reported cases of improved atherogenic lipoproteinemia in otherwise healthy patients who had added butter and/or MCT oil to their baseline diet. Our patient’s non-HDLc rose from 155 mg/dL (<50th %ile), prior to a higher SFA diet, to 189 mg/dL and then jumped to 216 mg/dL with an apoB of 133mg/dL (both > 80th percentile) after adding butter and MCT oil. This unfavorable effect is concerning from a public health perspective and individually increasing this patient’s risk of ASCVD.

Abstract #521

RELATIVE CONTRIBUTION OF OBESITY AND SERUM ADIPOPOINETIN LEVEL TO THE DEVELOPMENT OF HYPERTENSION: A COMMUNITY-BASED COHORT STUDY

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Yonsei University Wonju College of Medicine

Objective: Recent studies have demonstrated that serum adiponectin level is associated with blood pressure. We investigated the association between serum adiponectin level and new-onset hypertension, and the relative contribution of obesity and serum adiponectin level to the development of hypertension in normotensive men and women.

Methods: We analyzed 1,553 adults (584 men and 969 women) without hypertension, who had participated in a cohort study in both time periods from 2005 to 2008 for baseline and 2008 to 2011 for follow-up. We divided participants into gender-specific tertiles according to serum adiponectin levels. We defined the highest tertile of serum adiponectin as ‘high adiponectin’. Participants were stratified into 4 groups: the non-obese with high adiponectin; the non-obese with low adiponectin; the obese with high adiponectin; and the obese with low adiponectin.

Results: During an average of 3 years of follow-up, 79 men (13.5%) and 99 women (10.2%) developed hypertension. Low serum adiponectin level was an independent predictor of new-onset hypertension in men (Odds Ratio [OR]: 1.99; 95% Confidence Interval [CI]: 1.03-3.86). The obese men with low adiponectin had an increased risk of new-onset hypertension compared with the non-obese men with high adiponectin (OR: 2.80; 95% CI: 1.35-5.81), whereas the obese men with high adiponectin showed no significant difference in the risk of new-onset hypertension (OR: 1.04; 95% CI: 0.32-3.41). In postmenopausal women, the obese subjects with low adiponectin had an increased risk of new-onset hypertension compared with the control group (OR: 2.41; 95% CI 1.16-5.04).

Discussion: High serum adiponectin levels could stimulate the activity of endothelial nitric oxide synthase, which is associated with vasodilation. On the other hand, low adiponectin levels may increase the risk of new-onset hypertension by adverse effects on fatty acid metabolism and by the presence of oxidative and inflammatory injuries to the vasculature. Further studies are needed to elucidate the interrelationships among obesity, adiponectin, menopause and the development of hypertension.

Conclusion: Our findings suggest that high serum adiponectin levels might play a protective role against the development of hypertension in obese men and obese postmenopausal women.

Abstract #522

COMPARISON OF RISK FACTORS AND PRESENCE OF CORONARY DISEASE (CHD) IN DIABETIC VS NONDIABETIC PATIENTS TEMUCO REGIONAL HOSPITAL

Virginia Iturrieta, Marcela Jiménez, Luis Quiñiñir, Tatiana Vásquez, Benjamin Stockins
Universidad de la Frontera

Objective: To assess magnitude of association between risk factors and presence of CHD. To compare these parameters between MD v/s non-MD patients of Temuco Regional Hospital.

Methods: Retrospective cohort study. Included 552 patients who underwent elective coronary angiography. Age, sex, hypertension, obesity, smoking, and lipid profile was evaluated. The analysis was performed using Stata 11.1 (Chi 2, T Student, ANOVA and stratified analysis).
Statistical significance p < 0.05 were considered. The results were expressed as mean and SD.

**Results:** 552 patients were evaluated, 40.7% had diabetes and 59.3% without diabetes. Average age was 65.4 ± 10.4 MD and 61.9 ± 11.7 for non-diabetics (p < 0.01). Both groups showed 58 men and 63 % for DM and non-DM respectively (p 0.2). The RR of CHD in diabetic patients was 1.31 (1.04 - 1.66) p 0.01. In stratified analysis for CHD and MD adjusted for age (cut point 63 by mean) RR 1.21 (CI 1.03-1.4) was observed. The average value of total cholesterol was 170 and 174 (p 0.4), LDL 99 and 106 (p 0.06), HDL 38 and 40 (p 0.01), triglycerides 139 and 167 (p 0.01) for MD and non- MD respectively. The frequency of hypertension in CHD was 83.9% v/s 75.2% without CHD (p 0.02) with RR 1.1 (CI 1.01 - 1.2) p 0.02. 27.7% was obese, without increasing risk of coronary heart disease. For smoking: 21 patients and 13% for CHD (+) and CHD (-) respectively RR 1.24 (CI 1.04-1.48) p 0.002. In stratified analysis CHD and hypertension adjusted for smoking showed RR 1.28 (CI 1.01 - 1.63). Increased risk was not demonstrated to adjust these variables by total cholesterol and LDL altered levels. The presence of coronary disease according to higher LDL levels at 70 (p 0.02), 100 (p 0.09) and 130 (p 0.5) finding statistically significant for the first two were evaluated. Average waist circumference was 94.5 +11.5 cm, without difference between groups (p 0.5).

**Discussion:** This study showed that patients with MD have a higher prevalence of coronary heart disease (RR 1.31). After adjusting for age shows that older diabetic patients have 1.2 greater risk to present CHD, no sex difference between the groups was demonstrated. Patients with hypertension and also smoke have RR of 1.28 for CHD.

**Conclusion:** The risk of coronary heart disease increases with the addition of cardiovascular risk factors such as smoking, hypertension and older but no increased risk was observed when to the above variables were added in total, LDL cholesterol or triglycerides alterations.

**Abstract #523**

**PREVALENCE OF CARDIOVASCULAR RISK FACTORS IN SEMI-URBAN DWELLERS IN NIGERIA**

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**Objective:** The objective of this study is to identify and determine the prevalence of cardiovascular risk factors according to sex and age in semi-urban dwellers in a developing country.

**Methods:** This cross-sectional study included participants aged ≥18 years in the sub-urban community of Ogbomoso, Oyo State, Southwest Nigeria. Participants who gave informed consent and met the inclusion criteria were administered. Data on the following were collected: systolic and diastolic blood pressure, diabetes mellitus, obesity, dyslipidaemia, waist and hip circumference, urine protein, and sociodemographic parameters. These were analysed with SPSS version 18.0 software.

**Results:** The 750 participants [221(29.5%) male, 529 (70.5%) female] had a mean age of 61.7 years, with 21.5% overweight and 8.5% obese. Prehypertension was present in 30.4%, while 25.3% and 25.5% had stage 1 and stage 2 hypertension respectively. Hypertension was found to be highest among people in the age group of 61-80 years with the unemployed having the highest rate in their group (61.2%) as opposed to the professional workers, whose group had the lowest rate (40.0%). Diabetes mellitus was found in 8.8%, abnormal waist circumference in 32.0%, and proteinuria in 73.9%. Dyslipidaemia, as represented by low HDL-C, occurred in 20.5%. There were abnormal levels of TC in 5.5%, LDL-C in 16.7%, and TG in 3.3%, but majority of the subject had normal levels. Hypertension, proteinuria, diabetes, obesity and dyslipidaemia were all statistically significantly associated with age and sex.

**Discussion:** The results show that the prevalence of risk factors for developing cardiovascular events increases steadily with increase in the age of the population until after 80 years, after which the prevalence drops down rapidly. This is probably as a result of the fact that as most urban dwellers grow in age, they tend to reduce the amount of physical activity they engage in, especially after retirement, as opposed to rural dwellers who are still active even into their late years and as a result have a lower prevalence. Although Ogunmola et al in a rural based study shows that smoking and alcohol consumption also contribute to risk factors exposing the southwestern Nigerian population to cardiovascular risks.

**Conclusion:** This study shows that cardiovascular risk factors, such as diabetes, obesity and dyslipidaemia had a moderate to low prevalence in the semi-urban Nigerian community. However, the high prevalence of hypertension and proteinuria in this study suggests a high risk of the occurrence of a future cardiovascular event.
METABOLIC BONE DISEASE

Abstract #600

ADJUNCTIVE USE OF TERIPARATIDE IN SPINAL FUSION AND FRACTURES

Pablo Pazmino, MD, Elaina Barraza, RN

SpineCal

Objective: Few studies have reported on adjunctive use of biologic therapies to promote bony fusion and their prevention of future adjacent level vertebral body compression fractures. Teriparatide (Forteo) a drug commonly used for the treatment of the osteoporosis, rapidly enhances bone formation and increases bone strength by selectively promoting osteoblast activity. Forteo has been shown to directly stimulate bone formation and improve bone density, but there is a lack of evidence regarding its use in spinal fusion and nonoperative spinal fracture management. We have used Forteo following spine surgery in a selective cohort of patients who were at risk for pseudoarthroses or nonunion, and in select fractures which were treated nonoperatively.

Methods: Radiographs of 18 patients with documented osteoporosis were reviewed before and after a minimum of 12 months of Forteo treatment. Among them, 12 patients were treated with Forteo (minimum 3 months) (group I) after surgical fusion procedures, and 6 patients who sustained spinal fractures were treated with Forteo without surgery (group II). All patients were followed at 3 weeks, 6 weeks, 3 months, 6 months and one year with radiographs to confirm final bony fusion. At these time periods we measured our cohorts post treatment pain, VAS, and quality of life. Furthermore, for the surgical cohort (Group I) we measured radiographic fusion and bony cortico-cancellous bridging on postoperative CT scans. For the fracture population treated with Forteo alone, we measured kyphosis and wedge angle of the fractured vertebral body, and ratios of anterior, middle, and posterior heights of the fractured body to posterior height of the normal adjacent level vertebrae to ascertain any degree of adjacent level collapse or asymptomatic progression of osteoporosis.

Case Presentation: The progression of spinal cortical and cancellous fusion was shown in 100% of our surgical cohort (Group 1). At the last follow-up, mean increments of kyphosis and wedge angle were unchanged in Group 2 (6.3 and 5.3 deg) and in adjacent level vertebral bodies. In both groups, Forteo also demonstrated improved post treatment bone mineral densities in both groups.

Discussion: Each spinal fusion and fracture carries the potential to develop a nonunion, mal union, or pseudoarthrosis. Biologic therapies to promote and/or accelerate an otherwise problematic fusion may constitute a new treatment modality for patients who are at risk.

Conclusion: Forteo has the unique potential as a biological non-invasive strategy to improve and encourage bony healing and fusion in patients with certain fractures and prevent future fractures while halting detrimental side effects of osteoporosis.

Abstract #601

HYPOPHOSPHATEMIC RICKETS ASSOCIATED WITH GIANT HAIRY NEVUS

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PGIMS

Case Presentation: A 10 year old boy presented with difficulty in walking and progressive deformity of the lower limbs. History of abnormal skin pigmentation present since birth. Patient was born full term of non-consanguineous marriage. Physical examination revealed widened bilateral wrists, genu varum, mild scoliosis. Height was 107 cm (<3rd percentile). His skin was remarkable for the presence of few hairy nevi, largest one covering his entire back and shoulders. Other small nevi were present over his arms, legs and face. Investigations revealed serum calcium 8.7 mg/dL , serum phosphate 2.1 mg/dL and serum alkaline phosphatase 2685 U/L. 24 h urine collection showed creatinine, calcium and phosphate excretion of 0.12 g, 0.01 g and 0.17 g respectively. Fractional excretion of phosphate was 26.98%. Tubular resorption of phosphate was 73%. Serum iPTH was 127.7 pg/ml and serum vitamin D levels was 69 ng/ml. Atreial blood pH was 7.394. Urine pH was 5.3. Urine examination for glucose and amino acids was negative. Skeletal survey showed generalized osteopenia, metaphyseal cupping and fraying of long bones. Radiographs showed bowing of both upper and lower limbs. Bone scan revealed diffusely increased radionuclide uptake in the entire axial and peripheral skeleton, more prominent in calvarium, mandible and bilateral costochondral junctions suggestive of metabolic bone disease. Serum FGF-23 levels were raised (171 U/L). Patient was diagnosed as a case of CNN with hypophosphatemic rickets and started on phosphate supplement and calcitriol.

Discussion: Acquired forms of hypophosphatemic rickets have been reported to be associated with various tumors. The combination of hypophosphatemic rickets with ENS or giant hairy nevus is rarely reported. Other skin lesions that can occur in ENS are vascular nevi, hypopigmented macules and café au lait macules. The central nervous system abnormalities in patients with ENS include seizures, hemiparesis, developmental delay, mental retardation, abnormal cerebral gyration, underdeveloped temporal lobe and sensorineural deafness. Precocious puberty is also observed rarely in association with ENS. Surgical excision of
the nevus has been reported to improve or cure the metabolic derangement. Injection of the supernate from homogenized portion of excised tissue into experimental animals has been shown to induce excessive phosphaturia suggestive of the causative role of epidermal nevus. The nature of the phosphaturic factor in ENS is not well-understood, but elevated circulating FGF-23 levels has been reported in one patient with hypophosphatemic rickets.

**Conclusion:** This case illustrates the rare association of hypophosphatemic rickets with giant hairy nevus.

**Abstract #602**

**REVERSION FROM STAGE 2 (HYPERCALCEMIC) TO STAGE 1 (NORMOCALCEMIC) HYPERPARATHYROIDISM FOLLOWING PARATHYROIDECTOMY - CASE REPORT AND PROPOSED NEW TERMINOLOGY**

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USC Keck School of Medicine- Department of Endocrinology

**Objective:** Eucalcemia and persistent elevation of parathyroid hormone (PTH) post-parathyroidectomy for primary hyperparathyroidism (PHPT) has been reported to occur in approximately 25% of patients following successful parathyroidectomy. This outcome is under appreciated by the medical community. Its etiology remains unclear and its significance is controversial. Our objective is to present an interesting example of persistent elevation of PTH without hypercalcemia following removal of two parathyroid adenomas in a case of hypercalcemic hyperparathyroidism and to propose new terminology for this condition.

**Case Presentation:** A 57 year-old man presented with a history of kidney stones, Ca++ of 11.3 (8.6-10.3 mg/mL), and elevated intact PTH of 239 (10-65 pg/mL). Alkaline phosphatase was normal at 108 (40-115 U/L). DEXA showed osteoporosis of radius & spine. At surgery a 1.8 g left superior parathyroid adenoma was excised, and the intraoperative PTH (IOPTH) fell from 253 to 37. A small 0.2 g right inferior adenoma was also removed, and IOPTH fell further to 27. Post-op Ca++ was normal at 8.9. Six weeks post-op his PTH was high at 91. Subsequent testing at 6, 8, 10, 12 and 18 months post-op revealed persistently high PTH (range 91-149) and normal Ca++. He has been on supplemental Vitamin D since 6 months post-op. Despite 25(OH)D levels increasing from 19 to 66 (30-100 ng/mL) with Vit D therapy, he continues to have Stage 1 HPT at 19 months post-op. There has been no evidence of secondary HPT.

**Discussion:** We propose the term “Stage 1 hyperparathyroidism” for eucalcemic patients with high PTH, and “Stage 2 hyperparathyroidism” for those with both high PTH and high Ca++. Many cases of Stage 1 HPT, including this patient, could be cases of quiescent ideopathic parathyroid hyperplasia. The prevalence of elevated PTH in the general population is unknown and should be evaluated. Most patients with Stage 2 HPT are cured with surgery; however, some revert back to Stage 1 post-op. Less than 5% of such patients are reported to return again to Stage 2. It is likely that there are undetermined long-term detrimental effects of elevated PTH. Therefore, it is important to monitor these patients and rule out secondary causes, especially where treatable.

**Conclusion:** Stage 1 HPT post-op parathyroidectomy is not rare and may be detrimental. We believe use of the terms “Stage 1” and “Stage 2” HPT, indicating whether or not the patient is hypercalcemic, simplifies communication and suggests progressive pathophysiology. More information on the long-term outcome of patients reverting from Stage 2 to Stage 1 HPT is needed.

**Abstract #603**

**PREVALENCE OF VITAMIN D INSUFFICIENCY AND DEFICIENCY IN A SELECTED POPULATION OF WOMEN LIVING IN NEW JERSEY**

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Rutgers Robert Wood Johnson Medical School

**Objective:** The purpose of this study is to examine the prevalence of vitamin D deficiency (serum 25-hydroxyvitamin D concentrations ≤ 20 ng/ml) and vitamin D insufficiency (serum 25-hydroxyvitamin D concentrations 21 to 29 ng/ml) in women seen at the general internal medicine clinic of the Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ.

**Methods:** We reviewed 800 charts of female patients, aged 23 to 80 years, whose first routine annual physical was performed from June 2006 to Dec 2012. Exclusion criteria included: current or history of use of calcium or vitamin D supplements, current or history of undergoing treatment for osteoporosis or osteopenia, diagnosis of hyperparathyroidism or biochemical thyroid disease.

**Results:** Vitamin D levels were measured in 440 out of the 800 patients. 256 patients were excluded. Data for 184 patients were included. Among these patients, 67 patients had sufficient vitamin D levels; 70 patients had vitamin D insufficiency and 47 patients had vitamin D deficiency. Patients with vitamin D deficiency were younger (49.9 ± 11.8 years vs. 54.7 ± 11.7 years, p< 0.05) and had a higher body mass index (31.84 ± 7.82 kg/m2 vs. 27.37 ± 6.81 kg/
m2, p < 0.05) compared to patients with sufficient vitamin D levels. Vitamin D deficiency was more common in African American (16 out of 29 patients), Asian (1 out of 4 patients), and Hispanic populations (3 out of 9 patients) compared to Caucasians (17 out of 97 patients, p < 0.05).

Discussion: The reported prevalence of vitamin D deficiency ranges from 18 to 58% in various populations. In our study population, who visited the clinic for routine physicals without any known diseases of calcium or vitamin D metabolism, the prevalence of vitamin D deficiency was in the range of the reported prevalence. Fifty five percent of the women in our population were screened for vitamin D deficiency and insufficiency. The selection criteria used by their primary care physicians for screening was unknown. The benefits of screening for vitamin D deficiency at a population level is yet to be determined. Since we demonstrated differences in vitamin D levels within different ethnicities, age groups and BMI, screening may be appropriate in those select groups of individuals in which lower levels of vitamin D were found.

Conclusion: Due to the lack of standard criteria, there is diversity in selection of patients for screening vitamin D deficiency in a well outpatient general clinic. It may be important to identify which patients should be screened for vitamin D deficiency and insufficiency.

Abstract #604

HEMOCROMATOSIS PRESENTING AS OSTEOPOOROTIC FRACTURE: A CASE REPORT AND REVIEW OF THE LITERATURE

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Advocate Christ Medical Center

Objective: Hereditary hemochromatosis (HH) is an autosomal recessive disorder with a prevalence of about 1 in 300 Caucasians. It is characterized by progressive iron accumulation in parenchymal tissues leading to organ damage during the fourth or fifth decade of life. Patients usually present with fatigue, diabetes, thyroid dysfunction, arthropathy and hypogonadism. The prevalence of osteoporosis varies from 25-50 percent in HH but is almost never the presenting feature. We describe a case of hemochromatosis presenting with osteoporotic fracture.

Case Presentation: A 48 year old Caucasian (Irish) male with a past medical history of hypertension was evaluated for osteoporosis after sustaining a low impact fall and fracture of rib and tibial plateau. He reported low libido and had no history of previous fractures, steroid use, rheumatoid arthritis, dietary deficiency of calcium or vitamin-D and no family history of osteoporosis. Bone densitometry revealed osteoporosis (T-score of -2.6 at the lumbar spine). Physical examination was normal. CBC, CMP, thyroid function test, serum and urine protein electrophoresis and PTH were within normal limits. 24-hour urine collection for calcium, creatinine and cortisol was normal. 25-OH vitamin-D was low (22 ng/ml) and total testosterone level was low at 146 ng/dl. FSH, LH were inappropriately normal suggestive of hypogonadotropic hypogonadism. MRI of pituitary gland was reported normal. Iron studies revealed high serum iron (263 mcg/dl) and iron saturation (93%). He was referred for HFE genotype testing and found to have a homozygous p.Cys282Tyr genotype. Patient underwent a liver biopsy, which confirmed the diagnosis. Regular phlebotomy was initiated and repeat testosterone level was within normal limits after 6 months. For his osteoporosis he was treated with IV Zoledronic acid. Interestingly, our patient had been voluntarily donating blood since the age of 39 years, which likely helped him in reducing iron overload, and end-organ damage.

Discussion: Osteoporosis is a common disease characterized by low bone mass and microarchitecture disruption leading to susceptibility to fragility fractures. When osteoporosis is diagnosed in young males, a detailed work-up is necessary to exclude secondary causes such as alcoholism, myeloma, malabsorption, hypogonadism, hyperthyroidism, hyperparathyroidism, cushing’s syndrome and hemochromatosis. Excess iron reduces bone mineral density by inhibiting osteoblast activity and bone apposition.

Conclusion: Osteoporotic fracture is an extremely unusual presentation of hemochromatosis and our case highlights the clinical reasoning process, which led to the diagnosis of hemochromatosis in a patient presenting with osteoporotic fracture.

Abstract #605

TRADITIONAL SCREENING MODALITIES FOR BONE HEALTH MAY NOT BE APPLICABLE TO THE HIV PATIENT POPULATION

Kelly Stephens, MD1, David Rimland, MD2, Leon Rubinsztain, MD2, John Payan, MD2, Christopher Rentsch2, Vin Tangpricha, MD, PhD1

1. Emory University, 2. Atlanta VA Medical Center

Objective: We sought to investigate the utility of DEXA and FRAX scores in identifying the prevalence of subclinical vertebral fractures in HIV patients with vitamin D deficiency.

Methods: Our retrospective study was approved by the Emory IRB. We examined the electronic medical records of veterans seen at the Atlanta VA Medical Center from 2007
to 2010. We enrolled subjects who were HIV positive and vitamin D deficient (25-hydroxyvitamin D (25(OH)D)< 20 ng/mL). Bone mineral density was assessed by DEXA and the calculated 10 year fracture risk using the World Health Organization FRAX equation. Two independent radiologists reviewed lateral chest x-rays for the presence of subclinical vertebral fractures.

**Results:** We identified 342 adult subjects with HIV (median CD4 count: 489.5 cells/mm³ (IQR, 329.5-682.5)) and vitamin D deficiency (median 25(OH)D: 13.0 ng/mL (IQR, 9.0-16.0)). Overall 14.3% (n=49) of subjects met diagnostic criteria for osteoporosis per DEXA, and 54.3% (n=178) had osteopenia. The median risk of any osteoporotic and hip fracture by FRAX was 1.4% (IQR, 1.0-2.8) and 0.1% (IQR, 0.0-0.3), respectively, well below the recommended threshold for treatment. Yet, sub-clinical vertebral fractures by lateral chest x-ray were detected in 46.6% (n=108) of our subjects.

As compared to those without fractures, those with fractures had similar prevalence of osteoporosis (15.3% vs. 15.7%, p=1.00) and osteopenia (55.4% vs. 60.9%, p=0.42), and similar FRAX major (1.3% vs. 1.5%, p=0.02) and FRAX hip (0.1% vs. 0.1%, p=0.41) scores. Finally, neither osteoporosis and osteopenia status, FRAX scores, 25(OH)D level, CD4 count, body mass index, sex, calcium and parathyroid hormone levels, smoking history, nor renal function were predictive of those with fracture after multivariable analysis.

**Discussion:** Individuals with human immunodeficiency virus (HIV) are at increased risk for osteoporosis and fractures due to concomitant risk factors such as vitamin D deficiency, hypogonadism and anti-retroviral therapies. Whether traditional screening modalities for bone disease apply to the HIV infected population remains unclear. We found that a significant proportion of patients with HIV and vitamin D deficiency have fragility fractures. However, traditional screening tools for bone disease such as DEXA and FRAX score failed to identify those with fractures.

**Conclusion:** Our findings suggest that traditional screening tools for fragility fractures are not applicable to the HIV population. Whether lateral CXR or other screening tests should be used to assess for sub-clinical fractures and to help guide appropriate therapy in this high risk population warrants further study.

Abstract #606

**Fragility Fractures: The Interplay Between Age and Obesity**

Mahshid Mohseni, MD, Pooya Hosseinzadeh, MD, Miazong Wu, PhD, Abid Yaqub, MD, Omolola Olajide, MD, John Leidy, MD, Driscoll Henry, MD

**Objective:** Fragility fractures are epidemic and place a significant burden on health care resources in the United States. The effects of age and obesity on occurrence of different fragility fractures are not well defined. Obesity is shown to be protective against certain fragility fractures but predispose the patient to fractures at other sites. We studied whether age and obesity can interact to affect the fragility of specific bones and influence the site-specific fracture incidences.

**Methods:** Retrospective chart review of patients presenting with fragility fractures (low trauma) at a tertiary care hospital in 2011 was performed. Low trauma fractures were referred to those fracture occurring spontaneously or a fracture arising from trauma which in a healthy individual, would not result in a fracture. The fractures were categorized to groups based on fracture location. ANOVA analysis was used to investigate the interplay between age and obesity (measured as BMI) in different fracture groups.

**Results:** A total of 332 patients were included, with age ranging from 18-97 years old (66.5 ± 17.4), and BMI from 14.7-68.2 kg/m² (28.2 ± 8.0). Based on fracture mechanism and fracture site, these fractures were further classified into nine catalogues. One way ANOVA analysis showed that patients with hip/thigh and spine fractures were more aged and had ess BMI than those with ankle and wrist region fractures (P ≤ 0.05). Further Pearson correlation and Stepwise regression analyses suggested that hip/thigh and spine fractures exhibited significant age-BMI interacted effects (P ≤ 0.05).

**Discussion:** The interplay between age and obesity on fragility fractures differs among different skeletal sites. Patients with wrist and ankle fractures are younger and have higher BMI than patients presenting with hip and spine fractures. BMI and obesity show a significant inverse interaction in patients with fragility fractures of the hip and spine. This inverse relationship implies that these (hip and spine) fragility fractures are seen in younger patients with high BMI and in older patients with low BMI.

**Conclusion:** This study suggests age and obesity can interact to affect the fragility and fracture of some specific bones. Intervention specially designed to manipulate the interaction would be beneficial to the reduction of fracture risk.
Abstract #607

CINACALCET FOR MANAGEMENT OF TERTIARY HYPERPARATHYROIDISM ASSOCIATED WITH CHRONIC TREATMENT OF HYPOPHOSPHATEMIA IN AN ADULT WITH TUMOR INDUCED OSTEOMALACIA

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Case Presentation: A 52 year-old female was in good health until 1986, when she developed debilitating myalgias and a waddling gait. Labs showed serum phosphate 1.0mg/dl, calcium 8.6mg/dl, urine phosphate 1506g/24hr (400-1300), 25(OH)D 21ng/ml, 1,25(OH)2D 18pg/ml (15-60), mid-molecule PTH 246pg/ml (30-330) and no aminoaciduria nor glycosuria. Transiliac crest bone biopsy showed severe osteomalacia and she was given the diagnosis of vitamin D-resistant hypophosphatemic osteomalacia. Phosphate 4 g/day and calcitriol were initiated, but serum PO4 remained 1.6mg/dl. After 20 years she developed bone pain, worsening myalgias, fatigue and depression, with increasing Ca to 12.5mg/dl, Cr to 2.8mg/dl and iPTH to 823pg/ml. In 2009, she incidentally noted a mass on her forearm. PET scan showed hypermetabolic activity at that site. Pathology of the resected mass showed a 4.5cm phosphaturic mesenchymal tumor, mixed connective tissue variant. Serum and urine PO4 normalized and Cr improved postoperatively. She was titrated off phosphate supplements by 2011, but iPTH and Ca remained elevated. Hyperparathyroidism evaluation included urine Ca 244mg/24hr, mild osteopenia on DXA, two right extrathyroidal nodules ~1cm on neck ultrasound, and a focus at the upper right pole of the thyroid on sestamibi scan. She started Cinacalcet 30mg BID and Ca normalized to 10mg/dl with improvement of Cr to 1.39mg/dl and iPTH to 823pg/ml. In 2009, she incidentally noted a mass on her forearm. PET scan showed hypermetabolic activity at that site. Pathology of the resected mass showed a 4.5cm phosphaturic mesenchymal tumor, mixed connective tissue variant. Serum and urine PO4 normalized and Cr improved postoperatively. She was titrated off phosphate supplements by 2011, but iPTH and Ca remained elevated. Hyperparathyroidism evaluation included urine Ca 244mg/24hr, mild osteopenia on DXA, two right extrathyroidal nodules ~1cm on neck ultrasound, and a focus at the upper right pole of the thyroid on sestamibi scan. She started Cinacalcet 30mg BID and Ca normalized to 10mg/dl with improvement of Cr to 1.39mg/dl and iPTH to 53pg/ml. Eight months later, Cinacalcet was decreased to 30mg daily, with Ca and PO4 remaining normal and further improvement of Cr to 1.14mg/dl and iPTH to 34pg/ml.

Discussion: Tumor induced osteomalacia (TIO) is a rare cause of hypophosphatemia due to benign neoplasms of mesenchymal origin. This tumor produces FGF-23, which inhibits renal phosphate reabsorption and calcitriol production. Tertiary hyperparathyroidism (THPT) may result from chronic phosphate replacement due to phosphate complexing with calcium, causing hypocalcemia and stimulation of PTH secretion. THPT is described in children with inheritable forms of hypophosphatemia who require lifelong phosphate therapy. Parathyroidectomy is the standard treatment. In our case, the patient was treated medically with Cinacalcet. It remains to be seen if the hyperparathyroidism may resolve without surgical treatment, now that the impetus for PTH stimulation has been removed.

Conclusion: We believe this is the first reported case of managing THPT associated with chronic phosphate replacement therapy without surgical parathyroidectomy in an adult with a FGF-23 producing tumor. Medical therapy with Cinacalcet should be considered in patients with THPT associated with TIO after the tumor has been removed and phosphate therapy is no longer required.

Abstract #608

SYSTEMIC MASTOCYTOSIS: AN UNDER-RECOGNIZED CAUSE OF OSTEOPOROSIS

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Mayo Clinic

Case Presentation: A 44 year-old man was referred to endocrinology clinic for vertebral compression fractures not preceded by trauma. Besides having back pain, he felt well with no fevers, night sweats, vomiting, diarrhea, or weight loss. He ate a normal diet, which included dairy products, and had no other medical problems, past surgeries, allergies, or history of steroid use. His medications included calcium and vitamin D supplements, as well as acetaminophen and cyclobenzaprine for back pain. He worked as a farmer, chewed tobacco daily after quitting smoking 10 years prior, drank alcohol occasionally, and denied drug use. Family history was significant for his father who had asthma and osteoporosis with vertebral fractures. Physical exam revealed a well-appearing man with a BMI of 29 and normal vital signs. His sclerae were white, thyroid was normal in size and consistency, and he had no lymphadenopathy, kyphosis, or rash. Bone mineral density testing showed T-scores of -0.2 at the femoral neck, -0.7 at the lumbar spine, and +2.1 at the 1/3 radius. Laboratory evaluation revealed a normal CBC, albumin, calcium, phosphorus, creatinine, 25-hydroxyvitamin D, PTH, TSH, total testosterone, 24-hour urine free cortisol, kappa and lambda free light chains, and serum protein electrophoresis. Tryptase was elevated to 15.7 ng/mL (reference <11.5 ng/mL) and urine 11 beta-prostaglandin F2 alpha was elevated to 2995 ng/24 hrs (reference <1000 ng/24 hrs). Bone marrow biopsy showed scattered aggregates of atypical mast cells involving 5% of the marrow with coexpression of CD2 and CD25, positive staining for tryptase, and the KIT Asp816Val gene mutation. Systemic mastocytosis was diagnosed.
**Discussion:** Systemic mastocytosis is a rare cause of osteoporosis characterized by proliferation and infiltration of pathologic mast cells into extracutaneous organs, often including the bones. Associated skeletal fragility is thought to be caused by mast cell mediators such as tryptase, histamine, and cytokines. Interestingly, fracture risk is higher in men with this disease than in women and does not always correlate with bone mineral density. Other potential manifestations of systemic mastocytosis include pruritis, flushing, anaphylactic episodes, gastrointestinal dysfunction, neuropsychiatric changes, and diffuse pain. The disease can present, however, with isolated skeletal fragility, as illustrated by this case, making the diagnosis difficult.

**Conclusion:** Systemic mastocytosis should be considered in young patients, especially men, who present with fragility fractures and no other obvious cause of secondary osteoporosis. Serum tryptase is a useful screening test, but diagnosis requires bone marrow biopsy.

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**ATYPICAL FEMORAL FRACTURES: RADIOGRAPHIC AND HISTOMORPHOMETRIC FEATURES IN 19 PATIENTS**

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**Objective:** This study describes characteristics and histomorphometric and radiographic features of atypical femoral fractures (AFF) as seen in 19 cases referred for evaluation.

**Methods:** All patients referred for AFF evaluation were reviewed. Patients meeting the ASBMR criteria for AFF were further evaluated and tetracycline labelled bone biopsies were completed. Radiographs were reviewed by a musculoskeletal radiologist.

**Results:** All fracture lines were transverse or short oblique and 15 of 19 patients had thickened cortices on x-ray. We report 19 cases of AFF in patients on long term bisphosphonate (BP) therapy. 14 of 19 fractures occurred without a fall or direct femoral trauma with 5 cases occurring after a fall from standing height. All patients were female; average age was 65 years (range 23-80 years). 4 of 19 cases were of Chinese descent, 4 were East Indian, with 11 being Caucasian. Average BP durations of use was 9.8 years (range 6-15 years). 9 of 19 patients were on alendronate alone, 2 patients on risedronate alone, 6 patients on a combination and 1 patient on pamidronate and alendronate. 1 patient was on a combination of alendronate and denosumab. Prodromal thigh or groin pain was seen in 12 of 19 patients for 1 to 15 months prior to fracture. PPI use was present in 6 patients. 2 patients were on prednisone for rheumatoid arthritis and 2 on prednisone for asthma. 1 patient had osteogenesis imperfecta type IV with a history of multiple fragility fractures and experienced a femoral fracture after 12 years of IV pamidronate with features consistent with an AFF. All patients had 25OH Vit D levels >50nmol/L. 18 patients with radiographic features of AFF had been on a BP for > than 6 years. 1 patient had been on alendronate for 5 months. 8 of 19 patients had bilateral femoral fractures.

**Discussion:** A large number of patients with radiographic AFF features had mineralization abnormalities on tetracycline labelled bone biopsy. Decreased osteoid surface and mean mineralized trabecular width was seen in 6 of 11 biopsies. Diffuse label was noted in 5 of 11 biopsies. Mineralization abnormalities were noted in a significant number of patients with radiographic features of AFF. All patients had normal or mildly reduced serum vitamin D levels.

**Conclusion:** Histomorphometric features seen on bone biopsy in women sustaining an AFF in association with long term BP use included evidence of mineralization abnormalities and decreased bone formation. 1 patient had features of decreased bone formation and mineralization abnormalities with only 5 months of BP exposure. Improved understanding of the pathobiology leading to these fractures may be gained with further histomorphometric data in larger numbers of patients.

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**RESISTANT HYPERCALCEMIA OF MALIGNANCY TREATED WITH DENOSUMAB**

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SUNY Downstate

**Objective:** Hypercalcemia of malignancy is a well-recognized complication of advanced cancer that poses numerous risks for the affected patient, including renal failure, altered mental status, and even coma or death. Commonly used therapeutic agents include IV fluids, calcitonin and bisphosphonates. However, in some cases hypercalcemia persists despite use of all these agents. Denosumab is a monoclonal antibody that inhibits RANKL. RANKL mediates bone resorption and hypercalcemia by activating osteoclasts. Though currently
approved for management of osteoporosis, small cases series and ongoing clinical trials suggest that Denosumab has potent calcium lowering effects and is emerging as a new therapeutic option.

**Case Presentation:** A 55 year-old woman with a history of breast cancer presented with worsening rib and sternal pain. She also complained of abdominal pain and constipation. She denied headaches, confusion or urinary symptoms. Physical exam was remarkable for tachycardia to 123 beats per minute, mild painful distress, and mild tender hepatomegaly. Labs showed a corrected serum calcium of 14.4mg/dl (ref:8.4-10.3), alkaline phosphatase (ALP) of 469mg/dl (ref:20-125), and PTH of 8.9pg/ml (ref:14-72). 25-OH Vitamin D was 21ng/ml (ref:30-100), 1,25-Vitamin D was 18pg/ml (ref:18-72). Given her high ALP and low PTH levels, hypercalcaemia was attributed to diffuse lytic metastatic bone lesions of the chest/abdominal/pelvic on computerized tomography and skeletal survey.

The patient was started on IV hydration, calcitonin, and pamidronate. Following an initial decrease in serum calcium, 1 week post-therapy, the serum calcium rose to 14.8mg/dl. Despite a second dose of pamidronate, IV fluids and Furosemide, the serum calcium remained elevated. Due to the resistant nature of the hypercalcaemia, the patient received a single subcutaneous dose of 120 mg denosumab. After the dose, the patient’s calcium remained stable for 3 days, and then decreased precipitously, reaching a corrected nadir of 9.2 mg/dl. Unfortunately, due to her advanced disease, the patient deteriorated clinically, developed septic shock and expired.

**Discussion:** We describe a patient severe hypercalcaemia to malignancy that was resistant to intravenous hydration, calcitonin and bisphosphonates, however, demonstrated a dramatic response to denosumab. Its novel mechanism of action via inhibiting RANK ligand supports its role as a potential treatment of hypercalcaemia of malignancy. Clinically patients will need close monitoring for hypocalcemia.

**Conclusion:** Further investigation is needed to understand its full therapeutic effects and to determine its safety.

**Abstract #611**

**HYPERPARATHYROIDISM: DIAGNOSTIC DILEMMAS IN AN AFRICAN AMERICAN PATIENT POPULATION**

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**SUNY Downstate**

**Objective:** Primary hyperparathyroidism (PHPT) is the most common cause of hypercalcaemia in outpatients; because of potential complications, surgery is recommended. In contrast, Familial Hypocalciuriic Hypercalcemia (FHH) with similarly elevated serum calcium & parathyroid hormone (PTH) levels, is a rare autosomal dominant mutation of the calcium sensing receptor. Because of its benign course, FHH must be excluded in order to avoid surgery. In practice, the 24-hour urine calcium/creatinine clearance ratio (CCCR) distinguishes these as a personal or family history of hypercalcaemia is often absent. Data in Caucasians are the basis for currently published cut-off values: in 80% of FHH the CCCR is low, < 0.01 and is high in PHPT at > 0.02. In an urban clinic with primarily African American (AA) patients with hyperparathyroidism, we noted frequent low CCCRs in the FHH range. We sought to characterize this in a retrospective study and describe the biochemical findings unique to this population.

**Methods:** We evaluated 110/170 hyperparathyroid cases with complete data, mean age 62 years, 90% female, without renal disease. Cases were divided into 3 groups based on published CCCR: low (<0.01), intermediate (0.01-0.02), or high (>0.02) and analyzed clinical parameters of calcium metabolism including serum Vitamin D, PTH, creatinine & calcium. Data are mean±SD.

**Results:** Unexpectedly, the CCCR was 0.13±0.007 and most had no family history of calcium disorders. Only 20% had an expected high CCCR while 80% were intermediate (45%) or low (35%). There were no significant differences in serum calcium, PTH, 25 OH-vitamin D or creatinine. Data for 3 groups follow: low CCCR (0.006±0.002): Ca 10.93±0.46 mg/dl, PTH 137.99±122 pg/ml, Vit D 28.1±13 nmol/L; intermediate CCCR (0.013±0.003): Ca 11.07±0.73mg/dl, PTH 130.5±96pg/ml, Vit D 25.9±11 nmol/L, high CCCR: (0.024±0.004): Ca 11.2±0.68mg/dl, PTH 176.3±110pg/ml, Vit D 25.4±12 nmol/L. Over 50% of sestamibi scans (performed in 80%of cases) suggested parathyroid adenoma with no group differences. 27/29 with multiple 24-hr urine collections had a CCRR <0.02 validating this measure.

**Discussion:** Generally PHPT has high urine calcium excretion while FHH has low excretion. In our AA patients, 80% had CCCRs below the expected range despite a positive sestamibi scans suggesting parathyroid adenoma and is consistent with a recent report. The data were not affected by vitamin D, age, serum creatinine, calcium or PTH levels.

**Conclusion:** We conclude that in African Americans the 24-hour urine Ca/Cr clearance ratio does not distinguish the benign FHH from PHPT. Further studies are needed in AAs to prevent unnecessary surgery and understand the biology of the calcium sensing receptor.
Abstract #612

THE QUANTITATIVE ULTRASOUND CORRELATIONS WITH CENTRAL DXA REPORT: THE 65-YEAR CUT OFF (A ROMANIAN MENOPAUSAL WOMEN STUDY)

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Objective: The heel quantitative ultrasound (QUS) is a very accessible method to fragility fracture risk assessment. In areas with less DXA devices or economical issues the method is used in order not to provide the diagnosis of osteoporosis but to stratify the risk of fractures in different type of patients, especially women in menopause.

We analyzed the lumbar DXA correlation with QUS women less and over 65 years.

Methods: This is a transversal study in Romanian (Caucasian) population. The inclusion criteria were women in menopause (for at least one year in menopause, regardless surgical and natural menopause), left heel QUS and lumbar DXA data to be provided. The exclusion criteria were previous specific medication for osteoporosis or for fracture risk reduction (as bisphosphonates, SERM, teriparatide, denosumab, strontium ranelate); active cancers or metabolic bone diseases. All the patients had a QUS evaluation (GE Achilles) and DXA (GE Lunar Prodigy). Linear regression was used (SPSS21). The statistical significance was considered at p value of p<0.05.

Results: 322 women in menopause were included (mean age of 57 years). The group 1 included women <65 years (n=272), with mean lumbar BMD (Body Mass Density) of 1.05 g/cm\(^2\) and mean SI (QUS Stiffness Index) of 80.1. The group 2 included women ≥ 65 years (n=50), with mean BMD 0.9 g/cm\(^2\) and mean SI of 71.1. The linear regression between BMD and SI pointed a statistical significant correlation between lumbar BMD and SI in group 1 (r=0.4, p<0.0005) while the value of r was not statistically significant in group 2 (r=0.1, p=0.2).

Discussion: We choose the cutoff of 65 years because over this age the women in menopause should have a central DXA scan regardless the clinical risk factors for osteoporotic fractures, thus methods as QUS (which is less expensive) are more useful in younger postmenopausal women. So, the correlation with the golden standard DXA is important to be analyzed in different populations.

Conclusion: The correlation between lumbar DXA and heel QUS was established in menopausal women less than 65 years (medium, positive value of the correlation coefficient), but not in those of 65 years and more.

Abstract #613

HIGHER VALUE OF STIFFNESS INDEX AT HEEL QUANTITATIVE ULTRASOUND ASSOCIATES A STRONGER CORRELATION WITH FEMORAL NECK BONE MINERAL DENSITY?

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1. C.Davila UMPh, 2. Parhon Institute, 3. SCM Povernei

Objective: The heel quantitative ultrasound (QUS) is useful in fragility fracture risk evaluation but the golden standard method is the DXA report based on the values of Bone Mineral Density (BMD).

The QUS advantages as low cost, mobile devices and the use of ultrasound wave (and not X-Rays) should be taken into consideration. One of QUS parameters is stiffness index (SI) which is a combine parameter.

We analyzed the femoral neck DXA correlation with SI in menopausal women, using different cutoffs for SI values.

Methods: A transversal analyze in Caucasian women in menopause was performed. They all had a central DXA scan (including femoral neck BMD) with a Prodigy device, and a left heel QUS with an Achilles Insight device.

No women with previous treatment for osteoporosis was included, neither those with bone metastases or active Cushing’s syndrome.

The statistical tests were performed in SPSS21. The statistical significance was considered at p value of p<0.05.

Results: 197 women were enrolled. Based on the stiffness index values, three groups were formed: Group 1 (SI≤54) had a mean age of 58.8 years (n=12). Group 2 (54<SI≥79) had a mean age of 58.2 years (n=101). Group 3 (SI > 79) had a mean age of 55.4 years (n=84).

The femoral neck BMD values increased from group 1 to group 3: 0.8g/cm\(^2\), 0.92g/cm\(^2\), and 1.07g/cm\(^2\).

The correlation coefficient r (based on linear regression, and after controlling for age) was r=-0.2, p=0.5 in group 1; r=0.2, p=0.01 in group 2; and r=0.5, p<0.0005 in group 3.

Discussion: The use of cut off values regarding the ranges of stiffness index (the cut offs are known from several worldwide large cohorts) is useful in daily clinical practice to rapidly evaluate the patients with high fracture risk (low stiffness index) who may be treated for fracture risk reduction; medium fracture risk (who need further evaluations as DXA), and low risk of fracture (high level of SI) who need follow up.

Conclusion: Based on our study, the postmenopausal women with low risk of fracture (based on high and medium values of stiffness index, as assessed by the heel
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quantitative ultrasound) have a statistically significant correlation with femoral neck bone mineral density (a modest, positive correlation coefficient of correlation), but not the subjects with low SI.

Abstract #614

PTHRP INDUCED HYPERCALCEMIA BY MALIGNANT MELANOMA

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Objective: Describe a case and mechanism of hypercalcemia in malignant melanoma.

Case Presentation: A 48 year old woman presented 6 months after excision of a melanoma from her right mid back along with multiple metastases to the trunk. Histopathology of the lesions showed melanoma without an in situ component. Multiple subcutaneous masses were noted in the left shoulder and buttocks as well as palpable adenopathy of the left groin and bilateral axillae (Stage IV melanoma).

An MRI of the brain with and without contrast showed no metastasis however scattered enhancing subcutaneous scalp nodules concerning for metastasis were identified. A PET/CT demonstrated multiple hypermetabolic lesions in the thorax, pelvis, and extremities. No lesions were identified within the liver and bone scan was negative for metastases.

She received four treatments of Yervoy(Ipilimumab), which she tolerated well. Few days later, she was admitted to the hospital with serum calcium of 14.1 mg/dL (normal: 8.6-10.2), iPTH of 3pg/mL, and 25OHvitamin D of 24 ng/mL. Her PTHrP was markedly elevated at 110 pg/mL (normal 14-27). She received 4 mg of Zoledronic acid (Zometa) with normalization of her calcium within two days. Her calcium levels began rising again to 10.8mg/dL by three and a half weeks post treatment. She received a second dose of Zometa at that point.

Discussion: Hypercalcemia occurs in up to 20 to 30% of patients with cancer at some time during the course of their disease. Possible mechanisms include direct metastases to bone resulting in hypercalcemia by local osteolytic process, systemic secretion of parathyroid hormone (PTH)-related protein (PTHrP) by malignant tumors known as humoral hypercalcemia of malignancy (HHM), secretion of the active form of vitamin D, 1,25-dihydroxyvitamin D (1,25(OH)2D), and rarely by ectopic secretion of PTH by tumor cells. It is extremely rare for metastatic melanoma to cause HHM.

While the exact mechanism of PTHrP and hypercalcemia in metastatic melanoma is yet to be determined, high expression of PTHrP in melanocytic cells, both benign and malignant, without secretion of PTHrP is well established. Comparison of PTHrP levels in melanoma cell line culture medium and melanoma cell lysates suggests that the increase in serum PTHrP in melanoma is the result of cell death or necrosis. In reviewing our case, the timing of the patient’s development of hypercalcemia may be related to the onset of treatment leading to cell death and necrosis.

Conclusion: In the setting of hypercalcemia in a patient with malignant melanoma, PTHrP should be considered as a mechanism in the absence of bone metastases.

Abstract #615

PRESCRIPTION GONE HAYWIRE-TOO MUCH OF SUNSHINE VITAMIN

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Objective: To present a case of hypercalcemia in a treated case of pulmonary tuberculosis due to vitamin D toxicity resulting from wrong dispersion of prescription.

Case Presentation: 42 year old gentleman not formally educated, factory worker presented with generalized weakness and constipation for 1 month. No h/o fever, weight loss, night sweats, abdominal pain was noted. The patient had previously completed treatment for open pulmonary tuberculosis for 8 months 1 month back. On examination, patient was conscious, oriented. Vitals were stable. No lymphadenopathy, bony or muscle tenderness was seen. B/l inframammary & infrascapular fine crackles were noted. Investigations showed Hb:13g/dl (13.3-16.2), ESR: 34 mm(0-10); TLC: 11600/cumm (4000-11000); BUrea: 40mg/dL (20-40); S.Creatinine: 0.6mg/dL (0.6-1.2);S.ALP: 149 U/L (50-150); S.Protein:7.5mg/dL (6-8); S.albumin: 3.7mg/dL (3.5-5.5); S.globulin: 3.7mg/dL (2.5-3.5); HIV antibodies were non reactive; HBA1C: 6% (<6.5%); Sputum for AFB: stain & culture: sterile; S.calcium: 14.5mg/dL (8.5-10.5); S.ionised calcium:1.96mmol/dL (<0.15); S.25OH vitamin D (ELISA): >380nmol/L (100-300); 24 hour urinary calcium: 210mg/day (100-300); 24 hour urinary creatinine: 600 mg/day; Urinary calcium/creatinine ratio: 0.35 (<0.15); 25OH vitamin D (ELISA): >380nmol/L (10-145); S.PTH (CLIA): 7pg/mL (14-75); Ultrasound abdomen revealed normal kidney, no renal calculi; S.ACE levels: normal; Serum Electrophoresis: No M spikes; CECT thorax: fibrocavitatory changes in b/l upper lung field, no hilar lymphadenopathy; CECT abdomen no ileocecal thickening, lymph node. To rule out iatrogenic
vitamin D toxicity patient was asked to furnish all past prescriptions. He had been prescribed single intramuscular injection of Inj cholecalciferol 0.6 million IU along with anti tubercular chemotherapy for one month. However, due to misinterpretation by pharmacist/patient, he received 30 consecutive daily injections of cholecalciferol of 0.6 million I.U. i/m (total 18 million IU). A diagnosis of treated pulmonary Koch with fibrocavitary sequelae with hypercalcemia secondary to iatrogenic vitamin D intoxication was made. The patient was rehydrated with normal saline with forced diuresis with furosemide, intravenous pamidronate and steroids. Two weeks after therapy patient improved symptomatically and serum calcium levels were normalized to 10.4 mg/dl.

**Discussion:** Easy availability of high dose vitamin D preparations along with increased awareness of its role and association with large number of medical conditions has led to unbridled prescription and over the counter use of vitamin D often unsupervised.

**Conclusion:** Caution should be exercised while prescribing high dose vitamin D preparations keeping in mind the deleterious effects of overdosage.

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**Abstract #616**

**PRIMARY HYPERPARATHYROIDISM PRESENTING AS ISCHEMIC STROKE**

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1. Lady Hardinge Medical College, 2. PGIMER

**Objective:** To present a case of asymptomatic primary hyperparathyroidism who presented as ischemic CVA

**Case Presentation:** A 34 year old male presented with weakness of right half of the body, left sided facial deviation & slurring of speech for 4 hours. No history of CAD/ T2DM/ Hypertension. No h/o smoking/ alcoholism/drug abuse/Vitamin D supplements/ prolonged immobilization/frequent dialysis. No significant family history. On examination, BP was 200/100 mmHg; Pulse rate was 90/min. CNS examination revealed right UMN type VII CN palsy, right sided hemiparesis (power 3/5) & dysarthria. Rest systemic examination was normal. On investigations: Hb: 12.0 g/dl (12-16); FBS: 96mg/dl (70-110); S.Na: 140meq/L (135-145); S.K: 3.9meq/L (3.5-5.5); S.Ca: 11.5mg/dl (8.5-10.5); Corrected Ca: 10.7mg/dl; Phosphate: 2.7mg/dl (2.5-5.5); Albumin: 5.0mg/dl (3.5-5.5); Blood Urea: 37mg/dl (15-45); Creatinine: 1.1mg/dl (0.6-1.2); Liver function tests were normal. Total Cholesterol: 169mg/dl (150-200); HDL Cholesterol: 41mg/dl (30-65); LDL Cholesterol: 115mg/dl (50-150); Triglyceride: 65mg/dl (50-200). ANA was negative. PT/ INR was 1.26. HIV \(\frac{1}{2}\), HBsAg and Anti HCV Antibody were non reactive. VDRL/TPHA was non reactive. Serum homocysteine levels : 12µmol/L. 2D Echoangiography showed mild concentric LVH with LVEF = 60%. Carotid & renal artery Doppler was normal. USG abdomen and neck was normal. MRI brain showed a lacunar infarct in posterior limb of left internal capsule. Serum vitamin D (25-OH): 66.08nmol/L (75-150); S.PTH: 118.30pg/ml (14-75). DEXA scan showed osteopenia in lumbar region (T score: -1.8, Z score: -1.8). Tc99 SestaMIBI subtraction scan showed increased uptake in left inferior parathyroid gland s/o adenoma. CECT neck showed a nodular subcentimetric parathyroid adenoma abutting the posterior part of lower pole of left thyroid gland. A diagnosis of hypertension with Left Ischemic CVA with right hemiparesis with right UMN type VII cranial nerve palsy with primary hyperparathyroidism with Left inferior parathyroid adenoma.

**Discussion:** The increased risk of vascular morbidity/ mortality with raised PTH is mainly attributed to hypertension and associated left ventricular hypertrophy. However there are few case studies to highlight the association between raised levels of PTH & CVA in a case of primary asymptomatic hyperparathyroidism.

**Conclusion:** Through this case, it is our endeavor to highlight this lesser known but catastrophic morbidity of primary hyperparathyroidism and how we can diagnose this disease by reading into patient’s routine blood investigations thoroughly (serum Ca2+ levels).

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**Abstract #617**

**HIP FRACTURE: A SENTINEL EVENT FOR OSTEOPOROSIS DIAGNOSIS**

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1. Unity Health System, 2. University of Rochester

**Objective:** Osteoporosis is a silent disease until it is complicated by fractures. National osteoporosis foundation recommends initiating treatment for osteoporosis for patient >50 year old who have low trauma hip fracture. Similar to stroke or coronary artery disease the pharmacologic therapy for secondary prevention of osteoporosis should be initiated within the hospital. Our aim was to identify if patient with hip fracture received antiresorptive therapy and Calcium+Vitamin D after admission for hip fracture.

**Methods:** This is a retrospective chart review. Patients
>50 years old who were admitted to our hospital for hip fracture between 01/2011-12/2012 were included in this study.

**Results:** The study included 419 patients. 73% were female. 97.7% patients were Caucasian. 26% patients had prior diagnosis of osteoporosis and 16.5% had previous history of osteoporotic fracture. Prior to admission 43% and 30.6% patients were receiving Vitamin D and calcium supplement respectively, 9.8 % were on bisphosphonates and 2.2 % on calcitonin. At discharge 56.7% were prescribed Vitamin D and/or Calcium, 8.1% were continued on bisphosphonates and 2.4% on other antiresorptive therapy. Bisphosphonate therapy was stopped in a few patients for concern that it would interfere with fracture healing. Interestingly, prescription rate for calcium and/or vitamin D were higher in females as compared to males (62.1% vs. 41.6%, p=0.0004) and a similar significant trend was seen for any antiresorptive therapy (13.7% vs. 1%, p<0.0001).

**Discussion:** Osteoporosis poses a huge economic and societal burden with an annual estimated direct cost of 17 to 20 billion for osteoporosis related fractures. Hip fracture should serve as a sentinel and catastrophic event to alert all clinicians about underlying osteoporosis. This event provides an opportunity to initiate an aggressive treatment program through an interdisciplinary team prior to patient discharge. Our study shows that osteoporosis remains unrecognized and therefore untreated in patients with hip fracture. Current literature supports early initiation of bisphosphonate therapy including the intravenous form to facilitate callus formation and healing. Interestingly our study confirmed gender related discrepancy in favor of females for treatment of this particular disease.

**Conclusion:** Osteoporosis is grossly under diagnosed in this population. Formulation and enforcement of treatment guidelines for osteoporosis should be mandated in all hip fracture patients.

**Abstract #618**

**PREDICTORS OF MORTALITY IN OSTEOPOROTIC HIP FRACTURE**

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**Objective:** To identify various risk factors that may help in predicting mortality in patients presenting with osteoporotic hip fractures.

**Methods:** This is a retrospective study at a community hospital. All the patients with age 50 year admitted with a low trauma hip fracture between January 2011 to December 2012 were included in the study. Patient’s demographics, past medical history, risk factors for osteoporosis, complications and discharge disposition were collected. Analyses were performed using JMP 10.0.2. Significant p-value was considered as <0.05.

**Results:** Of the 419 patients included in our study, 72.8% were females and the median age of the entire cohort was 85 (IQR=79 to 89). 26 (6.2%) patients died during the admission. Significant risk factors for death on univariate analysis were: Age >88 years (p=0.006), past history of falls (p=0.01), COPD (p=0.001), patients not taking calcium prior to admission (p=0.03), patients on chronic steroids prior to admission (p=0.05), patients who developed Pneumonia (p=0.0001), MI (p=0.0004) or stroke (p=0.02) during admission and patients who only received medical management for hip fracture (p=0.0001). Interestingly, Vitamin D level (13ng/ml vs. 27ng/ml, p=0.03) and Calcium level (8.95mg/dl vs. 9.2mg/dl, p=0.04) measured during admission were significantly lower in patients who died. In a multivariate analysis of the above significant risk factors patients who developed Pneumonia and MI during admission, patients who only received medical management for hip fracture, and patients not taking calcium prior to admission were found to be the strongest independent predictors of mortality.

**Discussion:** Osteoporosis affects 10 million Americans and results in 1.5 million fractures per year. Hip fractures are associated with up to 20% 30 day mortality. With the knowledge of the risk factors that can help in predicting mortality, effective preventive strategies can be planned beforehand. Interestingly in our study, we found low levels of calcium and vitamin D on admission to be the predictors of mortality but due to our smaller sample size, but it was not significant on multivariate analysis. Several studies have reported other risk factors such as mini mental test score <6, admission hemoglobin <10g/dl, history of malignancy, but due to the retrospective nature of our study we were not able to analyze these variables.

**Conclusion:** Osteoporosis has grossly been underdiagnosed and additional mortality poses challenges to these patients. Risk factors which may predict mortality will help in planning strategies to prevent any complications. Larger scale prospective studies may be justified.
Abstract #619

OSTEOPOROTIC HIP FRACTURE: CURRENT PRACTICE AT A COMMUNITY HOSPITAL

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Objective: To identify current practice of care in patients presenting with Osteoporotic Hip Fracture at a community hospital and to detect areas for improvement.

Methods: We retrospectively collected 419 patients with Age of more than 50 year old presenting with low trauma Hip fracture from January 2011 to December 2012. Patient information included demographics, past medical history, treatment (medical/surgical) and complications (DVT, Pneumonia, Sepsis, Stroke, MI and death) during admission, medications at discharge, DEXA scan post discharge and discharge destination. Data was analyzed using JMP 10.0.2.

Results: Median age of the population was 85 years (IQR = 79 to 89) with 72.8 % females. Of the 419 patients, 387 (92.6%) patients underwent surgical intervention. Only 38.4 % of patients had their Vitamin D level checked during admission. In patients who died during admission, Vitamin D level was significantly low (13 IU vs. 27 IU, p = 0.02) as compared to those who did not die. Major complications noted were UTI (22.2%), Pneumonia (6.9%), MI (4.8%), Sepsis (1.9%), Stroke (1%), DVT (0.2%) and death (6.2%). At discharge, 56.7% patients received Calcium + Vitamin D, 8 % received Bisphosphonate and 2.4% received other antiresorptive therapy. 5% patients were discharged to home, 32.8 % to acute rehab unit and 54% to skilled nursing facility. Only 1.4% patients underwent a DEXA scan after discharge. Recurrent fracture was seen in 9.1 % of patients within a median of 282.5 days.

Discussion: Osteoporosis is a disease of aging population. With longer life span and increasing geriatric population we are seeing more cases of fragility hip fractures. After a hip fracture, risk of a subsequent fracture increases up to two fold. Hip fracture causes decline in activities of daily living and only 50% return to their baseline functional status. The goal of treatment should be recognizing the diagnosis of osteoporosis in all patients >50 year old who present with low trauma hip fracture and then treat for secondary prevention of osteoporosis related fractures. As noted in our study, only 67.1% of patients were prescribed treatment on discharge (calcium and Vitamin D and Antiresorptive therapy) and only 1.4% patients underwent a DEXA scan after they were discharged. The data we collected is similar to what has been seen in other studies. Hence not only in one hospital but on a national level there needs to be a campaign to improve treatment and follow rates of osteoporosis in patients who present to the hospital with hip fracture.

Conclusion: Treatment for Osteoporotic hip fracture in hospital is not adequate and more aggressive treatment should be initiated in hospital as part of discharge planning.

Abstract #620

DENOSUMAB-INDUCED REFRACTORY HYPOCALCEMIA IN A PATIENT WITH BREAST CANCER AND DIFFUSE OSTEOBLASTIC BONE METASTASES AND SURGICAL HYPOPARATHYROIDISM

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Objective: Denosumab, a human monoclonal antibody to the receptor activator of nuclear factor-xB ligand (RANKL), inhibits osteoclastic activation and has been shown to reduce skeletal-related events in patients with metastatic bone disease and breast cancer. However, denosumab is associated with hypocalcemia. Severe hypocalcemia post-denosumab administration has been reported in patients with severe chronic kidney disease, vitamin D deficiency, prior exposure to bisphosphonate, and gastrointestinal disease.

Case Presentation: We report a case of 59 year old female with severe, symptomatic hypocalcemia of 5 mg/dl (corrected level) with inappropriately low iPTH of 49 pg/ml 20 days after a single injection of 120 mg denosumab for extensive osteoblastic metastatic bone disease due to invasive breast carcinoma. Patient had a total thyroidectomy 10 years ago for a benign goiter; she had mild symptoms of hypocalcemia postoperatively managed by intermittent oral calcium (Ca), but was on no Ca at the time of the denosumab injection. Corrected Ca before denosumab was 8.6 mg/dl and 25-hydroxyvitamin D was 19 ng/mL. Renal function was normal. Despite escalating doses of oral Ca, calcitriol and ergocalciferol, she required multiple hospitalizations for symptomatic hypocalcemia and intravenous Ca infusions. Seventy-one days after denosumab treatment, her corrected Ca was 7.7 mg/dL while taking elemental Ca 4.5 grams tid, calcitriol 3 mcg tid, ergocalciferol 50,000 IU weekly, hydrochlorothiazide 12.5 mg daily, and magnesium oxide 500mg daily. Short-term use of teriparatide did not correct the hypocalcemia nor reduce the doses of other supplemental medications; this was discontinued for lack of efficacy and potential risk in the setting of bone metastases. While on teriparatide 40 mcg sc twice daily, the serum osteocalcin was

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132 ng/ml (9-42 ng/ml) and serum CTX beta crosslaps was 117 pg/ml (104-1008 pg/ml). Imaging showed disseminated osteoblastic bone metastasis. The patient had no evidence of gastrointestinal malabsorption and 1,25-dihydroxyvitamin D 10 days after initiating calcitriol was 182 pg/mL, indicating appropriate absorption.

**Discussion:** This is a unique case in which the presence of hypoparathyroidism, vitamin D deficiency and extensive osteoblastic bone metastasis contributed to recurrent profound hypocalcemia.

**Conclusion:** We hypothesize that the combination of active calcification of bone metastasis with marked elevation of osteocalcin with suppressed bone resorption combined with an inappropriately low iPTH and vitamin D deficiency led to profound hypocalcemia. Very high and escalating doses of calcium and vitamin D over a 2 month period were required to normalize serum Ca.

**Abstract #621**

**USE OF METHIMAZOLE AND DENOSUMAB IN THE TREATMENT OF HYPERTHYROID-ASSOCIATED OSTEOPOROSIS**

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**Objective:** To present a case which demonstrates the effect of methimazole and denosumab on bone mineral density (BMD) in a patient with hyperthyroid-associated osteoporosis.

**Case Presentation:** A 68 year-old female presented for further evaluation of her long-standing history of untreated hyperthyroidism. On exam, she had a mild tremor and a 2 cm right-sided thyroid nodule. Laboratory evaluation revealed TSH <0.005 uIU/mL (0.450 -4.500 uIU/mL), FT4 2.78 ng/dL (0.82-1.77 ng/dL) and T3 303 ng/dL (71-180 ng/dL). Radioactive iodine uptake was increased consistent with hyperthyroidism with relative photopenia of the left lower lobe. Biopsy of the photopenic nodule was benign. Given her risk factors, a DEXA was obtained. This revealed osteoporosis with lumbar spine and left femoral neck T scores of -2.8 and -4.1, respectively. Due to inability to perform self care since an aneurysm repair, she was not a candidate for radioactive iodine and was started on methimazole. For her osteoporosis, denosumab was initiated along with calcium and vitamin D. FT4 and T3 normalized within four months. Two years after treatment with denosumab and methimazole, repeat DEXA revealed significant improvement at the lumbar spine (T score -1.1) and left femoral neck (T score -2.6). This represented a 25.2% increase at the lumbar spine and 43.1% increase at the left femoral neck when compared to previous.

**Discussion:** In hyperthyroidism, thyroid hormone overstimulates osteoclastic-mediated activity resulting in cortical and trabecular bone resorption. Traditionally, hyperthyroid-associated osteoporosis is treated with antithyroid therapy along with calcium and vitamin D supplementation. The combination of methimazole and bisphosphonate therapy has also been shown to increase BMD. However, the use of antithyroid therapy in conjunction with denosumab in the management of hyperthyroid-associated osteoporosis has not been well described. Denosumab is a monoclonal antibody which binds to the receptor activator of nuclear factor-κB ligand (RANKL) and subsequently inhibits osteoclast formation resulting in decreased bone resorption and increased bone density. It has been approved for the treatment of osteoporosis in women with high risk of fractures and may lead to a greater increase in BMD when compared to alendronate with a similar safety profile.

**Conclusion:** Given that denosumab targets the underlying mechanism of hyperthyroid-associated osteoporosis, it is a logical treatment option. Our patient’s dramatic improvement in BMD suggests that methimazole in conjunction with denosumab hastens recovery of BMD in hyperthyroid-associated osteoporosis.

**Abstract #622**

**FRACTURE RISK IS HIGH IN PATIENTS ATTENDING DIABETES CENTRES**

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**Objective:** Osteoporosis is common in postmenopausal women and guidelines recommend bone mineral density (BMD) screening of all women (and men) over age 65. FRAX is a tool for the assessment of 10-year fracture risk in adults, incorporating clinical risk factors with or without BMD. FRAX does not include type 2 diabetes mellitus (T2DM) as a risk factor although patients with T2DM have increased risk for fragility fracture. Paradoxically, patients with T2DM have a higher BMD than expected given their elevated fracture risk. We hypothesized that there was a low awareness of osteoporosis in the T2DM population seen in diabetes centers and that their FRAX risk of osteoporotic fracture would be at least equal to the Canadian population.

**Methods:** We recruited consenting women over 65 years attending diabetes education centers at academic hospitals in Vancouver Canada in 2013. A questionnaire with FRAX risk factors and osteoporosis awareness questions was administered. FRAX scores were compared to published data from a similar age and sex matched Canadian population.
Results: In diabetic women, the 10-year major osteoporotic fracture risk was 12.9% (+/- 10.3) and the 10-year hip fracture risk was 4.4% (+/- 7.9). Only 24% of participants had ever had a BMD test; only 38% were taking calcium supplements and only 40% were taking vitamin D supplements. Published FRAX fracture risk estimates for similar age and sex-matched Canadians for major osteoporotic and hip fracture are lower; 11.6% (+/- 8.0) and 3.6% (+/- 5.1) respectively (p<0.001) for both major osteoporotic fracture and hip fracture.

Discussion: Guidelines would recommend BMD testing and fracture risk assessment in all of the T2DM women surveyed, with recommendations of appropriate calcium and vitamin D intake for all. Candidates for osteoporosis pharmacotherapy would be patients with FRAX > 20% or FRAX hip > 3%. Despite dietician, nurse, and academic endocrinologist care, a minority of patients attending academic diabetes education centers are meeting guidelines recommendations for osteoporosis assessment or therapy. FRAX without BMD would suggest that the majority of patients would meet guidelines criteria for pharmacotherapy. In addition, the calculated FRAX scores likely are underestimates since the FRAX algorithm does not integrate the risk conferred by T2DM.

Conclusion: We conclude that diabetes centre resources should be directed to attend to the demonstrated bone health needs of patients, including BMD, FRAX risk assessment, calcium, Vitamin D, exercise, and pharmacotherapy.

Abstract #623

RENAL OSTEODYSTROPHY - WHEN IS A BONE BIOPSY NEEDED?

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Objective: The prevalence of different types of renal osteodystrophy appears to have changed within the past 2 decades.

Case Presentation: 34-year-male was referred for osteoporosis management. He had ESRD secondary to obstructive nephropathy with two failed renal grafts. While on chronic immunosuppressant therapy including steroids for transplant, he developed disseminated histoplasmosis (including meningitis leading to seizures) and is now on lifelong prophylaxis with itraconazole and levetiracetam. He is currently on peritoneal dialysis. Bone density revealed severe osteoporosis (Z-score-3.0 in lumbar spine, -3.5 in total left hip, -3.2 in total right hip and -2.8 in forearm). Vertebral fracture assessment revealed T7,10,11,12 and L1 fractures. Trabecular bone density showed low scores for his age. C-telopeptide was 522pg/ml(70-780pg/mL). Vitamin D level was normal at 42ng/ml. PTH was 340pg/ml. PTH had been above 2000 in the past and he has been on Cinacalcet, calcium citrate and calcitriol for past 3 years for secondary hyperparathyroidism.

Despite his low Z-scores and multiple vertebral fractures, traditional methods of diagnosing osteoporosis cannot be used in patients with a low GFR. The important question then became, what type of underlying metabolic bone disorder did our patient have.

The patient was referred for a metabolic bone biopsy, which showed increased bone turnover with normal mineralization. We treated him with IV zolendronic acid to prevent future fractures. Denosumab was not chosen because of his history of severe and recurrent infections.

Discussion: Renal osteodystrophy can be of different types. 1)High turnover and high volume-Osteitis fibrosa associated with untreated secondary hyperparathyroidism. 2)Low turnover osteodystrophy-Adynamic bone disease that is usually caused by excessive use of calcimimetics, calcium and vitamin D supplements and calcium based phosphate binders used for treatment of secondary hyperparathyroidism. 3)Osteomalacia occurs when there is defective mineralization.

Osteitis fibrosa was the most common type of bone disease in CKD and ESRD patients 2 decades ago but adynamic bone disease is now the most prevalent. High bone turnover osteodystrophy, such as with osteitis fibrosa, could be treated with antiresorptive agents; however this treatment can be detrimental in adynamic bone disease where turnover is already low. PTH above 400 can indicate high turnover dystrophy whereas PTH less than 100 usually is seen in adynamic bone disease. However levels in between these are equivocal. The definitive diagnosis in these cases can be made only by bone biopsy.

Conclusion: Metabolic bone biopsy is helpful for accurate diagnosis of renal osteodystrophy.

Abstract #624

TERIPARATIDE TREATMENT (PRE-SURGICAL Versus POST-SURGICAL) IN THE OUTCOME OF ATYPICAL FEMUR FRACTURE

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Objective: Our objective was to describe the response to teriparatide in atypical femur fracture(FF) comparing pre-surgical versus post-surgical outcome in a same patient.

Methods: We describe a post-menopausal woman with
ABSTRACTS – Metabolic Bone Disease

We describe a 55 year old post-menopausal woman with rheumatoid arthritis on intermittent steroid, leflunomide and methotrexate for prolonged duration. She took oral alendronate for 5 years for osteoporosis. She initially developed pain in the left thigh which was radiologically confirmed as atypical FF and underwent intramedullary nailing (IMN) for the same. 2 months later bisphosphonates were stopped. 6 months later she developed nail displacement and comminuted fractures at the fracture site requiring repeat nailing. One year later, atypical FF was noted in the other limb and was referred to our Endocrine department. At the time of presentation, she had pain only during severe activity. Her calcium and vitamin D status were normal. She was advised injection teriparatide for three months. 3 months later, radiological imaging did not show sign of fracture healing. She then underwent IMN with continued teriparatide treatment. She is now one year post-surgical intervention. There was no pain in right thigh and fracture had shown signs of union. However, the left femur had not united.

Discussion: Atypical FFs are rare but serious side effects of bisphosphonate therapy in osteoporotic individuals. The management of this condition is based on expert views. Current recommendations of ASBMR include treatment with teriparatide in addition to surgical fixation. Our patient developed atypical FFs initially in the left femur and underwent IMN for the same which did not improve the surgical outcome. In the right femur, she developed atypical FF later which was treated with teriparatide for three months before proceeding with IMN. Pre-surgical treatment with teriparatide in our patient had had long term successful outcome with union of fracture compared to the left which was not treated with teriparatide before surgery.

Conclusion: Although this is a single case report, due to occurrence of bilateral atypical FFs in the same patient, this scenario is akin to a typical example of placebo controlled trial on teriparatide pre-surgical treatment versus post-surgical treatment. Teriparatide treatment did not improve short term fracture healing; however it did improve the long term outcome when compared with the other limb which received teriparatide later.

Abstract #625

PRIMARY HYPERPARATHYROIDISM MIMICKING METASTATIC MALIGNANCY

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Mayo Clinic

Objective: To describe a case of brown tumors of primary hyperparathyroidism mimicking metastatic cancer with hypercalcemia.

Case Presentation: A 58-year-old female with a history of Hodgkin lymphoma presented with left leg pain after a fall from standing height. Physical exam was notable for deformity of the left lower extremity and a large left sided neck mass. Left hip x-ray confirmed a sub-trochanteric femur fracture and a lytic lesion. Laboratory results revealed a serum calcium of 15.6 mg/dL, ionized calcium of 8.05 mg/dL, alkaline phosphatase of 399 units/L and a mild normocytic anemia. CT scan of the chest, abdomen and pelvis revealed a 3.5 x 2.5 cm peritracheal nodule and widespread “metastatic” lytic lesions. An ultrasound of the neck showed a solid mass encompassing the left lobe of the thyroid with sonographic features of malignancy. PTH returned 1510 pg/mL and vitamin D was undetectable. Sestamibi scan revealed increased uptake in a left neck mass suggesting a thyroid malignancy. FNA was positive for neoplastic cells with Hürthle cell features. The left femur required resection and endoprosthetic replacement. The pathology from the operation revealed a brown tumor of hyperparathyroidism. The patient underwent excision of a 5.3 x 3.5 x 2.2 cm left superior parathyroid adenoma that was adherent to the left lobe of the thyroid. Postoperatively, her laboratory values normalized. She successfully underwent rehabilitation and the bone lesions decreased in size by five months after her parathyroidectomy.

Discussion: In this setting, malignancy is high on the differential. In particular, parathyroid and thyroid carcinoma should be considered. Osteitis fibrosa cystica is now very rare in the United States and occurs more typically in patients with severe disease, especially those with parathyroid carcinoma. Brown tumors result from excess osteoclast activity and are composed of numerous multinucleated giant cells admixed with fibroblasts and associated with interstitial hemorrhage marked by hemosiderin deposition (resulting in a brown appearance).

Conclusion: Clinical suspicion and appropriate testing are critical for the diagnosis. FNA cytology can be challenging when parathyroid malignancy is in the differential diagnosis. In the setting of hypercalcemia and a mass on imaging, surgical resection is the treatment of choice. Additionally, a prior FNA can make histologic assessment of invasion difficult due to biopsy site changes and has a remote risk for tumor rupture or seeding tumor cells.
Abstract #626

**ATYPICAL PARATHYROID ADENOMA MASQUERADING AS A THYROID NODULE AND PRESENTING WITH SEVERE HYPERCALCEMIA.**

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**Objective:** To report a rare case of atypical parathyroid adenoma presenting as a thyroid nodule and severe hypercalcemia.

**Case Presentation:** A 27-year-old Caucasian woman with history of mild mental retardation presented to ER with severe nausea, vomiting and abdominal pain of one-day duration. She had no similar episodes in the past. She denied taking any over the counter medications and had no known drug allergies. On examination, she was afebrile, with BP 130/75 mm Hg and HR 90-100 beats/minute. She was confused and had generalized tenderness over her abdomen. Laboratory data revealed corrected serum calcium 15 mg/dl (8.5-10.5), intact parathyroid hormone level 413 pg/ml (12-72), 25 (OH) vitamin D 9 ng/ml (30-100), 1,25 dihydroxy vitamin D 76.5 pg/ml (10-75) and serum phosphate 3 mg/dl (2.5-4.8). Renal and thyroid function tests were normal. She was admitted with severe hypercalcemia secondary to primary hyperparathyroidism and started on intravenous (IV) normal saline and received 1 dose of IV pamidronate 60 mg. Thyroid ultrasound revealed a right dominant 2.8 cm complex, solid and cystic nodule with intranodular vascularity. Her calcium level improved to 9.8 mg/dl and was subsequently discharged. As outpatient, she was referred to an endocrine surgeon for dominant right thyroid nodule and primary hyperparathyroidism. She underwent biopsy of the right thyroid nodule, which was consistent with parathyroid neoplasm. CT scan of neck with 3D imaging reconstruction showed a large well defined nodule with peripheral enhancement suspicious for large right parathyroid adenoma. She underwent minimally invasive parathyrectomy and intra-operative PTH levels fell from 289 pg/ml to 15.8 pg/ml. Pathology was consistent with atypical parathyroid adenoma, with focal capsular distortion and increased mitotic activity. Post operatively; she was started on calcium and vitamin D supplementation. She is doing well and following in clinic.

**Discussion:** Atypical parathyroid adenoma along with parathyroid cancer is amongst rare causes of primary hyperparathyroidism. It is uncommon for an atypical parathyroid adenoma to present with severe hypercalcemia. Further, in her case the adenoma was masquerading as a thyroid nodule making the diagnosis challenging. Certain ultrasound characteristics used to distinguish a parathyroid adenoma from thyroid nodule include solid composition, hypoechoic appearance and presence of a feeding polar vessel. It is difficult to distinguish an atypical adenoma from parathyroid cancer both clinically and histologically.

**Conclusion:** This case highlights the importance of suspecting parathyroid adenoma mimicking a thyroid nodule, especially in patients presenting with primary hyperparathyroidism.

Abstract #627

**TRANSIENT OSTEOPOROSIS IN PREGNANCY**

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**Objective:** To recognize and manage an interesting clinical condition called transient osteoporosis.

**Case Presentation:** 29 year old healthy female, gravida 4, presented with gradually increasing bilateral hip pain during her 36th week of pregnancy. She had no history of hip pain in her previous pregnancies. Pain first started in her left hip and then the right hip was involved. By 4-5 days after onset she was unable to walk. At the time of presentation she was suffering from disabling pain in both hips. Range of motion in both hips was limited without any erythema or warmth. Complete blood count, sedrate were all normal. Hip ultrasound showed bilateral effusions. MRI showed diffuse edema of the femoral head and neck bilaterally without any evidence of avascular necrosis or septic arthritis. Articular cartilage was normal without any destructive lesions. In the absence of any other causes and negative laboratory results, a diagnosis of TOH was made. She received simple analgesics and bed rest and delivered a healthy baby at term. Cesarean section was chosen to avoid possible trauma to the hips during vaginal delivery. She improved significantly after delivery and after 2 months was completely normal without any pain or movement restrictions in the hip joints. Repeat MRI in due course showed complete resolution of changes.

**Discussion:** Transient bone marrow edema syndrome also known as Transient Osteoporosis (TO) is an uncommon disease which may present with spontaneous hip pain that may progress to immobility. The disorder mostly affects postmenopausal woman or during pregnancy (third trimester, less commonly after postpartum) and
it can be painful and incapacitating. Hip joint (76%) is most commonly affected but rarely it can affect other joints. It is usually unilateral and the left hip is most commonly affected due to cephalic presentation of the fetus which could lead to microtrauma. Pregnancy is the only recognized risk factor for bilateral involvement. It is not related to trauma. Symptoms begin with spontaneous pain in the hip and within few weeks the pain extends to the groin and thigh. Later it progresses to limping and disability. It usually improves with a conservative approach. Diagnosis is made by exclusion. MRI can typically detect disease within 48 hours after onset of symptoms. Patients attain normal bone mass and complete mobility in 2-12 months and pregnant woman recover 2-6 months after delivery. Fractures of femoral neck have been a reported complication.

Conclusion: There are multiple differential diagnoses for hip pain in pregnancy. TOH is an uncommon but self-limiting condition. Diagnosis helps accurate management. It is a benign disease which improves with conservative management.

Abstract #628

PRIMARY HYPERPARATHYROIDISM IN PREGNANCY

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Case Presentation: Primary hyperparathyroidism (PHP) in pregnancy is an uncommon condition that is associated with significant maternal and fetal complications. A 25-year-old African primigravid woman was admitted to the hospital at 9 weeks of gestation with nausea, vomiting and fever like symptoms. She has no known past medical or family history of high calcium problems. She had recently emigrated from Togo to United States. Initial laboratory evaluation revealed significant elevation of calcium 13.5 mg/dl (8.4 - 10.2 mg/dl) and low phosphate level of 1.3 mg/dl (2.2 - 4.5 mg/dl). Her intact PTH was 23.7 pmol (0.9 - 7.7 pmol), 25 OH vitamin D level was 14.7 ng/ml and 24-hour urine calcium was 500 mg (100-300 mg/24 h), indicating primary hyperparathyroidism with super imposed vitamin D deficiency. After intravenous hydration, calcium levels improved to 10.2 mg/dl and she was discharged. Repeat laboratory check done 2 weeks later showed recurrence of hypercalcemia (calcium - 12.2 mg/dl) and she was readmitted to the hospital. Neck ultrasound revealed an indeterminate 8 mm hypoechoic nodule along the deep surface of the left lobe of the thyroid gland suspicious for parathyroid lesion. An elective parathyroidectomy of left inferior parathyroid adenoma was performed at 13 weeks of gestation. Intraoperative PTH levels have dramatically decreased from 21.6 to 3.3 pmol/L confirming successful operation. At 3 weeks clinical follow up (16 weeks gestation) her pregnancy was uncomplicated.

Discussion: PHP in pregnancy confers high maternal and fetal complication rates of 67% and 80% respectively. Given the rarity of PHP in pregnancy, management recommendations are based on retrospective studies. In the world’s largest case series of gestational PHP, calcium >11.4 mg/dl is associated with exponential increase in the risk of fetal loss, based on this authors recommend parathyroidectomy when calcium level is above this threshold. Given the high risk of surgery in the first and third trimester, surgical intervention is reserved for second trimester of the pregnancy. Asymptomatic patients with milder hypercalcemia (<11.4 mg/dl) can be managed with conservative medical management such as low calcium intake, oral hydration and close fetal surveillance.

Conclusion: Primary hyperparathyroidism during pregnancy though uncommon, represents a preventable cause of fetal and maternal morbidity and mortality. In cases of severe gestational PHP, parathyroid surgery can be safely performed in the second trimester and is the most definitive treatment modality with optimal prognosis for both the mother and fetus.

Abstract #629

RECURRENT FIBROUS DYSPLASIA PRESENTING IN ADULTHOOD

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Case Presentation: Fibrous dysplasia (FD) is an osteoblastic lineage disorder cause by a post zygotic activating mutation of the gene encoding the alpha subunit of the stimulatory G protein which results in abnormal proliferation and differentiation of bone. FD is diagnosed mostly in childhood and adolescence with 90% of craniofacial lesions found before age 5. An adult patient was referred to our clinic with recurrent FD in skull with normal non contrast CT head done 5 years prior to presentation.

This is the case of a 60 year old female with history of headaches and chronic sinusitis who presented to the Endocrinology clinic for evaluation of a recurrent mass in the right frontal sinus concerning for fibrous dysplasia. Headache was the initial symptom with a normal non contrast CT scan of head done in 2003. ENT evaluated
patient on December 2008 for chronic sinusitis with maxillary CT scan that showed a mixed density lesion within the superior aspect of the right frontal sinus extending from the frontal calvarium. Surgery was done on March 2008 for reduction of mass with placement of small plates and screws. Final pathology of bone showed a reactive lesion with strongly positive histiocyte change CD68. Patient headaches returned in 2013. A non contrast CT of sinuses showed an heterogeneous expansile mixed density mass completely opacifying the right frontal sinus extending partially across midline to the medial aspect of the left frontal sinus, concerning for recurrent fibrous dysplasia. Bone specific alkaline phosphatase was normal (25.6 U/L), with normal liver and renal function. A Whole Body Bone Scan done in November 2013 showed monostotic fibrous dysplasia located at midline frontal bone.

Discussion: FD is a congenital disease of bone that can present in adulthood. What makes the presentation of our patient interesting is that at the age of 50 a non contrast CT of head was normal, and subsequent CT of the sinuses 5 years later showed a mass, with evidence of recurrence after surgical excision. Ongoing research has provided more understanding on the physiology of FD making way for new therapeutic options.

Conclusion: FD is a rare disease of bone that causes bone deformities and pain. Recent studies suggest that inhibition of IL-6 by targeting the IL-6 receptor with tocilizumab can reduce local disease. Other targets of disease treatment being studied include RANK-L and PTHrP. As more is understood on the mechanism of activation of cAMP newer treatment options can be made available.

Abstract #630

EFFECT OF ZOLEDRONIC ACID ON GFR IN RENAL TRANSPLANT PATIENTS

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Objective: Renal transplant patients are at extremely high risk to develop osteoporosis due to secondary hyperparathyroidism, pre-transplant metabolic disturbances, and use of glucocorticoid and calcineurin inhibitors. An effective treatment for osteoporosis is intravenous zoledronic acid. However, zoledronic acid is renally cleared and renal toxicity has been reported. It is not recommended in patients with a creatinine clearance < 35 mL/min. This study evaluates the effect of zoledronic acid on renal function in renal transplant patients.

Methods: This study was a retrospective chart review of post-transplant patients treated with zoledronic acid for osteopenia/osteoporosis compared with an age matched renal transplant control with normal bone mineral density and not treated with zoledronic acid. Renal function was reviewed at baseline, one month and one year following treatment or non-treatment. All patients had a baseline creatinine clearance > 35 mL/min.

Results: Eighteen renal transplant patients (average baseline GFR of 76 mL/min) were treated with 5 mg zoledronic acid administered intravenously over 60 minutes and compared to 17 controls (average baseline GFR of 83 mL/min). The GFR was slightly higher at one month in patients who were treated with zoledronic showing a mean increase of 4.11 mL/min compared to a decrease of 9.53 mL/min in controls (p = 0.046). At one year, the GFR was not statistically different between the two groups (decrease of 2.94 mL/min in cases versus increase 1.35 mL/min in control, p = 0.48).

Discussion: This study is significant because osteoporosis is frequently found in renal transplant patients and zoledronic acid is an effective treatment. The limitations of this study include its small size and conduction at a single site. It was also not a randomized controlled trial. However, zoledronic acid appears safe in transplanted kidneys with CrCl > 35 mL/min but a larger randomized controlled trial would be needed to know conclusively.

Conclusion: In this study, the use of zoledronic acid to treat metabolic bone disease did not cause acute kidney injury or decrease in renal function in renal transplant patients who have a baseline creatinine clearance > 35 mL/min.

Abstract #631

EVALUATION OF THE RELATIONSHIP BETWEEN HYponATREMIA AND FRACTURES

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Objective: Hyponatremia from a wide range of causes is frequently present in the elderly. Recent studies show an increased risk of fractures in patients with mild chronic hyponatremia. Hyponatremia is noted to upregulate osteoclast-mediated bone resorption.

Our project evaluates the relationship between hyponatremia and risk of incident fracture while controlling for bone density, age, and sex.
Methods: Study design: Retrospective, matched case-control study of patients at Lahey Hospital and Medical Center, age≥45y with DEXA and serum sodium obtained within a year prior to event of interest (fracture/non-fracture complaint).

Cases: Patients with an incident fracture between Jan 2005-May 2013. First fracture was used for cases with multiple fractures.

Controls: Patients with a non-fracture complaint over the same time period, matched 2:1 with cases on age (within 2y) and sex.

Hyponatremia: Absent, Mild (sodium 135-137 mmol/L), Moderate (sodium 130-134), Severe (sodium < 130).

Bone density: Normal, Osteoporosis (T-score < -2.5), Osteopenia (T-score -1.0 to -2.5).

Univariate and multivariable conditional logistic regression models were used to estimate risk of fracture associated with hyponatremia and bone density. Odds ratios (OR) and 95% confidence intervals (CI) were calculated. All statistical analysis was performed using SAS v9.3. All tests were two-sided with alpha=0.05.

Results: We identified 457 cases and 914 controls. 89% were female, 90% Caucasian with a mean age of 73±10 years. Hyponatremia was more prevalent in cases compared to controls. An unmatched test of proportions showed risk of fracture increased with severity of hyponatremia (test for trend, p<0.0001). Univariate logistic regression models showed a significantly higher risk of fracture in hyponatremia (chi-sq p<0.0001) and osteoporosis/osteopenia (p<0.0001). Controlling for presence of osteoporosis/osteopenia, the risk was 3-fold higher in mild [OR 3.0; (95% CI: 2.2, 4.2)], 4-fold higher in moderate [OR 4.4; (95% CI: 2.8, 7.0)] and 11-fold higher in severe hyponatremia [OR 11.1; (95% CI: 4.1, 30.5)]. Interaction between osteoporosis and hyponatremia was tested in the model and was non-significant. Vertebral fractures were strongly associated with worsening hyponatremia (test for trend: p<0.0001).

Discussion: Our study shows elevated risk of fractures in patients with hyponatremia, irrespective of bone density. The risk of fracture is increased with worsening hyponatremia.

Conclusion: The importance of recognizing and managing hyponatremia and its associated morbidity, which may include an increased risk of fracture, is highlighted.

Abstract #632

HYPERPARATHYROIDISM AND HYPERPARATHYROID BONE DISEASE IN A YOUNG NIGERIAN WOMAN; A CASE REPORT

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Objective: Hyperparathyroidism is over-activity of the parathyroid glands resulting in excess production of parathyroid hormone. It is a rare endocrine disorder, scarcely seen in our practice locale in Nigeria. Primary hyperparathyroidism is even rarer, compared to secondary hyperparathyroidism. Secondary hyperparathyroidism is more common as a result of increasing incidence of renal diseases.

Case Presentation: A 39 year old female post graduate student of Edo origin in Nigeria presented with complaints of bone pains and weight loss, passage of stones in urine, polyuria, nocturia and inability to walk. Bone pains were generalized and were associated with shortening and bowing of limbs with hunching of the chest and back. Bone pains progressed till patient became wheelchair bound. There is history of significant weight loss. Examination revealed a young woman, chronically ill-looking, small for age, sitting in a wheel chair, with kyphosis and a gibbus, pectus carinatum, bowing of the limbs with grade 4 finger clubbing. Other findings were essentially normal. Corrected serum calcium was 16 mg/ml (8.5- 10.5), phosphate was 3.5mg/ml (2.5- 4.5). Parathyroid was 274.0pmol/L (1.6- 6.9). Electrolytes, Urea and Creatinine were essentially normal, renal ultrasound scan showed nephrolithiasis. Skeletal survey revealed generalized osteoporosis of the bones with collapse of the chest wall & reduction of lung volume bilaterally, transverse fractures of proximal third of forearm bones with anterior-lateral displacement, extensive cortical resorption of the femurs. An assessment of primary hyperparathyroidism with hyperparathyroid bone disease was made. She was placed on tabs Cinacalcet and Alendronic acid and referred to the surgical team for parathyroidectomy.

Discussion: Challenges in management of this patient included difficulty in making diagnosis as a result of expensive investigations; difficulty in treating because the drugs are scarce and expensive and few surgeons are experienced in performing the surgery in this part of the world.

Conclusion: This is a case report of primary hyperparathyroidism and hyperparathyroid bone disease in a young Nigerian woman. Primary hyperparathyroidism is a rare endocrine disorder in our practice locale.
Abstract #633

DENOSUMAB USE IN PATIENT WITH BISPHOSPHONATE-RESISTANT HYPERCALCEMIA OF MALIGNANCY

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Case Presentation: A 62 year old male with stage IV laryngeal squamous cell carcinoma with lung metastases was admitted for asymptomatic hypercalcemia with an albumin-corrected calcium level 13.8mg/dl (reference range, 8.5-10.3). He had been getting zoledronic acid 4mg every 3 weeks for the prior two months for hypercalcemia of 12-13mg/dl. He denied using HCTZ, calcium or vitamin D. The patient had no known bone metastases. Phosphorus and creatinine levels were normal. Intact PTH 9pg/ml (11-54), PTH-related peptide 16pmol/l (<1.8), 25(OH)D 17ng/ml (30-100) and 1,25(OH)2D 134pg/ml (10-75) were diagnostic of HHM. After IV pamidronate, intravenous fluid hydration and calcitonin, he was discharged with corrected calcium down to 12. Despite an increase to weekly zoledronic acid and adding prednisone for elevated 1,25(OH)2D, he had four subsequent admissions with elevated corrected calcium as high as 14.2. Denosumab 120mg subcutaneously was added. His corrected calcium remained at 11.6 for the next two weeks. Subsequently, he experienced rapid disease progression and died.

Discussion: Hypercalcemia has been reported to occur in up to 20 to 30 percent of patients with cancer. It has 30-day mortality of 50%. We describe a patient with humoral hypercalcemia of malignancy (HHM) refractory to bisphosphonate and prednisone with apparent response to denosumab, a therapeutic monoclonal antibody that blocks RANK ligand.

Conclusion: 1: Denosumab, currently approved only for osteoporosis and bone metastases, may be an additional choice for refractory hypercalcemia. The literature suggests it may be more potent than zoledronic acid.

2: HHM with increased PTH-rp usually does not result in elevated 1,25(OH)2D. Our patient with elevated 1,25(OH)2D did not respond to prednisone unlike a similar reported case.

Abstract #634

THE GROWING PROBLEM OF DENOSUMAB INDUCED HYPOCALCEMIA: REPORT OF TWO CASES

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Case Presentation: Introduction: Denosumab, a monoclonal antibody against receptor activator of nuclear factor-kB ligand, is a potent inhibitor of osteoclast activation. This antiresorptive drug was initially approved for the treatment of postmenopausal women with osteoporosis. Indications for its use have now been expanded to include prevention of skeletal-related events (SRE) in patients with bone metastases from solid tumors, increasing bone mass in patients receiving androgen deprivation therapy for prostate cancer or aromatase inhibitor therapy for breast cancer, treatment of men with osteoporosis, and treatment of giant cell tumor of bone. Severe hypocalcemia has been reported in individuals treated with denosumab, including fatal cases.

Case 1: A 77-year-old male with prostate cancer metastatic to bone was treated with denosumab 120 mg for the prevention of SRE. Serum levels of calcium and 25-vitamin D were normal prior to treatment. The patient developed severe symptomatic hypocalcemia one week after the first dose of denosumab, with a nadir serum calcium level of 4.9 mg/dl. Management included administration of 90 grams of calcium gluconate intravenously over a ten day hospitalization, and the hypocalcemia was successfully corrected.

Case 2: A 65-year-old female with severe renal impairment requiring dialysis, short bowel syndrome on chronic total parenteral nutrition (TPN), and osteoporosis previously treated with ibandronate, was treated with denosumab 60 mg for fracture risk reduction. Despite optimization of serum calcium and 25-vitamin D levels with TPN adjustments prior to treatment, the patient developed severe asymptomatic hypocalcemia, with a nadir serum calcium level of 6.1 mg/dl five weeks after the first dose of denosumab. Management included increased intravenous calcium supplementation via the TPN, and the hypocalcemia was successfully corrected.

Discussion: Risk factors for this adverse reaction is not fully understood, but appear to include prior bisphosphonate use, renal impairment and malabsorption syndromes. As the indications for denosumab therapy have broadened, the incidence of denosumab-induced hypocalcemia is likely to increase. As highlighted by the two cases described in this report, hypocalcemia may occur in patients with or without underlying predisposing conditions, such as renal disease and short bowel syndrome.
**Conclusion:** A prospective postmarketing study is planned to assess the long-term safety of denosumab; until the incidence and risk factors for denosumab-induced hypocalcemia are better clarified by such research, we recommend close monitoring for this potentially serious adverse event.

**Abstract #635**

**PERSISTENT HYPERCALCEMIA - CASE OF PAGET'S DISEASE OF BONE (PDB) AND CONCURRENT PARATHYROID ADENOMA (PA)**

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**Objective:** Bone metabolism can be affected by common diseases such as primary hyperparathyroidism (PHP) and PDB. Each disease is characterized by distinct clinical and biochemical markers, however the pathophysiologic presentation may overlap. We present a rare case of persistent hypercalcemia due to PHP in the setting of PDB.

**Case Presentation:** An 82-year old woman with PDB presented to endocrinology clinic for evaluation of persistent hypercalcemia. She was diagnosed with PDB several years prior to current presentation without any history of treatment. Patient recently presented to the ER status post fall. Physical exam was unremarkable. Labs showed elevations of bone specific alkaline phosphatase, calcium, and iPTH. Serum creatinine, liver specific alkaline phosphatase, 25-hydroxy vitamin D, and PTHrP levels were normal. She was treated with IV fluids and calcitonin with brief improvement in calcium levels. A bone scan showed increased uptake in the bilateral hemipelvis, right-left femurs, hemi-calvarium bilaterally that seemed consistent with PDB. Patient was started on Cinacalcet, however her hypercalcemia persisted. A Sestimibi scan demonstrated increased uptake in the region of the right thyroid bed, consistent with PA. Surgery was scheduled for bilateral neck dissection including right parathyroidectomy. Following initial surgery, calcium and iPTH levels remained elevated. Repeat Sestimibi scan showed persistent uptake in the right mid and lower thyroid, suspicious for residual PA. Patient was treated with zoledronic acid due to persistent hypercalcemia. Repeat neck exploration was performed which showed an enlarged right retroesophageal / retrocarotid parathyroid, which was removed. iPTH level decreased to normal within 10 minutes.

**Discussion:** PDB is caused by a disturbance in osteoclast differentiation and function resulting in focal areas of increased bone turnover. Symptoms include bone pain with laboratory findings of elevated bone specific alkaline phosphatase and bone deformities of the axial skeleton seen on radiologic studies. Typically, calcium and phosphorus levels remain normal in PDB, however iPTH levels can be elevated in 15% of cases due to secondary hyperparathyroidism. PHP is characterized by increased bone resorption due to elevated iPTH, causing elevation in calcium levels. The presence of PA or hyperplasia is rare in patients with PDB, prevalence of 2-6%. Early identification is key in preventing consequential skeletal and extraskeletal comorbidities.

**Conclusion:** PDB and PHP have distinguishing clinical and laboratory features. Hypercalcemia in a patient with PDB should raise one’s clinical suspicion of a coexisting disorder of calcium metabolism, one of which is PHP.

**Abstract #636**

**THE CLUE IS IN THE PHOSPHORUS**

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**Case Presentation:** A 56 year old male runner presented with recurrent lower extremity stress fractures. DXA bone density (BMD) lowest T-score was -2.0 at the femoral neck. Biochemical evaluation revealed serum phosphorus 2.5 mg/dL (2.9-4.8), alkaline phosphatase 170 U/L (41-120), intact PTH 65 pg/mL (7-53), serum calcium 9.5 mg/dL (8.4-10.5), serum creatinine 0.88 mg/dL (0.60-1.20) and 25-hydroxyvitamin D 42 ng/mL (20-100). On calcium and vitamin D supplements, he continued to have bilateral stress fractures despite reduced activity. BMD T-score 1.5 years later was -2.8 and IV bisphosphonate was initiated with no improvement in a 2 year follow up BMD. Due to a decline in serum phosphorus to 2.0 mg/dL, urine phosphorus was measured, with tubular reabsorption of phosphorus calculated to be low at 76%. Fibroblast Growth Factor (FGF) 23 level was 201 RU/mL (≤180 RU/mL) and 1,25-dihydroxy vitamin D level was 30 pg/ml (18-72). He did not tolerate calcitriol and phosphorus treatment due to bone pain. PET/CT revealed small foci of activity in both lower extremities, one at the location of a palpable, small, subcutaneous nodule on the dorsum of the right foot. MRI of the foot confirmed a 1.2 x 1.4 x 1.8 cm low T2 signal intensity soft tissue mass. This was excised and pathology showed a phosphaturic mesenchymal tumor- mixed connective tissue variant. One week post-op, FGF 23 level was <50 RU/mL, serum phosphorus was 5.1 mg/dL, and 1,25-dihydroxy vitamin D was 386 pg/ml. The patient had a dramatic clinical improvement and resumed running within a few months.

**Discussion:** Tumor induced osteomalacia (TIO) is a rare paraneoplastic syndrome characterized by renal
phosphate wasting and hypophosphatemia. Patients typically present with severe hypophosphatemia, bone pain, muscle weakness and stress fractures. FGF 23 has been identified as a phosphaturic factor which inhibits sodium dependent phosphate reabsorption in the proximal renal tubules. It also inhibits 1-α hydroxylase and results in low or inappropriately normal 1,25-dihydroxy vitamin D level. Most tumors associated with TIO are benign and originate from bone or soft tissue. Tumor localization can be challenging, but is critical, as excision provides a definitive cure.

Conclusion: We present a unique case of TIO in which the serum phosphorus was slightly low and the FGF 23 level marginally elevated, yet a dramatic biochemical and clinical response was noted following tumor resection. This highlights the importance of considering this diagnosis and pursuing a detailed evaluation of hypophosphatemia, even if mild, in all patients with recurrent stress fractures. The case also illustrates that a BMD T-score <-2.5 does not always represent osteoporosis.

Abstract #637

A CASE OF PSEUДOHYPOPARTHRYOIDISM WITH INTRACRANIAL CALCIFICATIONS

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Objective: To highlight a case of pseudohypoparathyroidism (PHP) with incidental finding of intracranial calcifications.

Case Presentation: A 41 year old African American male presented with muscle cramps, perioral numbness and paresthesia of his hands and feet since his twenties. Medical history was significant for hypertension for which he was taking Amlodipine. There was no family history of endocrine or neurological disorders. Dietary intake of calcium was normal for his age. On physical examination, his height was 180 cm and his weight 90 kg with a BMI of 27 kg/m2. Trousseau’s and Chvostek’s sign were positive. There were no clinical features of Albright’s hereditary osteodystrophy. Initial laboratory studies (normal range in parentheses) were as follows: corrected serum calcium of 7.0 (8.4-10.2 mg/dl) with ionized calcium 3.5 (4.5–5.6 mg/dl), phosphorus 5.7 (2.5– 4.5 mg/dl), magnesium 1.9 (1.6–2.6 mg/dL), intact parathyroid hormone (PTH) 128 (15-65 pg/ml), 25-hydroxyvitamin D 16 ng/mL, 1,25-dihydroxy vitamin D 47 pg/mL, creatinine 1.1 mg/dL, albumin 4.6 g/dL, and alkaline phosphatase 78 U/L. Further work-up did not show any additional endocrine abnormalities. The electrocardiogram showed a long Q-T interval. Treatment was initiated with calcium and vitamin D supplementation. After a few therapeutic adjustments, the patient was able to achieve calcium homeostasis. During follow up, a CT scan of the head done to evaluate a complicated sinusitis revealed dense calcifications throughout both cerebral hemispheres and basal ganglia.

Discussion: PHP is a rare disorder due to a deficient end organ response to parathyroid hormone (PTH) resulting in hypocalcemia, hyperphosphatemia and elevated PTH levels. It is classified as types Ia, Ib, Ic and II based on distinctive phenotypes and pathogenesis. One of the unusual findings in pseudohypoparathyroidism is the incidental detection of basal ganglia calcification on CT scan of the head. The most common site for these intracranial calcifications is the globus pallidus. The calcifications may extend to the white matter and the thalamus leading to neurological manifestations like extrapyramidal signs and dyskinesia. Involvement of cortical matter is rarely identified.

Conclusion: Our patient has bilateral calcifications in cerebral cortices and basal ganglia as an incidental finding in PHP. In addition, the clinical presentation only involved the sensory system with no motor, cognitive or neuropsychiatric involvement. This case illustrates the importance of making an early diagnosis of PHP. Also, the presence of basal ganglia and cerebral cortical calcifications should prompt an evaluation for PHP.

Abstract #638

A CASE OF DOUBLE TROUBLE: PRIMARY HYPERPARATHYROIDISM AND HUMORAL HYPERCALCEMIA IN THE SAME PATIENT

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UC Denver

Objective: 1. To describe a rare case of hypercalcemia due to Primary Hyperparathyroidism (PHPT) and Humoral Hypercalcemia of Malignancy (HHM).

2. To advise aggressive screening of patients found to persistently elevated Parathyroid hormone-related peptide (PTHrP).

Case Presentation: A 72 yo male presented with confusion, fever, weight loss of 40 lbs over two months, calcium level of 14.7 mg/dL and albumin 2.8 g/dL. Parathyroid Hormone (PTH) was 147 pg/ml (10-56pg/ml) along with elevated PTHrP 6.8 pmol/L (<2.0pmol/L). Phosphorus was low at 2.0, 25 Vitamin D 15.6 ng/mL, 1-25 Vitamin D was 129.4 pg/ml. SPEP, UPEP, and TSH were normal. Sestamibi exam localized to right inferior lobe. CT scan of chest, abdomen, and pelvis did not
find pathological sources for PTHrP. Patient had right inferior parathyroidectomy that was positive for adenoma. Calcium fell to 8.3 mg/dL post op though calcium rose to 10.1 mg/dL at discharge and PTH was undetectable. PTHrP was still elevated at 4 pmol/L and 1-25 Vitamin D fell to 27 pg/ml with mental status improved. Patient was re-admitted 2 weeks later with delirium and calcium up to 11.9 mg/dL with albumin of 2 g/dL. PTHrP was up to 8.5 pmol/L. Repeat CT scan revealed rapidly expanding mass in soft tissue adjacent to prior right hip arthroplasty. Initial concern was for infection given fever, but biopsy revealed high grade epithelioid angiosarcoma. Due to patient’s poor functional reserve, he was treated conservatively with fluids, IV bisphosphonate, and calcitonin prior to discharge to hospice where the patient passed away.

**Discussion:** HHM is caused by tumors that release a peptide with close homology in the N-terminal sequence to PTH that binds with the type 1 PTH receptor. PTHrP can be elevated in certain tumors including squamous cell cancers of lung and head and neck, as well as breast, and renal, and rarely from neuroendocrine tumors and sarcomas though any tumor in theory could release it. Epithelioid Angiosarcoma is a rare neoplasm derived from cells lining blood vessels. There are no case reports of PTHrP being elevated in association with Angiosarcoma currently. Unfortunately we could not confirm our suspicion with autopsy or staining of the biopsy for PTHrP. Anywhere from 4-15% of patients with hypercalcemia in cancer are found to have PHPT as the cause. It is rare to find hypercalcemia caused by both elevated PTH and PTHrP. The exact occurrence of both HHM and PHPT is unknown. HHM has a poor prognosis with one study finding median survival time of 64 days even with treatment with bisphosphonates.

**Conclusion:** This case highlights the importance to consider PHPT as a cause of hypercalcemia in patients with cancer and to aggressively search for causes of elevated PTHrP.

**Abstract #639**

**HYPERPARATHYROIDISM WITH UNUSUALLY LOW PARATHYROID HORMONE LEVELS DIAGNOSED BY CALCIUM-LOWERING RESPONSE TO CALCIMIMETIC THERAPY**

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**Case Presentation:** Reliable assays for intact parathyroid hormone (iPTH) have greatly facilitated the diagnosis of hyperparathyroidism (HPT). However, in some cases iPTH levels remain within the assay reference range. We present a case of delayed diagnosis of primary HPT due to unusually low iPTH levels where HPT was confirmed by therapeutic effect of cinacalcet on hypercalcemia.

A 57-year-old ambulatory male was initially diagnosed with hypercalcemia four years before consultation, with multiple serum calcium levels 11-12 mg/dL (8.4-10.5). The iPTH level was 15 pg/mL (Beckman Coulter, 12-88), and hypercalcemia was attributed to hydrochlorothiazide (HCTZ). However, despite stopping HCTZ, hypercalcemia persisted and led to endocrinology referral. Repeat measurement of iPTH with a different assay was 2.47 pM (Abbott Diagnostics, 1.2-7.0), or approximately 23 pg/mL, and unaffected by 1:3 and 1:6 dilutions of serum. Urine 24 hr calcium was elevated (477 mg), but serum phosphorus, creatinine, total protein, albumin, parathyroid hormone related peptide (PTHrp), 25-hydroxyvitamin D, 1,25-dihydroxyvitamin D, TSH, serum and protein electrophoresis, angiotensin converting enzyme level, and cyclase activating and inactive PTH levels were all unremarkable. Parathyroid scintigraphy showed persistent uptake in the left lower neck that coincided with a 1 cm soft tissue density near the thyroid gland on cervical ultrasound. Unfortunately, fine needle biopsy yielded a specimen inadequate for histological evaluation.

**Discussion:** Though highly unusual, cases of primary HPT with suppressed or low normal iPTH levels are documented in the peer reviewed literature. When clinical suspicion is high, the diagnosis of primary HPT should be pursued after carefully excluding other etiologies of hypercalcemia. Empirical therapy with cinacalcet was started to determine if the patient’s hypercalcemia might be PTH-responsive. Calcium and iPTH levels at start of treatment were 11.8 mg/dL and 1.9 pM, respectively. Calcium level improved to 9.9 mg/dL on 30 mg cinacalcet daily and then increased to 11 mg/dL when the patient transiently stopped treatment. Cinacalcet was resumed and titrated to 60 mg daily, with calcium level falling to 9.4 mg/dL but iPTH remaining unchanged at 1.9 pM.

**Conclusion:** Calcimimetic agents such as cinacalcet lower serum calcium levels by activating the calcium-sensing receptor in parathyroid tissue and inhibiting the release of PTH. This case demonstrates that empiric treatment with cinacalcet can confirm PTH-dependent hypercalcemia before committing patients to surgical neck exploration in the atypical case of primary HPT where iPTH level does not accurately indicate PTH activity.
Abstract #640

OSTEOMALACIA ASSOCIATED WITH FANCONI’S SYNDROME: A CASE SERIES

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Objective: Fanconi’s syndrome is a disorder of the renal proximal tubules characterized by unselected decreased renal tubular reabsorption of phosphorus, glucose and amino acids. It is a rare cause of osteomalacia which is accelerated by inadequate renal reabsorption of calcium, phosphorus and decreased uptake of active vitamin D as well as a decrease in 1α-hydroxylation of vitamin D. Our objective is to describe clinical history, biochemical and radiographic studies, bone histomorphometry, if available, treatment strategies and response to treatment of osteomalacia associated with adult Fanconi’s syndrome.

Methods: We identified 4 patients (3 female and 1 male) who met criteria at Mayo Clinic Rochester and Jacksonville from 1995 to 2013 via retrospective chart review.

Case Presentation: Age at diagnosis of osteomalacia ranged from 26 to 65 years. All patients presented with lower extremity pain and except one of them, all had a history of a clinical fracture. One patient had pseudo fractures found on bone scan. Two patients had femoral neck fracture before the age of 60 years. One had multiple rib fractures. Three patients had Fanconi’s syndrome associated with monoclonal gammopathy. The diagnosis of osteomalacia was made clinically in all the patients. They all had elevated alkaline phosphatase, bone pain, and/or demineralization on x rays. None of the individuals in this series underwent iliac crest biopsy. One patient was diagnosed with osteomalacia 8 years after the diagnosis of Fanconi’s syndrome, but in all others, the diagnosis was made concurrently. One of the patients had secondary hyperparathyroidism. All patients had mild renal insufficiency. 1 of the 4 patients had been treated previously with bisphosphonates and teriparatide for stress fractures. All patients were treated with phosphate, and vitamin D supplementation and one patient required calcitriol in addition. One patient was prescribed calcium supplements and other 3 had adequate dietary calcium intake.

Discussion: Hypophosphatemia, low 1,25-dihydroxyvitamin D, chronic acidosis and renal insufficiency likely contribute to osteomalacia in these patients. Patients with Fanconi’s syndrome associated osteomalacia respond well to phosphorous, calcium and vitamin D supplementation, however not all patients require calcitriol. In recent times, most often the diagnosis is made clinically without need for bone histomorphometry.

Conclusion: Osteomalacia associated with Fanconi’s syndrome usually presents with similar symptoms as with other causes but providers need to have a high degree of suspicion and awareness of this association.

Abstract #641

VITAMIN D REPLACEMENT IN AFRICAN AMERICANS WITH COEXISTING PRIMARY HYPERPARATHYROIDISM AND VITAMIN D DEFICIENCY

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Objective: Primary hyperparathyroidism (PHPT) and vitamin D deficiency often coexist in clinical practice. Historically, there has been concern about replacing vitamin D in deficient patients with the theoretical risk of worsening hypercalcemia in preexisting PHPT. In African Americans, PHPT is more prevalent with more severe manifestations and vitamin D deficiency more pronounced compared to other ethnicities. The safety of replenishing vitamin D in this population has not yet been well documented.

Methods: This is a retrospective study of the effect of vitamin D repletion in 28 patients from our endocrinology clinic between 2005 and 2013 diagnosed with concomitant PHPT and vitamin D deficiency. Subjects with GFR ≤ 60 mL/min per 1.73 m2, malignancy, family history of hypercalcemia, on thiazide or lithium therapy, patients in whom the onset of hypercalcemia could not be identified were excluded for the study. Corrected serum calcium, phosphorus, magnesium, 25 hydroxyvitamin D (25-OHD), intact parathyroid hormone (PTH) and serum alkaline phosphatase (ALP) were measured before and 3 months after replacement with weekly 50000 IU Vitamin D.

Results: Serum 25-OHD levels increased from a mean of 13.9 ± 13.65 ng/mL to 36.31 ± 6.74 ng/mL (P < 0.0001) after replacing vitamin D. Mean corrected serum calcium level before treatment was 11.13 ± 0.4 mg/dL which increased after treatment to 11.45 ± 0.61 mg/dL (P = 0.00046). Intact PTH decreased from 159.64 ± 47.11 pg/mL to 131.93 ± 45.15 pg/mL (P < 0.0001) after vitamin D therapy. Serum ALP levels, though mostly in the normal range, decreased from 102.86 ± 28.27 IU/L to 94.86 ± 22.27 IU/L (P = 0.0010). Twenty-four patients had 24-hour urine collection, mean 24-h urine calcium excretion increased from 137.65 ± 39.21 mg/24 hour to 215.86 ± 49.78 mg/24 hour (P < 0.0001). Mean urine calcium/creatinine clearance ratio (Ca/Cr) was 0.010 ± 0.0045 before and 0.019 ± 0.022 after
vitamin D (P = 0.085). Creatinine levels remained stable throughout our study period. No new cases of fractures or nephrolithiasis were reported.

**Discussion:** For clinicians, the safety of replenishing vitamin D in PHPT especially in African Americans has been a concern. In our study, we observed that though the serum calcium levels increased slightly after treatment with high dose vitamin D, these levels were not dangerously high. We also noted our study population to have lower urine Ca/Cr with no significant change after vitamin D repletion.

**Conclusion:** Vitamin D repletion appears to be safe in African Americans with coexistent PHPT and vitamin D deficiency.

Abstract #642

**VITAMIN D SUPPLEMENTATION THERAPY - EFFICACY OF THREE DIFFERENT PROTOCOLS**

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**Objective:** To study the efficacy of vitamin D supplementation therapy with three different protocols.

**Methods:** Three groups (Gp) of patients were studied. Gp1 intensive treatment: oral Cholecalciferol 60,000IU/wk/8wks followed bimonthly for 12wks-monitored. Gp2 Parenteral Cholecalciferol 600,000IU given as a loading dose, 8wks later followed by oral Cholecalciferol 60,000IU bimonthly for 12wks, Gp3 similar to Gp1, but not monitored. All subjects received elemental calcium 1gm/d for the entire duration of study. Serum calcium (S.CAL), phosphorous (S.PHOS), alkaline phosphatase (SAP), 25OHD, PTH levels and other tests were determined at baseline (Wk 0), 8wks (Wk 8) and 20wks (Wk 20). Statistical analysis was performed using RMANOVA.

**Results:** The mean±SD of age in Gps 1, 2, 3 are 31.46±6.26, 44.63±13.8, 49.46±14.5yrs respectively. Baseline serum creatinine and albumin levels were normal in all 3 Gps. The mean± SD of S.CAL, phosphorous (S.PHOS), alkaline phosphatase (SAP-IU/l), 25-OH vitamin D (25OHD-ng/ml) deficiency (<20ng/ml), parathyroid hormone (PTH-pg/ml) levels and other tests were determined at baseline (Wk 0), 8wks (Wk 8) and 20wks (Wk 20). Statistical analysis was performed using RMANOVA.

**Discussion:** Despite varied responses of different biochemical markers, all three protocols were effective in bringing up 25OHD levels. But, S.CAL, 25OHD improved significantly in Gp2, compared to Gp1 & 3. In Gp2, 96% of subjects achieved 25OHD sufficiency and eucalcemia at the end of 5th month. Hence, Gp2, using initial parenteral administration was most efficacious therapy.

**Conclusion:** Oral administration of vitamin D can be efficacious in restoring vitamin D status although initial parenteral administration may slightly more efficacious.

Abstract #643

**SEVERE HYPOCALCEMIA FOLLOWING DENOSUMAB THERAPY IN PATIENTS WITH VITAMIN D DEFICIENCY**

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**Objective:** Hypocalcemia is a recognized adverse event in patients following denosumab administration occurring in up to 18% of patients. Severe or symptomatic hypocalcemia occurs in less than 1% with severe renal impairment (CrCl <30mL/min) conveying an increased risk. It is unknown whether screening for risk factors in addition to renal insufficiency and correction of them prior to therapy would reduce the likelihood of severe or life-threatening hypocalcemia.

**Methods:** We report three cases of denosumab-induced severe hypocalcemia in which vitamin D deficiency may have been a contributory factor.

**Case Presentation:** Patient 1 is a 75-year-old woman with history of hypothyroidism, osteoporosis treated with ergocalciferol 50k IU monthly, end-stage renal disease on hemodialysis who was treated with denosumab 60mg SQ.
Her pretreatment serum calcium and 25-OH vitamin D level were 9.2mg/dL (8.4-10.2) and 44.9ng/mL (31-100), respectively. The week after administration her calcium, PTH and 1,25 dihydroxy vitamin D were 6.6mg/dL, 299pg/mL (15-65) and <8pg/mL (18-72), respectively. Despite the drop in calcium she was asymptomatic but admitted for treatment with IV and oral calcium and vitamin D.

Patient 2 is a 61-year-old man with carcinoid tumor metastatic to liver, lung and clivus who was treated with chemotherapy, local radiation, octreotide and monthly denosumab 120mg SQ twice. He had normal renal function. His pretreatment calcium was 9.2mg/dL. Within several weeks, his post-treatment calcium, 25-OH D, and PTH were 4.3mg/dL, <4.0ng/mL and 1110pg/ml, respectively. He developed parasthesias, carpal pedal spasm, and a prolonged QT interval after the second dose. He was also admitted for treatment.

Patient 3 is an 87-year-old man with osteoporosis and CKD 4 was treated with denosumab 60mg SQ. His pretreatment calcium was 9.0mg/dL. One week after administration, his calcium and 25-OH D were 6.4mg/dL and 22.1ng/mL, respectively. He was asymptomatic and treated with oral calcium and vitamin D.

Discussion: The development of severe hypocalcemia is both life-threatening and costly often requiring hospitalization, parenteral calcium supplementation, and aggressive vitamin D repletion. Our experience suggests that 25-OH vitamin D and/or 1,25 OH2 vitamin D deficiency may enhance the risk of severe hypocalcemia following denosumab.

Conclusion: While further studies are warranted, we propose that until data is available that patients who are candidates for denosumab treatment be screened with serum levels of 25-OH D, 1,25 OH2 D, and PTH and that deficiencies be corrected prior to treatment.

Abstract #644

SEVERE PRESENTATION OF A BENIGN DISEASE: PARATHYROID ADENOMA MIMICKING PARATHYROID CARCINOMA

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Objective: Primary hyperparathyroidism most commonly results from an adenoma (85%), with less than 1% of cases due to carcinoma. Although the diagnosis of a parathyroid carcinoma vs. adenoma is often retrospective, symptoms of a carcinoma are typically more severe and lab abnormalities more marked. Calcium levels rarely exceed 15 mg/dL with an adenoma and intact parathyroid hormone (PTH) levels are usually less than twice the upper limit of normal in contrast to 3-10 times the upper limit of normal with a carcinoma. We present an unusually severe case of a parathyroid adenoma.

Case Presentation: A 71 year-old female presented to our hospital with fatigue, constipation, and rectal pain for one week. She had not sought medical care in many years, and denied any past medical history or medication use. Physical exam was significant for a large, mobile, firm mass in the region of the thyroid. Lab work was significant for a serum calcium (corrected) of 20.1 mg/dl, PTH 2533 pg/ml, 25 OH Vit D 6.2 pg/ml, creatinine 2.61 mg/dl, TSH 3.41 IU/ml, and free T4 1.11 ng/dl. Thyroid ultrasound showed a large, heterogeneous, right thyroid mass. Sestamibi scan showed a single parathyroid lesion extending posteriorly from the lower pole of the right thyroid lobe. The patient underwent surgery and was found to have an enlarged right inferior parathyroid gland posterior to the enlarged right lobe of the thyroid; right inferior parathyroidectomy and right thyroid lobectomy were performed. PTH on post-operative day 2 was 54.7 pg/ml. Pathology revealed the parathyroid was enlarged, encapsulated, and hypercellular but without necrosis, fibrosis, or elevated mitotic count. The thyroid revealed a dominant adenomatoid nodule in a background of multinodular goiter and chronic lymphocytic thyroiditis. Upon discharge, lab work revealed PTH 257.6 pg/ml, corrected calcium 7.8 mg/dL, phosphorous 1.8 mg/dL and creatinine 1.13mg/dL. The patient was subsequently lost to follow-up.

Discussion: This case demonstrates a severe presentation of an often benign disease. Making the diagnosis of a parathyroid adenoma vs. carcinoma is often difficult, as no single feature is pathognomonic of malignancy, although histologic criteria have been adopted. Elevated PTH after successful parathyroidectomy is common (12-43% of cases) and in this case likely due to hypocalcemia, hungry bone syndrome, and vitamin D deficiency.

Conclusion: The presentation of this case with severe hypercalcemia, severely elevated PTH, and a neck mass, while initially concerning for parathyroid carcinoma, ultimately proved to be the combination of a parathyroid adenoma and a benign thyroid goiter.
Abstract #645

OSTEOMALACIA - POSSIBLE CAUSE OF BONE LOSS

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Case Presentation: Osteomalacia should be considered in the differential diagnosis of bone loss. Bone biopsy is the only method to diagnose osteomalacia but is rarely used. Non-invasive methods commonly used to explore bone such as DXA and radiography do not differentiate between osteomalacia and osteoporosis.

We present you the case of a patient with important bone loss, osteomalacia being the most important mechanism.

Case report: Woman, 43 years old, with early menopause at 29 years and exudative enteropathy starting at age 31 for which she was constantly treated with corticosteroids. Patient presented to our department with severe bone loss (T score = -4.8 SD), very low 25-hydroxy-vitamin D level and secondary hyperparathyroidism. She had been previously treated with bisphosphonates and usual doses of calcium and vitamin D, but there had been no semnificative increase of BMD and 25-hydroxy-vitamin D level.

Discussion: Although the patient had risk factors for osteoporosis such as early menopause, corticosteroid use and inflammatory chronic disease, we considered osteomalacia as the main cause of bone loss because the inflammatory bowel disease leads to vitamin D malabsorption. This is confirmed by the very low vitamin D level and it’s improve associated with spectacular increase of BMD and 25-hydroxy-vitamin D level.

Conclusion: We emphasize the importance of exploring vitamin D metabolic status in osteoporosis patients. Appropriate supplementation with vitamin D and its plasma level monitoring for it’s proper absorption conformation are essential to therapeutic success.

Abstract #646

HYPERPARATHYROIDISM UNMASKED: ACUTE HYPERCALCEMIA FROM IMMOBILIZATION AND UNRECOGNIZED NORMOCALCEMIC PRIMARY HYPERPARATHYROIDISM

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Objective: To emphasize the role of immobilization as short as 3 weeks duration can unmask underlying normocalcemic hyperparathyroidism.

Case Presentation: Immobilization is a known cause of hypercalcemia (1) and has been implicated in the etiology of hyperparathyroidism by mechanisms which are not fully understood (2).

We describe a case of acute hypercalcemia diagnosed during 3 weeks hospitalization in a patient with an underlying normocalcemic primary hyperparathyroidism. A 65 y/o female was admitted with T5-T6 fractures of spine after a fall from syncope due to complete heart block. She had a diagnosis of osteoporosis at L4 and was taking weekly alendronate since 2011. She had no prior history of elevated calcium, and was ambulatory prior to hospitalization. She received permanent pacemaker but had a complicated hospital course requiring mechanical ventilation.

At 3 weeks of hospitalization, she was found to have serum calcium of 11.0 mg/dl, corrected calcium of 12.4 mg/dl, iCa 6.8 mg/dl, iPTH 206 pg/ml, creatinine 1.6 mg/dl (eGFR 60), Vit. D 25-OH 17 ng/ml(30-100), 1,25D2OH 23 pg/ml(18-72), Phosphorous 3.1 mg/dl, and TSH of 2. Despite receiving IV hydration (100 ml/h) for 4 days, her corrected calcium rose to 13.5 mg/dl. Next, patient received IV pamidronate 60 mg, and calcitonin 250IU x 4 doses in addition to IV fluids. Her corrected calcium improved from 13.5 mg/dl to 10.8 mg/dl over the next 24 hours. A repeat PTH was 216 pg/ml. Calcium remained within normal range during the rest of hospitalization and at the time of discharge. Thyroid ultrasound showed a solid nodule in the right thyroid lobe 10x9x9 mm. A parathyroid sestamibi scan was negative for any adenoma.

Discussion: This case discusses an acute unmasking of normocalcemic hyperparathyroidism following a short period of relative immobilization. Immobilization causes uncoupling of bone turnover with a reduction in bone formation and increase in bone resorption (3) with a rapid efflux of calcium from bone into the circulation causing hypercalcemia with appropriate suppression of PTH. Persistent elevation of PTH despite hypercalcemia favored a diagnosis of underlying primary hyperparathyroidism. Immobilization possibly contributed to patient’s hypercalcemia in the acute setting. One should be vigilant for acute hypercalcemia in an immobilized patient with normocalcemic hyperparathyroidism.

Conclusion: Normocalcemic hyperparathyroidism can be acutely unmasked by immobilization.
Abstract #647

PRESENTATION OF ECTOPIC INTACT PTH SECRETION BY A GYNECOLOGICAL CANCER

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Objective: To present a unique case of hypercalcemia from secretion of intact PTH by a cervical carcinoma.

Case Presentation: A 59-year-old Caucasian female with a past medical history of diabetes, hypertension, and hyperlipidemia was admitted to an outside hospital due to vomiting, dehydration and hypercalcemia. She was hydrated and given IV pamidronate but had no work up for the underlying cause of her hypercalcemia. She did however have a CT scan of the chest abdomen and pelvis, due to weight loss and vaginal bleeding, and it revealed a possible uterine mass and bilateral lung nodules. A month later she was admitted to our facility by the gynecology service for hypercalcemia, serum calcium of 16.7 mg/dl (8.6-10.6 mg/dl). Endocrinology was consulted and a work-up revealed an intact PTH 455 pg/ml (13-65 pg/dl), PTH-rp 1.1 pmol/L (<2pmol/L), 25-OH Vitamin D 9.3 ng/ml (30-150 ng/dl), LDH 563 U/L (300-600 U/L), CA125 134 U/ml (0-30 U/ml). A neck ultrasound did not reveal any parathyroid abnormalities. We were unable to get a parathyroid sestamibi scan. The patient was taken to the OR and found to have endo and exo cervical masses that extended into her vagina. Pathology revealed poorly differentiated carcinoma with components of squamous cell carcinoma, neuroendocrine carcinoma, and adenocarcinoma and immunostains performed showed that the tumor cells were positive for p16, CD56, synaptophysin and PTH. Her hypercalcemia was acutely treated with IV fluids, sub-Q calcitonin, and IV pamidronate. She was started on chemotherapy; paclitaxel, cisplatin, and bevacizumab. One month post discharge, after her second cycle of chemotherapy, the patient’s calcium was 7.2 mg/dl and intact PTH 229 pg/ml.

Discussion: Cases of ectopic secretion of intact PTH by a non-parathyroid tumor are rare in the literature and by gynecologic tumors, even rarer. Prior reports have documented two gynecological tumors from ovarian carcinoma and one from endometrial adenosquamous carcinoma.

Conclusion: This intriguing case documents a novel neoplastic cause of ectopic secretion of intact PTH by a poorly differentiated cervical carcinoma with components of squamous cell carcinoma, adenocarcinoma, and neuroendocrine carcinoma.

Abstract #648

EVALUATION OF BONE MINERAL DENSITY IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA(ALL) AND NON-HODGKIN’S LYMPHOMA(NHL)

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Objective: Acute lymphoblastic leukemia (ALL) and Non-Hodgkin’s Lymphoma (NHL) are the most common childhood and adolescence malignancy respectively. Due to the increasing survival of these children, today late side effects of treatment are important. Therapies such as corticosteroids, cytotoxic and radiotherapy effect on bone density and put the child at risk of osteoporosis and pathological fractures.

Results: This 3-year cross sectional study was performed in Dr. Sheikh Children’s Hospital in Mashhad on 50 children with ALL (n = 25) and NHL (n = 25). Half of them were received (n = 25) chemotherapy alone and half of them chemotherapy plus radiotherapy (n = 25). All children were in the remission phase. We assessed them by DEXA bone mineral densitometry (BMD) on the lumbar spine and femoral neck (hip). We also measured some bone biomarkers include calcium (ca), phosphorus (p), parathoromone (PTH), alkaline phosphatase (ALP) in plasma. Results by age, height, sex and Body Mass Index (BMI) were adjusted with a special software.

Discussion: In our study, since bone density in ALL patients is more decreased than patients with lymphoma (NHL), it can be due to type of disease and use more severe chemotherapy in ALL patients.

Conclusion: Given that 94% of children had abnormal bone density, seem to pay more attention to the metabolic status and BMD in children with cancer can develop appropriate strategies to improve health and quality of their life.

Abstract #649

A PERPLEXING DILEMMA OF PAGET’S DISEASE

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Objective: To present an atypical case of Paget’s disease.

Case Presentation: A 77 year old woman with medical history of degenerative disc disease of the lumbar spine presented with complaints of severe, progressive bilateral lower extremity pain and numbness. Elective L5-S1 discectomy and laminectomy in July 2012 resolved her pain. However, MRI prior to surgery raised concern for a T12 marrow lesion. A bone scan showed increased
calvarial and left distal tibial activity suggestive of Paget’s disease. Basic metabolic panel, complete blood count, calcium, PTH, vitamin D, TSH, and alkaline phosphatase (AP) were normal. Based on clinical presentation and history of Paget’s disease in her brother she was referred to Endocrinology for diagnosis clarification and treatment of suspected Paget’s disease. Bone specific AP was unremarkable and serum c-telopeptide crosslink (CTX) was 1012 pg/mL. The DXA scan was normal. Based on clinically asymptomatic disease and normal AP, bisphosphonates were not started. The follow up X-ray of the skull in October 2013 was significant for new lytic lesions and progression of diffuse Paget’s disease. The bone scan identified non-specific foci of increased radiotracer activity in the skull indicative of diffuse Paget’s. A skull CT with contrast was ordered to rule out malignancy and revealed lytic phase of Paget’s disease and an arachnoid granulation in the area of increased uptake seen on bone scan. Bisphosphonate therapy was recommended due to radiological progression of the disease and skull involvement.

**Discussion:** Polyostotic Paget’s disease with progressive skull involvement is usually associated with elevated AP. When AP is normal in asymptomatic patients, the best treatment is controversial. The UK and Canadian guidelines for treatment of Paget’s disease recommend treating patients with bone pain and biochemical evidence of active disease. Active asymptomatic Paget’s disease of the skull may be associated with higher risk for complications and treatment is considered acceptable. In cases of normal AP, other bone markers such as CTX may be helpful, though there are no standard values for her age group nor significant data to support the practice.

**Conclusion:** In rare cases, radiologically active Paget’s disease of the skull can present with a normal AP level. In this instance, other bone markers may be useful for evaluation of disease activity and follow up. Treatment with bisphosphonates should be considered in patients with radiologically active Paget’s disease of the skull even with a normal AP. Additional studies may need to be done to clarify the role of other bone markers and indications for treatment in atypical cases of Paget’s disease.

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**Abstract #650**

**ANIMAL MODELS OF OSTEOPOROSIS CORRELATE WITH CLINICAL BONE MARKER DATA IN WOMEN TREATED WITH OSPEMIFENE**

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**Objective:** To assess predictive value of bone markers in ospemifene treated animals compared to humans.

**Results:** SERMs have been shown to prevent osteoporosis and reduce fracture risk. Ospemifene 60 mg/day is a nonhormonal, oral, selective estrogen receptor modulator (SERM) approved for the treatment of moderate to severe dyspareunia in postmenopausal women with vulvovaginal atrophy (VVA). It has been shown to have bone-preserving effects in rats where inhibition of OVX-induced decreases in ash weight at the femoral and tibial epiphyses, increased tibial stiffness, improved bone markers and BMD changes, similar to estrogen supplementation were noted. Ospemifene 1-10 mg/kg reduced bone markers indicative of collagen degradation in a dose-dependent manner. The S-ICTP was reduced by 67-82% compared with OVX rats (p < 0.05), equivalent to the effects of raloxifene.

Two randomized phase II clinical trials of ospemifene on serum bone markers in postmenopausal women have been performed. Ospemifene 30, 60 and 90 mg/day was compared with raloxifene 60 mg/day (the approved dose for osteoporosis) over 12 weeks. Markers of bone resorption (urinary N- and serum C-terminal cross linking telopeptides of type I collagen (NTX and CTX), and markers of bone formation (serum osteocalcin, bone-specific alkaline phosphatase [bone ALP], and procollagen type 1 N and C peptides [P1NP and P1CP]) were measured at Baseline, 3 months on treatment and 2-4 weeks post-treatment in 118 post-menopausal women with a mean age of approximately 57 years. Changes in bone markers were comparable in the ospemifene 60 and 90 mg/day and raloxifene groups. A similarly designed second phase II randomized clinical trial evaluated ospemifene 30, 60, and 90 mg/day versus placebo on bone turnover markers. Ospemifene reduced bone markers in a dose-dependent manner in a study of 176 healthy post-menopausal women (mean age of ~57 years). NTX decreased in all dosage groups, whereas CTX decreased in the 90 mg/day group. Formation markers (P1NP, P1CP, and bone ALP) were significantly decreased in all treatment arms and P1NP and bone ALP statistically differed from placebo.

**Discussion:** Correlating animal models with human disease is often unreliable. However, in this large pre-clinical and
clinical program OVX-rats treated with ospemifene had similar reductions in markers of bone turnover as did post-menopausal women treated with ospemifene.

**Conclusion:** Bone turnover markers have been shown to correlate with fracture outcomes, thus the totality of the animal and human data support further evaluation of ospemifene as a treatment option for women desiring treatment of VVA and osteoporosis prevention.

**Abstract #651**

**MASSIVE ECTOPIC PARATHYROID LIPOADENOMA: A RARE CAUSE OF PRIMARY HYPERPARATHYROIDISM**

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**Objective:** Primary hyperparathyroidism (PHPT) is the most common cause of asymptomatic hypercalcemia. It is typically diagnosed incidentally as part of laboratory testing for other conditions and is often caused by a single, enlarged adenoma. Parathyroid lipoadenoma is a rare histologic variant, notable for its increased stromal fat component.

**Case Presentation:** A 70 year old African American male with a history of BPH was evaluated for hypercalcemia. His history was notable for a traumatic left femur fracture following a motor vehicle accident, but he did not have other clinical manifestations of hypercalcemia, such as nephrolithiasis or osteoporosis. After a thorough evaluation, including bloodwork revealing a total calcium 11.7 mg/dL, ionized calcium 6.9 mg/dL, phosphorus 2.8 mg/dL, PTH 314 pg/ml and 24 hour urine calcium 386 mg, he was diagnosed with PHPT. Both a neck ultrasound and a sestamibi scan failed to localize a parathyroid adenoma. A whole-body SPECT-CT was performed, demonstrating the absence of uptake in the neck, but localized an area of uptake, measuring approximately 3 cm, in the anterior mediastinum. Due to persistence of hypercalcemia and suspicion for an atypically located parathyroid adenoma, the patient underwent median sternotomy and excision of the mass. Intraoperative PTH measurement was 192 pg/ml at baseline, 165 pg/ml at time 0 and decreased to 74 pg/ml at 10 minutes and 48 pg/ml at 20 minutes post resection. The mass weighed 62 g and measured 13 x 5 cm. However, the nodular component weighed 31 g and intraoperative frozen section showed parathyroid gland in a stroma composed of sixty percent adipose tissue, consistent with lipoadenoma. The day following surgery, the calcium level normalized and PTH level was 36.3 pg/ml.

**Discussion:** Parathyroid lipoadenoma is a rare cause of PHPT. They can be recognized histologically by an increased amount of stromal adiposity, generally greater than fifty percent. They are also unique because they can be either functional or non-functional. Initially described in 1958, to date there are just over forty cases reported in the literature. While an ectopic location for a parathyroid adenoma is generally rare, the anterior mediastinum is the most common site for these.

**Conclusion:** Our case illustrates a unique cause of PHPT. Parathyroid lipoadenomas can pose a diagnostic challenge because they have the potential to be found in ectopic locations and may be difficult to distinguish during surgery due to the high fat content of the stroma. Our case illustrates how both preoperative SPECT-CT and intraoperative PTH measurement can help with diagnosis, particularly in the setting of ectopically located adenomas.

**Abstract #652**

**LOEYS-DIETZ SYNDROME AND INCREASED BONE FRAGILITY**

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**Objective:** Loeys-Dietz syndrome (LDS) is an autosomal dominant connective tissue disorder that has been associated with mutations in TGFβR1, TGFβR2, SMAD or TGFβ2. Patients have vascular and cutaneous abnormalities and may have skeletal and craniofacial manifestations. Although frequent fractures have been reported with LDS, the relationship of LDS with bone quality and fracture risk is unclear. Here we describe a LDS patient with a history of multiple fractures and severe debility.

**Case Presentation:** A 62 year old woman presented for evaluation of multiple fractures. Starting at age 39, she developed numerous low impact fractures, including right metatarsal fractures and vertebral compression fractures resulting in progressive back pain, deformity and debility. Due to the use of glucocorticoids for sinusitis, a presumed etiology of glucocorticoid induced osteoporosis was made. Her steroids were discontinued and she was treated with bisphosphonate therapy for 10 years, teriparatide for 2 years while also being on hormone therapy. She had a history of a thoracoabdominal aortic aneurysm dissection. Her two daughters died of ruptured aortic aneurysms. Physical examination revealed hypertelorism and retrognathia. She had pectus carinatum and severe kyphoscoliosis. Laboratory assessment revealed normal calcium, phosphorous, 25-OH vitamin D, PTH level, thyroid function, and protein electrophoresis. Celiac...
disease evaluation was negative. A DXA scan showed bone mineral density at the L1-L4 spine T score +1.6 (1.219 g/cm²), left femoral neck T score -1.5, (0.681 g/cm²), left total hip T score -1.6 (0.751 g/cm²), right femoral neck T score -1.8, (0.647 g/cm²) and right total hip T score -1.5 (0.755 g/cm²). Vertebral fracture assessment showed moderate to severe wedge and biconcave compression fractures extending from T11 to L4 vertebral bodies. Plain films revealed multiple vertebral compression fractures with severe kyphosis and healed rib fractures. Sequencing of TGFBR1 and TGFBR2, confirmed a heterozygous mutation in TGFBR1 gene (1460G>A).

Discussion: Low bone matrix quality, skeletal fragility and delayed bone healing is an increasing cause of morbidity and possibly mortality in LDS patients. Abnormal secretion of collagen type I from fibroblasts in LDS patients with TGFβR2 gene mutation could lead to impaired quality of the organic bone matrix resulting in increasing fracture risk. DXA study techniques provide limited information on the quality of bone structure and matrix.

Conclusion: For the practicing endocrinologist is important to know that DXA studies looking at bone mineral density in patients with LDS may not reflect the degree of bone fragility.

Abstract #653

HORMONAL REPLACEMENT THERAPY (HRT) AND BISPHOSPHONATES TO PREVENT BONE LOSS IN FUNCTIONAL HYPOthalamic AMENORRHEA (FHA): A SYSTEMATIC REVIEW AND META-ANALYSIS

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Objective: We conducted a systematic review and meta-analysis of studies that evaluated the effect of HRT and bisphosphonates in preventing bone loss in patients with FHA.

Methods: We performed a comprehensive search of several electronic databases. We included original controlled and non-controlled studies, prospective, and retrospective in nature that enrolled female patients of any age presenting with FHA, including athletic, weight-loss and stress-associated amenorrhea/oligomenorrhea. The efficacy of interventions were measured as a change in the number of fractures or change in bone mineral density. All outcomes were reported for a follow-up period of 8-48 months (Median is 12 months). The quality of evidence was conducted according to the GRADE recommendations.

Results: Nine studies with 280 patients that received different hormonal therapies met our eligibility criteria. All studies reported absolute bone mineral density at the level of the lumbar spine. Three studies reported BMD of the femoral neck. None of the studies reported fractures, z-score or t-score. Random-effects meta-analysis showed a statistically significant change in BMD of the lumbar spine in patients receiving hormonal therapy compared to patients receiving control with WMD=0.032 g/cm² favoring hormonal therapy. There was no significant effect of receiving hormonal therapy on BMD of the femoral neck. The extensive literature search yielded no studies to evaluate bisphosphonates in treating patients with FHA.

Discussion: The meta-analysis showed a statistically significant difference between the changes in the lumbar BMD in patients receiving hormonal therapy compared to control intervention. However the clinical implication of this improvement is not clear since none of the studies evaluated the effect on risk of fractures. The quality of this evidence according the GRADE approach was low due to the high risk of bias, imprecision (very small sample size) and indirectness as BMD is a surrogate outcome.

Conclusion: Low quality of evidence suggests the use of hormonal therapy may prevent bone loss in patients with functional hypothalamic amenorrhea/oligomenorrhea. Hormonal therapy was associated with a modest increase in lumbar spine density. Whether this effect translates into important patient outcomes such as fracture prevention with longer use is unknown. There is no current data to support the use of bisphosphonates in this population.
Efficacy and Safety of Liraglutide 3.0 mg for Weight Management in Overweight and Obese Adults: The SCALE™ Obesity and Prediabetes, a Randomized, Double-Blind and Placebo-Controlled Trial

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Objective: Obesity is associated with prediabetes, which is a high risk factor for development of type 2 diabetes (T2DM). This trial investigated the effects of liraglutide 3.0 mg, as adjunct to diet and exercise, on weight loss (co-primary endpoints: mean change in body weight [BW] and proportions of individuals losing ≥5% and >10% of BW), safety and tolerability in overweight and obese adults without T2DM over 56 weeks.

Methods: Individuals (BMI ≥27 kg/m2 with ≥1 comorbidity or ≥30 kg/m2) were randomized 2:1 to once-daily subcutaneous liraglutide 3.0 mg or placebo plus a 500 kcal/day deficit diet and exercise. Randomization was stratified by prediabetes status (according to ADA 2010 criteria) and BMI. Clinicaltrials.gov ID: NCT01272219.

Results: 2590 of 3731 randomized individuals (age 45.1±12.0 years, 78.5% female, BW 106.2±21.4 kg, BMI 38.3±6.4 kg/m2, 61.2% with prediabetes) completed 56 weeks (71.9% on liraglutide 3.0 mg and 64.4% on placebo). At week 56, individuals on liraglutide 3.0 mg had lost 8.0% (8.4 kg) of BW compared to 2.6% (2.8 kg) with placebo (estimated treatment contrast [ETC] -5.4% [5.6 kg], p<0.0001, ANCOVA; FAS, LOCF). The proportion of individuals achieving a BW loss ≥5% was 64% with liraglutide 3.0 mg and 27% with placebo (estimated odds ratio (OR) 4.8, p=0.0001, logistic regression). The proportion achieving BW loss >10% was 33% and 10%, respectively (OR 4.3, p<0.0001). BW loss was independent of prediabetes status at screening and baseline BMI. Consistent with BW loss, liraglutide 3.0 mg also reduced waist circumference (ETC −4.2 cm) and BMI (−2.0 kg/m2) (both p<0.0001, ANCOVA), and improved glycemia, blood pressure and lipids (not shown).

Discussion: Liraglutide 3.0 mg was superior to placebo on all co-primary endpoints and the safety profile was generally consistent with that of previous clinical trials with liraglutide in individuals with T2DM. The clinical significance of the imbalance in gallbladder disorder and pancreatitis events is currently unknown.

Conclusion: Liraglutide 3.0 mg, as adjunct to diet and exercise, was efficacious and generally well tolerated.

Office-Based Counseling for Weight Loss (WL): 52-Week Healthy Lifestyle Program (HLP) Developed for Lorcaserin Phase 3 Clinical Trials with Potential for Translation to Clinical Practice

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Objective: Obese and overweight individuals who lose 5% of body weight reduce comorbidity risk, and a 7% WL may prevent primary T2D. Lifestyle modifications, diet/exercise counseling, managing expectations, and a patient-centric approach can be effective in conjunction with pharmacotherapy for WL. The HLP, the 52-wk lifestyle modification program of diet/exercise counseling, is a model for WL management in real-world clinical settings and was used in three pivotal phase 3 trials of lorcaserin, a selective 5-HT2C agonist.

Methods: The HLP was administered to all patients in the trials (BLOOM, BLOSSOM, and BLOOM-DM) who received placebo or lorcaserin (N=7784, aged 18-65 years, BMI of 30-45 kg/m2 or 27-29.9 kg/m2 with ≥1 comorbidity). At each study visit the HLP included 15-min one-on-one diet/exercise counseling. Counselors received 4 hours of training that covered program components, roles and responsibilities, materials, counseling intervention elements, and action planning. Patients were given a pedometer, food and activity 5-HT2C agonist.
logs, and other educational resources. Patients were counseled to exercise for 30 min/day and to reduce their estimated energy requirements by 600 kcal/day (based on WHO criteria). At each visit, food and activity logs were reviewed. The HLP focused on office-based counseling supplying brief lessons on topics related to successful long-term WL. The 3 studies’ end points included absolute and percentage changes from baseline in body weight after 52 weeks.

**Results:** The HLP was successfully implemented in these trials. At week 52 lorcaserin- and placebo-treated patients (MITT) lost weight compared with baseline. HLP/placebo intervention resulted in 22.6% of patients without and 16.1% of patients with T2D achieving ≥5% WL, and 15.4% and 10.1% achieving ≥7% WL, respectively. Adjusted mean WL with HLP/placebo was 2.5 kg (2.5%) in nondiabetic patients and slightly less—1.6 kg (1.5%)—in patients with T2D (P<0.001 and P<0.0001, respectively). Patients without with and with T2D who received lorcaserin bid plus HLP had greater WL (5.8 kg [5.8%] and 4.7 kg [4.5%], respectively; P<0.001; P<0.0001).

**Discussion:** In patients with and without T2D, significant WL was achieved among those receiving placebo plus HLP, and a significant proportion of these patients achieved ≥5% WL. The HLP may be used alone or in conjunction with pharmacotherapy such as lorcaserin for additional WL benefits.

**Conclusion:** This office-based, patient-centric program provides an adaptable model that may be used by practitioners who treat overweight and obese individuals.

**Abstract #702**

THE ECONOMIC BURDEN OF HIGH BODY MASS INDEX (BMI) BY GLYCEMIC STAGE IN THE UNITED STATES

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1. Evidera, 2. Novo Nordisk Inc

**Objective:** Our study assessed the healthcare costs of being overweight or obese at different glycemic stages, including euglycemia, pre-diabetes (PreD), and type 2 diabetes (T2D).

**Methods:** For a sample of 153,561 adults (~50% males and ~97% white), we examined the electronic health records and insurance claims data between January 2004 and May 2013 provided by Geisinger Health System. T2D stage was defined by ≥1 T2D ICD-9 diagnosis code, ≥2 glycemic lab results (A1C ≥6.5% or FPG ≥126mg/dL), or use of non-metformin anti-diabetic (AD) drugs. PreD stage was defined by A1C 5.7-6.4% or FPG 100-125 mg/dL. Adults in euglycemic stage needed to be in this stage for ≥2 years before PreD or T2D, without AD drugs or elevated glycemic lab results. We excluded adults who had T1D, were underweight or had diseases associated with unintentional weight change. We censored data by pregnancy or the end of continuous enrollment. Healthcare resource utilization captured by the claims and associated costs (in 2012 value) were examined for each glycemic stage among adults with ≥90 days of data in the stage. The association between healthcare costs and BMI during a stage was estimated by generalized linear regression, adjusted for socio-demographics (age, gender, race, smoking, employment, insurance type and index year) and sampling weight. We estimated the marginal annual costs in people overweight or obese, defined by BMI (overweight: 25-29.9kg/m2; class I obesity: 30-34.9kg/m2; class II: 35-39.9kg/m2; class III: ≥40kg/m2), relative to those with normal BMI (18.5-24.9kg/m2).

**Results:** We identified 48,344 adults (mean age: 46; mean BMI: 29kg/m2) in euglycemic stage; 4,003 adults (age: 58; BMI: 33kg/m2) in PreD stage; and 10,105 adults (age: 60; BMI: 33kg/m2) in T2D stage. For people with euglycemia, the estimated annual marginal costs associated with overweight or obesity relative to normal BMI ranged from $330 for overweight to $1,814 for class III obesity (all P<0.05). For people in PreD stage, the annual marginal costs relative to normal BMI were only significant for class III ($2,224). For people in T2D stage, the annual marginal costs relative to normal BMI were significant for class II ($1,757) and class III ($3,816) (P<0.05).

**Discussion:** This is the first retrospective study to examine healthcare costs of high BMI within different glycemic stages. Drug use may be under-identified as enrollment in drug coverage was unknown.

**Conclusion:** A positive correlation between healthcare costs and BMI levels was observed for people with BMI=25kg/m2 during the euglycemic stage. With elevated or impaired glycemia, the correlation was mainly evident in people with BMI >35kg/m2.

**Abstract #703**

EFFECTS OF INTENSIVE LIFESTYLE MODIFICATION ON DIASTOLIC DYSFUNCTION IN PATIENTS WITH METABOLIC SYNDROME

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**Objective:** Preclinical stages of heart failure include metabolic syndrome (Stage A) and diastolic dysfunction (Stage B). Metabolic syndrome is associated with
Obesity

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Diastolic dysfunction as well as increased left ventricular mass. Knowledge is limited with regards to the effects of lifestyle intervention on diastolic dysfunction in patients with metabolic syndrome.

Methods: For this proof-of-concept study, we selected 26 patients with metabolic syndrome without known heart disease, and explored the effect of a 24-month standardized group lifestyle intervention on left-ventricular diastolic function. Function was measured at baseline and 24 months by transthoracic echocardiogram with tissue Doppler imaging. The lifestyle intervention focused on diet, physical activity and stress management, and aimed at remission of metabolic syndrome. Metabolic syndrome was defined using the modified criteria from the National Cholesterol Education Program. Diastolic dysfunction was evaluated using a standardized protocol based on established criteria from the American Society of Echocardiography.

Results: Of 26 patients with metabolic syndrome at baseline, 77% were women and 34% were Caucasian. The patients weighed 97.2±19.5 kg on average and 77% had pharmacologically treated hypertension. In response to the group lifestyle intervention, 54% of participants achieved remission of metabolic syndrome at the 24-month follow up (assuming the worst case scenario for missing metabolic syndrome assessment). The average weight loss was -2.6±8.1%. 73% (n=19) of patients completed the 24-month lifestyle intervention and follow-up assessment. 32% (n=6) of participants had diastolic dysfunction (grade 1) at baseline. Of these patients, 67% (n=4) showed resolution of diastolic dysfunction after 24 months of intensive lifestyle modification and 50% (n=3) showed resolution of both metabolic syndrome and diastolic dysfunction. One patient did not respond to the lifestyle intervention, progressing to diabetes mellitus and developing grade 1 diastolic dysfunction after 24 months.

Discussion: Our preliminary results suggest that patients with metabolic syndrome who adhere to lifestyle intervention can achieve improvement in diastolic function with only modest degrees of weight loss and are less likely to progress to diastolic dysfunction.

Conclusion: These findings are important in heart failure prevention, as the patients with persistent diastolic dysfunction have high likelihood of progression to clinical heart failure.

Abstract #704

Does the Body Mass Index of Parents Contribute to the Metabolic Risk of Their Offspring?

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Objective: The objective of this study was to establish the extent to which parental factors influence the metabolic health of their offspring. It follows on from an earlier finding of a gender assortative association (mother-daughter, father-son) in the body mass index (BMI) of healthy trios (mother, father and child) in a cohort of contemporary British children.

Methods: The study was designed as a prospective longitudinal cohort study. The study’s subjects were 226 healthy trios from a 1995 to 1996 birth cohort randomly recruited in the city of Plymouth, United Kingdom. Body mass index BMI and metabolic score (derived from natural log HOMA IR, triglycerides, total:high density lipoprotein cholesterol ratio) were measured at nine annual time points from 5 to 13y.

Results: The metabolic score was significantly associated with BMI in both genders and all ages. There were large and significant differences in the metabolic score between normal weight and overweight obese children. The metabolic score of overweight and obese girls was up to fourteen fold greater than that of normal weight girls. Parental BMI and metabolic status however, had little effect on these differences. Mixed effects modelling showed that, as the child’s BMI increased, the influence of parental factors became less relevant. Time lag analyses confirmed that weight gain preceded metabolic disturbances in the children.

Discussion: Neither the BMI or the metabolic status of either parent appears to explain the large difference in metabolic risk between their overweight and normal weight offspring. Our data suggest that a focus on preventing excess weight gain in early childhood is imperative to reduce metabolic risk subsequently.

Conclusion: The impact of obesity on the metabolic health of contemporary children is a function of their own weight gain, rather than that of their parents, and is therefore potentially preventable.
Abstract #705

RAPID REDUCTION IN INSULIN REQUIREMENTS IN PATIENTS WITH T2DM FOLLOWING IMPLANTATION OF AN ENDOSCOPICALLY-PLACED DUODENOJEJEUNAL BYPASS LINER (ENDOBARRIER)

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Objective: Determine the effect of implanting an endoscopic duodenojejunal bypass liner (EB) on insulin requirements in patients with T2DM.

Methods: Prospectively collected data from a nationwide data registry and medical records data for the first 100 patients in Australia who underwent EB treatment after successful implantation of this device were retrospectively reviewed. All patients were treated at either of two centers. Most were day-stay patients but the insulin-requiring patients at one center were admitted overnight and insulin withheld whilst non-fasting BSLs were monitored. At the other center a more gradual approach to insulin reduction was used. All patients were reviewed at 1-4 weeks post implant, and then 3 to 6 monthly. The EB devices were in situ for up to 12 months, when they were explanted endoscopically. Diabetes medications at explant or date of last follow-up, fasting BSL, HbA1c, other blood pathology results, and weight were recorded.

Results: Eleven (11%) patients had T2DM requiring insulin prior to EB treatment. The insulin requiring patients were significantly older (median 60 years, range 46-71) than the whole cohort (median 52 years (range 17 to 79 years) but there were no other significant demographic differences. Median BMI at implantation was 37 kg/m2 (range 29 to 57 kg/m2), median weight was 111 kgs (range 68 to 155kg). Median excess weight was 38kg. Median length of follow up after implantation was 132 days (range 9 to 458 days).

Insulin was completely ceased in 6 (54%) of the 11 patients. This was achieved within 24 hours of EB insertion in 3 patients, within 4 weeks in one patient, and within 12 months in 2 patients. All the remaining 5 patients decreased their insulin requirements, either in frequency, dosage, or both. Median HbA1c was reduced by 17% (baseline 8.8, last follow-up 7.3). All patients continued on their oral diabetes medications. Median weight loss was 11.1kg (range 3.2 to 20.0kg).

Discussion: The variable time to cessation of insulin probably reflects differing approaches to patient management in the two Australian treatment centers.

Conclusion: Insulin requirements were reduced or eliminated in all patients. The endoscopic duodenojejunal bypass liner (EB) is an effective treatment for T2DM.

Abstract #706

PRACTICE PATTERNS IN THE MANAGEMENT OF PATIENTS WITH OBESITY: RESULTS OF A NATIONAL SURVEY OF FIVE PHYSICIAN GROUPS

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1. Takeda Pharmaceuticals International, 2. CE Outcomes

Objective: While obesity is recognized as a major health problem, approaches to disease management vary. The primary aim of this study was to investigate practice patterns in obesity management by different physician types in the US.

Methods: A case-vignette survey was developed with input from literature reviews, clinical experts, and focus groups. The survey was piloted and distributed to a US national sample of 625 practicing physicians, which included endocrinologists (ENDOs), OB/GYNs, cardiologists (CARDS), family physicians (FPs) and internists (IMs) (n=125 per group) in July 2013. Six domains related to obesity evaluation and management were surveyed: perception/understanding of disease impact, pathophysiology, assessment/diagnosis, treatment approach, barriers to treatment, and resource needs.

Results: Of all physician groups, ENDOs were most familiar with obesity-related topic areas (5.5-7 points on a 10-point scale), but none of the physicians groups ranked as extremely familiar (8-10 points). With the exception of ENDOs, other physician groups demonstrated limited familiarity (1-5.5 points) with hormonal and neuroregulation of appetite and energy balance. Most ENDOs and FPs (~80%) were able to correctly classify a patient with class 1 obesity, compared with CARDS, IMs and OB/GYNs (~70%). More ENDOs, CARDS, and IMs (~80%) were able to correctly classify a patient with class 3 obesity than FPs and OB/GYNs (~70%). The majority of physicians stated that they would provide counseling about nutrition or physical activity for a patient with class 1 or class 3 obesity. FPs, IMs, and ENDOs were most often reported
comfort prescribing approved medication for weight loss (48%) and OB/GYNs the least often (7%). Across all physician groups, levels of 10% weight loss were considered more important than 5% loss in determining success of treatment. Motivation to lose weight and rebound weight gain were rated the most significant barriers to obesity management. Most physicians (68-80%) refer patients for weight loss information to commercial weight loss programs, followed by hospital/university (57-64%), payer (28-44%) and community based organizations and programs (27-47%).

**Discussion:** These data demonstrate that physicians recognize the negative health effects of obesity. However, levels of familiarity with the pathophysiology, diagnosis and management of obesity vary among physician groups.

**Conclusion:** These data indicate a need for expanded education and resources for health care providers who treat patients with obesity.

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**Abstract #707**

**CLINICAL OUTCOME REPORT OF WEIGHT MANAGEMENT PROGRAMS AT PALO ALTO MEDICAL FOUNDATION**

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**Objective:** The main objective of this report is to evaluate the clinical outcome of both surgical and non-surgical weight management programs at a large multi specialty group that serves multiple counties in the Bay area of Northern California.

**Methods:** By using electronic health record, a retrospective, cross sectional analysis of weight management programs was performed. Those who attended our non-surgical programs, New Weigh of Life and HMR in 2011 and 2012 were identified. We also identified those patients who had bariatric surgery performed between 2008-2012 by using CPT codes documented in our electronic health record.

**Results:** In 2012, we had 460,989 active adult patients with documented BMI in EHR. Of those, 33.3% were overweight and 20.4% were obese. 79% of overweight/obese patients had one or more of the four major co-morbidities including diabetes mellitus, hypertension, hyperlipidemia and sleep apnea. 269 patients participated in “New Weigh of Life” program with 77% completion rate. NWOL is based on diabetes prevention program. 39% of NWOL participants lost 5% or more of their initial weight. 364 patients completed HMR program with 87% completion rate. This program is based on low calorie diet with supervision. 86.5% of HMR participants lost 7% or more of their initial body weight. 965 patients had undergone bariatric surgery between 2008 and 2012. Gastric bypass patients had an average 88 Lbs weight loss 2 years after surgery. Lap band and sleeve gastrectomy patients had an average 34.5 Lbs and 79.4 Lbs weight loss respectively 2 years after surgery. There were improvements in HgA1c, fasting glucose, total cholesterol and triglycerides in all our programs.

**Discussion:** Compared with New Weigh of Life program, HMR program had significantly higher number of patients who achieved 5% or more weight loss. The completion rate was higher in HMR program. The average weight loss in 2 years was very similar in gastric bypass and sleeve gastrectomy patients, however, there were more significant drop in HgA1c and LDL cholesterol in gastric bypass patients compared with Lap band and sleeve gastrectomy patients. We offer shared medical appointments for the follow up of our post bariatric surgery patients. We have implemented tools in our EHR to remind our providers to order essential lab work for the follow up of post bariatric surgery patients.

**Conclusion:** This report shows that with meaningful use of electronic health record and education of providers to enter appropriate diagnoses and codes into EHR, long term clinical outcome and quality of our services can be monitored and reported. Our clinical outcome data for both non-surgical and surgical programs are comparable with nation-wide data.

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**Abstract #708**

**THE IMPACT OF BODY MASS INDEX (BMI) ON THE RISK OF PROGRESSION BETWEEN GLYCEMIC STAGES IN THE UNITED STATES**

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1. Evidera, 2. Novo Nordisk Inc

**Objective:** Overweight and obese people have increased risk of developing type 2 diabetes (T2D). This study aims to assess the impact of BMI on the risk of glycemic stage transitions, including progression from euglycemia (normal) to pre-diabetes (PreD) or to T2D directly without observation of PreD, progression from PreD to T2D, and reversion from PreD to normal.
Methods: For a sample of 153,561 adults (97% white), we examined the electronic health records and insurance claims data between January 2004 and May 2013 provided by Geisinger Health System. Adults with BMI <18.5 kg/m² or diseases associated with unintentional weight change were excluded. We segmented a person’s medical history into glycemic stages by searching backwards for: 1) T2D stage defined by ≥1 T2D ICD-9 code, ≥2 lab results meeting criteria for the diagnosis of diabetes (A1C ≥6.5% or FPG ≥126 mg/dL), or use of non-metformin anti-diabetic (AD) drugs; 2) PreD stage identified by A1C 5.7-6.4% or FPG 100-125 mg/dL; and 3) normal stage identified as ≥2 years (yrs) in the remaining medical history without AD drugs or elevated lab results. Reversion from PreD to normal was defined by euglycemic lab results. Weibull survival models, adjusted for age, gender, race and smoking, were used to estimate the transition relative risk associated with each BMI level (normal: 18.5-24.9 kg/m²; overweight: 25-29.9 kg/m²; class I obesity: 30-34.9 kg/m²; class II: 35-39.9 kg/m²; class III: ≥40 kg/m²). The analyses were censored by the end of continuous enrollment or pregnancy.

Results: Normal stage (mean duration: 5.1 yrs) was identified for 32,864 adults (mean age: 48; 44% male; mean BMI: 29). Of these, the rate of progression to PreD was 13 per 1,000 person-yrs, and 9 to T2D. The PreD stage (mean duration: 2.2 yrs) was identified for 4,483 adults (mean age: 58; 48% male; mean BMI: 33). Of these, the rate of progression to T2D was 84 per 1,000 person-yrs, and the rate of reversion to normal was 58. The adjusted risk of progression from normal to PreD relative to normal BMI (RR) ranged from 1.8 (overweight) to 9.5 (class III obesity); for normal to T2D, 1.8 to 6.5; for PreD to T2D, 1.3 (p<0.10) to 2.9; and for PreD to normal, ~0.7 across all overweight and obesity categories (P<0.05 except where noted).

Discussion: This is the first retrospective study to examine the relative risk of high BMI within glycemic stage. Since glycemic testing is not routinely done on all patients in clinical practice, the pre-diabetes stage is likely under-identified.

Conclusion: Positive correlation between risks of progression along the glycemic continuum and BMI levels was observed in a real-world US practice setting.

Abstract #709

POST-HOC EVALUATION OF THYROID NODULES (TN), BODY MASS INDEX (BMI), AND LEPTIN PLASMA LEVELS IN A LARGE COHORT OF PRIMARY CARE PATIENTS: CAN OBESITY LEVELS ELEVATE EARLIER DECADE PREVALENCE OF TN?

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Objective: Presence of nodules in thyroid is most frequent cause of endocrinopathy. Prevalence of thyroid nodules in United States is 3-10%. Twelve thousand cases of thyroid carcinoma are diagnosed annually. Prevalence of thyroid nodules (68%) higher than 7.5 MHz (33%). Several autopsy surveys, 37-57% of patients had thyroid nodules. Studies suggest prevalence of 2-6% palpation. Thyroid nodules have been proven to increase with age. Obesity as a factor has had mixed data. 81% of females and 70% of males have been found to have thyroid nodules upon autopsy examinations.

Methods: BMI Leptin set including thyroid scans, we are evaluating via post-hoc analysis plausible link between leptin plasma levels, BMI, and obesity on prevalence of both benign and malignant TN’s in over 600 patients. Cut point for nodules was .2 mm.

Results: Rate of malignancy in age group was greatest in patients >70 years (19 of 47 patients, 40.4%) followed by patients 21-30 years of age (37 of 125 patients, 29.6%). Blacks had lower rate of thyroid carcinoma than Caucasians. Discussion: Presence of nodules in thyroid gland of obese patients is often found. Insulin Resistance (IR) may induce increased thyroid proliferation, nodule volume and nodule formation. Evidence for obesity in thyroid carcinoma is inconsistent. In one study, obesity was associated with higher prevalence of thyroid cancer in women (Han et al. 2013). There have been mixed conclusions about the prevalence of thyroid nodules in obese patients with elevated leptin. Aging so far is the number one association with thyroid nodules. In this study we found that men with elevated leptin has increased nodules, women did not. Only one study evaluated role of serum leptin levels and TN without any conclusive association (de Sousa et al.
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2013). Earlier reports (Shah and Braverman 2012) BMI underestimates obesity prevalence, especially in women with high leptin levels (>30 ng/mL).

**Conclusion:** Aging is the key association for thyroid nodules, as there have been mixed observations about prevalence of thyroid nodules and obesity.

**Abstract #710**

**METABOLIC SYNDROME IN IKORODU: A COMMUNITY SURVEY**

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**Objective:** The concept of metabolic syndrome is still a subject of controversy among and between academic societies. The aim of this study is to determine the prevalence of metabolic syndrome in a rural area in ikorodu using the world health organisation eligibility criteria.

**Methods:** In collecting data for this study 47 participants were recruited into the study after obtaining consent from them through their opinion leader. The random blood sugar of all the participants were checked using a glucose meter machine. Impaired glucose tolerance value was taken as 140mg/dl or above. The waist circumference and the hip circumference of the participants were checked using a non stretch tape. The waist hip ratio (WHR) was then calculated for each participant, central obesity was defined as waist hip ratio >0.9 for male or WHR >0.85 for female. Also a body mass index (BMI) of >30kg/m² was taken as central obesity. The blood pressure was measured using a mercurial sphygmomanometer at heart level.

**Results:** A total of 47 participants were recruited into the study. The age range was between 25-72 years. Of these 24 (51.06%) participants were male while 23 (48.94%) participants were female. Three participants fulfilled the eligibility criteria for metabolic syndrome as outlined by world health organisation representing 6.4% of the study population. The male to female ratio is 2:1 in this study population. The female with metabolic syndrome was in her sixth decade of life. Of the two males one was in his sixth decades of life while the other was in his eighth decades of life.

**Discussion:** The determining factor in metabolic syndrome include insulin resistance amongst others. The aging process that results in atherosclerosis, loss of beta cells in the pancreas, amongst others are key factors in the pathogenesis of metabolic syndrome in the elderly but is not exclusively the cause as metabolic syndrome also occurs in the young patients and children.

**Conclusion:** The prevalence of metabolic syndrome in ikorodu is 6.4% (WHO CRITERIA). In our country Nigeria, more geriatric centers needs to be opened to cater for the elderly as they form a significant population of metabolic syndrome patients and because metabolic syndrome increases with age and who knows it may become a leading cause of morbidity and mortality in the elderly in the near future if not envisaged now and controlled ahead of old age.

**Abstract #711**

**PRE AND POST-OPERATIVE VITAMIN D LEVELS IN PATIENTS REFERRED FOR BARIATRIC SURGERY FROM NORTHERN ONTARIO COMPARED WITH SOUTHERN ONTARIO**

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**Objective:** To determine Vitamin D levels at baseline and six months post-operatively for patients referred for bariatric surgery as well as to examine any difference between patients from Northern Ontario versus Southern Ontario.

**Methods:** Data was obtained from the Ontario bariatric registry. Data for 461 patients from Northern Ontario and 573 patients from Southern Ontario were used in this study. The Northern Ontario region included results from the Sudbury and Thunder Bay area whilst the region of Southern Ontario encompassed results from the Guelph, Windsor, Hamilton, Humber, Toronto, Ottawa and Kingston areas. 25 hydroxy Vitamin D levels were taken at baseline and six months post-surgery (Roux-en-Y gastric bypass surgery or sleeve gastrectomy). The data was then organized via area and analyzed. The normal range for 25 hydroxy Vitamin D level is 75-250 nmol/L. If the pre-operative level was below the normal range, Vitamin D supplements were administered either as Vitamin D2 orally 50,000 IU once week x 6 weeks boluses or Vitamin D3 (generally around 2000 IU per day) orally. After surgery, almost all patients were on Vitamin D supplements when the Vitamin D levels were checked 6 months post-op.

**Case Presentation:** The average levels of 25 hydroxy Vitamin D for patients from Northern and Southern Ontario regions were calculated. The average level for
patients from Northern Ontario was 54.19 nmol/L (SD of 25.19) pre-operatively and 80.42 nmol/L (SD of 29.01) six months post-operatively. The average level for patients from Southern Ontario was around 54.64 nmol/L (SD of 25.95) pre-operatively and 81.59 nmol/L (SD of 29.06) six months post-operatively.

**Discussion:** As expected, Vitamin D levels were low at baseline in patients referred for bariatric surgery. Previous studies have shown that 25 hydroxy Vitamin D levels were inversely correlated with percentage body fat possibly secondary to alteration in tissue distribution. The 6 month post-operative Vitamin D level was in the normal range possibly due to better Vitamin D supplementation and weight loss post-surgery. Northern Ontario has harsher winters with less hours of sunlight compared to Southern Ontario. However, there was no significant difference between pre-operative and 6 months post-operative Vitamin D levels between these two regions.

**Conclusion:** Obese patients referred for bariatric surgery from Ontario in general are Vitamin D deficient. With supplementation, most patients had normal 25 hydroxy Vitamin D levels 6 months post bariatric surgery. There was no significant difference in 25 hydroxy Vitamin D levels pre-operatively or post-operatively between patients from Northern and Southern Ontario.

**Abstract #712**

**METABOLIC SYNDROME IN SURULERE: A COMMUNITY SURVEY.**

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**Objective:** Metabolic disorders can be acquired or congenital. Metabolic syndrome is a form of metabolic disorders with multisystemic effects. While metabolic activity in living man starts right from the time of conception through to ageing process or period of mortality, the morbidity it generates from onset to finish in the history of mankind is the mystery that the medical world seeks to address day by day from the time of Hippocrates. Metabolic syndrome is one of such morbidity. This paper aims to determine comparatively the prevalence of metabolic syndrome in surulere using three criteria.

**Methods:** This prospective study was done in Surulere Lagos during a free health outreach programme to the community. Surulere is an area located on the Lagos mainland in Lagos State, Nigeria, with an area of 23 kilometre square with 503,975 inhabitants, with a population density of 21,864 inhabitants per square kilometer. Their blood sugars were taken using a glucose meter. The blood pressures were taken using a mercurial sphygmomanometer. The waist circumference was taken using a non stretch tape following individual consent. The body mass index of each participant was computed.

**Results:** A total of 66 volunteers participated in the study. The age range was 18-88years. The eligibility criteria for metabolic syndrome as outlined by World Health Organisation was fulfilled by 7.57%. Criteria outlined by International Diabetic Federation (IDF) was fulfilled by 13.64%. Criteria outlined by National Cholesterol Education Program Adult Treatment Panel III (NCEP:ATPIII) criteria (2001) was fulfilled by 6.06% of the study population.

**Discussion:** The differences in definition and criteria of metabolic syndrome by different study groups gives different prevalence and different sex distribution for the same disease entity as shown in this study. It should be noted however, that even lean individuals may develop features of Metabolic Syndrome adding further to the complexity of its pathogenesis. While obesity can be a spot diagnosis in some instances especially when gross, the same cannot be said of metabolic syndrome as it involves underweights, normal weight, overweight and obese subjects.

**Conclusion:** The prevalence of metabolic syndrome in surulere is 6.06% (ATP III criteria), 7.57% (WHO criteria) and 13.64% (IDF criteria). Different criteria with different prevalence for the same disease entity.

**Abstract #713**

**PREVALENCE OF OBESITY IN RURAL RESIDENTS OF SOKOTO, NIGERIA.**

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**Objective:** Excess body fat (not mere body weight) is recognized as a risk factor for cardiovascular diseases, diabetes mellitus and gallbladder diseases. Numerous methods, varying in sophistication and expense, have been
used to estimate body fat content, but most of the methods are unsuitable for routine clinical assessment. Leg-to-leg bioelectrical impedance analysis (BIA) is a simple, portable, non-invasive, safe and highly acceptable to patient technique of body fat assessment for both children and adults. To determine the prevalence of obesity using anthropometry and bio-electrical impedance analysis, among a rural population of Sokoto, Nigeria.

**Methods:** This was a cross sectional study involving anthropometric measurements of body weight, height and body composition, using leg-to-leg BIA; among rural dwellers. Body Mass Index (BMI) was calculated as the ratio of weight (kg) per height squared in meter.

**Results:** Of the 183 participants recruited for the study, 105 (57.4%) were females while 78 (42.6%) were males. There was no significant difference between the proportions of males and females who responded. The subjects were aged 16-70 years, with a mean (SD) age of 42.8 (16.3) years. Using BIA, 14.3% and 7.7% had overweight and obesity respectively. While using BMI 17.3% and 4.2% had overweight and obesity respectively. The female subjects had significantly higher percentage body fat [26.2+8.5 vs. 8.6+4.3% (p=0.001)] than the males. The female subjects had higher waist circumference [80.9+10.6 vs. 77.9 +8.8 cm (p=0.129)] and body mass index [22.0+5 vs. 20.5+4.4 kg/m2 (p=0.121)] than the males. There was good correlation between %body fat and waist circumference (r=0.547, p<0.05).

**Discussion:** Overweight is relatively common in female rural residents of Northwestern Nigeria. The estimation of percentage body fat using BIA technique helps in further identifying overweight subjects more than the traditional anthropometric parameters.

**Conclusion:** BIA technique is recommended as part of screening measures for obesity and other cardiovascular risk factors.

**Abstract #714**

**EFFECT OF WEIGHT LOSS ON CONCOMITANT MEDICATION COSTS IN OBESE/OVERWEIGHT INDIVIDUALS WITH EDMONTON OBESITY STAGING SYSTEM STAGE 3 OBESITY RECEIVING PHENTERMINE/TOPIRAMATE EXTENDED-RELEASE**

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**Objective:** The Edmonton Obesity Staging System (EOSS), validated against NHANES data, categorizes obesity-related morbidity based on degree of comorbidities. This allows for identification of patients with the greatest need for clinical intervention. This post-hoc analysis of the CONQUER study stratified subjects receiving phentermine/topiramate extended-release (PHEN/TPM ER) or placebo (PBO) by their baseline EOSS score and evaluated the annual cost-offsets associated with changes in concomitant medication use, including medications for hypertension (HTN), dyslipidemia (DYSL), and type 2 diabetes mellitus (T2DM).

**Methods:** CONQUER, a Phase 3, double-blind, 56-week study, randomized 2487 obese/overweight subjects (body mass index [BMI] ≥27 and ≤45 kg/m2) with ≥2 weight-related comorbidities to PBO, PHEN 7.5 mg/TPM ER 46 mg (7.5/46), or PHEN 15 mg/TPM ER 92 mg (15/92). EOSS is scored as: 1=subclinical weight-related risk factors, 2=established weight-related chronic disease, 3=established end-organ damage. This analysis focuses on subjects in the EOSS 3 category using ≥1 concomitant medication at baseline or endpoint for the treatment of HTN, DYSL, or T2DM (ITT-LOCF). Cost-offsets in antihypertensive, lipid-lowering, and antidiabetic medication use were calculated by multiplying unit cost (Medi-Span’s PriceRx database) by the number of doses per day from baseline to week 56/end of treatment. The cost of PHEN/TPM ER was not included in this analysis.

**Results:** In total, 43 subjects in the PBO group, 31 in the 7.5/46 group, and 58 in the 15/92 group had an EOSS score of 3 at baseline and received ≥1 concomitant medication at baseline or endpoint. At baseline, mean weight (SD) was 104±18 kg. Baseline annual concomitant antihypertensive, lipid-lowering, and antidiabetic medication costs were $1245±1504, $1911±1705, and $1629±1647 for PBO, 7.5/46, and 15/92, respectively. At week 56, least-squares (LS) mean percent weight loss was -2.5%, -6.0%, and -8.0% for PBO, 7.5/46, and 15/92, respectively (P<.05 vs PBO). At end of treatment, annual concomitant medication costs decreased with PHEN/TPM ER and increased with PBO: $20±95, -$104±112, and -$109±81 for PBO, 7.5/46, and 15/92, respectively. Common adverse events were constipation, paraesthesia, and dry mouth.

**Discussion:** Among subjects with established end-organ damage, EOSS Stage 3, PHEN/TPM ER significantly reduced weight and decreased annual concomitant medications costs compared with PBO.

**Conclusion:** These findings suggest that PHEN/TPM ER-enhanced weight loss is associated with a reduction in annual medication costs vs PBO, even in subjects with end-organ damage.
Abstract #715

ASSESSMENT OF RESTING AND POST-EXERCISE ENERGY EXPENDITURE WITH PERSONAL MOBILE TRACKER MAY GUIDE PHYSICAL TRAINING FOR LONG-TERM OUTCOMES

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Objective: Obesity is the manifestation of calories intake exceeding energy expenditure (EE). EE is a result of myriad mechanisms, that not only involve the calories spent to sustain life at resting (resting EE, REE) and physical activities, but also the calories spent after physical activities. While calories spent during physical activities can be easily tracked with current technologies, calories spent at resting and after physical activities are more difficult to track. These calories can only be assessed with indirect calorimetry methods, which are restricted at clinical or sport facilities. Furthermore, the calories spent after physical activities are known as Excess Post-Exercise Oxygen Consumption, EPOC, and are essential to determine long-term efficacy of physical activity and exercise.

In the present study, the objective is to explore the value of personal resting and post-exercise EE (EPOC effect) tracking.

Methods: We used a personal mobile indirect calorimeter tracker (www.breezing.co), which enabled assessment of resting, pre- and post-exercise EE; and allowed quantification of EPOC associated with the capability of muscle mass growth for a training protocol applied 3 times a week for 6 weeks. The exercise protocol, named High Intensity Intermittent (HIIT), was chosen due to its simplicity, workout quality, and short time required (4 min per session with 8 rounds of 20 sec. repetitions alternated with 10 sec. of seated resting).

Study participants performed over 640 measurements of EE independently, using the mobile tracker. Two groups, one control group (CG, n=11) and one intervention (IG, n=19) group, performed EE measurements at the beginning, middle, and end of the study period. In the case of participants in the IG, the measurements were performed on the specific training day (HIIT day) and in 2-3 days of non-training (Non-HIIT days), and measurements were compared to those assessed in similar conditions on a normal day of the CG (control measurement day).

Results: Results showed significant statistical differences in the participants’ EPOC effect for HIIT day vs. Non-HIIT day, and vs. control measurement day (α=0.05). In addition, significant statistical differences were found in the muscle mass growth of the IG vs. CG. Furthermore, the participants of the intervention group with muscle growth of 6+% showed statistical significant superior EPOC effect than other participants (α=0.20).

Discussion: The overall results confirmed that EPOC effect was present in the HIIT training day.

Conclusion: Overall, the EPOC measurements performed by the study participants using the mobile tracker allowed early identification of stages of exercise training associated to long-term muscle mass growth.
OTHER

Abstract #800

AN UNUSUAL PRESENTATION OF FAMILIAL HYPERPARATHYROIDISM

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Objective: The importance of genetic testing in patients with a family history of parathyroid disease.

Case Presentation: A 21 year-old man with a medical history significant for “grand mal” seizures, vitamin D deficiency, and asthma was found to have hypercalcemia and a high intact parathyroid hormone (iPTH) after presenting with bilateral mandibular fractures sustained from a fall after a seizure. It was noted that his maternal grandfather had a parathyroid adenoma diagnosed late in adulthood and his mother had renal stones and a parathyroid adenoma diagnosed at age 32 years. Both his mother and maternal grandfather were cured by parathyroid surgery.

Relevant Laboratory and Imaging: Initial total calcium levels were elevated and peaked at 14.1 mg/dL. At that time he had a slightly elevated albumin of 5.0 mg/dL, therefore corrected calcium was 13.3 mg/dL. His iPTH was inappropriately elevated at 119 pg/mL, and phosphate was low at 1.3 mg/dL. He had two CT scans done, one in 2007 and another at the time of his mandibular fracture that showed a stable “retention cyst” in the floor of the maxillary antrum. Neck ultrasound was done on initial visit and it demonstrated a significantly enlarged right lower parathyroid, measuring 15 x 6 x 7 mm, which was hypoechoic with a typical feeding vessel.

Surgery and Genetic Testing: He underwent successful parathyroidectomy. Surgical pathology demonstrated a parathyroid adenoma, measuring 1.3 x 1.0 x 0.5 cm and weighing 530 mg. Given the unusual family history, he was referred for genetic testing, which demonstrated that he was heterozygous for a nonsense R120x mutation in the CDC73 (HRPT2) gene.

Discussion: Here we present a case of a young man with an unusual presentation of familial primary hyperparathyroidism. He has a newly found mutation that is consistent with jaw parathyroid syndrome. This is a nonsense mutation in the HRPT2 gene which encodes for parafibromin, a tumor suppressor protein. Absence of parafibromin is associated with parathyroid adenomas, carcinomas, and renal tumors. It is also associated with benign tumors of the mandible and the maxilla. It is unclear if his maxillary lesion is related to this new mutation, since the CT findings are not consistent with a calcified tumor.

Conclusion: This case demonstrates the importance of genetic testing in patients with a family history of parathyroid disease. In jaw-parathyroid syndrome lifelong surveillance for parathyroid cancer, jaw tumors, renal tumors, and, uterine tumors in women is recommended.

Abstract #801

STRATEGIES FOR ACHIEVING SUCCESSFUL PARATHYROID ADENOMA LOCALIZATION IN PRIMARY HYPERPARATHYROIDISM

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Objective: To evaluate the strategies used to always achieve success in correctly localizing parathyroid adenomas.

Methods: 112 consecutive parathyroidectomies performed since 2006 were reviewed in patients with symptomatic or asymptomatic primary hyperparathyroidism who underwent tri-imaging with 1. high resolution or 3-phase neck CT scan (with and without contrast) or neck MRI scan (with and without contrast); 2. MIBI-SPECT; and 3. ultrasonography to localize parathyroid adenomas. At least 2 of the 3 studies were required to be concordant before the operation, with one of the studies preferably MIBI-SPECT. When uncertainty arose, especially when MIBI-SPECT was non-localizing but ultrasound showed a possible adenoma, FNA for PTH assay was performed and found to be useful. Radionuclear localization of adenoma was performed during every case. Intraoperative PTH assay (iPTH) was utilized. Ionized calcium, PTH and Vitamin D 25-OH levels were obtained, and vocal cord function was assessed with mirror or fiberoptic examination pre- and post-operatively.

Results: There were no negative explorations in 112 consecutive cases, with 100% concluding with the removal of a frozen section proven parathyroid adenoma at the localized site. The cure rate, however, was not 100%, as we had several patients with multiple adenomas. Two patients had triple adenomas, and five patients had double adenomas. All patients were cured eventually. One patient had a double adenoma by CT scan, ultrasound and iPTH but not MIBI-SPECT (which showed only one), and was cured after one operation. Procedure duration was typically less than 30 minutes to removal of the adenoma with minimal dissection, and operations were done on an outpatient basis. No instances of vocal cord palsy occurred.

Discussion: Both ultrasound and MIBI have false negative rates of up to 35% in localizing parathyroid adenomas, while combining imaging studies show non-localization in 10-17%. Negative localization pre-operatively can be associated with significantly higher negative exploration rates in parathyroidectomy, and suboptimal localization may lead to more extensive or 4 gland, prolonged explorations when hyperplastic parathyroid tissue are not found in the expected localization.
locations. The expense of tri-imaging as described in this paper is offset by its precision in correctly localizing parathyroid adenomas and reducing operating time, potential complications, and need for re-exploration.

**Conclusion:** Using the algorithm above, parathyroid adenomas were always found in the expected locations, thereby minimizing operating time, potential complications, and need for re-exploration.

**Abstract #802**

**SEVERE HYPERCALCEMIA DUE TO CONCOMITANT PRIMARY HYPERPARATHYROIDISM AND GRAVES’ DISEASE**

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**Objective:** Mild hypercalcemia in ambulatory patients is most often due to primary hyperparathyroidism. However, hospitalized patients with severe, symptomatic hypercalcemia (calcium values greater than 14 mg/dl) often have malignancy. Concomitant endocrinopathies causing severe hypercalcemia are rarely reported. We report a case of severe hypercalcemia due to primary hyperparathyroidism and Graves’ disease.

**Case Presentation:** The patient is a 36 year old female with a history of asthma who presented to the Emergency Department with 1 week of altered mental status. Her symptoms were associated with increased weakness, dizziness and anorexia and unintentional weight loss 2 to 4 weeks prior to presentation. Her vital signs were remarkable for heart rate of 131 bpm, blood pressure 118/65 mmHg and respiratory rate of 25. Her physical exam was remarkable for dry oral mucosa, tremors and slow mentation. Her labs were remarkable for severe hypercalcemia, calcium of 18.2 mg/dl, as well as hypokalemia (2.4 mg/dl), hypomagnesemia (<0.2 mg/dl), and hypophosphatemia (2.6 mg/dl). Her renal function was normal, EKG showed sinus tachycardia. She was admitted to the MICU and received aggressive intravenous hydration, electrolyte replacement, calcitonin and pamidronate. Within a few days of treatment, her mental status returned to baseline and her calcium and other electrolytes improved. She was also found to have suppressed TSH of 0.008 uIU/mL and free T4 of 6.82 ng/dl. Thyroid scan was consistent with Graves’ disease so methimazole was started. PTHi was 499 pg/ml (12-65 pg/ml) and she underwent a parathyroid scan which was remarkable for a left lower pole adenoma. After stabilization of her electrolytes and hyperthyroidism, she underwent parathyroidectomy. After surgery, calcium and PTHi quickly normalized and stabilized within normal range. Pathology was consistent with 4 grams parathyroid adenoma.

**Discussion:** Hypercalcemia of malignancy is the most common cause for severe, symptomatic hypercalcemia in the hospitalized patient. Parathyroid carcinoma is a rare cause for hyperparathyroidism but may be considered when a patient presents with severe hypercalcemia and a 5 to 10 fold increase in PTH as our patient did. However, malignancy was not the cause for severe hypercalcemia in this case. Concomitant primary hyperparathyroidism and Graves’ disease causing hypercalcemia has been reported in the literature but is considered rare. In the vast majority of these cases, calcium values were less than 15 mg/dl.

**Conclusion:** Concomitant endocrinopathies is a rare cause of severe hypercalcemia, in our case the calcium level was markedly elevated at 18 mg/dl which to our knowledge has never been reported.

**Abstract #803**

**MULTIDISCIPLINARY TEAM IMPROVED DIABETIC METRICS IN THE INPATIENT HOSPITAL SETTING**

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Kaiser Permanente

**Objective:** To improve the quality of care by reducing hypoglycemia events, capturing Hemoglobin A1c (HgbA1c) labs, assuring follow up appointments scheduled within 7 days post discharge, and increasing patient satisfaction with diabetes education received during hospital stay.

**Methods:** Bi-weekly diabetic rounding by multi-disciplinary teams has proven to be effective on hospital floors allowing for timely assessment and nurse/physician education. Electronic medical record (EMR) provides data for real-time analysis including chart reviews, hospital census, missed HgbA1c lab opportunities, and follow-up appointments.

**Results:** From when the program started in October 2010 through December 2013, the numbers of patients experiencing hypoglycemia events during their hospitalization have been reduced by approximately 28.3%. The episodes of hypoglycemia decreased by
ABSTRACTS – Other

10.7% per day per patient. There was also a significant reduction in the duration of hypoglycemia (less than 70 mg/dL), and the incidence of severe hypoglycemia (less than 40 mg/dL).

HgbA1c labs captured have increased from 64% in 2010 to 91.3% in 2013. Follow up appointments scheduled within 7 days post discharge also increased from 53.1% in 2010 to 82.9% in 2013. Patient satisfaction with diabetes education improved from 56.2% in 2010 to 76% in 2013. Multidisciplinary root cause analysis (RCA) teams were formed to review and address improvement opportunities by the multidisciplinary teams. The findings were disseminated to primary care, hospitalists and specialty providers including nursing administration as a tool to educate and further raise awareness in both the inpatient and outpatient setting. The more severe cases were referred to the quality improvement department.

Discussion: Our overall performance shows a glimpse of the challenges and our constant improvement processes. Our integrated systems have allowed us to study and modify operational workflows to attain efficiency and sustainability. The use of bi-weekly multidisciplinary rounding teams is a cost effective technique of improving quality of inpatient diabetes care on a sustained basis. A key component of the sustainability of our program is the integration with the quality performance improvement department and the feedback it provides to each of the clinical departments involved in diabetes care within the hospital.

Conclusion: Our data indicates that biweekly multidisciplinary rounding team using an integrated system improves inpatient diabetic metrics in sustainable and cost effective manner.

Abstract #804

CARDIOMETABOLIC AND ENDOCRINE CORRELATES OF AGE, TOTAL BODY FAT, AND EXERCISE IN A HEALTHY MALE POPULATION

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Objective: To assess selective effect(s) of age, total body fat, and physical activity on hemodynamic indices, insulin sensitivity, endocrine function, adipokines, and inflammatory markers.

Methods: Sixty-nine healthy men age 19-78 yr and BMI 18-39 Kg/m2 were studied in the morning after overnight fasting. Study session consisted of: (1) blood collection for the measurements of glucose, insulin, TG, HDL, leptin, adiponectin, IGF-I, LH, FSH, free testosterone (FTe), E2, TSH, hsCRP, and TNF; (2) DXA for calculation of body fat; and (3) non-invasive assessment of cardiovascular risk via evaluating arterial stiffness by pulse wave velocity (PWV), left ventricular (LV) overload by augmentation pressure (AP), LV function by Ejection duration (ED), and coronary perfusion by subendocardial viability ratio (SEVR) using SphymoCor. Fat mass index (FMI) was calculated by dividing total body fat in Kg into height in meter to the power of 2. Fasting glucose and insulin concentrations were used to calculate peripheral insulin resistance using HOMA-IR formula. Multiple regression statistic was used for data analysis. Regression coefficients were standardized to eliminate the effect of variable scales, with standardized regression coefficient referred as beta.

Results: The results (beta:P) revealed significant association of: (1) FMI with SBP (0.26:0.024), DBP (0.37:0.0009), ED (0.39:0.001), SEVR (-0.037:0.0003), TG (0.24:0.05), HDL (-0.43:0.0002), HOMA-IR (0.55:0.0001), leptin (0.84:<0.0001), FTe (-0.30:0.0018), and E2 (0.28:0.02); (2) age with SBP (0.28:0.016), DBP (0.29:0.01), PWV (0.31:0.01), AP (0.72:<0.0001), IGF-I (-0.59:<0.0001), and FTe (-0.54:<0.0001); and (3) exercise with TG (-0.33:0.001).

Discussion: Advancing age in men is associated with decreased physical activity and increased body fat, which could confound the deleterious role of aging process per se. The results of this study in healthy men revealed age-independent role of increased body fat on BP; LV function, subendocardium perfusion, TG, HDL, leptin, and insulin resistance. Age-specific increases in arterial stiffness, SBP, and LV afterload would potentially be less consequential in the absence of abnormalities invoked by excess body fat. While decreased with advancing age in men, IGF-I and testosterone are not commonly pathological and rarely have clinical implications.

Conclusion: While in men, compromised somatotropic and gonadotropic function are primarily attributed to advancing age, cardiometabolic adversities except for indices of arterial stiffness, are the consequence of increased body fat, often associated with the aging process. The role of exercise is possibly underestimated, since this study was not designed for that purpose.

Abstract #805

NOT JUST “SOMATOSTATINOMA SYNDROME”, A PANCREATIC TUMOR SECRETING BOTH SOMATOSTATIN AND GASTRIN

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Objective: Somatostatinoma syndrome was first described in 1977 which includes diabetes mellitus, diarrhea and cholelithiasis. The inhibitory effect of somatostatin on insulin, cholecystokinin and digestive enzymes is thought to be the etiology of somatostatinoma syndrome. In 2012, a case of HIF2α gene mutation that led to coexisting somatostatinoma, paraganglioma and polycythemia
was reported. Mutation of this gene was associated with tumorigenesis and increased erythropoietin.

**Case Presentation:** A 69 year old man was referred to our endocrinology clinic in November 2012 for evaluation of two pancreatic masses which were found incidentally on CT scan. His past medical history included diabetes mellitus, chronic diarrhea, polycythemia of unclear etiology, gastric ulcer and cholelithiasis. Serum tests revealed elevated somatostatin, insulin, glucagon, gastrin and erythropoietin. Tissue samples from both masses stained positive for both somatostatin and gastrin. We are waiting for HIF2α gene result.

**Discussion:** The elevations in insulin, glucagon and gastrin were unexpected based on our knowledge of the inhibitory effect of somatostatin. Previous studies showed that gastrin stimulates both insulin and glucagon secretion, while somatostatin inhibits insulin and glucagon secretion to different degree. In this case, we postulate that excessive gastrin led to elevation of insulin and glucagon. As somatostatin suppressed insulin secretion more than glucagon secretion, there was a relative excess of glucagon over insulin which led to diabetes. Elevated gastrin caused gastric ulcer and diarrhea. This case also showed that pancreatic endocrine tumor can secrete more than one types of hormone simultaneously, and the clinical features of multi-hormone secreting pancreatic endocrine tumor were not described before. This is also the second case report of coexisting somatostatioma and polycythemia.

**Conclusion:** Symptoms that are characteristic of somatostatinoma syndrome are not always due to elevated somatostatin, which warrants measurement of multiple hormones when we evaluate somatostatinoma patients. And further research is needed to explain why pancreatic endocrine tumor can co-secret multiple hormones. Furthermore, we will need to find out the prevalence of HIF2α mutation in patients with somatostatinoma only versus patients with both somatostatinoma and polycythemia. The results will help us understand whether the coexistence of somatostatinoma and polycythemia is a separate disease entity that has a different pathogenesis pathway as compared with somatostatinoma alone.

**Abstract #806**

**A UNIQUE CASE OF INTRATHYROIDAL INTRAPARATHYROIDAL PARAGANGLIOMA**

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Rutgers Robert Wood Johnson Medical School

**Case Presentation:** A 55 year-old female who lived 200 miles from Chernobyl, USSR when the nuclear accident occurred, was concerned about her radiation exposure and requested a thyroid ultrasound which showed a 2.5 cm right lobe nodule. Plasma TSH was 1.54uiU/mL and free T4 was 1.1ng/dL. The pathology report from two separate FNAs conflicted; one indicated a follicular neoplasm, the other a benign goiter with negative BRAF and KRAS suggesting a benign nature. The patient returned for an FNA with the Afirma® gene expression classifier. There was a 40% suspicion for malignancy, identifying a genetic signature seen in medullary thyroid carcinoma. Plasma and urine normetanephrines and metanephrines were normal. Plasma calcitonin level was <2pg/mL (0-5), CEA 0.6ng/mL (0.0-4.7); calcium 9.3mg/dL and PTH 52pg/mL. She underwent a hemi-thyroidectomy to obtain a definitive histological diagnosis. Pathology revealed a 1.4 cm paraganglioma arising from an intrathyroidal parathyroid gland, surrounded by a rim of benign parathyroid tissue. The tumor stained positive for chromogranin A and S-100, highlighting sustentacular cells. Laboratory tests demonstrated mild elevation in chromogranin A of 6 nmol/L (0-5). Genetic evaluation showed the patient was negative for the familial paraganglioma syndrome genes (SDHB, SDHC, SDHD and SDHAF2). No additional surgery was recommended.

**Discussion:** Paragangliomas are rare neoplasms that arise in adrenal and extra-adrenal paraganglia of autonomic nervous system. Extra-adrenal paraganglia can be further divided into sympathetic and parasympathetic types. Although histologically indistinguishable, they differ in their secretory patterns. Parasympathetic paragangliomas occur predominantly in the head and neck; approximately 95% of such tumors are nonsecretory. These are frequently syndrome associated (MEN) or familial, correlated with increased mutations in the genes for succinate dehydrogenase (SDH) subunits A, B, C, and D, or SDHAF2 that encodes a protein required for flavination of SDHA.

**Conclusion:** Primary paragangliomas of the parathyroid are very rare with only two documented cases. We present, as far as we are aware, the first case of intrathyroidal intraparathyroidal paraganglioma. Due to lack of clinically characteristic features, distinct histologic patterns of paraganglioma include “zellballen architecture”. These tumors tend to be richly vascular; mitotic figures, necrosis, invasive growth and nuclear pleomorphism are generally absent. Immunohistochemically, neoplastic cells express chromogranin, synaptophysin and CD56, with S100 protein highlighting sustentacular framework.
Abstract #807

RATE OF ANAPHYLAXIS ASSOCIATED WITH INTRAMUSCULAR TESTOSTERONE INJECTIONS

Stephen Camper, PhD¹, L. Kallenbach, PhD², K. Summers, PhD³, L. Ma, PhD¹, N. Shusterman, MD¹


Objective: Intramuscular (IM) testosterone injections have been available since 1953 but significant immediate adverse reactions have not been emphasized. We sought to estimate the rate of anaphylaxis associated with IM testosterone injections using a large US electronic medical record (EMR) database. As a historical reference, we also present the experience from the FDA Adverse Event Reporting System (FAERS).

Methods: The Quintiles Practice Research database is the largest de-identified HIPAA compliant EMR database in the US, collecting data from 29,000+ providers (both primary and specialty clinics) in 49 states with records from ~16 million active patients. Study sample consisted of male patients who had received or were prescribed IM testosterone products during an outpatient visit between 1997 and 2012. Anaphylaxis cases were selected based on ICD-9-CM code of 995.0 (other anaphylactic reaction), or E932.1 (androgens and anabolic congeners causing adverse effect) occurring within 30 days of the testosterone visit. The relationship between testosterone injections and anaphylaxis was classified as “likely, probably, possible, unlikely” based on the clinical review of patient’s electronic medical records. The primary outcome was the number of patients with anaphylaxis per 10,000 patients.

Results: From 1997 to 2012, 56,427 unique patients were identified with exposure to IM testosterone products, and 38 potential cases (37 patients) of anaphylaxis associated with IM testosterone injections were found. Twenty-one cases (20 patients) were selected based on the 995.0 code and the rest were based on the E932.1 code. All of the cases based on the E932.1 code were classified as “unlikely” based on a paucity of supporting information describing the actual reaction. The remaining cases were classified as “likely” in 6 patients (6 cases), “probable” in 4 patients (5 cases), and “possible” in 10 patients (10 cases). Ten patients had a total of 11 “likely or probable” anaphylaxis cases, corresponding to a rate of 1.8 patients per 10,000 patients (95% CI: 0.7, 2.9). The rate for “likely, probable, or possible” cases was 3.5 patients per 10,000 patients (95% CI: 2.0, 5.1). In comparison, there were only 19 cases of anaphylaxis identified from FAERS from 1/1969 to 1/2013 (44 years).

Discussion: Our study showed that, although rare, anaphylaxis-related events have been documented to occur following IM testosterone injections.

Conclusion: Given the limitations of spontaneous reporting of adverse events for marketed products, EMRs can be utilized to complement FAERS in monitoring the safety of drugs, especially older drugs. Research funded by Endo Pharmaceuticals Inc.

Abstract #808

PERSISTENCE WITH TESTOSTERONE REPLACEMENT THERAPY

Stephen Camper, PhD¹, A. Puenpatom, PhD¹, C. Blanchette, PhD², L. Ma, PhD¹

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Objective: Very limited data exist on patient persistence with testosterone replacement therapy (TRT). Furthermore, no persistence data are available for the long-acting injection (LAI) formulation (Testosterone Undecanoate injection). Therefore, the objective of this study was to compare medication persistence and first switching patterns among patients initiating LAI with those using other testosterone formulations.

Methods: This was a retrospective database analysis of 17,385 patients receiving TRT in Germany between 2008 and 2012 based on the IMS® Health German Longitudinal Prescriptions (LRx) database. The main outcome measure was the percentage of patients who were persistent with their index TRT at 24 months from initiation.

Results: During the study period, patients receiving the LAI remained on their initial therapy significantly longer than patients receiving capsules, gels or short-acting injections (SAIs) (p<0.001). At three months, 70.1% of patients with the LAI were persistent with their initial TRT compared with 39.1% of patients receiving the gels and 14.7% of patients treated with the SAI. At 24 months, 20.2% of those receiving the LAI remained on their initial therapy vs. 9.7%, 5.7% and 0.5% for capsule, gels and SAIs, respectively. Sensitivity analyses showed consistent results. A total of 3,115 (17.9%) patients switched to a different product, with those starting on a LAI having the lowest switching rate (6.2%) and those starting with SAIs having the highest rate (24.2%).

Discussion: While persistence with TRT decreased substantially over time, treatment with the long-acting injection demonstrated higher persistence compared with the gels, capsule, and short-acting injections.

Conclusion: Persistence with treatment for low testosterone may be enhanced by the administration of testosterone utilizing a technology that prolongs the availability of drug and reduces dosing frequency. This research was supported by Endo Pharmaceuticals Inc. Malvern, PA.
Abstract #809

**PANCREATIC EXOCRINE AND ENDOCRINE DYSFUNCTION AFTER PARTIAL PANCREATECTOMY FOR VON HIPPEL-LINDAU ASSOCIATED PANCREATIC CYSTADENOMA**

Zijian Chen, MD, Jose Sanchez, MD, Emilia Lia, MD

Beth Israel Medical Center

**Case Presentation:** We present an interesting case of a 27 year old female diagnosed with von Hippel-Lindau (vHL) syndrome after subtotal pancreatectomy for pancreatic cystadenoma. The patient initially had multiple liver cysts discovered during prenatal ultrasound. Follow-up imaging post-partum revealed innumerable cysts in the pancreas, as well as several cysts in the kidneys. The patient’s main symptoms was early satiety. FNA revealed serous fluid. Hormonal evaluation did not show elevation in metanephrines nor tumor markers. The patient became more symptomatic and she decided to undergo subtotal pancreatectomy. Given pancreatic cystadenoma is associated with vHL, patient was evaluated by medical genetics. She tested positive for vHL. During the post-operative period, the patient demonstrated both fasting and postprandial elevations in blood glucose. She also developed several episodes of symptomatic hypoglycemia. Post-operative follow-up revealed normal cortisol levels, glycosylated hemoglobin of 5.9%, and C-peptide of 0.63ng/mL (0.8-3.1ng/mL) while concurrent glucose level was 12.1mg/dL. Further follow-up showed the patient to have fasting and post-prandial hyperglycemia. HBA1C increased to 6.6% six weeks after surgery, with elevated fructosamine, 340umol/L. In addition, she continued to have infrequent episodes of diaphoresis and tremors, which resolved with oral glucose intake. Glimepiride was started and the patient was instructed on management of hypoglycemia. However, her glucose continues to be elevated despite treatment.

**Discussion:** Pancreatic cystic disease is strongly associated with vHL (>70% in one study). Most of the pancreatic cystic disease is asymptomatic and discovery is usually incidental during imaging workup for unrelated pathology or during evaluation for patients who have vHL genetics. With symptomatic disease, surgical resection is the treatment. Serous cystadenoma is rarer than simple cysts in vHL. Although still typically asymptomatic, surgical resection is more difficult and extensive. Endocrine dysfunction after pancreatectomy is not unrecognized in literature. The incidence of diabetes mellitus is 20 to 50% after Whipple’s. Glucagon deficiency and hypoglycemia is another challenge. There is need to control both hyper and hypoglycemia after pancreatectomy.

**Conclusion:** We present a patient who presented with diffuse pancreatic cystadenoma discovered incidentally on prenatal ultrasound. Subsequently patient was diagnosed with vHL, with associated findings of renal cysts and central nervous system hemangioblastomas. In this patient, we review the management of pancreatic cystadenoma, as well as the sequela of the surgery.

Abstract #810

**MALIGNANT INSULINOMA PRESENTING WITH NEUROLOGICAL DEFICITS AND SEIZURES**

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**Case Presentation:** We present a case of a 65 year old male with a history of malignant insulinoma requiring chemical embolization. The patient presented with a history of weakness, irritability, hemiparesis, and seizures secondary to hypoglycemia. Initially patient was recommended to increase food intake, use of Acarbose, and steroids with some improvement of symptoms. Biochemical testing revealed high levels of c-peptide (12.5 ng/mL), proinsulin (70 pmol/L), and insulin (32.6 uIU/mL) while serum glucose was low (37 mg/dL). On imaging patient was found to have multiple lesions in both the liver and the pancreas. Liver biopsy revealed moderately differentiated carcinoma with possible neuroendocrine features. The patient had continued symptoms of hypoglycemia that were difficult to control, and was referred for hepatic artery embolization. The patient underwent two embolization procedures, encompassing the anterior and posterior segments of the right hepatic artery. The patient tolerated the procedure well, and had improvement of symptoms secondary to hyperinsulinemia. However, follow-up monitoring revealed both enlargement and new disease foci that are both intrahepatic and extrahepatic. Given the extensiveness of the disease, patient was started on somatostatin analog in effort to control rate of growth of these masses.

**Discussion:** Insulinomas are rare, with incidence of less than 4 cases per million person-years. Less than 10% are malignant, 10% present with multiple tumors, and the majority are sporadic. The exceptions are those associated with MEN1, which can occur in 6-10% of patients with the genetic susceptibility. There are not histologic criteria to differentiate between benign and malignant insulinoma, therefore biochemical and pathologic evaluation must be made. Successful treatment is based on completeness of surgical
Abstract #811

AN UNUSUAL CAUSE OF HYPOCALCEMIA

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St. Francis Hospital

Objective: To present an unusual but known cause of hypomagnesaemia induced-hypocalcaemia in a patient with chronic omeprazole ingestion for severe GERD.

Methods: In this report we present an unusual cause of hypocalcaemia in the setting of prolonged omeprazole ingestion.

Case Presentation: Our patient described features of magnesium deficiency such as weakness, muscle twitches, and fits with clinical signs of hypocalcaemia: a positive Chvostek’s and Trousseau’s Signs. Patient’s blood test revealed a low calcium ionized (0.75 mmol/l, 1.15-1.29) and magnesium level (1.2 mg/dl, 1.7-2.8). The total Vitamin D level was 54 ng/dl (30-100). His liver function tests, amylase and lipase were normal. With omission of the omeprazole 1 day after admission and replacement therapy, his ion levels normalized.

Discussion: Hypomagnesaemia is often undiagnosed and is associated with multiple biochemical abnormalities. Treatment focus should be aimed at stopping the proton pump inhibitors (PPI) and replacing the magnesium. There is some recent evidence indicating that improper use of PPI is rising.

Conclusion: Chronic use of PPIs is an unusual cause of hypocalcaemia. As with any medication it is important that PPIs should only be prescribed when appropriate, and mainly for FDA-approved indications. Continued monitoring and decision making on dose reduction/withdrawal is essential to avoid complications.

Abstract #812

PSEUDOHYPOPARATHYROIDISM PRESENTED AS BILATERAL SYMMETRICAL INTRACRANIAL CALCIFICATION

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Objective: Pseudohypoparathyroidism (PHP) is a rare disorder defined by end-organ unresponsiveness to parathyroid hormone (PTH). Type Ib PHP is characterized by resistance to PTH mainly in the renal tissue and in a few others tissues such as the thyroid, but without features of Albright hereditary osteodystrophy (AHO). This type is characterized by blunted nephrogenous cyclic-AMP (cAMP) response to exogenous parathyroid hormone (PTH).

Methods: In this report we present an adult onset presentation of PHP 1B confirmed with laboratory and genetic testing, who presented with multiple seizures.

Case Presentation: A 24 year African American male, presented with new onset seizure episodes since three days prior to admissions. Patient denied any muscle spasm, weakness, tongue biting, urinary incontinence. He was not able to remember the episodes and per witnesses it involved his whole body with shaking movements and eye rolling, and mouth drooling. Episodes were being provoked wit feeling unease at his throat and coughing. Patient had episodes of hand clenching when he plays piano since the ago of 20. On physical exam, trousseau and chvostek signs were present. CT head revealed Diffuse calcification of the BG (caudate and lentiform nucleus) and cerebellum (dentate nucleus) in a symmetric and bilateral pattern. This finding was confirmed with MRI. Blood tests revealed calcium: 5.6 mg/dl (8.5-10.5), ionized calcium: 0.55 mmol/l (1.15-1.29), phosphorus 6.1 mg/dl (2.40-4.30), 25 OH Vit D 17.6 ng/ml (30-100), PTH intact: 157 pg/ml (15-65), 24 h urinary calcium: 24 mg/24h (100-300). We started him IV calcium gluconate two times daily adjusted according to ionized calcium to keep the levels above 1.1, calciteriol 0.25 mg/day, and ergocalciferole 50000 units weekly for up to 8 weeks, patient’s calcium total and ionized level improved to normal values. With high-normal serum phosphate and normal alkaline phosphatase, and a lack of symptoms associated with osteomalacia, vitamin D deficiency alone was unlikely to be the cause of hypocalcaemia. There was no peculiar clinical features of Albright hereditary osteodistrophy. The diagnosis of PTH resistance (pseudohypoparathyroidism type Ib) was made clinically and patient was referred for a genetic test which confirmed the diagnosis.
Discussion: Pseudohypoparathyroidism presents with end organ resistance to PTH, associated with hypocalemia, hyperphosphatemia, and elevated PTH. Intracranial bilateral symmetric calcification can be seen in up to 50% of PHP cases.

Conclusion: It is extremely important to perform a complete biochemical analysis in order to distinguish PHP from other disorders in every patient presenting symptoms suggestive of hypocalcaemia.

Abstract #813

INCIDENCE AND SURVIVAL TRENDS OF RARE MALIGNANCIES OF THE THYROID, PARATHYROID, ADRENAL AND ENDOCRINE PANCREAS

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Objective: With the exception of papillary and follicular thyroid cancer, malignant tumors of the thyroid, parathyroid, adrenal and endocrine pancreas are uncommon. These rare malignancies present a challenge to both the clinician and patient as few data exist on their incidence or survival. We hypothesized that, due to incidental detection by radiographic imaging, there has been an increase in incidence and survival of these rare malignant tumors with a concomitant decrease in stage at presentation. We aimed to determine the most recent incidence and survival data of these rare malignant endocrine tumors, as well as trends in incidence over time.

Methods: We used the NCI’s SEER 18 database (2000-2009) to investigate incidence and survival of rare malignant tumors of the thyroid, parathyroid, adrenal, and endocrine pancreas. Rare tumors were defined as tumors with an incidence of less than 60 cases per 1,000,000 person-years. Tumors were categorized with the WHO classification systems. We collected data on incidence, gender, stage, size, and survival. Change in incidence was calculated between years 2000-2002 and 2007-2009.

Results: We found 39 types of rare malignant tumors in the organs studied in the SEER database. Malignant thyroid tumors had the highest combined incidence (100.8 per 1,000,000 person-years) followed by pancreas (4.0), adrenal (2.6) and parathyroid (0.4). Incidence for all endocrine organs combined increased 60% from 86.7 (95% CI 85.5 - 87.9) (n=20,360 per year) to 132.3 (95% CI 130.9 - 133.7) (n=33,900 per year) over the study period. The majority of the increase was attributable to rare tumors of thyroid, followed by pancreas, adrenal, and parathyroid. Five-year survival increased 1.38% (p<0.05) over time without any change in stage at presentation.

Discussion: We found that rare malignant endocrine tumors are more common than expected, and are as common as adenocarcinoma of the pancreas. We also noted a significant increase in incidence and a minimal improvement in survival. Because there has been no change in treatment for these tumors in this time period, the increasing rates may be due to increased incidental detection

Conclusion: We hope our data will improve survival of these rare tumors by making physicians more aware of these increasingly common malignancies.

Abstract #814

WHAT’S IN A NAME?: A TAXONOMY FOR THE DEFINITION OF MINIMALLY INVASIVE PARATHYROIDECTOMY

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Objective: In recent years “minimally invasive parathyroidectomy” (MIP) has become the procedure of choice for many surgeons, but the meaning of the term MIP is unclear. This is confusing for both the medical community and patients. We hypothesize that because the definition of MIP in the literature is so variable this term has little meaning. Our aim was to create a standardized taxonomy and terminology for MIP.

Methods: We performed a PubMed search using the terms: parathyroidectomy, minimally invasive, localized, focused, unilateral, radio-guided, video-assisted, and endoscopic. Review articles, and publications that did not comment on parathyroidectomy were excluded. Data were collected for: author, journal title, year published, and all described aspects of parathyroidectomy. Histograms of all descriptive terms were analyzed for frequency of use and time trends.

Results: We identified 1,010 articles, and analyzed 443 (44%) after applying the exclusion criteria. We found 18 words used in 75 different combinations to describe MIP. Publication time trends showed a non-parametric distribution between 1982 and 2013, with a median publication year of 2006. We established four categories that encompassed all 75 definitions of MIP, namely: 1. operative approach (open describing incision size, or endoscopic, robotic, video-assisted), 2. number of glands explored, 3. operative adjuncts (ioPTH, radio-guided, fluorescence-guided), and 4. anesthesia type. The words “focused”, “targeted” and “directed” are unclear and were replaced with actual gland number explored. Operative approach was the most commonly described attribute
and was mentioned in 47% (n=207) of the articles (mean incision size = 2.2 cm), followed by number of glands explored (blank % of articles), operative adjuncts [overall %] (iopth, radioguided, fluorescence guided), and finally anesthesia type [36% of articles (general [27% (n=120)] vs. local [9% (n=42)])

**Discussion:** The finding that there are 75 different definitions for MIP confirms that this term is too generic to be useful.

**Conclusion:** We propose a new, taxonomic format for describing MIP based on the four descriptive categories we identified in this study: [operative approach], [# of glands explored], parathyroidectomy using [operative adjuncts] under [anesthesia type]. For example, “2 cm, single gland parathyroidectomy using ioPTH under general anesthesia”.

Abstract #815

**RECONSIDERATION OF AMERICAN THYROID ASSOCIATION (ATA) STANCE ON POTASSIUM IODIDE (KI) PREVENTION AND NUCLEAR T/ERROR: POLICIES TO SAVE LIVES**

*Erroneous units for KI distribution.***

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**Objective:** Iodine-131 [131I] inhaled from Uranium fission (t1/2 8 days beta radiation) due to nuclear t/error may extend 300+ miles. ATA recommends KI distribution (50 miles) and availability to 200 miles. Department of Health (DOH) compliance of 130 mg KI dose distribution is near zero. Effective KI dose is needed before 8 hours after an event, in more vulnerable populations (i.e. children). Physicians, military, and political officials remain unconvinced of the necessity of the current dose recommendations.

**Methods:** Guideline review off FDA, ATA, CDC, USRC, UN, Councils on Radiation Protection and Measurement, World Nuclear Association recommendations; review of scientific literature and consultation with key NYS decision makers (i.e., commissioners of DOH/homeland security, governors, congressmen and generals) was conducted.

**Results:** 30 mg single dose of KI 99% and 15 mg 98% successful in blocking radiiodine absorption, on the first day. Continued suppression occurred with 15 mg KI (Sternthal, et al).

**Discussion:** Consensus opinions from policy makers have no confidence in the current dosing; therefore, the ATA needs to recommend distribution of the lowest effective prophylactic dose, make instructions user friendly, review alternative dietary sources and multiple exposures, and explain the broader I-131 medically related co-morbidities that can last 60+ years (i.e., x-ray of thyroid for acne) and extension of thyroid disease in areas from 200-5,000 miles from epicenter. Few scientists know the value of alimentary iodide (i.e. kelp [3 mg KI in ¼ teaspoon]) can protect like KI. Food industry does not use iodized salt, impacting distant regions (K-perchlorate is hazardous).

**Conclusion:** ATA and other agencies should revise recommendations for distribution to be 15 mg KI (3 mg scored) pills taken before 8 hours following an event (2 mg KI per 10 pounds and 7 days; 1 mg per 10 pounds is user friendly for families) (Sternthal, et al). Additional doses (i.e., 60 pills) because long-term food (milk) and water contamination or repeat events. Public knowledge of dietary iodide sources need to be readily available (in mg/tsp form). I-131 broader impact on health and long-term thyroid monitoring needs to be identified.

Abstract #816

**FAHR’S SYNDROME ASSOCIATED WITH PSEUDOHYPOPARATHYROIDISM**

Zarmen Israeli-Konaraki

**Objective:** To demonstrate the spectrum of hypocalcemia and Fahr’s syndrome.

**Case Presentation:** A 65-year-old man presented with chest discomfort and stiffness behind the head. A CT scan of the brain revealed bilateral basal ganglia and subcortical white matter calcification. The serum calcium was 6.7 mg/dl, albumin 4.2 g/dl, magnesium 2.0 mg/dl, phosphate 4.2 mg/dl, i PTH 223 pg/ml, 25-OH vit D 34 ng/ml, TSH 7.8 mIU/L, free T4 0.5, TPO antibody negative and thyroid ultrasound was normal. No history of seizures, tremor, headache, bone pain, constipation, or paresthesia off the face or extremities. The family history was negative for seizures, mental retardation, fractures or short stature. His height was 157 cm. No skull deformity, palpable goiter, Chvostek’s sign or shortening of metacarpals and metatarsals were noted. No tremors or rigidity were noted and deep tendon reflexes were depressed. A diagnosis of Fahr’s syndrome associated with pseudohyoparathyroidism(PHP) was entertained and he was started on calcitriol and calcium carbonate.

**Discussion:** To evaluate the etiology of hypocalcemia, a detailed history, physical exam and measurement of intact PTH, vitamin D metabolites, magnesium and phosphate levels are required. A diagnosis of PHP is suspected by the findings of an elevated serum intact PTH, hypocalcemia,
normal 25-OH- vit D and magnesium. The subtype Ib maybe considered with the involvement of parathyroid, possibly thyroid axis and lack of dysmorphic features of Albright’s osteodystrophy. The treatment includes calcitriol and calcium. The patients with hypoparathyroidism are at risk of intracerebral calcifications. Fahr’s syndrome is characterized by bihemispheric calcium deposition in basal ganglia and semiolval center. The clinical manifestations include rigidity, hypokinesis, mood disorders and subcortical dementia. Because of extensive intracranial calcification, this patient needs to be closely monitored for any incident neurological symptoms and signs and the hypocalcemia be corrected although the evidence for improvement is insufficient.

Conclusion: This case demonstrates an example of a very mild presentation of hypocalcemia and intracranial calcifications secondary to a rare condition. One should be cognizant of the spectrum of symptoms and signs associated with hypocalcemia, which may be from severe to none and clinical presentation of intracranial calcifications which may range from subclinical to extensive and debilitating. The discovery of Intracranial calcifications by imaging studies should prompt immediate measurement of serum calcium level for expedited intervention to prevent potential life-threatening complications of severe hypocalcemia and treatment of underlying conditions.

Abstract #817

PREVALENCE OF RETINOPATHY IN DIABETIC PATIENTS IN ASSOCIATION OF THEIR TREATMENT

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Objective: To determine the prevalence of retinopathy in patients with diabetes mellitus in an underdeveloped country.

Methods: Patients with type 1 and 2 diabetes mellitus (DM) were included in this study. In this cross sectional study, the results were analyzed using the $\chi^2$ (Chi-square) test with the SPSS 20.0 program ($P<0.05$).

Results: Out of 2419 patients, 1416 (58.5%) were females and 1003 (41.5%) were males. Total patients with type 1 DM were 526 with a mean age of 42.71 with SD of 13.71, but patients with type 2 DM, were 1892 with a mean age of 49.06 years and SD 9.74. Screening revealed: normal eyes finding (NEF) 51.9%, mild Non proliferative diabetic retinopathy (NPDR) 11.2%, moderate (NPDR) 5.1%, severe (NPDR) 0.8%, very severe (NPDR) 0.2%, proliferative diabetic retinopathy (PDR) 0.4%. The incidence of advanced eye disease (AED) was more common in NIDDM patients than in IDDM patients. NEF and very severe NPDR were more common in patients who had taken oral hypoglycemic drugs compared to insulin treated patients. Mild NPDR, moderate NPDR, severe NPDR, PDR, and AED were more common in patients who had taken insulin than oral hypoglycemic agents.

Discussion: In underdeveloped countries proper screening for diabetic retinopathy screening are not often performed. To our knowledge this is the first cross sectional study of DR prevalence in diabetic patients in Lahore, Pakistan.

Conclusion: Proper screening is required for diabetic retinopathy in underdeveloped countries.

Abstract #818

INSULIN USE BEYOND DIABETES

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Objective: To highlight non-diabetic uses of insulin and glucagon

Case Presentation: A 31-year-old woman was brought to the emergency department (ED) by a friend after ingesting approximately 46 tablets of metoprolol succinate 100 mg and 45 tablets of 50 mg equating to just over 6500 mg between 1:00 p.m. and 8:00 p.m. in a suicide attempt. She was also suspected of ingesting an unknown amount of atenolol. Her past medical history consisted of mitral valve prolapse, postural orthostatic tachycardia syndrome, and history of psychiatric disorders including anorexia nervosa requiring a PEG tube placement, major depression, and previous suicidal attempts. She lived alone and worked as a social worker. She smoked cigarettes, rarely imbibed alcohol, and had a remote use of marijuana in the past. Upon arrival, she was lethargic and drowsy, but able to carry on a conversation. In the ED, her vitals were stable with pulse ranging from 70 to 80s. EKG revealed normal sinus rhythm with a rate of 75 bpm and without ST-segment changes. By midnight, she became bradycardic to 60’s with blood pressure of 70/40s. She received two liters of normal saline IV at 250 ml/hr. After consulting poison control center, glucagon 1mg IV push was given followed by 5 mg/hr with titration parameters. She was admitted to the intensive care unit and placed on 1 to 1 observation. She continued to receive aggressive IV fluids, but because of limited stock of glucagon, it was discontinued after 12 hours. Insulin drip along with 10% dextrose were started at a rate of 0.5 units/kg/hr with titration to keep systolic BP >100. The rates of insulin were as high as 160 units/
hr, but this led to hypokalemia, and hypophosphatemia. She underwent hemodialysis on the 2nd hospital day. Her blood pressure and heart rate gradually improved and by the 4th hospital day, the patient had fully recovered.

**Discussion:** Apart from the realm of diabetes and diagnosis of growth hormone deficiency, insulin has been used for its multiple pleotropic effects in different medical conditions ranging from growth media for cell cultures, glucose-insulin-potassium solution in cardiology, narcoanalysis, deep insulin coma therapy, wound healing, and treatment of intoxication from calcium channel blockers and beta blockers. Our case illustrates the beneficial effects of insulin with dextrose in beta-blocker toxicity since the large amount of glucagon necessary for treatment are seldom available.

**Conclusion:** Insulin with dextrose is a readily available and cost-effective alternative to glucagon in order to protect myocardial activity in the event of beta-blocker poisoning. Close monitoring of serum potassium and phosphate is an essential component of this approach.

Abstract #819
WHERE IS THE PARATHYROID ADENOMA?
INITIAL SURGICAL APPROACH WITHOUT LOCALIZATION STUDIES FAILS TO LOCATE THE ADENOMA

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**Objective:** Although it is recommended that patients with hyperparathyroidism should undergo localization studies to determine the location of the adenoma, surgery is often performed without these studies in some centers. Hereby we report a case where initial surgical approach without localization studies failed to restore eucalcemia in a patient with hyperparathyroidism.

**Case Presentation:** A 68 year old male with a history of nephrolithiasis, headaches and recurrent persistent hypercalcemia was evaluated. Left hemithyroidectomy and parathyroidectomy were performed in 2011 without any localization studies, but despite surgery, hypercalcemia persisted. At presentation in our clinic laboratory tests showed a serum calcium of 14.2 mg/dL with an intact PTH level on 221.6 pg/mL. Twenty four hours urine calcium was elevated (436 mg/24 hrs). A parathyroid scan was revealed a focal area of increased uptake in the superior aspect of the chest (below the sternal notch approximated in the region of the manubrium of the sternum). Neck, chest and abdominal CT scans were performed and this revealed an enhancing lymph node in upper anterior mediastinum posterior to the manubrium of sternum. Given these findings, persistence of symptoms and imaging reports a decision was made to consult cardiothoracic surgery for midsternotomy and excision of an adenoma which was highly suspected to be parathyroid adenoma. A radical thymectomy and excision of a parathyroid adenoma were performed. A parathyroid adenoma 2 cm in size within the left upper pole of thymus was confirmed by histological examination. Patient tolerated the procedure well and was discharged home with a serum Ca of 8.8 mg/dL and intact PTH level of 10.0 pg/mL.

**Discussion:** At present surgical excision of the parathyroid adenoma offers the only permanent, curative treatment for primary hyperparathyroidism. Localizations studies help the surgical approach and generally used in developed countries.

**Conclusion:** Five to ten percent of patients undergoing neck surgery for hyperparathyroidism have recurrent or persistent disease. In such cases, ectopic parathyroid adenoma should be suspected in the anterosuperior mediastinum as the location of the ectopic tumor. Accurate localization studies are mandatory in patients undergoing reoperative surgery although it is also recommended prior to initial surgery.

Abstract #820
SODIUM THIOSULFATE - AN EMERGING HOPE FOR CALCIPHYLAXIS

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**Objective:** To present a case of calciphylaxis responding to sodium thiosulfate (STS).

**Case Presentation:** A 53 year old nonsmoker female presented with 2 months history of worsening painful rash. It initiated as erythematous rash involving proximal digits and later involved bilateral lower extremities and left breast with associated early necrosis. She had end stage renal disease (ESRD) secondary to type 2 diabetes mellitus and was on hemodialysis. Patient noted generalized weakness but denied fever, arthralgia, previous thrombotic events, recent travel or change of medications. Medications included insulin, atenolol, enalapril, sevelamer, nephrocaps and vitamin D2. Examination showed dry necrotic bilateral proximal second and third digits. Open ulcers with eschars were observed over legs, left lateral breast, right dorsal second toe and left buttock. Chemistry profile revealed elevated intact parathyroid hormone (PTH) (127 pg/mL) and low
Chronic Lithium use for bipolar ICU after she had a flame burn causing inhalational injury

A 56 year old female with a history of bipolar disorder, diabetes and Lithium therapy. Lithium induced NDI presenting 6 years after stopping after cessation of therapy. Here we describe a case of mechanism. Effects of Lithium can persist for many years chronic use and causes impairment of the ADH signaling (NDI). Lithium accumulates in the distal tubular cells with up to 50% of the patients resulting in nephrogenic DI disorders can cause impaired kidney concentrating ability Case Presentation: Marshall University

Yanal Masannat, MD, Omolola Olajide, MD, FACE

OF CESSATION OF LITHIUM THERAPY

A CASE OF NEPHROGENIC DI AFTER 6 YEARS OF CESSATION OF LITHIUM THERAPY

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Marshall University

Case Presentation: Chronic Lithium use for bipolar disorders can cause impaired kidney concentrating ability in up to 50% of the patients resulting in nephrogenic DI (NDI). Lithium accumulates in the distal tubular cells with chronic use and causes impairment of the ADH signaling mechanism. Effects of Lithium can persist for many years after cessation of therapy. Here we describe a case of Lithium induced NDI presenting 6 years after stopping Lithium therapy. A 56 year old female with a history of bipolar disorder, diabetes mellitus, COPD and atrial fibrillation who was admitted to the ICU after she had a flame burn causing inhalational injury for which she was placed on mechanical ventilation. She developed polyuria and a rising serum sodium seven days after admission with urine output of 6-8 liters per day and serum sodium ranging from 150-162 mEq/L. On examination, she was intubated. Her BP 146/72 mmHg, pulse 116/min, respiratory rate 31/min and temperature 99.2 F. She was started on IV D5W at 150 ml/hr initially, DDVAP 0.1 mg twice a day, HCTZ 25 mg BID and Indomethacin 50 mg BID through PEG feeding tube. However, the response was suboptimal and an endocrinology consultation was obtained when serum Na was 160 meq/L and urine output was 8100 ml in the past 24 hours prior to consultation. Review of her past history was significant for remote use of Lithium from 1977 - 2007 for treatment of bipolar disorder which was stopped in 2007 when she developed Lithium toxicity. It was thought that parenteral administration of DDVAP would be more appropriate and orally administered medications might not be completely absorbed. The patient was started on DDVAP 0.1 mcg SQ on PRN basis when polyuria of >300 ml/hr in two consecutive hours develops. Patient had a total of 6 doses of DDVAP over the course of three weeks and serum Na has improved and stabilized at 140-145 meq/L upon discharge to a long term care facility. Discussion: Our patient showed partial response to SQ DDVAP as evidenced by a declining serum Na and reduced urine output. With fluid adjustment and DDVAP on a PRN basis, a normal Na level was eventually achieved. However, it must be mentioned that maintaining fluid balance is a challenge for clinicians especially in sedated patients who cannot utilize their thirst mechanism. Appropriate and timely intervention and close follow up should be implemented in these situations. Conclusion: Patients who have been treated with Lithium should be closely monitored for development of DI especially in situations where access to water or the thirst mechanism is impaired. Physicians should be aware that Lithium effects on the kidney can persist for many years after cessation of therapy.

Abstract #822

THE ENDOCRINOPATHIES OF MALE ANOREXIA: AN UPDATE AND CASE SERIES

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Objective: Anorexia nervosa (AN) is a serious disorder with associated morbidity and mortality, most commonly diagnosed in females. Existing literature on male anorexia is sparse and a review of the endocrine effects of AN in
men has not been previously published. Our objective is to highlight the clinical characteristics of AN in males as a routinely overlooked cause of multiple endocrinopathies and systemic illness in hospitalized patients.

Methods: We present 4 cases (2 cases at The Mount Sinai Hospital, 2 cases at Long Island Jewish Medical Center) of young men with hormonal dysfunction due to underlying AN. Pertinent de-identified data was collected from a chart review of cases seen on the endocrinology consult service at both hospitals. IRB approval was not required for an observational report of the cases presented.

Case Presentation: Four young men with AN demonstrated evidence of multiple systemic complications from severe caloric and protein malnutrition. Mean age at diagnosis was 21.75 years (range 20-24 years). The most common endocrinopathies seen in this male cohort were abnormal thyroid function tests, hypogonadism, and hypercortisolemia, associated with bradycardia, gastroparesis, hypothermia, acute systolic heart failure, and erectile dysfunction. Clinical findings poorly correlated with severity of endocrine dysfunction, indicating complex and multifactorial interactions. Most of the clinical effects from these endocrinopathies resolved with improved caloric intake and nutrition.

Discussion: AN is a psychiatric disease with systemic consequences, most commonly diagnosed in females. This clinical case series highlights the association of AN in men with multiple endocrinopathies. The heterogeneous presentations and varying degrees of clinical manifestations in our cohort emphasize the challenge in diagnosis. Increased awareness of AN in male patients is important since prevalence rates are likely underestimated. Appropriate diagnosis and nutritional intervention can restore the metabolic dysfunction in a majority of cases.

Conclusion: AN is an under-appreciated disease in men and a cause of multiple endocrinopathies. A multidisciplinary approach to treatment is needed as most endocrine dysfunction can be restored with psychological and nutritional support. Further studies on males with eating disorders are needed to optimize diagnosis and treatment.

Abstract #823

CARNEY COMPLEX [CC]: UNIQUE ENDOCRINE AND NON-ENDOCRINE DIAGNOSTIC - THERAPEUTIC CHALLENGES AND BIOLOGIC MYSTERY

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Objective: To describe the clinical and therapeutic challenges observed during the management of a 9 year child with Carney Complex.

Methods: Clinical course (a) Cushing’s syndrome - ACTH independent [hypercortisolemia, elevated 24-hour urinary Cortisol, mildly enlarged adrenals on MRI; Liddle’s test - paradoxical cortisol response diagnostic of Primary Pigmented Nodular Adrenocortical Disease PPNAD; confirmed by histopathology]; (b) somatostatin receptor positive [Ga68 DOTANOC PET] recurrent osteochondromyxoma [benign locally invasive myxomatous lesion], presenting as sphenoid sinus mass (erosing the floor of sella and contiguous with pituitary); (c) incidental [no palpable nodule], somatostatin receptor positive [Ga68 DOTANOC PET] papillary carcinoma of the thyroid with nodal metastases; (d) bilateral extensive testicular microcalcification - on ultrasound. Numerous sequential surgeries the child has undergone include: (a) laparoscopic bilateral adrenalectomy; (b) total thyroidectomy with lymph node dissection, radioactive iodine ablation of residual thyroid; (c) repeated
transphenoidal resections [4 surgeries and subsequent rapid regrowth upto 8.5 cm, over a period of 3 years] of the sphenoid sinus mass [with resultant bilateral proptosis and total / near total visual loss], after which the neurosurgery team and international experts “gave up”. At this stage [apparent no role for chemotherapy or brachytherapy], after Ethics Committee approval and informed consent / assent, he underwent gamma knife radiation of the osteochondromyxoma [20 % tumor size reduction, marginal improvement of vision after 4 months].

Case Presentation: Medical therapy has included hydrocortisone, fludrocortisone and thyroxine. Follow up: 50 months. He is under surveillance for late development of other features of CC. Genetic analysis was negative for PRKAR1A mutation. Serial echocardiograms were normal, without any evidence of atrial myxomas. Exuberant keloid formation [surgical scars- neck, abdomen, thigh] was observed [described for the first time in CC], and appears to be one more manifestation of CC pathobiology. Investigations of parents and a brother were normal.

Discussion: Osteochondromyxoma of bone is very rare [4 cases; 2 recurrences - one fatal]; the present case representing the most aggressive, and the first report of gamma knife radiation therapy. Somatostatin receptor positivity [neuroendocrine tumor marker] of the osteochondromyxoma and papillary thyroid carcinoma remains enigmatic.

Conclusion: The rare and yet incompletely understood Carney’s complex continues to be a clinical and biologic challenge.

Abstract #824

PATTERN OF UNDERWEIGHT AND OVERWEIGHT IN LAGOS

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Objective: The aim of this study is to determine the pattern of underweight and overweight among Lagosians.

Methods: The sample size was 118 participants that were randomly selected in Lagos. The weight of each individual was determined with a weighting scale in kilogram. The height of each participants was also determined in metres. The body mass index was computed using the formula body mass index is equal to weight in kilogram divided by height in metres square. (BMI=weight in kilogram/height in metres square). Each individual consented to the taking of measurements from them. Demographic data were obtained excluding names.

Results: In the study population of 118 Lagosian with age range 18-88years, 3.39% (4 participants) were underweight. 25% of the underweight was male while 75% were female. One each of the underweight are in the third, fourth, fifth and sixth decade of life. None of the underweight had short or tall stature. In contrast, 39.83% (47 participants) of the study population were overweight. Of the overweight participants 34.04% (16 participants) were male while 65.96% (31 participants) were females.

Discussion: Human weight is a subject of great concern not only to individual but also to the society and the medical world. Underweight and overweight is associated with medical condition of prognostic importance. Some disease condition cut across both sides of normal weight as they are seen in both underweight and overweight subjects, some commoner in underweight some commoner in overweight while some are almost exclusively seen in underweight individuals. The normal human weight is body mass index of 18.5kg/m2 - 24.9kg/m2. Underweight is body mass index less than 18.5kg/m2 while overweight is body mass index between 25-29.9kg/m2. While some apparently well individuals may appear underweight, it is also observed that some obsessed, overweight or normal subjects may become underweight by virtue of pathologic condition.

Conclusion: Overweight is commoner among Lagosian than underweight.

Abstract #825

SEVERE LIFE-THREATENING HYPERCALCEMIA POST THYROIDECTOMY IN A PATIENT TREATED WITH CALCITRIOL AND CALCIUM CARBONATE

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Objective: We describe a patient presenting four days post thyroidectomy with severe hypercalcemia resulting in pancreatitis and long term pancreatic dysfunction.

Case Presentation: A 33 year-old female, with nontoxic multi-nodular goiter underwent total thyroidectomy due to swallowing discomfort and cosmetic defect. Thyroid pathology result was benign. Baseline calcium was 10.2 mg/dl (n 8.6-10.3). She is diabetic on three oral medications with good control. Her surgery was uneventful and her parathyroid glands were preserved. Post-operatively her PTH level was suppressed to < 4 pg/ml (nl 12-88), and the
ionized calcium level was low, 1.11 mmol/l (n 1.14-1.33). She was started on calcitriol 0.5 mcg and calcium carbonate (CaCO3) 2500 mg in liquid form, both twice daily. She was discharged home to taper her calcium supplement and calcitriol after five days. She returned to the hospital four days post-op with abdominal pain. Laboratory work up revealed triglyceride level 163 mg/dl, amylase 631 U/l (n 28-100), lipase 1293 IU/l (n 8-57), calcium 18.7 mg/dl, ionized calcium greater than 1.91 mmol/l, phosphorus 3.9 mg/dl (n 2.4-4.7), PTH 4 pg/ml, 25-OH Vitamin D level 22.2 ng/mL, WBC 11,500/mcl, neutrophils 77 %, liver enzymes and bilirubin were normal. CAT scan and ultrasound of abdomen showed ascites and pancreatitis without cholecystitis. Her condition deteriorated rapidly requiring intubation and mechanical ventilation. Her calcium and calcitriol were stopped. She was given calcitonin and IV hydration which normalized her calcium level. She developed loose stools and worsening of diabetes. She was discharged home ten days later on insulin in addition to her oral diabetes medications. Follow up after discharge showed an increase in HgA1C from 6% to 9.3% in 12 weeks and worsening diarrhea. Subsequently, she was diagnosed with pancreatic insufficiency and required pancreatic enzymes. Her diabetes improved with higher doses of insulin. Her calcium remained normal.

Discussion: Calcitriol and CaCO3 are generally acceptable post thyroidectomy with an incidence of hypercalcemia up to 4.5 %. The absorption and bioavailability of CaCO3 were shown to be higher in tablets that dissolve faster. Liquid CaCO3 probably would have an even higher absorption rate than tablets. The dose of CaCO3 used in most literature is two to three grams daily and using five grams in our patient may have contributed to hypercalcemia. Severe hypercalcemia is a known cause of pancreatitis.

Conclusion: The liquid CaCO3 in conjunction with calcitriol intake may exaggerate calcium absorption and precipitate hypercalcemia which can be life threatening and results in long-term pancreatic dysfunction.

Abstract #826

THYMIC AND BRONCOPULMONARY CARCINOID TUMORS IN PATIENTS WITH MULTIPLE ENDOCRINE NEOPLASIA TYPE 1: THE MAYO CLINIC EXPERIENCE FROM 1977-2013

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Objective: Describe the clinical presentation of thymic carcinoid (TC) and bronchial carcinoid (BC) tumors in patients with multiple endocrine neoplasia type 1 (MEN1).

Methods: We performed an electronic search of the medical records to identify patients with a billing code for MEN1 who were seen in the Mayo Clinic from 1977 to 2013. This initial group of records was reviewed and MEN1 was diagnosed based on current clinical guidelines criteria.

Results: A total of 348 patients fulfilled the diagnostic criteria for MEN1. The mean age at diagnosis was 37.2 years, the majority of the patients were women (56%) and the average duration of follow up was 7.6 years. The prevalence of BC was 4.9% (n=17) and 2.0% for TC (n=7).

The mean age at diagnosis of BC was 45.1 years, the majority of the patients were men (61%), and 5 were smokers (39%). The majority of the patients (77%) were diagnosed on routine screening. Three patients died during follow up (23%), but BC was not the confirmed cause of death. None of the patients had distant metastasis at diagnosis or follow up. Residual disease was present in 1 patient and 4 patients (31%) developed local recurrence with only one requiring further intervention.

All 7 patients with TC were men, 4 (57%) were symptomatic at diagnosis and three were smokers (43%). The mean age at diagnosis was 43 years. At the time of diagnosis none of the patients had distant metastasis but three were found to have advanced local disease. Of the four patients with negative surgical margins 3 were found to have recurrence. Three of the patients died (43%) from TC complications.

Discussion: We report the clinical features of TC and BC in 20 of our 348 patients with MEN1 over 36 years at Mayo Clinic. The prevalence of BC was 4.9% and 2.0% for TC, which is similar to previously reported series of BC (5%) and TC (2.6-8%) in MEN1. BC has been reported as having a female predominance; however, the majority of our patients were men. Our results are consistent with previous reports in which the majority of the patients were diagnosed by routine screening and did not develop metastatic disease. TC has been previously reported to have a male predominance in most of the Western case series and are usually symptomatic at diagnosis, characteristics which are compatible with our findings. Only 1 of our patients was free of recurrence during follow up and three patients (43%) died due to TC, compatible with previous reports of aggressive behavior.

Conclusion: TC and BC tumors are an uncommon, but important component of MEN1. BC were most commonly diagnosed during routine screening and associated with an indolent course. TC were predominantly seen in men and associated with a more aggressive behavior.
Abstract #827

FOUR YEARS OF GROWTH HORMONE THERAPY IN TURNER SYNDROME

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Objective: Turner syndrome (TS) is one of the most common causes of short stature in females; several distinct phases of growth have been identified in girls with TS: -mild intrauterine growth retardation -slow growth during early infancy -delayed onset of the “childhood phase” of growth and -a prolonged adolescent growth phase. Adult height of patients with TS is 20 cm shorter than in general population. The cause of growth failure in TS remains unclear. Growth hormone (GH) therapy improves height outcome in girls with TS; results depend on age at diagnosis, duration of therapy and doses of GH. The aim of our study was to evaluate growth and safety during the first 4 years of GH treatment in patients with TS.

Methods: Turner syndrome (TS) is one of the most common causes of short stature in females; several distinct phases of growth have been identified in girls with TS: -mild intrauterine growth retardation -slow growth during early infancy -delayed onset of the “childhood phase” of growth and -a prolonged adolescent growth phase. Adult height of patients with TS is 20 cm shorter than in general population. The cause of growth failure in TS remains unclear. Growth hormone (GH) therapy improves height outcome in girls with TS; results depend on age at diagnosis, duration of therapy and doses of GH. The aim of our study was to evaluate growth and safety during the first 4 years of GH treatment in patients with TS.

Results: The mean height SDS score increased from -3.61 at baseline to -1.37 at 4ys. Main gain over 4ys was 23.55cm. The mean weight SDS score increased from -1.28 at baseline to -0.68 at 4 ys. Bone age was delayed at diagnosis by a mean value of 1.17ys and after 4ys the delay decreased to 0.22ys. Safety profile: There were no cases of diabetes mellitus, impaired glucose tolerance or malignancies; four patients had transient increase in fasting glucose(>100<126mg/dl); two patients developed hyperthyroidism and were treated with L-thyroxin.

Discussion: In TS ,GH and IGF levels are normal during childhood and growth impairment is clinically evident before the period when the activity of GH-IGF axis is decreased. GH therapy is capable to accelerate growth and to increase adult height. Delayed diagnosis of TS has a negative impact on growth outcomes.

Conclusion: GH treatment was associated with highly significant changes in growth at girls with TS. In our study height velocity was maximum (8.53cm/yr) in the first year of GH treatment; the improvements in growth declined in the second (6.85cm/yr), third (4.11cm/yr) and fourth year (4.05cm/yr). GH therapy had a favorable safety profile.

Abstract #828

A CASE OF SEVERE SYMPTOMATIC HYPOCALCEMIA FROM HIV RELATED HYPOPARATHYROIDISM

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Objective: To report a rare case of severe resistant symptomatic hypocalcemia from primary hypoparathyroidism attributed to HIV infection.

Case Presentation: A 54-year-old Caucasian lady presented to our clinic with a 2-year history of persistent hypocalcemia requiring multiple hospitalizations. Her symptoms were muscle cramps, tingling and perioral parasthesias. Her medical history is significant for HIV diagnosed 2 years ago, gastric bypass surgery done 15 years ago, HTN and COPD. She denied any history of prior neck surgery or radiation. There is no family history of autoimmune disease. Her vital signs were stable with an unremarkable physical exam. Pertinent medications included calcium carbonate, vitamin D3, calcitriol, Atripla (Efavirenz/ emtricitabine/ tenofovir disoproxil), HCTZ and inhaled budesonide/formoterol. Laboratory testing showed total calcium of 5.7 mg/dl [8.4-10.2], serum albumin 3.9 mg/dl, ionized calcium 2.7 mg/dl [4.5-5.5], serum magnesium 1.7 mg/dl [1.7-2.7], serum phosphate 6.3 mg/dl [2.7-4.5mg/dl] and intact PTH 7.6 pg/ml [15-65 pg/ml]. She had normal 25 (OH) vitamin D, 1,25 dihydroxy, vitamin D and renal function tests. She was diagnosed with primary hypoparathyroidism attributed to HIV infection.

Symptomatic hypocalcemia from primary hypoparathyroidism. Anti calcium sensor receptor antibody (CaSR) and NALP 5 antibodies were tested and found to be negative. During subsequent clinic visits, doses of calcium supplements and calcitriol were titrated and she was started on magnesium oxide. Despite of above, she continues to require calcium carbonate 2500 mg TID, calcium citrate 1900 mg BID and calcitriol 0.5 mcg TID. Last corrected serum calcium level is 9.18 mg/dl. She is being considered for teriparatide therapy.

Discussion: Hypocalcaemia is an infrequent phenomenon in HIV infection, mostly attributed to Vitamin D deficiency, hypoalbuminemia or pharmacotherapy. Hypocalcaemia has been well described in patients following gastric bypass surgery; however, it is associated with secondary hyperparathyroidism. Tenofovir can rarely cause
hypocalcemia as part of Fanconi’s syndrome, along with hypophosphatemia and normal or slightly elevated PTH levels. Our patient has hypocalcemia with low PTH levels, consistent with primary hypoparathyroidism. With the absence of neck surgery, and an unlikely autoimmune etiology (negative antibody testing, late onset, absence of family history and associated conditions), HIV infection is considered as the principal etiology. This has been rarely reported in literature. Mechanisms explaining hypoparathyroidism in HIV infected patients are not well described.

Conclusion: Intact PTH levels should be measured in HIV infected patients presenting with hypocalcemia. HIV infection has been reported to be associated with primary hypoparathyroidism.

Abstract #829

RARE THYROID TUMOR IN AN ELDERLY FEMALE

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Objective: Review the differential diagnosis of thyroid paraganglioma

Case Presentation: 69 year old female with a past medical history of a cervical cancer and benign goiter 44 years ago, for which she received radiation plus hysterectomy and left partial thyroidectomy respectively. One year ago, patient presented with weight loss, anemia and syncope. A colonoscopy found a poorly differentiated mucinous colonic carcinoma. PET/CT Scan revealed 4.2cm left adrenal lesion. The core needle biopsy showed crowded cells with hyperchromatic nuclei with cells in a more fibrous-appearing background and it was positive for synaptophysin and negative for cytokeratin and TTF-1. The biopsy of the thyroid gland revealed a neuroendocrine tumor consisting of tumor cells with predominantly isolated single nuclei. The immunochemistry showed synaptophysin in most tumor cells and chromogranin was weakly to moderately positive. The tumor did not stain for epithelial markers. A rare cohesive group of cells of less than 1% exhibited expression of keratins and cytokeratin AE1-AE3, CAM 5.2 and CK7. Staining demonstrate a rare group of cells that stain positive for TTF-1. CDX-2 was negative. LCA, CD3 and CD20 all were negative. Physical examination was positive for right thyroid lobe enlarged at 2-3cm.

Discussion: This tumor is usually difficult to diagnose because it is rare and potentially malignant. This tumor is rarely functional, like in this case that found incidentally. In the differential there are 2 other tumors: medullary carcinoma of thyroid and hyalinizing trabecular adenoma of the thyroid. Morphologically these tumors are similar, so immunochemistry is very important to differentiate them. It is important to distinguish between them because of the prognosis and management. Thyroid paragangliomas are keratin, cytokeratin markers negative. The string stain for synaptophysin marker is another characteristic of thyroid paragangliomas. MCT stains positive for TTF-1, compared to thyroid arangliomas that are negative for this marker. The absences of CD markers in this particular case were helpful to rule out lymphomas. The treatment is surgery. Radiation is indicated only if surgery is not feasible.

Conclusion: Thyroid paraganglioma is a rare entity that should be consider in the differential of neck masses.

Abstract #830

RAISED HS CRP IN 1ST TRIMESTER MAY NOT PREDICT GDM

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Objective: It is estimated that 10% of women who get pregnant every year in India develop GDM, usually in the last trimester. It is recommended that a pregnant woman should undergo a test at the 12th week to diagnose early gestational diabetes as Indians belong to high ethnic group for developing GDM. So there is a need for identifying some marker of inflammation to predict GDM. To determine if raised hsCRP in 1st trimester has any predictive value for diagnosing GDM.

Methods: This is a prospective, unicentric, non interventional longitudinal study. During the study period, 200 pregnant women reporting for antenatal care before 16 weeks of pregnancy for the first time were tested for presence of hs-CRP in blood in addition to the standard antenatal tests to predict GDM subsequently. These women were followed up in the antenatal clinic and underwent oral glucose challenge test (OGCT) with 50 g of glucose between 24 and 28 weeks of gestation, and the standard 3 hour oral glucose tolerance test (OGTT) was done if the value of plasma glucose in OGCT exceeded 140 mg%. GDM was diagnosed as per the modified criteria of Carpenter and Coustan. In females diagnosed having GDM, HbA1c values were also done. Reference values for hs CRP were Low risk< 1.0 mg/dl High risk > 2.0 mg/dl.

Results: The hs-CRP was abnormal in 88 cases. These 88 cases were followed up in the antenatal clinic and OGCT was done at 24-28 weeks. The OGCT was found abnormal in 47 cases. These abnormal OGCT cases underwent OGTT Test during 24-28 weeks. 16 out of these 47 cases were diagnosed having GDM (18.8%). All these 16 GDM cases (abnormal OGTT) underwent HbA1c test & it was found to be more than 6.5%.
Abstract #831

BRIDGING THE GAP - ENHANCING HEALTH CARE PROVIDERS’ KNOWLEDGE AROUND ENDOCRINE AND FERTILITY ISSUES IN SURVIVORS OF CHILDHOOD CANCER

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Objective: Endocrine late effects are the most common long-term sequelae in pediatric and adult survivors of childhood cancer. Previous studies have shown that health care providers lack sufficient awareness of late effects of cancer therapy. We developed a continuing education program to enhance providers’ knowledge, comfort and performance in caring for childhood cancer survivors. Here we present the impact of our regional conference on participants’ knowledge of endocrine late effects.

Methods: Evidence based curriculum for the one-day conference was designed to stimulate interest and provide salient information on essential areas of survivorship care. Participants completed a 20-point pre- and post-test questionnaire at the beginning and end of the conference respectively to assess their knowledge and understanding. Six of the 20 questions (30%) were based on endocrinopathies. The responses to questions were anonymous and analyzed using SAS statistical software.

Results: There were 35 participants (13 MDs, 12 RN/APN, 2 SW, 8 other), the majority practicing clinical oncology. Thirty one pre-test and 29 post-test questionnaires were completed. Out of the 6 questions focused on endocrinology, only 2 in the pre-test, and 4 in the post-test were answered correctly by > 50% of the respondents. When asked which pituitary hormone is most radiosensitive, only 58% correctly recognized it to be growth hormone in the pre-test; however the response improved to 93% in the post-test (p=0.0017). On the other hand, 94% of the pre-test and 100% of the post-test responses were correct for the potential long-term effects of radiation on the thyroid gland. Chemotherapy agents causing hypogonadism were identified poorly in both pre (35%) and post tests (38%). Participants’ awareness on the incidence of premature ovarian failure after stem cell transplant improved from 13% to 69% (p<0.001). Most participants underestimated (5-25% vs. 50%) how often oncologists referred women for fertility preservation before cancer therapy. Awareness on experimental procedures for female fertility preservation, although improved was still limited to 59% of post-test respondents.

Discussion: Health care providers lack knowledge in several areas related to endocrine and fertility issues in cancer survivors. This knowledge gap was only partially filled by participation in a one-day conference. Our next steps include the use of webinars and practice improvement initiatives with the goal of reaching more providers regardless of their geographic location.

Conclusion: Continuing educational programs will help elevate providers’ knowledge and therefore will likely improve their comfort and performance in caring for childhood cancer survivors.

Abstract #832

METABOLIC PROFILE POLYCYSTIC OVARY SYNDROME (PCOS) IN MAPUCHE ETHNICITY PATIENTS AND CHILEAN GENERAL POPULATION

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Objective: To compare the metabolic profile of PCOS in clinical Mapuche ethnicity and one general population case-control study was conducted.

Methods: We included patients between 18-42 years old, with PCOS Rotterdam criterion. In 181 patients Mapuche ethnicity (PM) and control group (CG) was divided. Insulin resistance (IR) was assessed using HOMA (nv 0.35 and 4.5 ulu/mL). The thyroid status as TSH values (vn: 0.35 and 4.5 ulu/mL). The analysis was performed using Stata 11.1 with Chi 2, T Student, ANOVA and stratified analysis.
**Results:** Evaluated 181 patients 20.9 % (n = 38 ) PM, this average age was 26.4 ± 6 years, menarche 12.5 ± 1.5 years, compared to 28 and 12.5 years respectively for CG . In Mapuche: mean BMI was 32.7 ± 6.4, 20 and 65 % were overweight and obese respectively, in the CG average BMI 31.9 ± 6.4, 30.5 % overweight and 57 % obese (p 0.1). When comparing the groups according to age and BMI by linear regression p value was 0.01, between > and < 27 years: OR 2.37 (CI 1.16 - 4.8) p 0.009 for obesity. Average insulin level was 5.8 ± 4.2 MP and CG 4.5 ± 2.8 (p 0.1). HOMA in the CG presented 89.5% IR, versus 80% in MP (p 0.1). Both groups showed significant association with obesity comparing IR, OR 2.8 (CI 0.93 - 8.4) p 0.05. Average glycemia for PM was 103.3 ± 6.9 mg/dl and 97.2 ± 1.9 mg/dl in CG (p 0.2). Average values total cholesterol, LDL and HDL for MP were 189.2, 110.2, and 41.4 respectively, being lower than CG (194.7, 116.2 and 46%) with p = 0.1. Triglycerides were higher in MP 176 v/s 162 (p = 0.4). The association between obesity and dyslipidemia was being significant for low levels of HDL, OR 2.64 (CI 1.01 - 8.4) p 0.02. Dyslipidemia by age, both groups showed an association between low HDL, OR 2.5 (CI 1.05 - 6.3) p 0.02 and high triglycerides, OR 2.01 (CI 1.01 -4.4) p 0.05. Prevalence of subclinical hypothyroidism (SCH) was 9% in both groups.

**Discussion:** The MP had a higher percentage of obesity and lower levels of total cholesterol, LDL, HDL and triglycerides higher (not significant). However, both groups showed > RI risk (OR 2.8) and low HDL (OR 2.6) in obese. The older increased risk of low HDL (OR 2.5) and high triglycerides (OR 2.01) was observed. Stratified analysis showed significant association between low levels of HDL and obesity independent of age (OR 2.65).

**Conclusion:** Mapuche ethnicity was 20.9%, less than 31% of the ethnic group in the region. This study found no statistically significant differences in clinical and metabolic variables by race.

**Abstract #833**

PREVALENCE OF 25 HYDROXYVITAMIN D SUFFICIENCY IN HEALTHY SUBJECTS IN COSTA RICA

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**Objective:** The aim of the study was to determine the concentration of 25 hydroxyvitamin D (25-OH D) and examine the level of sun exposure and dietary vitamin D intake were estimated using a questionnaire. Fifty four females aged 35.8 ± 10.2 years; body mass index (BMI) (kg/m2) 27.1 ± 5.9, waist circumference 90.0 ± 14.1 cm and 26 males aged 36.2 ± 10.6 years, BMI 27.5 ± 5.0, waist circumference 86.6 ± 8.5 were included. All of the subjects were normocalcemic, three were hypertensive; none had renal insufficiency and neither history of thyroid dysfunction or gastrointestinal disease. Two subjects used to take vitamin D and calcium supplements.

**Results:** In the whole group, 25-OH D concentrations were 24.0 ± 7.0 ng/dl; in females 22.7 ± 6.4 ng/dl and in males 26.6 ± 7.7 ng/dl, p = 0.02. Vitamin D deficiency was seen in 28 % of the females and in 38 % of the males and insufficiency in 57 % and 38 % of females and males, respectively. PTH concentrations were 39.8 ± 17.5 pg/dl; in the nine subjects with high PTH concentrations, the 25-OH D was below 30 ng/dl. No association was found between 25 OH D and anthropometric measurements. Fifteen individuals drank at least one glass of milk daily corresponding to a 25% of vitamin D recommended daily allowances and, low sunlight exposure was documented in 52 % of the study subjects.

**Discussion:** In this healthy free-living population, the prevalence of 25-OH D sufficiency was 18 %. This was an unexpected finding considering the fact that the study population lives in a sun-replete latitude. Changes in lifestyle, long working indoor hours and the widespread use of sunscreens may explain our results. Intake of dietary sources of vitamin does not seem to influence 25-OH D levels. Furthermore, it is not known whether the secondary hyperparathyroidism associated with low 25-OH D, seen in a 10 % of this young population, would have an impact on bone health in the long term.

**Conclusion:** A larger study is needed to confirm these findings. However, it would be recommended to take public health actions such as education programs related to healthy sunlight exposure or vitamin D supplementation, specially in high risk populations like urban and indoor workers.
Abstract #834

VARIATION OF QUANTITY OF FOOD CONSUMED DURING RAMADAN (FASTING) AND NON-FASTING DAYS IN SRI LANKAN MUSLIMS

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Objective: Fasting during the month of Ramadan is a religious obligation and belief for healthy Muslims. The aim of the present study was to quantify the food consumption during a full week of fasting (Ramadan) and to compare the quantity of food consumed during a non-fasting week in three divisional secretariat areas of Kandy and Matale districts of Sri Lanka.

Methods: This study was done during 2nd to 8th of July 2013 and 1st week of September 2013 in Warakamura area in Matale district and Akurana and Inigala areas in Kandy district of Sri Lanka. Non-probability convenient sampling technique was used and a questionnaire was used to collect data from ninety (90) families. The selected households were visited by the second author and asked to keep a record of food items used for a week, during Ramadan and non-Ramadan period. The investigator visited the house by end of the week and filled the questionnaire, interviewing the chief occupant of the house and by going through the records. Analysis was done on MS Excel and SPSS version 16. Independent paired t-test was used to assess associations and P<0.05 was considered statistically significant.

Results: The following food items were consumed significantly higher during Ramadan than during non-Ramadan period (P ≤ 0.05): Cooking oil (in Kg) 1.01±0.65 Vs 0.52±0.25, curd (in measures of 500g) 2.07±1.55 Vs 0.19±0.45, sugar (Kg) 3.57±1.24 Vs 2.06±0.98, potatoes (Kg) 1.12±0.92 Vs 0.55±0.37, chicken (Kg) 1.46±0.84 Vs 0.98±0.59, beef (Kg) 1.28±0.65 Vs 0.96±0.53 and onion (Kg) 2.97±3.02 Vs 1.22±0.62. The following food items were consumed less during the Ramadan than during non-Ramadan periods, which were statistically significant (P<0.05): Rice (Kg) 3.22±1.73 Vs 4.44±2.14, wheat flour (Kg) 2.13±1.35 Vs 2.83±2.09, coconut (in numbers) 4.21±3.49 Vs 5.03±2.48, milk powder 0.67±0.43 Vs 0.82±0.31, green vegetables (Kg) 1.94±0.88 Vs 3.77±7.9, dhal (Kg) 0.29±0.29 Vs 0.45±0.36, , masala powder (Kg) 0.22±0.23 Vs 0.16±0.12, chili powder (Kg) 0.1±0.06 Vs 0.13±0.1, fresh fish (Kg) 0.44±0.47 Vs 0.69±0.48, dry fish (Kg) 0.01±0.03 Vs 0.15±0.15.

Discussion: Muslim devotees are expected to eat less and healthy during the month of Ramadan. However, our study shows that there is a significant increase in consumption of unhealthy food items such as oil, curd, sugar, meat items and during Ramadan compared to non-Ramadan period. Most of the healthy food items such as vegetables and fish were eaten less during Ramadan.

Conclusion: This seems contradictory to teachings of Islam. Health education programs may be helpful in changing this pattern.

Abstract #835

MADELUNG’S DISEASE - AN UNUSUAL CASE OF A RARE DISEASE

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Objective: To report a rare and unusual case of a Cambodian female with Type 1 Madelung’s disease.

Case Presentation: A 31-year-old Cambodian female was referred for evaluation for possible Cushing’s syndrome. She presented with symmetrical weight gain around the neck, upper body, and arms over a 3-year period. The patient’s social history includes five years of alcohol consumption, two years of 1 L of hard alcohol daily followed by three years of 72-oz of beer daily. Neck/chest CT revealed prominent subcutaneous adipose tissue in the posterior portion of the neck extending to the upper back and arms with normal muscle appearance of the shoulder girdle and latissimus dorsi region. Laboratory studies revealed total cholesterol of 221mg/dL, HDL of 58 mg/dL, triglycerides of 407 mg/dL, fasting glucose of 101 mg/dL, Hemoglobin A1C of 5.1% and a TSH of 2.212 mU/L. Testing for Cushing’s included mildly elevated AM cortisol x 2, but normal diurnal variation of cortisol and midnight salivary cortisol of 0.05 nmol/l.

Discussion: The patient’s clinical presentation is consistent with Madelung’s disease (benign symmetric lipomatosis). Madelung’s disease is a rare metabolic condition characterized by massive diffuse accumulations of benign adipose tissue distributed in a symmetrical pattern. The male to female occurrence ratio is 30:1, and most frequently manifests during midlife. Madelung’s disease is classified as Type 1 (“Madelung’s collar”), and Type 2. Type 1 primarily affects men, especially of Mediterranean Caucasian decent, and presents with lipomas around the neck, shoulders, and arms that may extend to the mediastinum and potentially obstruct the
trachea and vena cava. In contrast, Type 2 is usually exhibited in females presenting with a “stereotypical obese” profile with lipomas extending around the hips and thighs with the absence of tracheal and vena cava compression. More than 90% of patients with Madelung’s disease have been linked to chronic alcohol consumption, however the mechanism is poorly understood and abstinence from alcohol does not reverse the disease. This patient’s history, physical examination, and radiological imaging are consistent with Type 1 Madelung’s disease.

**Conclusion:** Madelung’s disease is an unusual condition that is rare among females, especially in those with Type 1 disease. Madelung’s disease should be considered in patients with abnormal fat distribution and heavy alcohol consumption. In Type 1, important characteristics leading to diagnosis are symmetry, diffuse deposition of adipose tissue, and excessive adipose tissue with markedly thin musculature. The forearms and legs are often spared from lipomas.

**Abstract #836**

**ASYMPTOMATIC SEVERE HYponATREMIA**

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**Objective:** To present a relatively asymptomatic man with serum sodium of 98 meq/L.

**Case Presentation:** A 42-year-old male with cirrhosis of liver due to alcoholism presented to emergency department with shortness of breath and fatigue. Over the past couple of months he noted progressive abdominal distension, pedal edema, loss of appetite and intermittent nausea and diarrhea. His only oral intake had been at least a case of beer per day and water. Physical examination revealed a moderately built, malnourished male who was alert awake and oriented x 3. Vital Signs were: temperature 97.9 o F, blood pressure 146/87 mm Hg; pulse 128 per minute and respirations 26/minute, 100% saturation on 3 liters of nasal cannula. His mucosa was dry. Lung and heart exam was normal. Ascites was present with no abdominal tenderness. Spider angiomata and abdominal wall collateral vessels were noted. Pedal edema was present. Labs showed a serum sodium of 98meq/L (which was reconfirmed), Creatinine 0.7mg/dL, albumin 2.8g/dL, Total Protein 7.3g/dL, glucose 136 mg/dL, Total cholesterol 96mg/dL, Triglycerides 77 mg/dL, serum alcohol level 50mg/dL, serum osmolality 220mOsm/kg, urine osmolality 456 mOsm/kg, random urine sodium < 5mmol/L and fractional excretion of sodium was 0.16%. Thyroid and cortisol studies were normal.

Treatment for hyponatremia was initiated with intravenous infusion of 0.9% normal saline at a rate of 85 ml/hr. The serum sodium improved gradually to 109 meq/L in 48 hours. He had some symptoms of agitation attributable to alcohol withdrawal which were stabilized with sedation but had no neurological sequelae from hyponatremia. 4 days since admission his sodium was 115 meq/L but was noted to have a decline in urine output. He was then started on a regimen of albumin infusion and subsequently intravenous bumetanide was added for diuresis. His serum sodium continued to improve gradually and by the time of discharge (after 12 days); his serum sodium was 135 meq/L.

**Discussion:** This was a unique case of severe hyponatremia with relatively modest to no symptoms. The hyponatremia in our patient was of multifactorial etiology. His effective arterial blood volume was depleted (despite clinical signs of hypervolemia) superimposed on his underlying beer potomania, malnourishment and lack of dietary solute intake.

**Conclusion:** This is one of the lowest serum sodium levels ever reported, especially in a patient who was alert, awake and oriented x3 and had minimal symptoms of hyponatremia. His 10 day road to recovery was uneventful without neurological sequelae.

**Abstract #837**

**ENDOCRINE ABNORMALITIES IN A YOUNG PATIENT WITH WILSON DISEASE**

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**Objective:** Wilson disease is an autosomal recessive inherited genetic disease that leads to impairment of cellular copper transport. Endocrine abnormalities, including amenorrhea, infertility and hypoparathyroidism were reported. The aim is to present a case of Wilson disease with both ovarian and bone involvement.

**Methods:** Pituitary MRI and pelvic ultrasound were performed. Bone mineral density was assessed by lumbar spine DXA.

**Case Presentation:** C.C. 28 years old woman, diagnosed with Wilson disease and cirrhosis, presented for secondary amenorrhea. The patient denied significant headaches, narrowing of visual field, galactorrhoea, acne, hirsutism. Endocrine examination was normal. Biochemical data revealed hypergonadotropic hypogonadism (serum estradiol < 20 pg/ml, FSH= 12.1 IU/L, LH= 16 IU/L), normal prolactinemia (5.46 ng/mL), normal androgen levels (total testosterone= 0.42 ng/mL, DHEAs= 141.3 μg/dL, 17 hydroxy progesterone= 1.08 ng/mL). Pituitary function and pituitary MRI were also normal. Normal
antimullerian hormone values were noticed (AMH=10.89 ng/mL). The patient also showed low mineral density for age (BMD= 0.831 g/cm2, T score= - 2.9 SD, Z score= - 2.9 SD). Hypoparathyroidism was ruled out by normal serum levels of calcium (10 mg/dL) and PTH (44.62 pg/mL); mild vitamin D insufficiency was noticed (25 hydroxi vitamin D= 27.3 ng/mL). D-penicillamine treatment (1.25 g/day) was administered. A wait-and-see policy was adopted for secondary amenorrhea. We aim to reassess the patient if menstruation does not appear after serum ceruloplasmin normalization.

Discussion: In patients with Wilson disease, amenorrhea is often reported, but its mechanisms are incompletely elucidated. An interference of ovarian follicular aromatase activity possibly due to copper intoxication could explain ovarian disturbances. Risks for low bone mineral density in our patient with cirrhosis include hypogonadism and vitamin D insufficiency. Wilson’s disease is also known to cause bone loss independent of liver dysfunction.

Conclusion: Regular endocrine assessment is necessary in patients with Wilson disease.

Abstract #838

NOT ALL HYPONATREMIA IS SIADH: SEVERE POLYURIA IN A PATIENT WITH CEREBRAL SALT WASTING SYNDROME

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Objective: Electrolyte abnormalities, especially hyponatremia, are very common in patients with brain injury. The most common cause of hyponatremia in this population is syndrome of inappropriate antidiuretic hormone secretion(SIADH); however it is important to recognize less common causes of hyponatremia, such as cerebral salt wasting syndrome (CSW) as it has important clinical implications. We present a case of hyponatremia and severe polyuria in a patient with a subarachnoid hemorrhage (SAH) and highlight the diagnostic challenges in differentiating between SIADH, central DI and CSW.

Case Presentation: Pt is a 27 year old female with past medical history of hypothyroidism, who was admitted for severe headache. She was found to have a SAH on CT scan and underwent aneurysmal coiling. On post-op day 3, she was noted to have polyuria(>8 L/day) with a serum sodium of 123 mmol/L, low urine specific gravity and a normal kidney function. She was thought to have central DI and started on desmopressin as well as sodium chloride tablets. Polyuria persisted with urine output as high as 36 L/day while receiving fluid replacement with normal saline. On post-op day 6, the hyponatremia was corrected but the polyuria continued. An endocrine consult was requested and IV hydration, salt tablets and desmopressin were subsequently held. Patient was noted to be clinically volume depleted and had increased thirst. Her urine output was greater than 200cc/hr for more than two hours and laboratory testing revealed urine osmolality of 509 mmol/kg, urine sodium of 224, serum sodium of 134 mmol/L, serum osmolality of 270 mmol/kg and uric acid level of 0.8 mg/dL. These values are consistent with CSW. Patient was started on mineralocorticoid supplementation and intravenous fluid replacement with normal saline. Over the course of 10 days, she reached and maintained euvoicmic state with normal serum sodium on salt tablets, oral hydration and fludrocortisone. CSW resolved in two weeks and all therapy was discontinued.

Discussion: This patient with CSW had an unusual presentation of significant polyuria and hyponatremia which was initially treated as central DI. This case emphasizes the importance of determining the etiology of hyponatremia prior to initiating treatment of electrolyte abnormalities in patients with brain injury. A key distinguishing factor between CSW and SIADH is the patient’s fluid volume status.

Conclusion: The combination of physical examination findings together with the biochemical profile prior to initiation of therapy is crucial for appropriate and timely management. Treatment includes fluid restriction, salt tablets and vasopressin receptor antagonist in SIADH versus fluid replacement and mineralocorticoid in CSW.

Abstract #839

PRIMARY HYPERPARATHYROIDISM DURING PREGNANCY- WORK UP AND MANAGEMENT: A CASE REPORT

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Objective: Primary hyperparathyroidism is more common in older age groups but 5-10% cases are diagnosed during childbearing age. We are presenting a case of primary hyperparathyroidism work up and treatment during pregnancy.

Case Presentation: 18 year old female G2P0A1 @ 23w presented with recurrent pyelonephritis, kidney stones and hypercalcemia. She had pyelonephritis and obstructing renal stones few months ago requiring right ureteral stent, followed by right nephrostomy tube due to obstructed stent and pyelonephritis. Patient had a first trimester miscarriage during the first episode of pyelonephritis and was advised
further workup of hypercalcemia. Workup during this admission revealed high-ionized calcium (6.70 mg/dl), low phosphorus (1.9 mg/dl), inappropriately high PTH (204.6 pg/ml), low albumin (2 g/dl), high 24-hour urine calcium (705 mg/24h), low vit D level (19 ng/ml), normal 1,25 vit D and normal PTHrp, suggestive of primary hyperparathyroidism. Head & neck Ultrasound did not visualize parathyroid glands. After discussion between MFM, ENT and nuclear medicine, Sestamibi scan was obtained with 10 mCi of Tc-99m(half of usual dose). It showed parathyroid adenoma in the upper mediastinum and MRI chest without contrast confirmed the finding. Since admission she was treated with intravenous fluids, Lasix and Cinacalcet, with no improvement in calcium. After explaining risks and benefits she underwent mediastinoscopy and removal of mediastinal parathyroid adenoma by CT surgery. Post operative course was uneventful and ionized calcium normalized to 4.80 post operatively.

**Discussion:** Diagnosis of primary hyperparathyroidism is important during pregnancy as hemo dilution, hypo albuminemia, increased urinary calcium excretion, high fetal calcium requirements can mask primary hyperparathyroidism, when suspicious, check corrected or ionized calcium. If untreated it is associated with both maternal and fetal complications. Norman et al described 15 of 77 patients who underwent Para thyroidectomy during second trimester had a good outcome and the rest of the pregnancies had a higher than expected miscarriage rate during late first trimester or early second trimester. Fetal loss was seen at all levels of elevated maternal calcium but most were above 11.4 mg/dl. Review of limited available literature revealed unsuccessful exploratory surgery eventually requiring Tc-99 m localization. In our patient with Sestamibi scan we were able to localize adenoma to mediastinum and surgically remove in timely manner.

**Conclusion:** In view of higher Pregnancy loss in untreated Hypercalcemia early and aggressive work up may be beneficial but risk benefits of Sestamibi scan needs to be carefully evaluated on an individual basis.

Abstract #840

TOXIC TUMS

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**Case Presentation:** A 74 year old lady with past medical history of hypertension, osteoarthritis, reflux esophagitis and rheumatoid arthritis was brought in to the E.R. by family member for altered mental status. As per the relative, symptoms started two days back and were gradually worsening. The patient was recently admitted in different hospital for Clostridium Difficile Colitis and was discharged with a bottle of TUMS for heart burn, in addition to her previous medications. On examination patient was afebrile with a blood pressure of 148/96 mmhg, heart rate of 106/min., respiratory rate of 20/min and oxygen saturating of 99% on room air. A full body inspection did not show any signs of trauma. Patient appeared lethargic but was arousable and there were no signs of focal neurological deficits. Examination of rest of the systems was benign. Labs showed sodium 142, potassium of 3, chloride of 101, bicarbonate of 34, BUN 29, Creatinine 1.7(baseline 1.3), blood glucose of 111 and calcium of 15.4 (8.4-10.2 mg/dl). CBC and LFT was normal. Urinalysis was negative. A 12 lead EKG showed sinus tachycardia. A chest X-ray was normal. CT scan of head and Spine were normal. Endocrine workup revealed a PTH intact level of 7 pg/ml, a PTHrp within normal range, Vitamin D 25(OH) 39ng/ml, Vitamin D 25(OH)D2 <4pg/ml, Phosphorus 2.7, and negative SPEP and UPEP. Patient was started on I.V. fluids with closed monitoring. Over the course of time patient’s calcium level trended down and her mental status improved. After around 48 hours patient was fully awake, alert and oriented and her calcium levels and BMP were within normal range. On asking, patient revealed that she consumed around 50 tablets of TUMS in last one week because she found it “tasty”.

**Discussion:** Milk alkali syndrome consists of the triad of hypercalcemia, metabolic alkalosis and renal insufficiency associated with the ingestion of large amounts of calcium and absorbable alkali. Once a classic cause of hypercalcemia, this syndrome almost completely disappeared due to use of new therapies of peptic ulcer disease. However, this disorder is making a comeback, and now is the third leading cause of hypercalcemia after primary hyperparathyroidism and malignancy.

**Conclusion:** Three factors are responsible for the increase in incidence of milk alkali syndrome: Readily available over the counter calcium carbonate preparations; emphasis on calcium therapy for the prevention and treatment of osteoporosis; use of calcium carbonate to minimize secondary hyperparathyroidism in patients with chronic renal failure. It is very important to educate patients on correct use and consumption of the available calcium formulations to prevent life threatening consequences.
**Abstract #841**

**SCREENING FOR OSTEOPOROSIS IN POST MENOPAUSAL FEMALES IN A UNIVERSITY BASED OUTPATIENT RESIDENCY PROGRAM**

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**Objective:** United States Preventive Services Task Force recommends screening for osteoporosis in all women 65 years and older by Dual Energy X ray Absorptiometry (DXA scan). The rate of bone mineral density screening with DXA scan is varied in different primary care settings. The goal of our study is to identify percentage of female patients 65 years or older who got screening DXA scan at our facility.

**Methods:** We conducted a retrospective cross-sectional study and analyzed information by reviewing patient charts. Study population included female patients 65 and older at our primary care practice. Data was obtained as per a pre-defined questionnaire focusing on patient’s demographics, insurance information, past medical problems, history of previous fracture, and any documented osteopenia by X-Ray. If DXA scan was not done, we looked at patient’s office visits to the PCP in calendar year 2012 to determine whether or not it was ordered and what was the main reason for not ordering the test. Statistical analysis was performed on the data collected.

**Results:** We looked at 1988 patients presenting for care from August 2012 to December 2013. We included 109 established (seen at least 3 times in our practice) female patients who were 65 or older. 58 out of 109 eligible females (53.2%) had DXA done compared to 51 who did not (46.7%). Demographic characteristics between these two groups were similar regarding age (average of 70.9), race ($P = 0.73$) and insurance provider (85% with Medicare and Medicaid). The average weight was calculated to be 175.5 lbs. There was just one patient who had an order for DXA but did not get it done. Of 51 patients who did not get DXA scan, only 6 (11.8%) had documentation regarding the reason for not ordering the test.

**Discussion:** Osteoporosis is a common problem among older women and the burden is related to the increased incidence of fractures. We found the rate of screening to be 53% in eligible patients at our facility, where residents in training learn to function as a primary care physician under direct supervision of faculty preceptors. Most unscreened patients had no documentation on their charts regarding why the test was not done.

**Conclusion:** We need to educate our residents to improve osteoporosis screening and proper documentation. Studies such as this can help residency programs increase awareness regarding osteoporosis screening and help in reducing preventable morbidity and curtail health care costs. We have recently started using an Electronic Medical Record (EMR) in our outpatient practice. We plan to re-evaluate the rate of osteoporosis screening after a year of implementing EMR at our practice.
PITUITARY DISORDERS / NEUROENDOCRINOLGY

Abstract #900

CEREBRAL SPINAL FLUID LEAKS COMPLICATING MEDICAL THERAPY OF GIANT PROLACTINOMAS

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**Objective:** We present two cases of giant prolactinomas treated with dopamine agonist (DA) therapy with variable outcomes.

**Case Presentation:** Case 1: A 75 year old male presented with vertigo and headaches for 6 months. Visual field testing was concerning for right optic nerve compression. MRI showed a 32 x 24 x 17 mm sellar and suprasellar lesion invading bilateral cavernous sinuses. The floor of the sella turcica was depressed, with no evidence of the optic chiasm compression. Studies showed a prolactin of 716.9 mg/ml. The patient was started on bromocriptine 2.5 mg daily. Four weeks later he was hospitalized for meningitis and reported clear nasal drainage for 3 weeks. Repeat MRI revealed a 33 x 22 x 25 mm mass with erosion inferiorly through the floor of the sella at the level of the intercistern septum, involving the sphenoid sinus. Beta 2 transferrin was present in the nasal discharge.

Case 2: A 46 year old male presented with 2 months of progressive headaches, left sided vision loss, unsteady gait and right sided epistaxis. On confrontational visual fields the right eye had a temporal field hemidefect and the left eye had no light perception. MRI showed a large, multilobulated 90.7 x 86.3 x 82.8 mm mass involving the sella turcica. There was erosion through the sellar floor into the sphenoid sinuses bilaterally, the right posterior ethmoid air cells and posterior right nasal cavity. Mass effect was demonstrated on the optic chiasm with encasement of the optic nerves. Prolactin level was >1000 mg/ml and bromocriptine 10 mg daily was started. MRI two months after therapy showed a decrease in tumor size to 79.5x 51.1x 59.7 mm and a decreased prolactin level of 17.66 mg/ml. The patient had no further episodes of epistaxis.

**Discussion:** Prolactinomas are the most common hormone secreting pituitary tumor. Cerebral spinal fluid (CSF) rhinorrhea may be a presenting symptom of massive invasive prolactinomas or may develop following DA therapy caused by unplugging of an eroded area in the skull base as a result of tumour shrinkage. DA-induced CSF rhinorrhea should be considered when starting DA in patients with massive invasive prolactinomas who develop a nasal discharge or salt-like taste in the throat. Glucose oxidase tests for CSF leaks are inaccurate and lack specificity. A CSF leak is diagnosed by nasal fluid biochemical analysis of a glucose level more than 30 mg/dL or presence of beta-2 transferrin.

**Conclusion:** CSF leakage is a rare complication of DA therapy. Reduction in tumor size is not a good predictor of potential CSF rhinorrhea. Close follow-up is required when DA therapy is initiated for massive invasive prolactinomas.

Abstract #901

HYPOPITUITARISM SECONDARY TO IPILIMUMAB THERAPY IN PATIENTS WITH MELANOMA

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**Objective:** To describe a case series of patients with advanced melanoma who developed hypopituitarism after treatment with ipilimumab.

**Case Presentation:** We describe a series of eight patients who presented with non-specific symptoms such as fatigue and dizziness following therapy with ipilimumab for advanced melanoma. The mean age of the patients at the time of presentation was 64.8 years. There were four male and four female patients. The time to onset of symptoms from start of therapy ranged between 7-16 weeks. The dose of ipilimumab used was 3mg/kg in all but two patients who received a dose of 10mg/kg. Pituitary hormone levels were abnormal to varying degree in the patients though most cases required therapy with a glucocorticoid and levothyroxine. ACTH was measured in seven patients and found to be between 2-16 pg/mL (7-69 pg/mL). Random cortisol was checked in all patients and found reduced in five ranging from 0.6 to 1.6 mcg/dL (morning reference range of 5-23 and evening reference range of 3-16 mcg/dL). Free T4 was reduced in four patients who had a correspondingly low TSH. Insulin like growth factor-1 (IGF-1) was measured in six patients and found decreased in all four male patients. Prolactin level was checked in six patients and found inappropriately normal in two patients. LH was decreased in four. FSH was checked in seven patients and found to be inappropriately normal in three. LH was decreased in four and inappropriately normal in two patients. Testosterone was low in all four male patients. Prolactin level was checked in six patients and was low in two. MRI sella was normal in two and showed changes consistent with hypophysitis in five patients. One patient had a hypermetabolic pituitary gland noted on PET scan with a normal pituitary on MRI.

**Discussion:** Ipilimumab, a monoclonal antibody against the cytotoxic T-lymphocyte antigen-4 (CTLA4) receptor, has been shown in studies to improve survival in patients with advanced melanoma. However, inhibition of CTLA4 induces side effects termed as “immune-related adverse events” which includes endocrinopathies- hypophysitis and more rarely thyroiditis and adrenalitis. In recent trials, the incidence of hypophysitis
Induced by anti-CTLA monoclonal antibodies is less than 5%. Symptoms may occur 6-12 weeks after initiation of therapy as observed in our case series. Furthermore, patients with anti-CTLA hypopituitarism often require lifelong therapy with glucocorticoids.

**Conclusion:** Hypopituitarism though a less common side effect of ipilimumab, can be life threatening if left untreated. Therefore physicians should have a high index of suspicion for hypopituitarism when evaluating patients on ipilimumab therapy presenting with non-specific symptoms.

**Abstract #902**

**SEVERELY ELEVATED GROWTH HORMONE LEVELS IMPACT SURGICAL OUTCOMES IN ACROMEGALY- EMORY UNIVERSITY EXPERIENCE**

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**Objective:** Transphenoidal adenectomy (TSA) is first-line treatment for acromegaly. While surgical cure is negatively influenced by cavernous sinus invasion, the impact of preoperative growth hormone (GH) levels is equivocal. Our aim is to determine the impact of preoperative GH levels on biochemical remission after TSA.

**Methods:** This is a retrospective case series of 79 consecutive acromegaly patients operated between 1994-2013. All had their first TSA performed at Emory, immunohistochemically confirmed GH adenomas, and follow-up >3 months. Biochemical remission was defined as normal IGF-1 during follow-up >3 months in the absence of adjuvant therapy. We calculated Youden indices to determine the threshold for GH levels to predict biochemical remission. We compared the characteristics of the 2 groups as defined by the GH threshold.

**Results:** Lack of cavernous sinus invasion was the only predictor of remission in multivariate analysis. Lower preoperative GH was a predictor in univariate analysis. We calculated a preoperative GH of 40ng/mL as the GH threshold for remission (sensitivity 97%, specificity 42%). Group A (GH>40) comprised 19 patients (9 men), age 43±13, median follow-up of 37.7 months (5.6-112.2). Tumor diameter was 2.7±1.0 cm, preoperative GH 136±176 and IGF-1 of 1032±301 ng/mL. Immediate postoperative GH was 62.1±201.7. Three patients (15%) had remission at 3 months, but 2 recurred within 2 years. Adjuvant therapy resulted in normal IGF-1 in 9/16 at a median 20 (11-34) months postoperatively.

Group B (GH≤40) comprised 60 patients (25 men), age 47±13 median follow-up of 42.6 months (3-186.8). Tumor diameter was 1.6+/-.10 cm, preoperative GH 11.1±9.8 and IGF-1 of 745±327. Immediate postoperative GH was 3.5±5.4. Thirty five patients (58%) had remission at 3 months with no recurrence during follow-up. Adjuvant therapy resulted in normal IGF-1 in 19/25 patients at median of 26 (3-91) months.

Group A had larger, more invasive tumors, higher preoperative IGF1 levels, higher immediate postoperative GH and more residual tumors at 3 months (p<0.05). Although mean age was not significantly different between groups, age at surgery peaked at 25-35 years in group A and 45-55 in group B. The 2 groups were not significantly different regarding tumor immunostaining for prolactin or CAM5.2.

**Discussion:** Preoperative GH levels are an important predictor of biochemical remission when significantly elevated. The relationship of GH elevation and cavernous sinus invasion should be further defined, as should the molecular fingerprint and the potential role of preoperative medical treatment in this group of patients.

**Conclusion:** GH levels >40ng/mL negatively impact surgical remission after TSA in acromegaly.

**Abstract #903**

**ADULT DIAGNOSIS OF A RARE PEDIATRIC DISORDER**

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**Case Presentation:** A 59 year old man presented to our endocrinology clinic for HPA axis evaluation. Four years prior the patient developed seizures and part of this work up included an MRI which revealed a hypothalamic hamartoma. Seizures were medically controlled and he was asymptomatic until noting vision changes after a traumatic head injury. MRI showed slight expansion of the mass and formal visual field testing confirmed bitemporal hemianopsia. He was not having signs of pituitary dysfunction other than drinking 7-8 liters of fluid daily. Cortisol axis was intact with an 8am level of 17.4μg/dL.
Gonadal axis was intact with FSH, LH, and testosterone in the normal range. Thyroid axis was intact with free T4 of 0.8µg/dL. Prolactin and IGF-1 were in the normal range. Serum sodium was 138mEq/L with a urine osmolarity in the upper half of the normal range. He underwent debulking of the hamartoma and visual defects improved. Hypopituitarism was not found post-operatively. His polydyspia, attributed to dipsogenic DI caused by the mass, resolved. Interestingly, his daughter, a 29 year old female, was also diagnosed with seizures during this time period and underwent evaluation with the same finding of a hypothalamic hamartoma. Both patients had had polydactyly with prior surgical correction. The daughter underwent genetic testing which revealed a novel heterozygous single base pair deletion in exon 13 on the GLI3 gene causing a frameshift mutation. Further investigation into family history revealed multiple members in previous generations with polydactyly and/or seizures.

Discussion: Pallister-Hall syndrome (PHS) is a genetic disorder secondary to an inherited autosomal dominant or de novo mutation in GLI3 gene. The syndrome was first described in 1980 by Hall and Pallister. Current diagnostic criteria require presence of hypothalamic hamartoma and polydactyly in addition to positive family history. Diagnosis is confirmed with genetic testing. Due to variable penetrance other clinical anomalies including sydactyly, dysplastic nails, midline defects, imperforate anus, and renal and genitourinary abnormalities can also occur. Patients are often diagnosed in early childhood due to structural defects or development of seizures and it can be lethal in infancy if undiagnosed hypopituitarism or respiratory tract anomalies exist.

Conclusion: PHS is considered rare, however prevalence is unknown. It is possible that many cases exist in those with polydactyly and asymptomatic hypothalamic hamartomas. Since most diagnoses are made in the pediatric population, our report adds to the few cases detected in adulthood in the literature.

Abstract #904

ROLE OF TEMOZOLOMIDE IN AGGRESSIVE PITUITARY TUMORS

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Objective: Pituitary carcinomas are rare and are defined by the presence of metastasis within or outside the CNS but not contiguous with the primary sellar tumor. We report a case of malignant prolactinoma refractory to medical therapy, radiation and surgery wherein temozolomide was used successfully to cause biochemical and radiological improvement.

Case Presentation: A 66 year old female presented in 1998 with headaches and vision loss of 2 weeks duration and was found to have a prolactin secreting pituitary macroadenoma with hemorrhage and compression of the optic chiasma. She underwent trans-sphenoidal surgery. She presented again 8 years later with similar complaints and was found to have a recurrent pituitary tumor with prolactin of 1300 ng/ml. Prolactin nadired at 800 ng/ml with increasing doses of cabergoline and she underwent a second trans-sphenoidal surgery with surgical pathology showing 3 mitotic figures/10 HPF and MIB-1 index of 40%. A third TSS was performed in 2008 for significant regrowth of the tumor followed by a 5 week course of fractionated radio-surgery. Prolactin nadired at 575 ng/ml but rose again to 3488 ng/ml despite high dose cabergoline therapy. A fourth TSS was performed in November, 2010 for apoplexy following which she received 6 cycles of temozolomide with significant radiological tumor reduction and biochemical response. Four more cycles of temozolomide were administered a year later for progression of disease which resulted in radiological and biochemical stabilization of the prolactin secreting tumor. She developed cranial nerve XII palsy due to local tumor invasion and was found to have bone metastasis to the spine and hip. She was discharged to hospice and has currently been started on Capecitabine in combination with temozolamide.

Discussion: Pituitary carcinomas are extremely rare, constituting 0.2% of all pituitary tumors. Current treatments for pituitary carcinomas include repeated debulking operations, conventional radiotherapy or radiosurgery and systemic chemotherapy. Temozolomide is a novel alkylating prodrug, approved for use in refractory glioblastoma multiforme. The first report of temozolomide use as a salvage therapy to treat aggressive pituitary carcinomas appeared in 2006. Research is underway to identify biomarkers that can be used to predict tumor aggressiveness and recurrence.

Conclusion: TMZ is the first chemotherapeutic agent to show substantial response in the management of aggressive pituitary tumors. Reliable predictive markers of tumor aggression and chemotherapy efficacy need to be identified. Greater understanding of the molecular pathways of malignant transformation and progression would provide new tools to develop targeted therapies.
Abstract #905

A NOVEL MUTATION ASSOCIATED WITH MEN-1 SYNDROME TWENTY YEARS AFTER ZOLLINGER ELLISON SYNDROME (ZES) DIAGNOSIS: A CASE REPORT

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Case Presentation: A 60-year-old male presented to the ER with symptoms of skin flushing, diarrhea, and fatigue for two months, nearly twenty years after a ZES diagnosis. He was found to be profoundly anemic. EGD was suspicious for a gastric mass. Subsequent CT guided duodenal biopsy was consistent with a neuroendocrine tumor, which stained for chromogranin and synaptophysin. Labs revealed a gastrin of 30,253 pg/ml (<100), PTH 110 pg/ml (10-65), prolactin 65 ng/ml (2-18), 24 hour urine 5-HIAA 50.3 ml/L (<6), histamine >100 nmol/L, and chromogranin A 193,600 ng/ml (0-50). Serum calcium was normal. Octreotide scanning found diffuse stomach and retroperitoneal uptake. CT of the abdomen showed multiple hypervascular nodules within the duodenum, gastric body, and in the tail of the pancreas, all consistent with gastrinomas. Thyroid ultrasound revealed bilateral hypoechoic areas suspicious for enlarged parathyroid glands. Pituitary MRI was negative. Genetic testing identified a heterozygous sequence variant mutation of the MEN1 gene (amino acid change p.Val40_Leu41del) in a dominant mode of inheritance, not previously described to be associated with MEN-1 syndrome. The patient was started on Omeprazole. Due to persistent episodes of skin flushing and loose watery stools, he was started on short acting Octreotide and then transitioned to Octreotide LAR once a month. Within one week of therapy, the patient reported significant improvement of his flushing and diarrhea. Gastrin levels decreased to 3102 pg/ml, histamine decreased to 9 nmol/L, and chromogranin A decreased to 9970 ng/ml. His anemia improved following iron infusions. Notably, his family history is significant for a maternal uncle who died at a young age of a perforated stomach ulcer. His mother underwent a subtotal gastrectomy and a parathyroidectomy and one of his two daughters was found to have a prolactinoma. Today, the patient remains well and has opted for continued medical therapy.

Discussion: MEN1 is an autosomal dominant endocrine cancer syndrome with high penetrance. The MEN1 gene consists of 10 exons on chromosome 11q13, which codes for a 610 amino acid nuclear protein, Menin, which plays a role in tumor suppression. Interestingly, the rate of de novo mutations is estimated at 10% for MEN1 in general, and as high as 25% for MEN1 patients with ZES. Over 1300 germ line and somatic mutations in the MEN1 gene have been described, and include missense, nonsense, and deleterious mutations.

Conclusion: We describe the first case of this possible MEN1 sequence variant mutation. The association of his proband sequence with MEN1 syndrome in his affected family members is pending confirmation via genetic testing.

Abstract #906

SUCCESSFUL LONG-TERM MANAGEMENT OF REFRACTORY CUSHING’S DISEASE WITH PASIREOTIDE: A CASE REPORT

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Objective: In a recent 12-month Phase III study (NCT00434148), pasireotide reduced urinary free cortisol (UFC) in most patients with Cushing’s disease (CD). Moreover, UFC reductions were associated with improvements in health-related quality of life (QoL) and the clinical signs and symptoms of CD. Patients who experienced clinical benefit were eligible to participate in an extension phase of the trial.

Methods: Here we report a patient who achieved sustained UFC control and improvements in the clinical signs and symptoms of CD for >5 years with pasireotide.

Case Presentation: A 67-year-old man underwent transphenoidal surgery for CD, but UFC elevation persisted (167 µg/day [ULN, 50]), indicating surgical failure. He enrolled in the Phase III study and received pasireotide 600 µg BID (increased per protocol to 1200 µg BID). At baseline, his appearance was distinctly Cushingoid, with marked truncal obesity (weight, 97.8 kg; BMI, 31.2 kg/m^2). He was able to care for himself, but unable to carry on normal activity or do active work (Karnofsky performance status [KPS]=70). Beck depression inventory (BDI) and CushingQoL scores were 32 and 41.7, respectively. Within 3 months, his UFC normalized and, except for isolated transient elevations, this effect has endured for >5 years. Signs and symptoms of CD also improved rapidly and, after 5 years’ treatment, he continues to display only minor signs and symptoms of disease (KPS=90). Although BDI and CushingQoL were recorded only for the first 12 months of treatment, these indices improved similarly (10 and 66.7, respectively, at Month 12), and the patient’s personal reports throughout the extension are consistent with sustained disease control.
Fasting plasma glucose and HbA1c worsened on treatment. While metformin, glyburide, or rosiglitazone alone did not improve his glycemic status, his hyperglycemia was brought under good control with insulin and continues to be well controlled on this antidiabetic regime. Initial weight loss (-11.9 kg at Month 12) was reversed following a debilitating knee injury, but his activity has increased significantly since total knee replacement. At most recent follow-up, his weight was 6.2 kg below baseline and insulin dose was reduced.

**Discussion:** This case illustrates successful long-term control of hypercortisolism and significant, durable improvements in clinical symptoms of CD, depression, QoL, and functional status with pasireotide.

**Conclusion:** Our findings support other observations that pasireotide can induce significant, rapid, and enduring improvements in patients with CD. Additional trials are planned to study the long-term benefits and risks of pasireotide treatment and to optimize concomitant antidiabetic management.

**Abstract #907**

**PET+ PITUITARY INCIDENTALOMA**

**Harmeet Narula, MD, FACP, FACE**

**Objective:** To describe an interesting case of an incidental pituitary mass seen on PET scan in a man with 2 cancers (lymphoma & a synchronous SCC Larynx)

**Case Presentation:** 82 year old man with recently diagnosed Non-Hodgkins Lymphoma of the neck & a synchronous laryngeal cancer was referred to endocrinology clinic for evaluation of an incidental sellar uptake on a surveillance whole body PET scan. The patient denied any headache or visual symptoms. He complained of mild fatigue and attributed it to his ongoing chemotherapy (he initially received R-CHOP and subsequently was on monthly rituximab). He also received XRT for his laryngeal cancer. He had a history of longstanding primary hypothryoidism and was on a stable levothyroxine dose for years. On physical examination, he did not appear acromegalic or Cushingoid, visual fields were intact, thyroid was normal and no neck lymphadenopathy was palpable. The rest of his physical exam was unremarkable. On labs, his Prolactin was normal at 8 ng/mL, TSH 1.1 mIU/L, Free T4 1.64 ng/dL, Testosterone 407 ng/dL. MRI of the pituitary gland revealed a 1cm lesion. The mass was stable on repeat imaging after 5 months.

**Discussion:** Incidental pituitary lesions are common; 10% of the population may have an incidental pituitary abnormality. PET scans are routinely used in the staging & surveillance of various malignancies. Many incidental abnormalities may be seen on PET scans, and in some tissues (like the thyroid), a PET + focal incidentaloma has a greater risk of malignancy. With pituitary lesions, there does not appear to be an increased risk of malignancy even when FDG PET uptake is seen. In a recent review by Hyun et al, only 40% of pituitary uptake on PET was associated with pituitary pathology (rest was physiologic uptake), and of these, almost 90% were benign pituitary adenomas, even though >90% of the PET scans in this study were performed in patients with known or suspected malignancies. We suggest a conservative approach (as the vast majority of these lesions appear benign), unless atypical features suggestive of a pituitary metastasis/malignancy are present (heterogenous mass with bony destruction on MRI, or with Diabetes insipidus and/or hypopituitarism or multiple cranial nerve palsies).

**Conclusion:** Incidental pituitary uptake can be seen on FDG PET scanning, in patients with known or suspected primary malignancies; most of these lesions are benign pituitary adenomas. Endocrinologists, oncologists and radiologists should be aware of this, so they may appropriately evaluate & manage these patients.

**Abstract #908**

**PITUITARY ADENOMA INCIDENTALLY DETECTED ON PARATHYROID SESTAMIBI IMAGING**

**Harmeet Narula, MD, FACP, FACE**

**Case Presentation:** 67 y morbidly obese WM, hx gastric bypass, recurrent calcium oxalate kidney stones, prostate cancer, DM2, HTN, Hyperlipidemia & Gout was sent by his PCP for an endocrine evaluation for elevated PTH and ‘rule out hyperparathyroidism’. As part of the ‘work-up’, the PCP performed a parathyroid sestamibi scan which revealed no abnormality in the parathyroids but incidentally revealed increased uptake in the sellar area. The patient denied any headaches, or visual symptoms. On examination, his visual fields were intact and he did not appear acromegallic or Cushingoid. On labs, his Serum calcium was between 8.5 to 9.0 mg/dL, with albumin 4.1 gm/dL, iPTH 158 pg/mL, Serum creatinine 0.96 mg/dL and 25-hydroxy-vitamin D 28 ng/mL, consistent with secondary hyperparathyroidism. Pituitary workup revealed a Serum prolactin 5.8 ng/mL, Testosterone 953 ng/dL, SHBG 77 nmol/L, TSH 0.9 mIU/L, Free T4 0.9 ng/dL. MRI of the pituitary gland revealed an 8 mm pituitary microadenoma. This was stable on imaging 5 months later.

**Discussion:** Incidental pituitary abnormalities are common; 10% of population has an incidental pituitary abnormality. Tc99 Sestamibi is commonly performed to localize parathyroid adenomas in patients with biochemically
confirms primary hyperparathyroidism. Normal pituitary gland does not take up sestamibi but pituitary adenomas may also take up Tc99 sestamibi, and may be incidentally seen on parathyroid scans or cardiac stress tests (Kojima et al, 2001). Craniopharyngiomas do not take up Tc99-MIBI but many other CNS malignancies, including astrocytomas & glioblastoma multiforme do. 

**Conclusion:** Endocrinologists, radiologists and nuclear medicine physicians should be aware of sellar uptake on sestamibi imaging, so they may evaluate these patients appropriately.

**Abstract #909**

**HYPOPARATHYROIDISM & OTHER ENDOCRINOPATHIES IN A THALASSEMIA PATIENT: THE EFFECT OF IRON OVERLOAD**

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**Objective:** To describe hypocalcemia due to hypoparathyroidism induced by hemochromatosis in a thalassemia patient.

**Case Presentation:** A 28 year old Saudi Arabian male, with beta thalassemia major, transfusion dependent and had received >1000 blood transfusions in life, presented to the hospital with a transfusion reaction. The past history was significant for splenectomy. His labs showed hypocalcemia, with calcium of 6.5, normal albumin, high Phosphorus 9.8 & magnesium 1.8. Concurrent PTH levels were 25mg/dl. EKG showed QTc of 480 msec. Subsequent worsening of his renal function was associated with recurrent hyperphosphatemia of 10.2 and low ionized calcium of 0.85. Low 25, OH Vitamin D levels were present. Persistent hypocalcemia and hyperphosphatemia was seen even with improved renal function. Calcium levels checked 1 year ago were normal. His brother also has thalassemia major and parents have diabetes. On examination, thyroid was normal, Chvostek's and Trousseau sign were positive. Testicular exam showed bilateral small testiciles. Further work up showed HbA1C of 7.2%, low testosterone, FSH, & LH values. Pituitary MRI, showed possible diabetes, but normal adrenal function (based on cosyntropin test), normal prolactin levels. He was treated with recombinant PTH, calcitriol and ergocalciferol. Topical testosterone gel improved his energy levels and libido.

**Discussion:** Hypoparathyroidism is a rare consequence of iron overload in thalassemia major patients requiring frequent transfusions. The mechanism includes iron infiltration of the gland. This classically presents in the second decade of life, more common in males and splenectomized patients. The anterior pituitary is sensitive to iron overload causing short stature, hypogonadism, acquired hypothyroidism and hypoparathyroidism. Glucose intolerance and osteoporosis are also common. Bone disease is multifactorial due to hormonal deficiency, bone marrow expansion, calcium and vitamin D deficiency.

**Conclusion:** Physicians should be aware that many endocrine glands may be affected in thalassemia patients due to iron overload by repeated transfusions. Early recognition and prevention of these endocrine complications, by early onset and regular chelation therapy, can improve quality of life and psychological outcome.

**Abstract #910**

**CONGENITAL PITUITARY STALK DEFORMITY**

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**Case Presentation:** A 20 year old female with a history of diabetes mellitus presents with primary amenorrhea and normal secondary sexual characteristics. No associated headaches, visual changes, galactorrhea, or hirsuitism. She denies sexual activity, never used OCPs or progesterone, and has no history of brain trauma. Gynecological exam revealed Tanner stage IV with normal external genitalia. Internal exam was declined. Pregnancy test was negative. Laboratory work showed FSH 3.9, estradiol <18, LH 3.7, Prolactin 7.3, free testosterone <12. Thyroid studies, IGF-1, DHEA, 17-(OH) progesterone, and 24-hour urine cortisol were normal. A pelvic ultrasound showed normal ovaries and uterus. Radiographic bone age was that of an 18 year old. Karyotyping resulted in 46 XX. This patient was diagnosed with hypogonadotrophic hypogonadism. An MRI brain was done to look for an etiology (see images). The imaging displays hypoplasia of the pituitary gland without any visible stalk. There is a focus of enhancing tissue at the midline of the median eminence, posterior to the optic chiasm. This may reflect ectopic posterior pituitary tissue. What is the diagnosis?

**Discussion:** Findings, along with clinical history, conclude that this patient has pituitary stalk transection syndrome with probable ectopic posterior pituitary...
ABSTRACTS – Pituitary Disorders/Neuroendocrinology

A previously healthy 25-year-old man was diagnosed with an unusual case of Pituitary stalk transection syndrome, a congenital structural deformity of her pituitary stalk. The patient developed hypogonadotrophic hypogonadism with low FSH and LH, resulting in low estrogen production from a congenital structural deformity of her pituitary stalk.

Conclusion: Pituitary stalk transection syndrome, although classically viewed as a sheering force causing disruption of the stalk, can present atraumatically as a result of a congenital structural deformity of the stalk itself.

Abstract #911

HOW MUCH CORTISOL DO WE NEED?

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University of Buffalo

Case Presentation: A 31 year old Caucasian male with history of hypothyroidism, viral meningitis and marijuana abuse presented to hospital with altered mental status. Patient was given intravenous Dextrose by paramedics at home when his blood sugar was 20 mg/dl. Upon arrival to the ER his blood sugar was 16 mg/dl but his mental status improved. He denied any skipping of meal the previous day but reported having diarrhea and upper respiratory symptoms (dry cough) for a week. He had 3 hospitalizations for hypoglycemia precipitated by various infections prominently after being diagnosed with viral meningitis 6 years ago. He complained of mild fatigue and inability to gain weight, but denied any other symptoms of hypothyroidism, headache, visual problems, and sexual dysfunction. Initial vital signs and physical examination were unremarkable. CBC and CMP were normal. Insulin (<2mcU/ml), proinsulin (<5pmol/L) and C-Peptide (<0.1ng/ml) levels were suppressed appropriately for hypoglycemia. His cortisol level at 6 AM was <0.8mcg/dl. He failed ACTH stimulation test with cortisol being <0.8mcg/dl at 30 and 60 min after 250 mcg of intravenous cosyntropin administration. Old records revealed undetectable cortisol levels in the past (<1mcg/dl, 5 years ago). Surprisingly he was not started on any corticosteroids. Other endocrinology work up at 7AM showed ACTH <1.1 pg/ml(N 7.2-63.3), total Testosterone 166 ng/dl(300-1200), SHBG-95.4 nmol/L( 16.5-55.9), LH-7.5 mU/ml( 1-8), FSH-2.4 mU/ml( 1-11), IGF1-11 ng/ml (71-241) and Prolactin 3.2 ng/ml(N0-17). His thyroid function with levothyroxine supplement showed TSH of 1 mcU/ml (0.4-5) and FT4 of 0.9ng/dl (0.8-1.8). MRI of pituitary is pending. He was started on oral hydrocortisone which improved his fatigue and episodic hypoglycemia.

Discussion: The patient was diagnosed with panhypopituitarism with undetectable cortisol levels. MRI pituitary is pending at present. Such recurrent severe hypoglycemic episodes appear to be from secondary adrenal insufficiency precipitated by infectious process. Recurrent severe hypoglycemia as isolated presenting symptom of glucocorticoid deficiency is uncommon. Other uniqueness of this case is the survival of the patient with undetectable cortisol level without any steroid supplementation.

Conclusion: We describe an unusual case of panhypopituitarism with chronic glucocorticoid deficiency presenting with severe recurrent hypoglycemia. Adrenal insufficiency as a cause of hypoglycemia is well documented, but a person living with undetectable levels of cortisol for years, is being described for first time in literature.

Abstract #912

A UNIQUE CASE OF A DOPAMINE-SECRETING CERVICAL PARAGANGLIOMA

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Objective: Head and neck paragangliomas (HNPGL) are uncommon and rarely secrete catecholamines. A limited number of dopamine-secreting HNPGL have been reported. We present a case of a dopamine-secreting cervical paraganglioma and discuss preoperative evaluation.

Case Presentation: A previously healthy 25-year-old man presented with six months of dysphagia. He had also been experiencing episodes of lightheadedness, blurry vision, and syncope for two years, and noted that swallowing often triggered these symptoms. He denied having palpitations, sweats, anxiety, headache, nausea, diarrhea or flushing. He had no family history of adrenal or extraadrenal tumors, or conditions associated with familial paraganglioma syndromes.

On physical examination the patient was normotensive and not orthostatic. Oropharyngeal exam revealed left tonsillar prominence with rightward deviation of the uvula. Mouth opening with neck extension triggered lightheadedness. Fiberoptic exam showed partial immobility of the left
vocal cord and large left pharyngeal mass. Neck CT imaging revealed a 6 cm hypervascular mass in the left carotid sheath with features suggestive of a paraganglioma. MIBG scan was confirmatory and no other tumors were identified.

Laboratory evaluation revealed significant elevations of serum dopamine (769 pg/mL, ref. < 48 pg/mL) and 24hr urinary dopamine (951 μg/24hr, ref. < 510 μg/24 hr), and elevations of serum normetanephrine (241 pg/mL, ref. < 145 pg/mL), 24hr urinary norepinephrine (190 μg/24hr, ref. <135 μg/24hr) and normetanephrine (794 μg/24hr, ref 82-500 μg/24hr). Serum metanephrine and 24hr urinary metanephrine were within the normal range.

The patient will undergo tumor embolization followed by surgical resection. Preoperative management includes alpha-adrenergic receptor blockade with doxazosin, with beta-adrenergic receptor blockade as needed.

Discussion: Patients with dopamine-secreting HNPGL are unique in that they are often normotensive, as dopamine-induced vasodilation may oppose the vasoconstrictive effects of norepinephrine. The most common presenting symptoms, as in our patient, are often related to mass effects. Patients with HNPGL often have germline mutations in the succinate dehydrogenase (SDH) gene, specifically mutations in subunits C and D. Our patient has a 3-year-old son, and our patient's genetic screening is pending. Dopamine-secreting HNPGL are associated with an increased risk for malignancy, though our patient does not have evidence for metastatic disease.

Conclusion: We present a case of a rare dopamine-secreting cervical paraganglioma. This provides an opportunity to review the presentation and evaluation of this unique tumor.

Abstract #913

SYMPATHOMIMETIC AMINES PROVIDES MARKED RELIEF OF CHRONIC TREATMENT REFRACTORY MIGRAINE HEADACHES

Jerome Check, MD, PhD1, Rachael Cohen, DO2, Joanne Liss, MT3, Diane Check, BS3


Objective: The endocrinologist is frequently asked to find a solution to severe headaches looking for a hormonal connection as a complication of estrogen therapy, premenstrual syndrome, pituitary tumor, hypertension, pheochromocytoma or hypoglycemia. The sympathetic nervous system controls cellular permeability. Pain in various locations including severe treatment refractory migraine headaches have anecdotally been improved by treating with the sympathomimetic amine dextroamphetamine sulfate allegedly by improving sympathetic tone by replacing the defective neurotransmitter. With restoration of sympathetic function the cellular permeability defect is corrected and inflammatory elements are precluded from absorbing into brain tissue. The objective of this study was to evaluate the efficacy of dextroamphetamine sulfate treatment in a series of women with chronic migraines refractory to standard therapy.

Methods: A prospective observational study was performed in women with severe chronic migraine headaches refractory to standard therapy. To be eligible the women had to have severe headaches for at least 3 years and have failed to gain improvement from beta blockers, topiramate, and ergotamine preparations. Only women with prior complete neurologic work-up excluding any brain lesions as the cause of the headaches were selected. Dextroamphetamine sulfate was started at 15mg extended release capsules and could be increased by 10-15mg up to 60mg. Each patient was asked at 6 months to simply state whether the sympathomimetic amines provided 1) no relief, 2) mild relief, 3) moderate improvement, 4) complete or almost complete eradication. The questionnaire was repeated at 1 year for those remaining on therapy.

Results: Twenty-two women with an average duration of headaches for 13.8 years were enlisted (age range 31-64, avg. 41.7). Only 1 woman reported no improvement and stopped therapy whereas 17 of 22 (77.3%) reported almost or complete relief of headaches at 6 months and 1 year. Four other women reported moderate relief.

Discussion: Dextroamphetamine sulfate has been reported to dramatically improve migraine headaches including ocular migraines, and headaches associated with intracranial hypertension and temporal mandibular joint syndrome. However, anecdotes fail to provide information on the percentage of cases that are successful.

Conclusion: Dextroamphetamine sulfate is highly effective for treatment refractory migraines as evidenced by a high success rate in a series of women with severe headaches.
Abstract #914

MYSTERIOUS SYNCOPAL EPISODES

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Case Presentation: We present a mysterious case of a 44 year old lady with medical history of chronic migraine headaches, fibromyalgia, chronic back pain, PTSD, multinodular goiter who had multiple hospital admissions and ER visits in recent months for syncopal episodes. These episodes were sudden in onset, lasted for 5-20 minutes and were associated with post syncope drowsiness and fatigue lasting for hours. The episodes were not related to exertion or postural changes. On physical examination she was found to be orthostatic and had bulky thyroid. Extensive neurological and cardiac work up including EEG, CT scan head, CTA head and neck, telemonitoring and echocardiogram were unremarkable. CBC, BMP and thyroid function tests were within normal range. 1 mcg cosyntropin stimulation test showed baseline cortisol levels of less than 1.5 mcg/dl, 11.7mcg/dl at 15 minutes and 14.6mcg/dl at 30 minutes, which was an inadequate response. The aldosterone level was <1.6 ng/dl at baseline and 30 minutes (4.0-31.0 ng/dl). MRI head showed no pituitary abnormality. Hence the diagnosis of central adrenal insufficiency was made and patient was started on hydrocortisone. Patient had no history of chronic steroid use or radiation exposure. She was on chronic oxycodone therapy since 2007 for back and neck pain which most probably led to the suppression of HPA axis causing central adrenal insufficiency. Oxycodone was discontinued and patient was started on lidocaine patch with short acting morphine for breakthrough pain. Patient was followed up in endocrinology clinic with marked improvement in symptoms.

Discussion: The use of opioids for chronic non cancer pain has increased substantially and the proportion of office visits for chronic musculoskeletal pain in which opioids were prescribed has doubled from 8 % in 1980 to 16% in 2000. Studies have shown that acute administration of morphine without exogenous stress caused a rise in corticotrophin releasing hormone whereas exogenous stress as well as repeated daily doses of morphine caused a significant lowering of plasma and pituitary ACTH concentrations and hypothalamic CRH content.

Conclusion: It is hypothesized that narcotic analgesics exert their hormonal effects by altering the release of neurotransmitters in the CNS. δ - and κ-opiate receptors appear to be involved in the control of ACTH release. Adrenal insufficiency often presents with vague and non-specific symptoms. As physicians we should consider central adrenal insufficiency as one of the side effects of chronic opiate therapy and have a low threshold to test patients for this.

Abstract #915

CUSHING’S DISEASE AND PANHYPOPITUITARISM

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KUMC-W

Case Presentation: Cushing's disease is characterized by ACTH-dependent hypercortisolism in which the source of excess ACTH is the anterior pituitary. It is primarily treated with surgical resection; however, refractory cases can be treated medically. Panhypopituitarism, by contrast, is characterized by insufficient secretion of pituitary hormones. To our knowledge, we report the first case of a patient presenting with the simultaneous onset of pituitary Cushing's disease and panhypopituitarism in the absence of a compressive pituitary adenoma. The patient's Cushing's disease was treated successfully with mifepristone.

A 62 year-old male was referred for evaluation of hypogonadism. Symptoms upon presentation included fatigue, diffuse muscle weakness, weight gain, central adiposity, easy bruising, headache, night sweats, orthostatic symptoms, decreased libido, and erectile dysfunction. Medical history was significant for diabetes, hypertension, prostatism, esophagitis, and sleep apnea. Pertinent physical findings included central adiposity, moon facies, increased neck circumference, and diffuse ecchymoses. Upon laboratory evaluation he was found to have panhypopituitarism manifested by central hypogonadism, central hypothyroidism, and a low prolactin level. He was found to be hypercortisolemic, with a 24 hour urine free cortisol level of 137 μg (0-50 μg/24 hours) and no suppression to low dose dexamethasone administration. Initial MRI of the pituitary failed to reveal an adenoma. CT of the chest, abdomen, and pelvis was negative for neoplastic processes. Inferior petrosal sinus sampling lateralized the excess ACTH to the right petrosal sinus.

The patient chose to delay surgery. He was placed on mifepristone 300 mg.P.O. daily. A follow up MRI approximately 4 months after initiating mifepristone showed shrinkage of the pituitary gland. He had improvement in his Hemoglobin A1c level, weight loss, and decreased ecchymosis, as well as a subjective improvement in headache.

Discussion: Hypopituitarism can be explained by genetic mutation such as PROP-1 mutation, yet there are no known reports of a patient with simultaneous onset of panhypopituitarism in the absence of pituitary compressive pituitary adenoma and central Cushing's disease. Medical treatment with mifepristone without surgery decreased the size of the pituitary and improved clinical signs/symptoms of Cushing disease.

Conclusion: We report a patient presenting with
the simultaneous onset of pituitary Cushing’s and panhypopituitarism in the absence of a compressive pituitary adenoma. Mifepristone may be an option for patients with Cushing’s disease who are not candidates for surgery.

Abstract #916

AN INTERESTING CASE OF PITUITARY MACRO-ADENOMA PRESENTING AS SYMPTOMATIC INTERNAL CAROTID ARTERY COMPRESSION

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Objective: Obstruction of the internal carotid artery by a pituitary tumor is a rare occurrence, particularly in the absence of pituitary apoplexy. Pituitary macroadenomas can invade the cavernous sinus and rarely cause occlusion of the internal carotid artery (ICA).

Methods: In this case report we present a patient with symptomatic carotid compression by a pituitary adenoma without evidence of apoplexy.

Case Presentation: A 67 y.o. male patient presented with a right sided weakness, and three months history of progressive loss of vision on both eyes. Physical exam showed a bitemporal hemianopsia. The MRI revealed a 2.7 cm pituitary mass likely a macroadenoma, which was extending into the suprasellar cistern and was displacing the optic chiasm, and laterally the mass was pressing on cavernous portions of both internal carotid arteries. Also there was evidence of an acute stroke in the left pons. There was no radiologic evidence of apoplexy. Hormone studies at that time was consistent with panhypopituitarism, his prolactin level was initially 29 ng/ml (elevated but not at the extend of prolactinoma,) and a dilutional test showed even lower prolactin level of 21 ng/ml, so patient was diagnosed with a non-functioning pituitary adenoma. Surgical resection of the tumor and ICA decompression via the transsphenoidal route resulted in prevention of further symptoms. Histopathologic analysis confirmed a non-functioning pituitary adenoma without evidence of hemorrhage or intra-tumoral infarction. Among these 6 patients, 5 children (83.33% of them ) undergone radiation and 4 patients( 66.66% of them) had ALL. There was 2 (4% total) cases of subclinical hypothyroidism but with normal height. According to BMI(body mass index) access 2(4% total ) patients had overweight.

Discussion: Children with malignancies especially ALL patients received reradiation are at high risk for GHD. Although chemotherapy alone in ALL children also can lead to short stature. GHD in adolescence can lead to a decrease in Lean Body Mass, obesity and osteopenia.

Conclusion: Most patients with symptomatic obstruction of the ICA by a pituitary tumor have been reported as a result of apoplexy. In this case report, we present a patient with symptomatic carotid compression by a pituitary adenoma without evidence of apoplexy.

Abstract #917

EVALUATION OF GROWTH HORMONE DEFICIENCY (GHD) IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) AND NON-HODGKINS LYMPHOMA(NHL)

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Objective: Acute lymphoblastic leukemia (ALL) is the most common childhood cancer and non-Hodgkin's lymphoma (NHL) is the most common childhood cancer. These children may suffer from some late effects of treatments such as endocrinopathies like thyroid, pituitary, metabolism disfunctions. Growth Hormone Deficiency (GHD) is one of the causes of short stature.

Methods: During a 3 years cross-sectional research in Dr Sheikh children hospital in Mashhad, we studied on 50 children with ALL( n=25 ), NHL( n=25) who received chemotherapy alone (n=25) or plus radiation ( n=25 ). Patients with height less than 5th percentile, were evaluated for GHD via insulin stimulating test. Also for short stature workup in all patients thyroid function test were done.

Results: We found 6 (12%) children with height less than 5th percentile who 5 (83.33% of them or 10% of total) had GHD. There was no statistical correlation between type of disease also type of treatment and GHD( respectively p-value = 0. 667, 0.189 ) due to small sample size. Among these 6 patients, 5 children (83.33% of them ) undergone radiation and 4 patients( 66.66% of them) had ALL. There was 2 (4% total) cases of subclinical hypothyroidism but with normal height. According to BMI(body mass index) access 2(4% total ) patients had overweight.

Discussion: Children with malignancies especially ALL patients received reradiation are at high risk for GHD. Although chemotherapy alone in ALL children also can lead to short stature. GHD in adolescence can lead to a decrease in Lean Body Mass, obesity and osteopenia.

Conclusion: In our study ALL patients who received radiation had unfavorable state for height and endocrine side effects. So it seems more attention to radiotherapy complications in children with cancer especially ALLs is needed to improve their quality of life.
Abstract #918

GRANULOMATOUS SELAR MASS: WHAT COULD IT BE?

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Objective: A number of different pathologies can present as a sellar mass. Granulomatous lesions are rare and tuberculosis of the pituitary is even more uncommon.

Case Presentation: A 46 year old female presented to the clinic one year ago with severe headache and problems with her vision. She had weight loss but denied fever. Review of systems was otherwise negative. Physical exam revealed visual field defects (bitemporal hemianopsia). MRI showed 18 X 10 X 17 mm well defined lobulated sellar/supra sellar mass.

Baseline labs were, Na 144 mmol/L (135-145), K 5.0 mmol/L (3.5-5.1), TSH 0.11 µIU/dL (0.27-4.2), Total T4 5.36 µg/dL (5.1-14.1), Total T3 150 ng/dL (80-200), Cortisol 1.49 µg/dL (>18), Estradiol <20 pg/mL and Prolactin 16.1 ng/mL (1.9-25). She had trans sphenoidal resection of the tumor. The pathology was suggestive of granulomatous inflammation. Considering the possibility of tuberculosis the patient was started on anti tuberculosis therapy. She was also started on Levothyroxine 25 mcg daily, Hydrocortisone 25 mg daily (in divided doses) and DDAVP nasal spray one puff daily. 4 months later she felt much better, did not have any headaches and the visual fields improved. Labs showed Estradiol 29.2 pg/mL, FSH 13.8 mIU/mL, TSH 2.93 µIU/mL (0.27-4.2), Total T4 8.81 µg/dL (5.1-14.1), Total T3 150 ng/dL (80-200), Cortisol 1.49 µg/dL (>18), Estradiol <20 pg/mL and Prolactin 16.1 ng/mL (1.9-25).

On subsequent follow up 9 months later, she continued to do well. Labs showed Estradiol 23.9 pg/mL, FSH 13.8 mIU/mL, LH 4.11 mIU/mL, Prolactin 5.48 ng/mL (1.9-25), Na 138 mmol/L (135-145), Cortisol 10.58 µg/dL (>18), TSH 3.4 µU/mL (0.27 - 4.2), Free T4 1.03 ng/L (0.8-1.9), Total T4 8.98 µg/dL (5.1-14.1). The MRI revealed an empty sella. The patient was gradually weaned off anti tuberculosis therapy, and continued on the hormone replacement.

Discussion: Pituitary tuberculosis is extremely rare, and should be considered as a diagnostic possibility when the pathology reveals granulomatous inflammation. Other granulomatous pituitary lesions include Wegener's granulomatosis, idiopathic giant cell granulomatous hypophysitis and Takayasu's disease.

Conclusion: Pituitary tuberculosis should be in the differential for a sellar mass, particularly in developing countries, as medical management could be an option.

Abstract #919

UNRECOGNIZED MASKED CEREBRAL SALT WASTING CAN COMPLICATE MANAGEMENT OF DIABETES INSIPIDUS

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Objective: Cerebral salt wasting syndrome (CSW) is diagnosis of exclusion and remains a controversial diagnosis. Development of CSW in the setting of Diabetes insipidus (DI) creates a very complicated problem of water metabolism with severe consequences.

Methods: We present a case in which management of DI was complicated in the setting of initially unrecognized CSW syndrome.

Case Presentation: 51 year old female presented with a supra-sellar mass. A sub-frontal craniotomy was performed. Patient was also noted to develop a DI and exhibited a classic tri-phasic DI response post operatively. On post op day 7 patient was aphasic and disoriented due to a posterior MCA infarct. On post op day 12, patient's urine output increased exponentially in spite of 8 mcg of DDAVP resulting in 2 liters of negative fluid balance. Blood sodium decreased from 146 mmol/L to 123 mmol/L over a 6 hour period and patient developed a seizure.

Blood pressure maintenance required vasopressors. Work up revealed a high plasma renin activity, low aldosterone level and elevated urine sodium. Patient was clinically dehydrated. Development of hyponatremia in the setting of a negative fluid balance along with an increased requirement for dDAVP suggested development of CSW syndrome. Based on the clinical diagnosis fludrocortisone 0.1 mg twice daily was started. Patient's clinical and fluid status improved very shortly. By the second day patient had a positive fluid balance of 700 cc.

Discussion: CSW is characterized by hyponatremia and extracellular fluid depletion due to inappropriate sodium loss in the urine. Urine osmolality is inappropriately high in the presence of hyponatremia due to increased release of ADH. Our formulation was that CSW was masked in this case because of lack of an ADH response due to DI. Providing dDAVP to control urinary volume caused by CSW resulted in overt manifestation of underlying CSW with acute hyponatremia.

Clinical dilemma in this case was that administration of dDAVP was inevitable to control volume loss and maintain an appropriate BP in a patient who had stroke and have been requiring more than 1000 cc of fluid resuscitation per hour. Impairment in aldosterone secretion and excess natriuretic factors have been implicated in CSW. Our patient had a low aldosterone concentration. Nevertheless, diagnosis
should be made clinically since waiting for aldosterone level results can delay the diagnosis by 2 to 3 days.

**Conclusion:** CSW syndrome can occur in a patient with CNS injury as can DI. Existence of both complicates the recognition of the syndrome and delays appropriate treatment. Addition of fludrocortisone to dDAVP can help manage this complicated picture and prevent severe hyponatremia.

**Abstract #920**

**PITUITARY ADENOMA WITH HEMORRHAGE: IS IT APopleXY?**

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**Case Presentation:** A 23 year old African American female presented due to fall. She suffered injury to her chest, did not hit her head nor lose consciousness. Had headache at the time of presentation. Clinical exam was benign. Chest X-ray and CT head was done. Chest X-ray was normal but CT head showed pituitary adenoma with possible hemorrhage prompting to get an emergent MRI. MRI confirmed the evidence of pituitary adenoma with hemorrhage. Adenoma was located centrally and extended posteriorly to sella. She was emergently sent to the nearest ER. From there she was transferred to a referral center due to lack of Neurosurgery. Headache had resolved by then. Was evaluated by Neurosurgery and Endocrinology, pituitary biochemical work up was within normal limits. Visual fields were normal.

**Discussion:** Apoplexy means sudden episode of impairment of cerebral function. Classical pituitary apoplexy refers to a clinical syndrome characterized by sudden onset of headache, vomiting, visual impairment and decreased consciousness caused by haemorrhage and or infarction of the pituitary gland. Macroadenomas tend to have increased risk. It is usually associated with hemorrhage, hemorrhagic infarction or bland infarction. Increased arterial blood supply and incomplete maturation of blood vessels have been attributed to increased risk of apoplexy. Common precipitating factor is hypertension. Other causes include head trauma, anti coagulants, dopamine agonists, cardiac surgery, pituitary dynamic testing and history of irradiation. Clinical manifestations depend on timing of the presentation and frequently occurs in an undiagnosed pituitary tumor. Manifests with Endocrine and or Neurological features and can mimic subarachnoid hemorrhage, bacterial meningitis or stroke. Neurological manifestations are due to rapid increase in size of the intra-sellar contents, leading to increase in the intra-sellar pressure. Common symptoms include sudden, severe headache usually retro orbital, ocular palsies, decreased visual acuity and visual field defects specifically bitemporal hemianopia, meningism, and cerebral ischemia. Pituitary hormonal deficiency with adrenocorticotroph hormone deficiency is more common than thyrotrophin and gonadotrophin deficiency. Low serum prolactin levels at presentation usually indicate high intrasellar pressure and indicate poor recovery from hypopituitarism after decompressive surgery.

**Conclusion:** Pituitary apoplexy is a clinical syndrome and not a radiological diagnosis. Asymptomatic pituitary haemorrhage and or infarction detected on routine imaging or during histopathological examination are not considered apoplexy unless they have neurological, endocrine or ophthalmologic features.

**Abstract #921**

**A SILENT CORTICOTROPH ADENOMA REVEALED BY SEVERE CUSHING’S DISEASE AFTER TWO PITUITARY SURGERIES**

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**Objective:** Subtypes of non-functioning pituitary adenomas who may differentiate into functioning adenomas are silent corticotroph adenomas (SCA). We present the rare case of a silent corticotroph macroadenoma which became hypersecreting after two pituitary surgeries.

**Case Presentation:** FG, a 50 years old man was twice operated for compressive non secreting pituitary macroadenoma (NFPA). After the first surgery he developed hypopituitarism and needed replacement therapy for all the hormonal lines. Several months after the second surgery he developed the clinical features of Cushing’s syndrome (CS). Hormonal dosages showed: high levels of cortisol without circadian rhythm, high level of ACTH and the lack of suppression at 1 mg overnight and high dose Dexamethasone suppression tests. The CT scans (thorax and abdomen) and the normal level of chromogranin A excluded an ectopic ACTH secretion and the final diagnosis was Cushing’s disease. The immunohistochemistry with ACTH antibodies of the previously resected pieces of the pituitary adenoma (Rb anti HuACTH polyclonal NIDDK in dilution 1/1500) showed parcelar positive staining, confirming the diagnosis of silent corticotroph adenoma. As the patient refused a third pituitary surgery, he was referred for conventional fractioned external beam radiation therapy, in a total
dose of 120 Gy in three consecutive cures, associated first with Cabergoline (3 mg/week), then with Ketoconazole (800 mg/day). As the high levels of cortisol recurred and the clinical evolution was severe, he was subjected to bilateral adrenalectomy. The pathological exam showed micronodular and diffuse hyperplasia of the cortical region of both adrenal glands. After surgery, a replacement therapy with Prednisone 7.5 mg/day and Fludrocortisone 0.1 mg/day was started. Consequent to adrenalectomy, the clinical features of CS improved progressively: 18 Kg weight loss, disappearance of the cushingoid habitus, normalization of the blood pressure, improvement of the biochemical parameters (glycaemia and serum lipids) and a better quality of life.

**Discussion:** The SCA represent only 4,6% of NFPAs and the transformation into an functional corticotroph adenoma is extremely rare. SCA are invasive, act more aggressive then NFPAs requiring repeated surgical procedures and radiotherapy. The mechanism of transformation of a previously SCA in Cushing's disease is not yet elucidated, but there are several hypotheses proposed.

**Conclusion:** We present the rare case of a silent corticotroph macroadenoma which became hypersecreting after two pituitary surgeries.

**Abstract #922**

**THE EXPLODINGHEADACHE OF MY LIFE**

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**Objective:** Pituitary apoplexy should be considered in a patient who presents with a sudden onset of headache, visual field abnormalities and ocular muscle paresis.

**Case Presentation:** 50 yrs old gentleman presented to the emergency in a state of altered consciousness of few hours. The patient's attendants gave a history that the patient had severe headache which was associated with several episodes of effortless vomiting and sudden vision loss. No history of headache anytime before this episode was elicited. On examination, patient was in altered consciousness (GCS= E2 V2 M4), blood pressure was 70/40 mm Hg, pulse rate - 100/min, thready and extremities were cold and clammy. On general physical examination fine wrinkles were noted around lateral margins of mouth and eyes (crow feet appearance), as well as the scantiness of hair all over the body, especially pubic hair, axillary hair and facial hair. The nipple areola complex was hypopigmented and gynaecomastia was present. Testicular volume was reduced to 10 cm3 along with soft consistency suggestive of secondary testicular atrophy. On ophthalmological examination, complete absence of vision in the left eye and temporal hemianopia in the right eye was noted. Bilateral pupils were non reacting and dilated. On investigations, RBS= 105mg/dl, S.Na =140 meq/l (135-150), Hormonal profile revealed reduced values of Serum FSH <0.66 mIU/ml (1.55-9.74), Serum LH <0.216 mIU/ml (1.8-7.8), Serum Testosterone (total) <0.170nmol/l (4.56-28.2) and Serum Prolactin= 2.2ng/ml (3.3-18.6), S.Cortisol = 70.4 nmol/l (123-626) and Serum TSH = 1.53 mIU/l (0.5-5.0). NCCT head revealed rounded mass of 2.2 X2.5 cm with peripheral rim calcification in suprasellar region with intrasellar extension. Contrast enhanced MRI showed a dumbbell shaped mass compressing the optic chiasma. The patient was given intravenous hydrocortisone, intavenous fluids and underwent urgent surgical decompression. Histopathology showed blood clots, fibrin, inflammatory cells, surrounding acidophilic cells suggesting pituitary prolactinoma with haemorrhage. A final diagnosis of macroprolactinoma with pan hypopituitarism with pituitary apoplexy with left secondary optic atrophy with right temporal hemianopia was made. Patient was started on appropriate hormone replacement therapy and continues to do well.

**Discussion:** Pituitary apoplexy is a rare but potentially life-threatening condition caused by either haemorrhage or infarction of the pituitary gland. Surgical intervention is needed in case of vision loss, ophthalmoplegia and altered sensorium.

**Conclusion:** Headache though ubiquitous in nature and perplexing for the clinician may have sinister implications and must not be treated lightly.

**Abstract #923**

**HIDING IN PLAIN SIGHT: MACROPROLACTINEMIA**

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**Objective:** Macroprolactinemia manifests with a predominance of higher molecular mass prolactin, >150kDa. The prevalence of macroprolactinemia in hyperprolactinemic populations has been reported between 15-46%. While clinical symptoms are less frequent in macroprolactinemic patients, they cannot be differentiated from true hyperprolactinemic symptoms.

**Case Presentation:** A 36-year-old woman with history of intermittent amenorrhea and elevated prolactin noted in 2002 presented for management of the same. She had an MRI brain at time of diagnosis, which did not show any pituitary abnormalities. She had been on bromocriptine
since time of diagnosis until her first pregnancy in December 2009. Her second pregnancy was in June 2011 and she stopped breast feeding August 2011. Both pregnancies were normal. She did report stress at home. She was restarted on cabergoline March 2012 but then lost to follow up for 1.5 years, during which time she was not compliant with medication. Menses had resumed in the interim, but she had developed galactorrhea. She had been on an OCP for 5 months, which she stopped 1 month prior to follow up. Thyroid function tests were normal since diagnosis. Prior to repeating workup for hyperprolactinemia, including repeat imaging, she was assessed for macroprolactinemia. Prolactin was checked via gel filtration (to remove macroprolactin) and found to be normal: 20.1ng/mL (Reference range: 2.8-26.0ng/mL). Due to the persistence of notable bothersome galactorrhea, she was continued on low-dose cabergoline.

**Discussion:** Some medications can raise prolactin, including estrogen and H2 blockers but this patient's prolactin was elevated long before the birth control pill was started. Stress is also reported to raise prolactin levels but they would not be expected to remain constantly elevated as in this patient. While clinical signs and symptoms of elevated prolactin are not common with macroprolactinemia, they are present in this patient. It is remarkable that she developed various manifestations of elevated prolactin, yet retained fertility. Her prolactin level never rose over 100-110ng/mL as would be expected with a prolactinoma, though she was off medication for a prolonged period, which led us to suspect macroprolactinemia.

**Conclusion:** Though macroprolactinemia is not common, it is important to recognize this entity as a possibility when working up hyperprolactinemia, especially in those patients with negative imaging and prolactin levels that do not change in the absence of treatment.

**Abstract #924**

**ECTOPIC ACTH SECRETING PITUITARY ADENOMA WITHIN THE SPHENOID SINUS**

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**Case Presentation:** A 38-year old woman reported weight gain, hirsutism and bruising. Clinically she appeared ‘classically’ cushingoid. Investigations revealed 24 hour urine free cortisol of 278 µg (0-50), ACTH 121 pg/ml (6-48); 8am serum cortisol of 17 µg/dL and 14 µg/dL after 1 mg overnight and 2 day low dose dexamethasone suppression test (DST), respectively. There was >50% decrease in serum cortisol after an overnight high dose (8mg) DST. The sella appeared normal with no pituitary mass present on magnetic resonance (MR) imaging. Computed tomographic (CT) scan of chest, abdomen and pelvis was unremarkable.

Inferior petrosal sinus sampling (IPSS) did not demonstrate a significant central to peripheral (C/P) ACTH ratio, of either 2:1 before, or 3:1 after administration of CRH. The test was interpreted as non-diagnostic due to the lack of proper IPS catheterization based on a C/P ratio of <1.3 for prolactin. ACTH response to CRH in peripheral blood during IPSS was > 50%. CT of the head revealed an incidental lesion in the right sphenoid sinus which was also present on MR imaging and felt to be an incidental polyp. Considering the picture as a whole, with corresponding absence of any abnormality on chest, abdomen and pelvis imaging we elected to operate.

Two small (3-4 mm) pseudo-encapsulated lesions on the right side of the pituitary were removed which were negative for a corticotroph adenoma. A soft polypoid 5 mm lesion in the inferior aspect of sphenoid sinus was identified, removed and demonstrated ACTH positivity on immuno-histochemical staining. The patient developed hypocortisolism post-operatively (nadir cortisol of 1.3 µg/dL) at 48 hours after surgery. At 44 months post-surgery, she remains in remission.

**Discussion:** Ectopic corticotroph adenomas are a rare but important cause of ACTH-dependent hypercortisolism. They are especially important in the setting of patients with ‘MR-negative’ Cushing’s disease or in patients in whom surgical exploration of the sella has not induced biochemical remission. In our experience over the past 9 years, performing surgery on 115 patients with biochemically-defined Cushing’s disease, we have had 2 cases of ectopic ACTH adenomas located solely within the sphenoid, for an incidence of 1.7%.

**Conclusion:** Ectopic corticotroph adenomas can be a diagnostic challenge in patients with Cushing’s disease; failure to recognize one may lead to a sellar exploration that fails to find an adenoma and induce disease remission. The presence of a sphenoid ‘polyp’ as an etiology of ACTH-dependent hypercortisolism should prompt the clinician not to overlook this often regarded ‘incidental’ radiological finding.
Abstract #925

APOPLEXY OF RCC- AN UNCOMMON OCCURRENCE THAT MIMICS PITUITARY APOPLEXY

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Einstein Medical Center

Objective: Rathke's cleft cysts (RCC) are congenital, non neoplastic cysts that are asymptomatic in the majority of patients. RCC apoplexy is a rare complication and a fairly new entity that has been underdiagnosed in the past. Further the clinical presentation mimics the syndrome of pituitary apoplexy. Here we report a patient acutely presenting with pituitary apoplexy-like picture who was found to have RCC hemorrhage on follow up.

Case Presentation: A 29 yr/o African American gentleman presented with the worst headache of his life. Physical examination revealed normal visual fields and acuity and a nonfocal neurological exam. The patient had a CT head which showed a hyperdense 12mm sized sellar lesion. MRI revealed a 1.5 *1.7 *1.3cm sellar mass with homogenously increased T1 and T2 signals without contrast enhancement. The patient was managed conservatively for pituitary apoplexy. Hormone analyses revealed low TSH, low T4 and low testosterone levels. All other hormones were within normal limits. Patient declined surgical intervention. The patient was started on thyroxine and testosterone replacement therapy and was closely followed. Over the following months he came off of all replacement therapies and all hormonal assays have since been within normal limits. Repeat MRI revealed a Rathke's cleft cyst with hemorrhagic debris in it, found to be compressing on the pituitary tissue.

Discussion: Rathke cleft cysts are benign congenital remnants of the Rathkes pouch found in about 15 to 22% of routine autopsies. Most RCCs are asymptomatic. Common symptoms are headache, visual disturbances or mild endocrinopathies from suprasellar extension/compression. Hemorrhage into RCC is a relatively rare occurrence. No specific precipitating factors have been defined. Patients with RCC apoplexy tend to present with sudden onset severe headache and visual disturbances just as pituitary apoplexy but certain distinguishing features have been described. RCC hemorrhages tend to produce smaller mass lesions, less severe symptoms and have lower prevalence of pituitary dysfunction. Important radiological features include hyperintense T1 and T2 signals, nonenhancing wall and a pathognomonic intracystic nodule seen in 70% of cysts. The ultimate diagnosis is given by surgical removal and pathological examination.

Conclusion: RCC hemorrhage is a close mimic of pituitary apoplexy and needs to be considered in the differential diagnoses of sellar masses. Management is similar to pituitary apoplexy. Prudent radiological and clinical examination can help differentiate the two while pathological analysis provides the definitive diagnosis.

Abstract #926

DIABETES INSIPIDUS: A RARE COMPLICATION OF ACUTE MYELOID LEUKEMIA

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Case Presentation: A 19-year-old woman presented to the ER with 24 hour history of fevers and bilateral axillary lymphadenopathy. Initial lab investigation revealed hemoglobin 9.2 g/dL, platelets 146 K/uL, and white cell count 3.4 K/uL with a neutrophil count of 0.03 K/uL. Circulating blasts (15%) were identified on peripheral smear. Bone marrow aspiration confirmed the diagnosis of acute myeloid leukemia (AML). Cytogenetic studies of bone marrow aspirate demonstrated trisomy 13 (in a setting of near tetraploidy). A staging MRI of the brain showed no structural abnormalities. Patient underwent induction 7+3 regimen with idarubicin and ara-C. Clinical course was complicated by neutropenic fevers, mucositis and oral ulcers. Because of the latter, the patient had reduced oral intake and rapidly developed hypernatremia up to 171 mOsm/L (from admission serum Na of 138 mmol/L) with serum osmolality of 354 mOsm/kg and urine osmolality of 155 mOsm/kg. Urine output was 5-6 L/day. Clinical and laboratory data was consistent with diabetes insipidus (DI) and, in retrospect, the patient reported polydipsia and polyuria for two years. She was treated with IV hypotonic fluids with resolution of the hypernatremia. Two weeks after the onset of hypernatremia, the patient reported weakness on her right side. Repeat MRI of brain showed abnormal signal intensity within the pons suggestive of osmotic demyelination syndrome. Bone marrow biopsy performed 14 days after induction of chemotherapy showed no blasts. A water deprivation test conducted 4 weeks after the induction chemotherapy showed resolution of DI. She continued to be in remission with no clinical symptoms of DI.

Discussion: Little is known about the pathogenetic mechanisms involving the rare occurrence of DI in AML. While some patients have leukemic infiltration of the neurohypophysis on MRI, others have no such structural abnormalities. Karyotype abnormalities involving chromosome 7, 20 and 3 have been associated with AML and DI (monosomy 7, monosomy 20 and 3q21q26).
Several potential mechanisms have been postulated that may predispose these patients to DI: abnormal expression of neutrophil migration gene in monosomy 7 cases, abnormal thrombocytosis seen in 3q21q26 interfering with DDAVP level or function, and overexpression of EVI-1 gene in 3q21q26. DI has not been reported with trisomy 13 in AML. This rare cytogenetic abnormality has been associated with dedifferentiation of blast cells and poor prognosis. 

**Conclusion:** Since DI often precedes the diagnosis of AML and may not be associated with structural abnormalities on MRI, a complete blood count should be considered in patients with central DI without obvious cause.

**Abstract #927**

**AN UNUSUAL CAUSE OF SECONDARY ADRENAL INSUFFICIENCY**

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**Case Presentation:** A 54 year old female with a history of idiopathic premature ovarian failure at age 30, with no pituitary imaging at that time, and post-ablative hypothyroidism from Graves’ disease was admitted with hypotension, tachycardia, and acute kidney injury. Previously, she had required 3 medications for management of hypertension and reported unintentional weight loss over the past months. A cortisol stimulation test done in the afternoon showed a baseline cortisol of 1.6 mcg/dL with stimulation to 8.3 mcg/dL. Pituitary labs revealed an adrenocorticotrophic hormone of 11 pg/mL (0-46 pg/mL) with paired cortisol of 2.1 mcg/dL, free thyroxine of 0.9 ng/dL with thyroid stimulating hormone (TSH) of 0.031 microU/mL, follicule-stimulating hormone of 6 mU/mL with estradiol of <20 pg/mL, insulin-like growth factor of 72 ng/mL (53-191 ng/mL) and prolactin of 58 ng/mL. Imaging showed a fusiform, left internal carotid artery cavernous aneurysm measuring 21 x 11 mm with expansion into the sella causing displacement of the pituitary gland and involving the origin of the left ophthalmic artery. She was treated with stress dose steroids before undergoing craniotomy with clipping and bypass of the aneurysm and involving the origin of the left ophthalmic artery. She was treated with stress dose steroids before undergoing craniotomy with clipping and bypass of the aneurysm. Post-operatively, she developed blindness of her left eye, thought to be due to the aneurysm and/or surgical repair. Notably, she had an intact adrenal axis upon testing six months post-operatively, with adrenocorticotrophic hormone of 58 pg/mL and paired cortisol of 13.4 mcg/dL. She is now off corticosteroids.

**Discussion:** Internal carotid aneurysms causing hypopituitarism have been reported in a small number of case reports in the literature. In the only larger study of this condition, the prevalence of hypopituitarism due to an intrasellar aneurysm was 0.17%. In this retrospective review, none of the patients had recovery of pituitary function. Notably, our patient did have recovery of her adrenal axis. In retrospect, we hypothesize that the etiology of her premature ovarian failure was secondary hypogonadism. The patient's development of secondary hypothyroidism could have caused inappropriate dosing of levothyroxine since TSH was being used to guide adjustments.

**Conclusion:** Internal carotid aneurysms are a rare cause of hypopituitarism. In the scant literature covering this topic, hypopituitarism is typically permanent. Our patient had recovery of her adrenal axis after surgical repair of her aneurysm, underlying the importance of reassessment of adrenal function post surgically in these patients.

**Abstract #928**

**COCAINE INDUCED PITUITARY APOPLEXY AND PANHYPOPITUITARISM**

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**Objective:** Chronic cocaine use has been implicated in panhypopituitarism. Acute cocaine intoxication resulting in pituitary apoplexy and panhypopituitarism has not been reported in literature.

**Case Presentation:** A 54 year old African American gentleman presented to the emergency room with the onset of headache 2 hours after snorting a gram of cocaine and ongoing since 1 week. Headache was described as severe, throbbing, in the right parieto-occipital area radiating to the entire head; not relieved with Ibuprofen. There was associated dizziness and difficulty ambulation. His physical exam was normal. His labs revealed a failed pituitary-thyroid axis:TSH 0.196(0.4-5mcU/mL), Free T4 0.61(0.8-1.8 ng/dl); a failed pituitary-adrenal axis: AM cortisol <0.8(4-20 mcg/dl), ACTH <1.1(7.2-63.3 pg/ml), cortisol 30 minutes and 1 hour post 250 mcg Cosyntropin were 9.5, and 11.2 mcg/dl respectively; a failed pituitary-gonadal axis: LH 0.3(1-8 mu/ml), Testosterone <20(300-1200 ng/dl), SHBG 40.2(19.3-76.4 nmol/L) and low prolactin levels of 1(0-17ng/ml). ANCA (Anti-Neutrophil Cytoplasmic Antibodies) were negative. Enhanced MRI of Brain showed a large complex sellar mass 2cm x 2.2 cm with hemorrhagic components and partial erosions of the dorsum and floor with mild suprasellar and parasellar extension into cavernous sinus regions. Surgical decompression was deferred due to normal visual acuity and absent visual field defects. He received stress dose of glucocorticoids followed by maintenance dose and discharged on it with levothyroxine replacement. The patient has been lost to follow up.
Discussion: We hereby report a case of panhypopituitarism resulting from pituitary apoplexy induced by single intra-nasal cocaine use. While the association of cocaine use with myocardial infarction and stroke has been well described, pituitary apoplexy and panhypopituitarism resulting most likely from severe vasoconstriction of hypophyseal vessels need special mention. Panhypopituitarism associated with chronic cocaine use is rare with only two cases reported to date, one with human neutrophil elastase anti neutrophil cytoplasmic antibody (HNE-ANCA) associated granulomatous pituitary inflammation associated with CIMDL (Cocaine induced midline destructive lesions) and pituitary necrosis without apoplexy in the other case.

Conclusion: We suggest that the diagnosis of cocaine induced pituitary apoplexy should be considered in subjects presenting with severe headaches after cocaine inhalation.

Abstract #929

NSAID-INDUCED SYMPTOMATIC, SEVERE HYponATREMIA IN A PATIENT WITH DIABETES INSIPIDUS

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Case Presentation: Patient is a 46 yo F with h/o DI, who presented to the ER for evaluation of AMS, abdominal discomfort for 3 days. Patient has had DI for 16 years for which she was on nasal DDAVP but switched to PO. Patient states recently she had been drinking a lot of water to try to relieve her constipation. At the same time, patient has also been taking Pamprin, which contains naproxen, for her back pain. Physical Exam was notable for mild epigastric tenderness to palpation. CT A/P and MRI brain were unremarkable. Chemistry was notable for Na of 117 and the rest of laboratory was unremarkable, including normal TFTs and lipid profile. Urine osmols were 396 and serum osmols were 237. Patient was admitted to hospital for treatment of Symptomatic hyponatremia. She was initially put on 800 ml fluid restriction and her DDAVP was held, but Na stayed the same. Therefore, she was started on 3% NS at 50 cc/hr x 2 hours and Na increased to 123. Patient also diuresed well and output increased to about 6500cc throughout admission. On last day of hospitalization, Na was 130 and patient was discharged on desmopressin 100 mcg nasal spray BID. Patient's HA, nausea, and dizziness improved and constipation was relieved with enema.

Discussion: ADH works by increasing production of renal prostaglandins, which then work by negative feedback blocking ADH hydroosmotic and vascular effects. When someone takes NSAIDs, it blocks the inhibitory prostaglandin effect, leading to increased ADH induced water reabsorption. This results in a reduction of plasma Na+ concentration. Normally, the fall in serum Na will diminish ADH secretion and decrease water retention, however in patients with non-suppressible ADH release such as volume depletion or SIADH, there is no negative feedback, creating worsening hyponatremia. In our patient with central diabetes insipidus, she was taking Pamprin, containing naproxen for her back pain. This medication blocked her prostaglandin production, reducing her free water excretion, which normally would be balanced out by a decrease in ADH release. However, she was also taking DDAVP which acted similarly to non-suppressible ADH release, worsening her hyponatremia and leading to her presenting symptoms, which all resolved with temporary holding desmopressin and correction of her hyponatremia.

Conclusion: NSAIDs can lead to hyponatremia, but in a patient with Central Diabetes Insipidus on DDAVP, it can worsen the hyponatremia to critical levels.

Abstract #930

REGIONAL PHEOCHROMOCYTOMA: CASE PRESENTATION IN A YOUNG FEMALE

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Case Presentation: A 31 year-old female with a medical history of newly diagnosed hypertension and Type 2 Diabetes Mellitus presented with significant, unintentional loss of weight of 1 year's duration, associated with paroxysmal symptoms of palpitations, diaphoresis and flushing. Differential diagnoses considered in this young, non-obese lady included a pheochromocytoma, thyrotoxicosis, and occult malignancy. Biochemical evaluation revealed elevated levels of urine catecholamines and metanephrines, 35-70 times the upper limit of normal. CT (Computer Tomography) Abdominal Pelvis showed a 9 x 8.7 x 7cm mass lesion with necrosis arising from the left adrenal gland. She was managed pre-operatively with Phenoxybenzamine and Atenolol as for a left pheochromocytoma, and underwent an open left adrenalectomy.

Discussion: In this young patient, there was no family history of paragangliomas, and no associated features of familial syndromes such as Von Hippel-Lindau syndrome, MEN 2 (Multiple Endocrine Neoplasia), or Neurofibromatosis Type 1. In view of the large tumour size and the presence of tumour necrosis, there was an index of suspicion for a malignant pheochromocytoma. A 2-centimetre liver lesion was seen on initial CT
staging scans, which was further characterised on MRI (Magnetic Resonance Imaging) to be a simple liver cyst. A benign, subcentimetre right lung nodule was also found. Unfortunately, histopathological analysis revealed a pheochromocytoma with regional disease. There was invasion of a vein, and 1 out of 6 lymph nodes sampled. Post-adrenalectomy, a repeat 24-hour urine specimen for catecholamines/ metanephrines showed persistent mild elevation: Urine Norepinephrine 576nmol/day (72-505), Urine Normetanephrines 2698nmol/day (480 - 2424). An MIBG (metaiodobenzylguanidine) scan was negative for distant metastasis. 

**Conclusion:** This young female will require lifelong surveillance for tumour recurrence. In view of an initial negative MIBG scan, other modalities of surveillance could include an In-111 octreotide or 18F-fluorodeoxyglucose positron emission tomography (PET) scan, which is currently not available at our centre. 

**Abstract #931**

**SLIPPED CAPITAL FEMORAL EPIPHYSIS WITH GROWTH HORMONE DEFICIENCY TREATED WITH GH.**

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**Objective:** To demonstrate that slipped capital femoral epiphysis (SCFE) caused by Growth hormone (GH) deficiency can be successfully treated with GH after surgical fixation.

**Case Presentation:** hypothyroidism, growth hormone supplementation, hypogonadism, and panhypopituitarism can cause SCFE. Obesity and adolescent age are other predisposing factors.

Orthopedical side effects can occur with GH therapy. SCFE, Legg-Calvé-Perthes disease, carpal tunnel syndrome and scoliosis have been reported in a large number of children treated with GH.

A 13 years young boy who was on adequate Thyroxine since last two years, was brought for poor linear growth (Growth rate velocity - 4.0 cm per year), He had acanthosis nigricans, weight more than 95th centile and height less than 5th centile. IGF-1 - 65 ng/ml, found to have peak GH of 1.78 ng/ml at 120 minutes with Glucagon stimulation. Gd enhanced MRI showed a hypoplastic pituitary. Other biochemical and hormonal parameters were unremarkable. Bone age was 12 years. He was started with GH therapy at a dose of 0.03 mg/kg/day. After about 3 months of GH therapy the child had recurrent pain in left hip joint with a limp in gait. This was diagnosed as SCFE and GH was stopped and it was treated with screw fixation. The parents later revealed that this kind of pain was also present even one month before starting GH however as it was not so severe and there was no limp so it was ignored. But symptoms worsened after the GH therapy. After 6 months of surgery, GH was restarted. The GRV increased to 9 cm per year with GH. Presently the child is doing well on GH, Thyroxine and supportive therapy. A close watch is kept on the other hip joint which will be prophylactically fixed in near future.

**Discussion:** GH deficiency and GH therapy both can produce SCFE. The adolescent age, obesity and hypothyroidism have also contributed. This case demonstrate this unique situation where GH deficiency led to SCFE which was treated with GH successfully.

**Conclusion:** Hence before starting GH, SCFE must be suspected in a child who complaints of hip pain. It should be treated surgically first and then GH can be given. If a previously normal child develops hip pain while on GH therapy, SCFE should be ruled out and GH should be withdrawn as continuation of GH may worsen it. In this situation also GH can be restarted after surgical fixation.

**Abstract #932**

**A RARE CASE OF PROLACTINOMA AND HYDROCEPHALUS FROM AQUEDUCT STENOSIS PRESENTING AS ACUTE PSYCHOSIS IN AN AFRICAN AMERICAN MAN**

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**Objective:** To present a rare case of prolactinoma with compensated hydrocephalus (CH) from aqueduct stenosis presenting as acute psychosis.

**Case Presentation:** 47 year old African American man with no significant past medical or surgical history was brought in by family for bizarre behavior (delusions, hallucinations, social withdrawal, aggression and a lack of personal care) for 2-3 months. On examination, he appeared disheveled, visual exam was normal for field of vision and had no gait abnormalities. Other systems were normal. CT scan of head showed CH with aqueduct stenosis. MRI of brain with contrast enhancement additionally showed a pituitary adenoma of 1.5 x 1.6 cm. Endocrine evaluation disclosed an elevated prolactin of 1219 (3-18 ng/ml), ACTH was 18 (7.2-63.3 pg/mL), IGF-1 was 226 (121-237 ng/ml), a total
A 47 year old man presented with this is a rare case of prolactinoma and review of the literature reveals a single case of hyperprolactinemia and psychosis are two disorders of the pituitary should be considered as a potential etiology for psychosis or just a silent bystander. Dopamine agonist is used in the former while dopamine antagonist in the latter. It is important to observe that not all elevations in prolactin can be explained by reciprocal changes in dopamine secretion. Not much is known about the interactions between dopamine and other chemicals that stimulate prolactin, generally known as prolactin releasing factors. It is unclear in our case if CH was also a potential etiology for psychosis or just a silent bystander.

**Conclusion:** This is a rare case of prolactinoma and hydrocephalus from aqueduct stenosis presenting as acute psychosis. For patients with prolactinoma and psychosis, the endocrinologist and psychiatrist should work together to monitor tumor size, serum prolactin levels, and adherence to antipsychotic medication. There is a theoretical risk of psychiatric decompensation with dopamine agonists. Aripiprazole might be a rational choice as a first-line antipsychotic agent in such patients. Disorders of the pituitary should be considered as a differential in the work up of patients with atypical psychotic presentation.

**Abstract #933**

**MASSIVE CORONARY ANEURYSMS, AN UNUSUAL FINDING IN ASSOCIATION WITH ACROMEGALY**

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Tulane-BRG

**Objective:** The existence of pathologic vascular changes associated with acromegaly are well supported by the literature. We describe a case of an acromegalic man who presented with ST elevation MI and massive coronary aneurysms.

**Case Presentation:** A 47 year old man presented with 30 min of substernal chest pressure radiating to his left shoulder, shortness of breath and diaphoresis. PMH includes acromegaly diagnosed at 37. PSH includes transsphenoidal resection of pituitary adenoma. PE revealed an anxious man with protruding supra-orbital ridges and coarsened facial features. EKG showed 4-5 mm of ST elevation in V2-V5. Troponin was normal. Coronary angiography was notable for a 29 X 70 mm proximal-mid LAD aneurysm, beyond which the coronary vasculature could hardly be visualized. A 15mm dia RCA aneurysm and a 13 mm dia left circumflex aneurysm were seen without evidence of arteriosclerosis. Lacking a target for stent placement, the patient was admitted in ICU and was treated with aspirin, clopidogrel and low molecular weight heparin. Coronary CT angiogram confirmed the previously described aneurysms, and showed lack of flow distal to the LAD aneurysm, intact flow through the RCA and circumflex artery, and an anomalous take off of the LAD proximal to the aneurysmal lesion. CT angiography of the patient's head, thoracic aorta, abdominal aorta and femoral arteries showed no evidence of aneurysmal disease. He was discharged to cardiology follow up with an EF of 40%.

**Discussion:** Review of the literature reveals a single case of peripheral femoral aneurysm in a patient with acromegaly. Although there is a strong correlation between acromegaly and intracranial aneurysms, our patient presented with coronary aneurysms so it is interesting to know if both are related or if this rare coronary aneurysm is a separate entity in itself. This patient lacked the major risk factors for aneurysmal disease. Coronary imaging showed no evidence of atherosclerosis. He had no history of Kawasaki's disease, vasculitis, Ehlers Danhos, or Marfans syndrome, which represents the vast majority of non atherosclerotic coronary aneurysms. This patient's coronary ectasia is unusual in both its extent throughout the coronary vasculature, as well as the magnitude of coronary dilatation when compared to other cases of coronary ectasia. In summary, we describe a case of an acromegalic man presenting with anterior MI secondary to thrombosed massive LAD aneurysm.

**Conclusion:** Such a unique case is striking in light of the correlation between acromegaly and intracranial aneurysm, and raises the possibility that acromegaly can be associated with coronary aneurysms.

**Abstract #934**

**CUSHING'S SYNDROME RESULTING FROM A BRONCHIAL CARCINOID TUMOUR IN A YOUNG NIGERIAN MALE.**

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University of Benin Teaching Hospital

**Objective:** To report a rare case of Cushing's syndrome resulting from bronchial carcinoid tumor.

**Case Presentation:** A 25 year old presented in our clinic with a history of weight gain of 2 years duration with associated increased appetite and 1 year history of...
progressive breathlessness and exertional dyspnea. There was no history of paroxysmal nocturnal dyspnea, cough or palpitations. He also developed polyuria, polydipsia with nocturnal diarrhea. He had no past history of diabetes mellitus and there was no history of steroid or alcohol use. Physical examination revealed a young man with hyper-pigmentation of the knuckles and multiple violaceous striae on both arms, trunk with few punctuate spots on the trunk. His weight was 102kg, height- 1.94m, BMI - 27.1 waist circumference - 105cm, hip circumference - 109cm. He had a pulse rate of 76bpm, regular normal volume; blood pressure was 130/80mmHg. Investigations done showed hypokalaemia (2.0 mmol/L) and hyponatraemia (128mmol/L) respectively. Impaired glucose tolerance and a normal fasting serum lipid. 24 hour urinary free cortisol was 38.75µg/dl (ref<50µg/dl). Cranial computer tomography scan was normal. He was admitted a month after presentation and managed for congestive cardiac failure secondary to uncontrolled hypertension in NYHA class IV precipitated by a right lobar pneumonia in a patient with Cushing's syndrome. At this time further evaluation could not be carried out because of our limitations. He opted to seek further treatment in the United Kingdom. At presentation, in the A&E department (in UK), his random cortisol was 1846nmol/L, ACTH 278.5ng/l and a 24hr urinary free cortisol excretion of 6421nmol/24hrs (all values were elevated). An MRI of the pituitary was unremarkable. An Octreotide SPECT showed high selective uptake of a solitary focus in the right lower lung zone, this was done after a chest CT showed nodules in the right lung zone. A diagnosis of Cushing's syndrome secondary to an ACTH secreting bronchial tumour was made. The tumor was removed and he recovered subsequently. He was discharged home 3 months later.

**Discussion:** We had challenges in identifying the source of cortisol in this patient as appropriate investigations could not be done due to the non-availability of the laboratory tests in a underdeveloped country.

**Conclusion:** Cushing’s syndrome resulting from bronchial carcinoid in the young is quite rare, though it is more common in males. Age of occurrence is usually between the ages of 40-60 years. In this case, the patient was 25years and has no history of smoking. A high index of suspicion is necessary to make such a diagnosis in this age group.

**Abstract #935**

**USE OF BROMOCRIPTINE FOR NON-FUNCTIONING PITUITARY ADENOMA DURING PREGNANCY**

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The University of Texas Medical Branch

**Objective:** Management of pituitary macro-adenoma during pregnancy may be clinically challenging, independently of tumor's functional status. In addition to potential tumor growth, pituitary enlargement due to lactotroph hyperplasia may displace macro-adenoma and result in compressive symptoms that compromise maternal and fetal well-being. We describe a case of a non-functioning pituitary macro-adenoma managed conservatively with bromocriptine throughout pregnancy.

**Case Presentation:** A 25 year old Hispanic female, G3P2A0, presented to the emergency room 8 weeks into her pregnancy with recurrent severe frontal headaches, nausea and vomiting. Patient had no symptoms suggestive of pituitary hormone deficiency or excess. Patient had been evaluated at an outside hospital 10 weeks prior for a complaint of severe headache; a 7 mm pituitary adenoma was found on brain MRI. She was hemodynamically stable and the remainder of her physical exam was unremarkable. Brain MRI without contrast was obtained and revealed a 1.8 x 1.3 x 1.0 cm sellar mass that extended into the right suprasellar region with optic chiasm impingement. Anterior pituitary hormones were evaluated: TSH: 0.35 mIU/mL, Free T4: 1.13 ng/dL, Prolactin:40.4 ng/mL, IGF 1: 65 ng/mL, LH: 0.34 mIU/mL, FSH: <0.2 mIU/mL. Serum cortisol increased from 13.8 to 37.6 mcg/dL after 250 mcg intravenous cosyntropin. Formal visual field testing was normal. Multidisciplinary team discussions recommended conservative management. Since pituitary macro-adenoma was impinging on the optic chiasm, bromocriptine 2.5 mg a day was started to prevent pituitary growth and possible displacement of the macro-adenoma. The patient tolerated the bromocriptine well and reported an improvement in her headaches. She had no visual complaints during gestation. Patient had a spontaneous vaginal delivery at 35 weeks and had no post partum complications.

**Discussion:** During pregnancy the pituitary gland increases in size by 100 - 130 % mainly due to lactotroph hyperplasia. Resulting tumor growth may displace the pre-existing macro-adenoma towards the optic chiasm and result in compressive visual defects. Dopamine agonists do not affect the original tumor size but can prevent lactotroph hyperplasia and tumor displacement. Our patient likely benefited from the effect of bromocriptine on pituitary enlargement.

**Conclusion:** Current guidelines for management of non-functioning pituitary macro-adenoma suggest transsphenoidal surgery if patient has visual field defects, optic chiasm compression or severe headaches. Use of dopamine agonists may prevent physiological growth of the pituitary gland and postpone need of neurosurgical intervention during pregnancy.
Abstract #936

ACROMEGALIC “ADENOMIA” PRESENTING AS DYSPHONIA

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Objective: Acromegaly, with an incidence and prevalence of 3 and 60 cases per million tends to presents insidiously. We describe a case of a 59-year-old woman who presented with dysphonia.

Case Presentation: A 59-year-old woman with a medical history of hypertension, hyperlipidemia and diabetes mellitus presented with deepening of her voice. She reported widening of her hands and feet for five years as well as an enlarged tongue, intermittent headaches and blurry vision. Physical exam significant for left eye temporal hemianopsia, frontal bossing, widen nose, macroGLOSSIA and bilateral enlarged hands and feet. MRI of the head revealed a 1.7 x 3.3 x 2.9 cm mass expanding the sella and compressing the optic chiasm. Growth hormone (GH) returned at 149 mg/mL with an insulin-like growth factor (IGF-1) level of 1123 ng/mL. Transsphenoidal resection was performed with improvement of vision the following morning. Three days later, GH and IGF-1 were 3.6 mg/mL and 564 ng/mL respectively. Immunohistochemistry for GH was positive.

Discussion: GH, secreted by the pituitary gland stimulates the liver to secrete IGF-1, with both hormones primarily effecting skin and connective tissue growth. Acromegaly may present subtly with headache, jaw prognathism and acral enlargement or overtly with cranial nerve defects, congestive heart failure and cardiac/respiratory failure. Overgrowth of skull, facial bones and cartilage may result in frontal bossing, prognathism, enlarged facial features as well as deepening of the voice. Vocal changes are typically described as lowering of frequency. Williams et al described 14 patients undergoing hypophysectomy, eight whom had acromegaly. These patients had a lower mean fundamental frequency, which rapidly increased postoperatively.

Although dysphonia is only one of the potential subtle presentations of acromegaly, it is important to note that the average time to diagnosis is 10 years after the onset of symptoms. Patients may present to a variety of healthcare providers including an ophthalmologist with visual complaints, a dentist with jaw pain or a gynecologist with menstrual irregularities. Early diagnosis and treatment is imperative due to the significant complications.

Conclusion: We described a case of a 59-year-old woman who was brought to medical attention when her voice changed. Acromegaly if identified and treated early has high cure rates. Although there is a 2 to 2.5 times increased mortality, this has been attributed to the co-morbidities associated with condition. As our medical society becomes more specialized, it is important not only to focus on individual medical conditions but also to realize sometimes there may be an underlying “giant” problem.

Abstract #937

GROWTH HORMONE THERAPY IN A CHILD WITH GERMINOMA: A FATAL CASE REPORT

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Objective: Our objective was to describe the fatal event associated with growth hormone (GH) therapy due to delayed diagnosis of sellar germinoma.

Methods: We describe a 12 year old girl with panhypopituitarism and diabetes insipidus (DI) due to sellar germinoma.

Case Presentation: 12 year old girl presented with polyuria, polydipsia and nocturia and failure to gain height. There was no headache, visual problem or recurrent vomiting. There was history of trauma before the onset of symptoms due to accidental fall without loss of consciousness. Her hormonal profile showed: estradiol 26pg/ml, cortisol 2.78µg/dl, prolactin 17.5ng/ml, LH 0.50 miu/ml, FSH 0.30miu/ml, IGF-1 25ng/ml and urine osmolality 169 mosm/kg. Her bone age was 5 year and 9 months. GH stimulation test was not done at that time. She was diagnosed as DI and panhypopituitarism. MRI sella showed stalk thickening with non-visualisation of posterior pituitary bright spot. She was treated with hydrocortisone, thyroxine, GH and vasopressin nasal spray. One year later, she attended another endocrinologist and was re-evaluated. She had gained 10cm in the preceding year. Glucagon stimulation test confirmed GH deficiency. She was continued on GH(4.3 units daily). Repeat MRI was not done. One more year later, she presented with loss of vision on one eye. Repeat MRI sella showed sellar and suprasellar lesion of size 4x4x3cm. She underwent tumor excision which was reported as germinoma. She later underwent radiotherapy and few days post-radiotherapy, she expired.

Discussion: The indications and use of GH therapy are increasing worldwide. The potential adverse events include development of leukemia, recurrence of central nervous system tumors, and other minor side effects like edema, arthralgia, etc. The absolute contraindications
are active malignancy, retinopathy and uncontrolled diabetes mellitus. A study published in JCEM (1997) stated normal brain MRI scans that show isolated pituitary stalk thickening merit follow-up with serial brain MRI for early detection of an evolving occult hypothalamic-stalk lesion. Williams textbook of endocrinology also stated that MRI should be repeated every 3 to 6 months, especially in children, in whom enlargement may indicate germinoma. Failure to diagnose this malignant disease earlier had resulted in the initial 2mm stalk thickening growing in to an invasive 40 mm size lesion following GH therapy.

**Conclusion:** Any child presenting with DI and stalk thickening should be suspected of germinoma and have an MRI sella done for the same and if initial MRI is normal, repeat imaging every 3 months is needed. GH therapy is lethal in such a presentation.

**Abstract #938**

**ATYPICAL PRESENTATION OF PITUITARY APOPLEXY**

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**Case Presentation:** Pituitary adenomas are a common cause of intracranial neoplasms. They can be classified as microadenomas if <1.0cm or macroadenomas if >1.0cm. Pituitary apoplexy is a condition presenting most commonly as sudden onset headache, visual disturbances and confusion due to hemorrhage of a pituitary tumor. We present a case of a patient who did not have the classical presentation but rather presented with nausea, vomiting and confusion.

A 63 year-old Vietnamese male with a PMH of Hemoglobin E-beta thalassemia presented with a 5-day history of nausea, vomiting, generalized weakness, and confusion. He denied headaches, changes in vision or hearing, chest pain, shortness of breath, abdominal pain, diarrhea, urinary symptoms, neurologic deficits, sick contacts, tobacco, alcohol and illicit drug use. Vitals on admission BP 87/58, P 76, RR 12, Temp 98.2. Physical exam revealed a lethargic appearing gentleman but was otherwise normal. Labs included Na 104 mmol/L, K 3.9 mmol/L. CT head showed a 14 x 15 x 16 mm pituitary macroadenoma without evidence of acute bleed or infarct. MRI demonstrated a 15mm x 18mm hemorrhagic pituitary adenoma. Hormonal investigations included cortisol 1.28 ug/dL, ACTH 52 pg/mL, TSH 0.180 uIU/mL, FT4 0.89 ng/dL, LH 0.92 mIU/mL, FSH 2.7 mIU/mL, IGF <25 ng/mL, and prolactin 12.7 ng/mL consistent with a nonfunctioning adenoma. Blood pressure and electrolytes improved with glucocorticoid and mineralocorticoid therapy. Over the subsequent days, he became abulic, non-verbal but alert, with new onset rigidity of his extremities and posture. Work-up including LP, EEG, blood and urine cultures was unrevealing. Repeat CT and MRI were unchanged and not suggestive of central pontine myelinolysis. Visual fields were grossly normal but he could not interact sufficiently to undergo formal visual field testing. Given the significant change in neurological status, transphenoidal pituitary resection was performed. Surgical biopsy showed a pituitary adenoma with hemorrhage and hematoma. His mental status improved and was discharged to a short-term rehab facility.

**Discussion:** Pituitary apoplexy, although an uncommon event, is potentially life threatening. The reported incidence of pituitary hemorrhage ranges from 10 to 27%. Manifestations in patients vary and may be the result of either pressure effects or hormone secretion. They frequently mimic other metabolic and intracranial processes and without high index of suspicion it may be hard to diagnose.

**Conclusion:** We hope that our case presentation will add to the existing literature of atypical presentations of tumor apoplexy that include lethargy and decrease level of consciousness without severe headache or visual disturbances.

**Abstract #939**

**ATYPICAL PRESENTATION OF A PITUITARY MACROADENOMA - A POTENTIALLY MORE AGGRESSIVE, INVASIVE AND LESS COMMON SUBTYPE**

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**Case Presentation:** A 71 year old gentleman presented with insidious onset of blurring of vision in left eye. He had no headache or other neurological deficit. MRI revealed a large pituitary macroadenoma with suprasellar extension tenting the optic chiasm and extending superior laterally towards the left extending into the left cavernous sinus encasing the internal carotid artery. Pituitary hormone profile including adrenocorticotropic hormone (ACTH), cortisol, growth hormone (GH), insulin-like growth factor (IGF-1) and thyroid stimulating hormone (TSH) were normal except for central hypogonadism
pre-operatively with luteinizing hormone (LH) 1.15mIU/mL, follicle stimulating hormone (FSH) 1.4mIU/mL, prolactin 7.9ng/mL, total testosterone 50.93ng/dL and free testosterone 9.5pg/mL. He underwent partial central inferior debulking and diagnostic biopsy of the mass via transphenoidal endoscopic approach. Pathology showed pituitary adenoma with MIB-1 / Ki-67 labeling index focally>3%(up to 5% focally). Immunostain for GH, LH, FSH, TSH and Prolactin was negative with rare ACTH immunostain positivity. P53 immunostain revealed rare scattered positivity. In combination of MIB-1/Ki-67 labeling index focally >3% and clinically adenoma with extrasellar extension with invasion revealed by MRI, this pituitary adenoma is consistent with atypical type of pituitary adenoma.

Discussion: Atypical pituitary adenomas are adenomas with atypical morphologic features suggestive of aggressive behaviors including invasive growth and potential for recurrence. These features include elevated mitotic index and MIB-1 labeling index greater than 3%. Ki-67 is an antigen which is routinely examined in all pituitary adenoma specimens. Increasing level of this antigen is correlated with the speed of tumor growth, invasion of the tumor and tumor recurrence. In 1996, the study of Thapar et al. revealed that the 3% or more increase of Ki-67 index is a useful marker of distinguishing invasive from noninvasive adenomas and this threshold level is accepted by the World Health Organisation. It has been reported that increase in MIB-1 nuclear labeling, with accompanied low p53 staining, was found in atypical, invasive, recurring pituitary adenoma.

Conclusion: Atypical pituitary adenoma is the intermediate form of adenoma between the common benign adenoma and exceedingly rare pituitary carcinoma. While the total resection of these masses is difficult, high mitotic activity also contributes to their high rates of recurrence. For this reason, these masses should be carefully followed post-operatively and additional treatment should be provided to prolong recurrence time as reported in retrospective European case series.

Abstract #940

A CASE OF SHEEHAN'S SYNDROME - UNDIAGNOSED FOR OVER 40 YEARS.

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UPMC Mercy

Case Presentation: Patient is a 74 year old Caucasian female who presented to outside hospital with dizziness and a syncopal episode. Was transferred to our hospital for cardiac catheterization which revealed severe CAD. She underwent CABG. Post op course was complicated requiring an ICU stay of 2 weeks. She developed cardiogenic shock and required extended ventilator support. Patient was subsequently transferred to in-patient rehab. She continued to complain of feeling cold and listless all the time, fatigue, poor appetite, nausea and vomiting, epigastric pain, diarrhea, postural dizziness and feeling depressed. Her blood pressure was as low as 86/50 mm Hg. Fasting glucose values were low 38 - 62 mg/dl. Sodium was low 120 -127 mMol/L. At this point, more than a month after patient was admitted to the hospital, endocrinology was consulted. At age of 32 years, patient had severe postpartum hemorrhage requiring hysterectomy followed by inability to lactate. Labs showed TSH 2.85 uU/ml normal, free T4 0.3 ng/dl low, and free T3 88 pg/dl low, am Cortisol 5.5 ug/dl low, ACTH 6 pg/ml low, somatomedin < 16 low, FSH 7.7 mLU/ml, LH 2.2 mLU/ml, prolactin 1.5 ng/ml were normal. Patient was initially treated with stress and then maintenance glucocorticoids. Levothyroxine was started after the initial replacement of glucocorticoids. MRI pituitary showed empty sella configuration.

Patient was diagnosed to have chronic secondary hypopituitarism due to Sheehan's syndrome with acute decompensation due to stress of surgery etc. Clinical improvement was dramatic. Family said for years she just sat and stared and they thought she was depressed. And only abnormality found was chronic hyponatremia. Now she is a new person, animated and active.

Discussion: Sheehan's syndrome occurs as a result of ischemic pituitary necrosis secondary to severe post partum bleeding. Its frequency is decreasing worldwide and it is a rare cause of hypopituitarism in developed countries owing to advances in obstetric care. History of postpartum hemorrhage, failure to lactate and cessation of menses are important clues to the diagnosis. Our patient reported severe postpartum hemorrhage requiring hysterectomy at age 32. Diagnosis of Sheehan syndrome was made, which had been undiagnosed for 43 years.

Conclusion: Diagnosis of Sheehan's syndrome is commonly missed and delayed but this is one of the longest intervals that has been reported. Clinicians should have a high index of suspicion of the disorder in patients with pertinent obstetric history. Meticulous history taking and examination will help in early diagnosis and treatment. This will reduce the mortality and morbidity and greatly improve the quality of life in these patients.
Abstract #941

A RUMOR OF PRIMARY HEPATIC NEUROENDOCRINE TUMOR

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Objective: Primary hepatic neuroendocrine tumor is a rare curable disease.

Case Presentation: A 53 year old man presented with abdominal pain, bloating and 60 pound weight loss. Physical exam showed a large firm right upper quadrant mass extending 15 cm below the costal margin. Imaging showed a 15 x 13 cm solid mass in the right hepatic lobe. Liver function tests were normal. HCV, HBV and HIV serology were negative. Serum AFP was 0.1 ng/mL and levels of CEA, CA 19-9, βhCG, and LDH were normal. An ultrasound-guided liver biopsy showed tumor cells with large nuclei within eosinophilic cytoplasm. Tissue immunohistochemistry was positive for CK7, and negative for CK20, TTF-1, mucin, Melan-A, HMB-45, and HSA. Tumor cells were “signet ring-like” and positive for neuroendocrine markers synaptophysin, chromogranin A, and CD56. Serum C-peptide, chromogranin A, and gastrin levels were borderline. Colonoscopy, upper endoscopy, octreotide scan, PET/CT scan, MRI and triple phase CT of the abdomen, and MRI of the brain did not show extrahepatic disease. A diagnosis of primary hepatic neuroendocrine tumor was made. Until then, metastatic carcinoind tumor was the working diagnosis. The patient underwent surgical resection of the mass, where he was found to have Stage III (T3aN0Mx) disease. He is currently alive and well eight months postoperatively.

Discussion: Primary hepatic neuroendocrine tumor (PHNET) is a rare disease where both surgical resection and liver transplant are potentially curative. The rarity of PHNET, 0.3% of all neuroendocrine tumors, makes it extremely difficult to diagnose prior to biopsy or resection. Easily mistaken for metastatic neuroendocrine tumor (NET), the diagnosis of PHNET should fulfill two criteria: 1) NET characteristics on biopsy and 2) extrahepatic sites of primary NET must be excluded. Given these lesions are considered metastases until proven otherwise, diagnostic modalities for locating the primary NET include octreotide and PET scans, as well as endoscopic evaluation. According to a review article of PHNET in 2011, common features are abdominal pain on presentation, a single lesion with right liver lobe predilection, and endocrinologic silence. Three immunohistochemical markers associated with PHNET are chromogranin A, synaptophysin, and CD56.

Conclusion: Because metastatic NETs are common, clinicians should have a high degree of suspicion for PHNET after a negative workup for extrahepatic primary disease. Unlike metastatic NETs, resection and liver transplant are potentially curative in PHNET, making proper diagnosis of this condition key.

Abstract #942

INCIDENTALLY DISCOVERED ACTH SECRETING PITUITARY ADENOMA ON A SESTAMIBI SCAN IN A PATIENT WITH HYPERPARATHYROIDISM

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Objective: We are reporting a case of pituitary ACTH secreting adenoma incidentally discovered on Sestamibi scan of parathyroids, done for the workup of normocalcemic primary hyperparathyroidism (pHPT).

Case Presentation: 49 year old Caucasian lady with no significant medical history was referred for evaluation of pHPT. She reported increased thirst, urination and weight gain of 10 lbs in one year. Paired corrected calcium/albumin/Intact PTH levels on two separate days 3 months apart were 9.82 mg/dl/ 4.66g/dl/ 63.9 pg/ml and 10.0 mg/dl/ 5.0g/dl/ 58.9 pg/ml (N:8.6-10.2 mg/dl/ 3.5-5.2g/dl/ <65 pg/ml respectively). Vitamin D-25 OH level was <65 pg/ml (N:50). Sestamibi scan of parathyroids, done for the workup of pHPT. She reported increased thirst, urination and weight gain of 10 lbs in one year. Paired corrected calcium/albumin/Intact PTH levels on two separate days 3 months apart were 9.82 mg/dl/ 4.66g/dl/ 63.9 pg/ml and 10.0 mg/dl/ 5.0g/dl/ 58.9 pg/ml (N:8.6-10.2 mg/dl/ 3.5-5.2g/dl/ <65 pg/ml respectively). Vitamin D-25 OH level was <65 pg/ml (N:50). Sestamibi scan did not reveal parathyroid adenoma but there was radio-ligand uptake in the midline at the skull base, in a location consistent with pituitary adenoma. Serum cortisol levels(7:15 am):17.4 mcg/dl and 24hr urine cortisol level was 1169 mcg/24hr (N:170-1200) respectively. Urinary calcium/creatinine ratio: 299ng/g creat (N<275). Sestamibi scan did not reveal parathyroid adenoma but there was radio-ligand uptake in the midline at the skull base, in a location consistent with pituitary adenoma. Serum cortisol levels(7:15 am):17.4 mcg/dl and 24hr urine cortisol level was 1169 mcg/24hr (N:170-1200) respectively. Urinary calcium/creatinine ratio: 299ng/g creat (N<275). Sestamibi scan did not reveal parathyroid adenoma but there was radio-ligand uptake in the midline at the skull base, in a location consistent with pituitary adenoma. Serum cortisol levels(7:15 am):17.4 mcg/dl and 24hr urine cortisol level was 1169 mcg/24hr (N:170-1200) respectively. Urinary calcium/creatinine ratio: 299ng/g creat (N<275). Sestamibi scan did not reveal parathyroid adenoma but there was radio-ligand uptake in the midline at the skull base, in a location consistent with pituitary adenoma. Serum cortisol levels(7:15 am):17.4 mcg/dl and 24hr urine cortisol level was 1169 mcg/24hr (N:170-1200) respectively. Urinary calcium/creatinine ratio: 299ng/g creat (N<275). Sestamibi scan did not reveal parathyroid adenoma but there was radio-ligand uptake in the midline at the skull base, in a location consistent with pituitary adenoma. Serum cortisol levels(7:15 am):17.4 mcg/dl and 24hr urine cortisol level was 1169 mcg/24hr (N:170-1200) respectively. Urinary calcium/creatinine ratio: 299ng/g creat (N<275). Sestamibi scan did not reveal parathyroid adenoma but there was radio-ligand uptake in the midline at the skull base, in a location consistent with pituitary adenoma. Serum cortisol levels(7:15 am):17.4 mcg/dl and 24hr urine cortisol level was 1169 mcg/24hr (N:170-1200) respectively. Urinary calcium/creatinine ratio: 299ng/g creat (N<275). Sestamibi scan did not reveal parathyroid adenoma but there was radio-ligand uptake in the midline at the skull base, in a location consistent with pituitary adenoma. Serum cortisol levels(7:15 am):17.4 mcg/dl and 24hr urine cortisol level was 1169 mcg/24hr (N:170-1200) respectively. Urinary calcium/creatinine ratio: 299ng/g creat (N<275).
ml suggesting ACTH dependent Cushing’s syndrome and contrast enhanced CT scan of chest, abdomen and pelvis not showing an ectopic source of ACTH. MRI of pituitary done on 2 separate occasions 3 months apart was normal. Inferior Petrosal Sinus Sampling(IPSS) showed a central to peripheral ACTH ratio of > 3.0, with a lateralization to the right. Trans-sphenoidal resection of the 40% of the pituitary gland revealed an ACTH producing corticotroph adenoma.

**Discussion:** Tiktinski et al. have reported pituitary incidentalomas on sestamibi scan done for evaluation of parathyroids, however their secretory nature, was not studied. Further investigations are needed to clarify the role of Sestamibi scan in the diagnosis of imaging negative clinical and subclinical pituitary Cushing’s disease and other secretory pituitary tumors.

**Conclusion:** We hereby report a subclinical case of pituitary ACTH secreting adenoma not visualized on MRI but incidentally discovered on a Sestamibi scan done for parathyroid evaluation.
Abstract #1000

STATUS OF TESTOSTERONE LEVELS OF PATIENTS ADMITTED TO A TERTIARY CARE HOSPITAL

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Objective: Urban lifestyle with altered habit culture, extensive use of mobile phones, deranged food habits and irrational sleep timings, is resulting in low testosterone levels and infertility. Men in the age group of early 30’s and 40’s are tired, sleepless and lacking libido because of low levels of testosterone. We undertook a study to determine if there were any other susceptible diseases that testosterone deficient patients were prone to. A total of 110 males from different strata of society, admitted to a medical unit in a tertiary hospital, were studied and their low testosterone levels were co-related for concomitant pathology.

Methods: A hospital based retrospective analysis of 110 males, who were admitted between February and October 2013 for a range of clinical conditions. Their testosterone levels were noted and a comparative analysis of their history and clinical conditions was carried out.

Case Presentation: 1) PREVALENCE

Assuming the definition of testosterone deficiency to be less than 260ng/dl (Tietz Fundamentals of Clinical Chemistry), it was observed that 60% of these patients were testosterone deficient.

2) AGE

a) The highest prevalence was noticed in the age group from 60 to 69 years - 78%
b) Almost equal deficiency (about 60%) was seen all through third to sixth decades of life.

3) CONCOMITANT COMORBIDITIES

a) Amongst the study population, interestingly 68% patients suffering from testosterone deficiency had infections.
b) The rest of the study group was randomly distributed amongst surgical (7%), Cardiac(6%), Gastrointestinal(4%),Diabetes and others(23%) causes for admission.

4) DISTRIBUTION OF INFECTION

Of the 60% who had infections, Bacterial infections were 66%; Viral infections were 19%; Parasitic infections were 15%

Discussion: Low Testosterone levels affect diverse physiological processes in the body and have a target action on multiple cells and organs. While dipping testosterone levels can produce subjective symptoms, documented low levels have been seen to have to a direct impact on ‘T’ cell and ‘B’ cell immunity. The fact that two-thirds of the deficient patients had to be hospitalized for the treatment of infections indicates the absolute need to screen the susceptible urban population and treat before they fall prey to the morbidity of infections.

Conclusion: The hypothesis that normal testosterone protects men against infection is probably borne out by this analysis. The fact that more than 60% of deficient patients were admitted with diverse infections, the immunoprotective action that testosterone lends to men needs to be explored. It would thus be wise to start a screening program amongst the susceptible male population in the community in view of loss of valuable man-hours.

Abstract #1001

METABOLIC DISORDERS AND THEIR CORRELATION WITH TESTOSTERONE LEVEL IN CAUCASIAN MALE PATIENTS

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1. “National Institute of Endocrinology”, 2. Enmedic

Objective: Metabolic syndrome is widely recognized as an important public health problem; its prevalence has increased substantially in the recent decades. The relationship between metabolic syndrome and testosterone levels is one of the longest running controversies in endocrinology.

Aim: The objective of the study is to show correlation with Metabolic syndrome or its components and testosterone level in male patients. We also study the influence of testosterone replacement therapy on obesity and insulin resistance in men.

Methods: 165 subjects were screened but only 94 subjects with 30-65 years and BMI 27.0 - 48.0 kg/m2 were enrolled in the study. The following analyses were done: Anthropometric study, Biochemical Measurements, ultrasonography of the abdomen and prostate. According to the laboratory and clinical condition we divided patients into three groups. The appropriate treatment was prescribed to all patients. 1) First group with obesity and androgen deficiency we used diet and physical activity. 2) Second group with androgen deficiency, obesity and insulin resistance, we used diet, physical activity and metformin. 3) Third same group as second group with androgen deficiency, obesity and insulin resistance, we used testosterone, metformin, diet and physical activity.

Results: In all investigated patients abnormal lipid profile and increased level of leptin was observed, all patients had decreased level of free testosterone and had inversely correlated with the degree of obesity and insulin resistance. After three months of treatment: We had some positive results cholesterol, triglyceride and LDL levels decreased, and HDL increased. Free testosterone level increased in all groups but...
the best results was in III group which was treated by diet, physical activity, metformin and testosterone. HOMA-IR decreased in all group but I and III group had alike result. BMI decreased in all groups but bets results was in III group. leptin level after treatment was approximately same in all groups, but compared best results was achieved in III group.

Discussion: These small observations suggest that an inverse relationship exists between serum androgens, obesity and insulin sensitivity. Low testosterone levels have also been found to be associated with dyslipidaemia and hypertension.

Conclusion: As our small study had shown testosterone therapy reduces insulin resistance and obesity in male patients and also decrease total cholesterol level. These observations suggest that an inverse relationship exists between serum androgens, obesity and insulin sensitivity.

Abstract #1002

ABSTRACT WITHDRAWN

Abstract #1003

HYPERANDROGENISM IN POSTMENOPAUSAL WOMAN ASSOCIATED WITH INSULIN RESISTANCE, LIPODYSTROPHY, NONALCOHOLIC FATTY LIVER DISEASE (NAFLD) AND UNCONTROLLED TYPE 2 DIABETES

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Case Presentation: 60 yr old female was referred in 2006 for hyperandrogenism. She was diagnosed at 18 y/o with PCOS and had history of ovarian cysts and menstrual irregularity. Facial hair present for decades, worsened with menopause and significant scalp hair loss and frontal balding. She had increased libido, but denied clitoromegaly. She had diabetes type 2 since 2001 with severe insulin resistance requiring 400 units insulin per day. She also had lipodystrophy with central truncal and abdominal visceral fat accumulation and depletion of peripheral subcutaneous fat in arms, shoulders, thighs, buttocks. Laboratory tests showed total testosterone of 208 (2-45ng/dl), DHEA-S of 204 (29.7-182.2 microg/dL), LH 24 (5.2-62.0mIU/ml), estradiol of 15 ( normal <20 pg/ml) which trended up to 76pg/ml in 2013 and transaminitis. Pelvic Ultrasound showed a symmetrical bilateral ovarian enlargement and CT showed normal adrenal glands with cirrhosis and splenomegaly. She refused surgery and medical therapies and the testosterone has risen to 433ng/dl.

Discussion: Although the initial consult was for hyperandrogenism, the combination of insulin resistance, NAFLD, Diabetes type 2 and PCOS seem unlikely to be by chance. Insulin resistance is associated with all of the above. We suspect that different organs or tissues may have different susceptibilities to the insulin resistance. Furthermore, the more severe the insulin resistance, the more likely that adverse pathology to multiple organs. Severe insulin resistance is seen with lipodystrophy as with the other entities. We suspect that our patient might have hyperthecosis because it is associated with severe insulin resistance and also the fact that the ovaries are not atrophic, no tumor has been discovered over seven years, and is similar to the cases reported by Castell et al. Surgery is planned for April 2014.

Conclusion: Hyperandrogenism may be associated with severe insulin resistance, and other insulin resistance diseases may be present, including NAFLD, Diabetes, Lipodystrophy.

Abstract #1004

A PATIENT WITH ELEVATED TESTOSTERONE AND GONADOTROPINS: IS IT SECONDARY HYPERGONADISM?

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Case Presentation: A 64- year old man was referred to Endocrinology section for evaluation of very high testosterone levels. Gonadal profile measured as the patient was complaining of fatigue and erectile dysfunction. Other Medical problems include chronic smoker, type 2 diabetes treated with insulin, chronic liver disease secondary to hepatitis C virus and depression. Physical exam showed normal testicular exam and no gynecomastia. Total testosterone level of more than 6000 ng/dl (241 - 827). Repeated blood work revealed a total testosterone of more than 1500 ng/dl free testosterone 16.65 ng/dl ( 5.0-21.0), beta-HCG <1 mIU/mL ( 0-3), alpha subunit 1.9 ng/mL (< 0.6 ng/ml ), sex hormone binding globulin (SHBG) 158.3nm/l (19.3-76.4), LH 15.3 mIU/ml (1.2-10.8), FSH 9.5 mIU/ml (0.7-10.8), total estradiol 50.5 pg/ml (7.6-42.6). Other results include, TSH 0.70 uIU/ml (0.4 - 4.0), albumin 3.6, alkaline phosphatase 79, AST 77 units/L (12 - 34), ALT 110 units/L (10 - 55). MRI of pituitary was done without any evidence of pituitary adenoma. Total testosterone level of more than 1045 ng/dl, free testosterone 10.5 ng/dl, SHBG 188.6 nm/l, LH 13 mIU/ml , FSH 9 mIU/ml , total estradiol 52.5 pg/ml, a free estradiol was came back 0.4 pg/ml ( 0.2-1.5 pg/ml).
Abstract #1005

CLINICAL FEATURES AND TREATMENT OF ENDOCRINOLOGICAL PCOS

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Objective: It is well known that the patients of polycystic ovarian syndrome (PCOS) were often complicated with obesity in the American and European countries. However, there are many normal body weight PCOS patients in Japan. Present study was performed to elucidate the endocrinological backgrounds between normal weight and obese patients of PCOS.

Methods: 443 cases of PCOS (LH/FSH>1, LH hyper-secretion by Gn-RH loading, hypothalamic anovulation, polycystic changes in the ultrasonic examinations) were subjected under the enough informed consents. They were divided into two groups by their BMI; normal (group N, 375 cases): less than 25, and obese (group O, 68 cases): more than 25. Then, the incidence of the complication of NIDDM (diagnosed by 75g glucose tolerance test; GTT), plasma FSH, LH, prolactin (PRL), estrone (E1), estradiol (E2), testosterone (T), androstenedione (A) and leptin (Lp) levels were investigated.

Discussion: The interesting features are: elevated LH level with high total testosterone and estradiol with normal free testosterone and low free estradiol level. This patient has elevated SHBG as a result of hepatitis C and chronic liver disease. SHBG bind both testosterone and estrogens. An elevated SHBG level explains the high total testosterone and high total estradiol. Gonadotropin levels are controlled via a negative feedback from free testosterone as well free estradiol. Estradiol exerts a strong negative feedback on the pituitary and decreases the release of gonadotropins. Therefore, in this patient, the elevated LH level can be attributed to either the low free estradiol level or to partial testosterone resistance. In view of elevated LH and elevated testosterone levels, other possibilities include gonadotroph adenomas and HCG secreting tumors. HCG levels being low, rules out HCG as the culprit. MRI pituitary has no evidence of pituitary adenoma.

Conclusion: Patients with chronic liver disease may have elevated SHBG causing high total testosterone and estradiol. Free estradiol may become so low that it loses its ability to suppress gonadotropins. The resulting elevated gonadotropins and high total testosterone may mimic a picture of secondary hypergonadism. A partial testosterone resistance can’t be ruled out as well.

Abstract #1006

SUICIDE ATTEMPT IN AN 18-YEAR-OLD PATIENT WITH MASSIVE BILATERAL GYNECOMASTIA AND AMBIGUOUS EXTERNAL GENITALIA

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Objective: To report a case of attempted suicide as a complication of intersex at puberty.

Methods: The case history, physical findings, hormonal results, findings at exploratory laparatomy in a patient with ambiguous genitalia is reported.

Case Presentation: Patient is an 18-year-old secondary school student who presented with a history of a small penis from birth and enlargement of both breasts of 2-years duration. There was no galactorrhea. The left testis was undescended. He was circumcised few days after
birth. Patient was reared as a male (the only male of the family). Father is deceased. His life was uneventful until he developed massive bilateral painless gynecomastia. He was constantly being mocked by other children and he attempted killing himself by jumping into a river in a bid to drown but was rescued. A local church donated some money to assist the patient to “remove” the breasts. Physical examination revealed a young “male”, height was 158 cm, axillary hair and pubic hair were present. Pulse rate was 80 beats /min, Blood pressure was 120/80 mmHg. Matured ‘female-type’ breasts were present. The penis was small (2cm long), right ‘testis’ was in the right scrotum while left testis was undescended. There was perineal hypospadia. No vaginal orifice was seen. Hormonal results were FSH 8.4 u/L (1.0-14.0), LH 0.5 u/L (0.7-7.4), human prolactin 13.1ng/ml (1.5-12.0), progesterone 0.5ng/ml (0.1-1.0), estradiol 61.5 pg/ml (15-60) and Testosterone 1.3ng/ml (3.5-8.6). Buccal smear microscopy showed squamous epithelia whose nuclei have Barr bodies Karyotype was not done as patient could not pay it. Pelvic ultrasound scan showed a male pelvis. No uterus, ovary or adnexal mass was seen. The clinical impression was that of true hermaphrodite.

Bilateral mastectomy were done. Exploratory laparotomy was done to remove the undescended left testis but a rudimentary uterus with the cervix prolapsed into the right scrotal sac and a left ovotestis in the left inguinal canal were seen. These were removed surgically. The perineal hypospadia was repaired. The small penis was scheduled to be modified by hormonal therapy.

**Discussion:** The challenges of managing an intersex patient in a resource-constraint locale will be discussed.

**Conclusion:** This case highlights a rare complication of discordant secondary sexual characteristics of an intersex patient at puberty.

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**Abstract #1008**

**AN UNUSUAL CASE OF VIRILIZATION**

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**Case Presentation:** Virilization, as a part of hyperandrogenism syndromes, is a rare clinical finding, upon encounter it is critical to identify the underlying cause, which can be challenging in certain cases. A 59 year old african american lady was evaluated for a follow up in endocrinology clinic for diabetes management. She complained of hoarseness for a year and a half, which was evaluated by ear, nose and throat specialists and was treated with proton pump inhibitors with no improvement. And upon further questioning she had decrease level of energy, increased libido, excess body hair as well as deepening of her voice. Upon physical exam she was found to have severe hirsutism (Ferriman-Gallway score of 24), facial acne, increase muscle mass and clitoromegaly (4 cm). Laboratory testing revealed significant increase of total and free testosterone of 1040 ng/dL and 9.4 ng/dL respectively (normal ranges 8-40 ng/dL and 0.3-1.9 ng/dL respectively). The rest of the hormonal profile,
including lutenizing and follicular stimulating, were all compatible with her postmenopausal state. Abdominal and pelvic computed tomography showed a left ovarian heterogenous mass, with normal right ovary and adrenal glands. The same findings were confirmed on a pelvic ultrasound. The patient was referred to a gynecologist and she agreed to have bilateral oopherectomy. The pathology of the left ovary showed a steroid cell tumor. The patients labs were obtained 3 months after the surgery and it showed a significant reduction in total testosterone level down to 79 ng/dL. By then the patient felt better and her hirsutism improved mildly.

Discussion: Our case illustrates a rare form of ovarian tumors presenting with clinical signs of hyperandrogenism. Although these clinical signs progress rapidly, the detection of the tumor may be delayed.

Conclusion: The recognition of such ovarian tumors through identifying their clinical manifestations is critical to institute the appropriate therapy early in the progression of the disease for prevention of future morbidity and mortality.

Abstract #1009

INFLUENCE OF THE CONCLUSION OF A RECENT LARGE COOPERATIVE STUDY IN CHANGING STANDARD PROTOCOL OF INDUCING MENSES IN ANOVULATORY WOMEN WITH OLIGOAMENORRHEA PRIOR TO INITIATING OVULATION INDUCTION WITH ANTI-ESTROGEN AND OUTCOME

Jerome Check, MD, PhD1, Joanne Liss, MT2, Diane Check, BS2


Objective: A recent prospective study found higher pregnancy rates in anovulatory women who just initiated clomiphene citrate without first inducing menses compared to those given progesterone withdrawal menses. The objective of this study was to 1) determine following presentation of these data at journal club the influence that this study would have on prescribing clomiphene with or without induction of menses, 2) to determine if the study would have similar findings when prescribing letrozole for a similar group of anovulatory women with oligomenorrhea, 3) comparisons would be made as to pregnancy rates with or without progesterone withdrawal in women taking clomiphene citrate and in women taking letrozole.

Methods: A retrospective review was performed of all first cycles of attempts to induce ovulation with either clomiphene citrate 50mg x 5 days or letrozole 2.5mg x 5 days in anovulatory women with oligomenorrhea. If a dominant follicle of 18-24mm with a serum estradiol >200pg/mL was not achieved within 10 days of the last tablet the dosage was doubled and follicular evaluation continued unless luteinization occurred. Some cycles according to physician preference were started without induction of menses no matter how long before was their previous menses and others were given medroxyprogesterone acetate for 13 days and follicle maturing drugs started on day 5. Clinical pregnancy and miscarriage rates were determined in their first ovulation induction cycle. Intrauterine insemination was performed if post-coital tests were poor.

Results: There were 21 first cycles using letrozole and 42 using clomiphene. Menses were not induced in 18/21 (86%) letrozole cycles and 24/42 (57%) clomiphene cycles. Clinical pregnancies occurred in 4 (22.2%) letrozole cycles without induced menses with 1 miscarriage vs. 4/24 (16.6%) clomiphene cycles, no miscarriage. One of 3 (33.3%) letrozole cycles with menses induced achieved a clinical pregnancy vs. only 1/18 (5.5%) of clomiphene cycles. There were no miscarriages.

Discussion: Though the endometrial thickness was higher with clomiphene without induced menses vs. menses induced (11mm vs. 9.5mm) one cannot explain the trend for lower pregnancy rates in women with induced menses because of thinner endometrial since the thickness was 9.5mm for those conceiving with letrozole.

Conclusion: The aforementioned study influenced a change in our normal pattern of inducing menses such that 66.6% of ovulation induction cycles did not use progesterone withdrawal. Pregnancy rates were in keeping with the aforementioned study of clomiphene since the pregnancy rates were higher without induced menses.

Abstract #1010

HIGH ESTROGEN AFTER INJECTABLE TESTOSTERONE IS RELATED TO AGE

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Objective: To describe our experience of treating 35,711 hypogonadal men with injectable testosterone and the effects on estrogen levels.

Methods: Data was extracted from our electronic health record (Advance MD) of the multi site Low T Centers across the United States. Altogether 35 Centers were examined.

Results: 7,215 (20.2%) out of the 35,711 patients had estradiol levels > 42.6 pg/ml. Estradiol was measured
using Electro-chemiluminescence immunoassay (ECLIA) through Lab Corp. The results: 132/989 (13.4%) of > 65 years; 3753/16955 (22.1%) 45-65 years; 2,968/15,857 (18.7%) 25-45 years; 7/215 (3.3%) of < 25 years patients had high estradiol levels. The difference between extreme age groups (< 25 and > 65) was statistically significant using a chi square test (p=0.013) with a chi statistic of 6.105.

Discussion: It is known that injectable testosterone can lead to higher estradiol and dihydrotestosterone (DHT) levels through peripheral conversion. Estradiol is converted from testosterone through aromatization in adipose tissue. Aromatase is localized in the endoplasmic reticulum where it is regulated by tissue-specific promoters that are in turn controlled by hormones, and cytokines. In general, as men age, there is a higher proportion of body fat compared to lean muscle mass. This may imply greater conversion to estradiol and does explain the higher levels in the middle aged men. As anticipated, because of less body fat, young men < 25 years had the lowest amount of conversion to estradiol. Paradoxically, after 65 years there appears to be a leveling of conversion, and this may be related to lower treated testosterone levels in this age group.

Conclusion: Presently, it is unclear as how to manage high estrogen in men, but our data suggest a high prevalence of conversion to estrogen and is correlated with age. Further research is needed; but we suggest that the activity of aromatase is affected with aging, leading to the changes observed.

Abstract #1011

A CASE OF PHENOTYPIC MALE 46 XX OVOTESTICULAR DSD WITH SYNDROMIC FEATURES

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Case Presentation: Although 46 XX testicular DSD has an incidence of 1:20,000, ovotesticular DSD is very rare and has been reported in 500 individuals worldwide. A 14 year 2 month old ex 31 week premature African American phenotypic male was referred to the pediatric endocrinology clinic for hormonal evaluation. The patient was born with ambiguous genitalia: perineoscrotal hypospadias, with a small phallic structure, bilateral inguinal hernias and asymmetry of the labioscrotal folds. Extensive evaluation at birth resulted in male sex assignment. He was subsequently lost to endocrine follow up.

In the interim, patient was sporadically followed by the geneticist for short stature, facial dysmorphism including prominent eyes with hypertelorism, depressed nasal bridge, and dysmorphism of extremities. There were concerns for filamin gene mutation and otopalatodigital spectrum disorders. Postpubertally, the patient had a normal male phenotype. Only after several visits with the geneticists, the karyotype was discovered to be 46XX with an inconsistent SRY pattern.

Pelvic and scrotal ultrasound revealed: 9-cm right utricular Mullerian structure, bilateral gonads in the scrotum and a multi-septated mass inferior to the presumed right testicle. Lab evaluation showed: Total Testosterone 249 ng/dL, DHT 43 ng/dL, Estradiol <5.1, SOX-9 duplication or deletion: Negative.

Gonadal biopsy showed fragments of both testicular and ovarian tissue on the left. On the right, testicular tissue, immature for age with peritubular fibrosis was found. Segments of ovarian tissue were found in the cyst-like structure adjacent to the right testicle. Evaluation of gonadal tissue showed a 46 XX karyotype with no evidence of SRY by FISH.

Discussion: The etiology of 46 XX ovotesticular DSD often remains unclear. Known causes include SRY translocation, hidden mosaicism for SRY or other Y sequences, loss of function mutations in RSPO1, and 46,XX/46,XY chimerism.

Assessment of our patient reveals an inconsistent SRY analysis. Gonadal biopsy confirms 46,XX ovotesticular DSD. Our patient also exhibits syndromic features. Perhaps a mutation in a filamin gene can also influence gonadal development through its importance in embryonic development. Since ovotesticular tissue is usually dysgenetic, removal of the tissue is recommended due to risk of malignant transformation.

Conclusion: This is a rare case of 46XX phenotypic male with ovotesticular DSD of undetermined etiology. The presence of SRY is not the only pathway to development of testicular tissue. Disordered ovarian development and mutations in genes necessary for ovarian maintenance may result in yet to be discovered accessory pathways that lead to development of testicular tissue.

Abstract #1012

CYCLIC ANGIOEDEMA AND URTICARIA IN A YOUNG WOMAN

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Objective: The cyclic rise and decline of female sex hormones during the reproductive period affect multiple organs. It is not generally known that hypersensitivity to endogenous progesterone can lead to anaphylaxis. We present a unique case of autoimmune progesterone hypersensitivity.
Case Presentation: A previously healthy 24-year-old female (G0P0, menarche at age 14) was referred for cyclic angioedema and anaphylactic-like reactions for 6 months. Episodes tended to start 5-8 days prior to menstrual periods and last until the final day of menses. She experienced variable degrees of lip/throat swelling, diffuse urticaria, abdominal pain and diarrhea. Twice she had hypotension and syncope that required ER treatment with epinephrine, antihistamines and prednisone. RAST tests for environmental and food allergies and tests for mastocytosis, hereditary angioedema and carcinoid were negative. Her only medication was ortho tri-cyclen, started one month prior to the onset of her illness. The intradermal progesterone test was positive. The oral contraceptive pill was discontinued. Treatment with cetirizine, loratadine and Benadryl were prescribed 10 days prior to the menstrual period and until the final day of menses with steroids available PRN. On this monthly treatment she has had no subsequent episodes.

Discussion: Autoimmune progesterone hypersensitivity occurs during the luteal phase when progesterone levels increase. The onset varies from menarche to the postpartum state. The mechanism remains unknown. Like our patient, some cases were induced by synthetic exogenous progestins. Diagnosis is often made with positive skin test. Anti-histamines provide symptomatic relief. Steroids’ side effects make regular use unattractive. Desensitization was successful in case reports. Severe cases may require medically induced anovulation. Conclusion: Early recognition of autoimmune progesterone hypersensitivity is important because untreated disease severely affects the life and the reproductive health of susceptible individuals.
demonstrated a 2.5 cm yellow nodule [Histopathology: Steroid cell tumor]. Post-op, the androgen levels returned to normal, with restoration of menses by three months, and complete regression of hirsutism and alopecia on follow up. **Discussion:** Hirsutism or virilization in pre- or post-menopausal women may be due to increased testosterone levels caused by an androgen-secreting tumor. The preoperative localization of small ovarian or adrenal androgen-secreting tumors is difficult, wherein conventional imaging techniques [ultrasound, CT, MRI] are negative, necessitating pre- or intra-op selective adrenal and ovarian vein catheterization and sampling [abnormal steroid gradients between peripheral and organ vein levels]. **Conclusion:** Functional FDG PET imaging provides easy and non-invasive localization, facilitating early diagnosis and prompt surgical excision of small ovarian androgen producing hilus cell tumors.

**Abstract #1014**

**A CHALLENGING CASE OF PREMENOPAUSAL HYPERANDROGENISM**

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**Objective:** Ovarian steroid cell tumors account for less than 0.1% of all ovarian tumors. They are a unique cause of female virilization and can imitate or coexist with congenital adrenal hyperplasia (CAH). Due to their rarity, there is limited data on malignant potential or response to therapy. We report a challenging case of hyperandrogenism in a premenopausal patient found to have a steroid-cell ovarian tumor.

**Case Presentation:** A 47-year old, gravida 3, para 1 presented for evaluation of hirsutism and elevated testosterone. She had been previously diagnosed with polycystic ovarian syndrome, and treated with metformin and medroxyprogesterone with mild improvement in her oligomenorrhea. Subsequent evaluation showed testosterone 333ng/Dl, 17-OH Progesterone (17-OHP) 953 ng/Dl, with normal thyroid, prolactin, luteinizing hormone, and normal luteinizing hormone, follicle stimulating hormone, and normal follicle stimulating hormone, luteinizing hormone, and normal estradiol, and normal progesterone. She had been previously treated with a testosterone gel preparation which produced hirsutism. She had a 2cm left ovarian cyst. Cosyntropin stimulation produced no significant change in 17-OHP. Adrenal and ovarian vein sampling were nondiagnostic, and she was started on dexamethasone for presumed non-classic CAH. 8 years later, the patient relocated and initial examination revealed acanthosis and severe hirsutism. Her dexamethasone dose was increased to 2mg daily, but still did not suppress her testosterone and 17-OHP. Repeat pelvic US showed normal adnexal masses. A sonohysterogram was performed, revealing an 11.8cm solid left adnexal lesion. CT showed a left adnexal mass 10.4x5.9cm and a right adnexal mass 4.9x4cm. She underwent surgical staging and debulking with total abdominal hysterectomy and bilateral salpingo-oophorectomy. Pathology was consistent with an 11cm left ovary malignant steroid cell tumor not otherwise specified.

**Discussion:** This case is unique in that pelvic US failed to detect the large ovarian mass, and adrenal/ovarian vein sampling was nondiagnostic. The elevated 17-OHP, rarely associated with these tumors, may be associated with co-existing non-classic CAH, further complicating the diagnosis.

**Conclusion:** Ovarian steroid cell tumors are rare and can present with hyperandrogenism and rarely hyperestrogenism. Extreme elevations of testosterone should prompt comprehensive investigation of an ovarian source even in patients with CAH.

**Abstract #1015**

**CLOMIPHENE CITRATE: A CHEAP AND EFFECTIVE APPROACH TO HYPOGONADISM**

Gregory Dodell, MD

**Objective:** The number of young men being screened and treated for hypogonadism has risen exponentially. During the past 5-years there has been an increase in testosterone prescriptions by 170%. Obesity, depression, and inadequate sleep are common features in these patients. Exogenous testosterone replacement suppresses the hypothalamic-pituitary-gonadal axis, which inhibits spermatogenesis. Clomiphene, a selective estrogen receptor modulator, enhances the endogenous production of testosterone, therefore maintaining fertility. Clomiphene is a generic oral medication.

**Case Presentation:** A 35-year-old male presented for an evaluation of hypogonadism and azoospermia. He was diagnosed with hypogonadism at the age of 23. He had previously abused an oral androgen preparation to lose weight and build muscle mass. He became symptomatic when he stopped. At that time, symptoms included decreased libido, fatigue, and emotional lability. The work-up by a previous physician demonstrated a normal MRI of the pituitary gland, a low total testosterone of 47 ng/dL, and normal prolactin and thyroid function tests. He was initially treated with a testosterone gel preparation which was subsequently changed to a depot preparation. A semen analysis demonstrated azoosperma, which concerned him and his wife. At the initial visit, he started a trial off of depot testosterone to reassess his pituitary function. A short 4-week trial demonstrated a total testosterone of 192 ng/dL, LH 4.6 mIU/ml, FSH 9.3 mIU/ml. He was symptomatic
and complained again of low libido, fatigue, and emotional lability. He was started on a trial of clomiphene 50 mg every other day. After 6-weeks his total testosterone was 542 ng/dL (FSH 25.6 mIU/ml and LH 6.9 mIU/ml). He responded well clinically and he has not experienced any side effects. A repeat sperm analysis demonstrated a total sperm count of 30 million (normal range 40-500 million). His wife became pregnant via IVF.

**Discussion:** Clomiphene is an off-label medication for hypogonadism, despite its demonstrated effectiveness since the 1960’s. It is a cheap and convenient (oral) mechanism to enhance endogenous testosterone production in young men while also maintaining fertility. Its effect on testosterone elevation has been demonstrated as compatible to that of testosterone gel preparations and may be preferable to patients since there is no concern about contaminating others or having frequent injections.

**Conclusion:** The management of young men with secondary hypogonadism should include a discussion about desired fertility and a focus on addressing potential underlying etiologies such as depression, inadequate sleep and an unhealthy diet.
THYROID DISEASE

Abstract #1100

VALIDATION OF A MOLECULAR CLASSIFIER FOR PREOPERATIVE IDENTIFICATION OF MEDULLARY THYROID CANCER IN THYROID NODULE FINE-NEEDLE ASPIRATION BIOPSIES

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Objective: Cytopathological evaluation of thyroid fine-needle aspiration biopsy (FNAB) specimens may not raise preoperative suspicion of medullary thyroid cancer (MTC), as it misses over one-half of these uncommon, yet aggressive, neoplasms. Additionally, serum calcitonin screening for MTC has a high false positive rate, which results in a low positive predictive value (PPV). We report results from a large, prospective validation of an mRNA-based expression signature (MTC Classifier) to preoperatively identify MTC in FNAB samples.

Methods: Prospectively, we conducted cytology on 50,430 consecutively received thyroid nodule FNAB samples. Among the 15.5% indeterminate samples (Bethesda categories III and IV), we performed the Afirma Gene Expression Classifier (GEC) to reclassify samples as benign or suspicious, and also used the MTC Classifier to identify MTC. We similarly evaluated an additional 2,673 prospective FNAB samples identified as indeterminate, suspicious or malignant (Bethesda III-VI) by locally read cytopathology. Clinical details were obtained for patients with MTC signatures or cytological features that suggested MTC. The MTC Classifier was also performed on 215 consecutive likely malignant specimens (Bethesda V-VI) to calculate incidence of the MTC signature.

Results: The MTC Classifier identified an MTC signature in 0.2%, 0.5%, 1.0%, and 1.8% of consecutive nodules with Bethesda category III-VI cytologies, respectively. The PPV for the MTC Classifier was 98%, and the single false positive was another neuroendocrine tumor (paraganglioma). In MTC-confirmed patients, basal serum calcitonin was <20 pg/ml in 7.5%, and unsuspected MEN2 germline mutations were identified in 10%. No MTC was found in 5 cases where cytology raised suspicion for MTC but the MTC Classifier did not, suggesting a high negative predictive value (NPV).

Discussion: In the largest thyroid FNAB study evaluating the incidence of MTC to date, an MTC Classifier identified all 39 histologically confirmed MTC cases, whereas only 15 (38%) were suspected or diagnosed as MTC by cytology. The MTC Classifier has high PPV for preoperatively identifying MTC among indeterminate thyroid nodules when used with the Afirma GEC, and also among FNABs deemed suspicious or malignant by cytopathology.

Conclusion: The preoperative genomic identification of MTC is expected to alter patient care, solidifying the need for timely, more thorough surgery, and necessitating preoperative screening for life-threatening concomitant pheochromocytoma.

Abstract #1101

THYROTOXIC CARDIOMYOPATHY: A STUDY OF THREE CASES

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Objective: To report the clinical course of thyrotoxic cardiomyopathy in 3 patients.

Methods: Three patients with thyrotoxic cardiomyopathy seen in our clinic are reported.

Case Presentation: #1: Mrs. G.C. is a 49 years old female presenting with 2 weeks history of breathlessness on exertion, one week history of progressive pedal swelling and four days history of dry cough with orthopnea, paroxysmal nocturnal dyspnea and palpitation. She has no past history of thyroid disorders. She was cachectic with fine tremor of the outstretched fingers and a goiter (Stage 11 WHO classification), tachycardia with S3 gallop rhythm. Her EKG result showed, irregular R-R interval, ventricular premature complexes, and atrial fibrillation. Thyroid function test showed elevated free triiodothyronine (T3) 18.59pg/ml (normal 2.5-3.9pg/ml), elevated free thyroxine (T4) 4.17ng/dl (normal 0.58-1.64ng/dl) and TSH was 0.61uIU/ml (normal 0.34-5.6uIU/ml). She was managed as a case of congestive cardiac failure secondary to thyrotoxic cardiomyopathy, and associated atrial fibrillation. She was managed with s.c clexane, i.v. furosemide, and carvedilol ,digoxin, candesartan, aspirin, aldactone, carbimazole and propranolol. She improved significantly with this treatment.

#2: Miss K.G. is a 27 year old patient with Grave’s disease diagnosed 10 months prior to presentation. She presented with breathlessness of 3 days duration which occurred at rest with associated palpitation, orthopnea, paroxysmal nocturnal dyspnea pedal edema and cough. She was previously treated with carbimazole and propranolol with poor compliance; she was managed as a case of thyrotoxic heart disease with imminent heart failure.

#3: Mrs. O.A. is a 55 year old female who presented with 2 months history of breathlessness which occurred during domestic work and progressed to breathlessness at rest with
associated orthopnea and paroxysmal nocturnal dyspnea. She had a history of a goiter 30 years ago which regressed. Family history confirmed that her mother, sister and an aunt had goiter. Physical examination revealed: goiter (WHO grade II) with exophthalmos and cardiomegaly. Thyroid function test showed suppressed TSH with elevated T3 and T4. She was managed as a case of thyrotoxic cardiomyopathy.

Discussion: In Nigeria today, thyroid disorders remain the second most common endocrine disorder with diverse metabolic sequelae. Thyrotoxic heart disease can present with sinus tachycardia, systemic hypertension, arrhythmias or dilated cardiomyopathy.

Conclusion: Thyrotoxic heart disease can affect both the young and elderly patients with hyperthyroidism. A nationwide multicenter study is advocated to determine its incidence in Nigeria.

Abstract #1102

ABSTRACT WITHDRAWN

Abstract #1103

PULMONARY HYPERTENSION AND RIGHT HEART FAILURE COMPLICATING HYPOTHYROIDISM

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Objective: To report a case of pulmonary hypertension and heart failure complicating hypothyroidism.

Case Presentation: A 41-year old Nigerian woman presented with 4 weeks history of dyspnea, weakness and easy fatiguability. She had a thyroidectomy thirteen years ago following a diagnosis of hyperthyroidism at another tertiary hospital. She was commenced on L-thyroxine, post- thyroidectomy but she discontinued medication and follow up care 3 years prior to this presentation. Examination revealed a young, lethargic woman with hypothermia, bilateral pitting pedal edema, slow mentation, tender hepatomegaly, elevated JVP, and a tricuspid regurgitant murmur with a palpable and loud pulmonary component of the second heart sound (P2). Thyroid function test was in keeping with hypothyroidism. ECG revealed right axis deviation, right atrial enlargement and right ventricular strain. Transthoracic echocardiography revealed right atrial enlargement with severe tricuspid regurgitation, elevated right ventricular/pulmonary artery systolic pressure (70.9mmHg), diastolic dysfunction, no effusion or clots. Right heart catheterization was not done as facility for cardiac catheterization was not available. An assessment of right sided heart failure and pulmonary hypertension secondary to hypothyroidism were made.

Discussion: Thyroid dysfunction is recognized to have major effects on the pulmonary and cardiovascular system, but heart failure and pulmonary hypertension is reportedly rare in hypothyroidism. Pulmonary hypertension is a life-threatening condition with poor prognosis if left untreated. The diagnosis of pulmonary hypertension is often delayed as was the case in our patient because the initial symptoms are often non-specific. In our patient, the history of thyroidectomy several years earlier and symptoms suggestive of hypothyroidism helped in reaching a diagnosis. Although limitations exist as to the use of echocardiography in the assessment of patients with pulmonary hypertension, it is still a useful test especially in resource-poor settings like ours. Early treatment of pulmonary hypertension is indicated because advanced disease may be less responsive to therapy.

Conclusion: Thyroid function tests are indicated in persons with pulmonary hypertension especially when there are symptoms suggestive of hypothyroidism. All patients must be adequately counselled before thyroidectomy, on the need for lifelong levothyroxine therapy and a means of tracking patients who default from follow up should be put in place.

Abstract #1104

INCIDENCE OF SECONDARY PRIMARY MALIGNANCIES IN THYROID CANCER PATIENTS TREATED WITH DOSIMETRY BASED RADIOIODINE THERAPY

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Objective: To determine whether the use of dosimetry based radioiodine therapy decreases the risk of developing secondary cancers compared with prior published studies.

Methods: A retrospective chart study was conducted on patients who received radioiodine via dosimetry in the Nuclear Medicine Department at Abington Memorial Hospital (AMH) from 1988-2005. Follow up data was obtained for these patients through chart review from the Endocrinology Department and cancer registry at AMH. Only 245 patients were included in the study based on inclusion and exclusion criteria.

Results: 35 of the 245 (14.3%) patients developed secondary cancers, with breast cancer and prostate cancer being the most common followed by melanoma, lymphoma, bladder cancer, colorectal cancer, ovarian cancer and leukemia. A sub group analysis did not reveal
a difference in the incidence of secondary cancers based on the type of primary thyroid cancers. However, there was statistically significant (p value <0.001) difference in the incidence of secondary cancers based on the stage of primary thyroid cancer (31.6% for stage 3 and 4 vs. 8.6 % for those with stage 1 and 2). The mean follow up for the study was 12.2 ± 4.8 years (range 5-32 yrs) and the mean latency to developing secondary cancer was 8.7 ± 5.8 years. Seven of the 35(20%) patients developed secondary cancer within 2 yrs and if these were to be excluded, the incidence drops down to 11.4%. The mean cumulative radiation dose was higher in the group with secondary cancer (268 ± 353.2 milli curie (mci) vs. 170.3 ± 176.7 mci) without statistical significance. There were fewer deaths (1.4%) in the group without secondary cancer compared to those with secondary cancers (14%).

Discussion: The incidence of secondary cancers in our study was 14.3% and it drops down to 11.4%, if secondary cancers occurring within 2 yrs of receiving radioiodine were to be excluded (too early to be related to Radio-iodine). This was comparable to prior published studies which reported an incidence of 4.8-13.5%. In these studies although the method of radioiodine dosing was not specified, it was most likely the empiric method. The group that developed secondary cancer had higher number of stage 3 and 4 primary thyroid cancers and received higher mean radiation doses. However, a subgroup analysis did not reveal a dose dependent relationship between cumulative radiation dose and occurrence of secondary cancers.

Conclusion: The incidence of secondary cancers in our study (14.3%) was comparable to the prior published studies (4.8-13.5%). Patients that developed secondary cancers received higher mean radiation doses, and had stage 3 and 4 primary thyroid cancers at baseline.

Abstract #1105

ACUTE BULBAR PALSY A RARE MANIFESTATION OF THYROTOXICOSIS

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Objective: This case is reported to state that thyrotoxicosis be considered in the differential diagnosis of dysphagia of obscure etiology.

Methods: A 49 year old woman presented sudden onset of dysphagia, dysphonia, weight loss and weakness since 12 week. She had difficulty in swallowing both solids and liquids. Many times accompanied by coughing & choking sensation. She had lost 12 kg over last 3 months. Her voice was a whisper. She was emaciated and irritable. Her BP was 160/70, Pulse 126 but she had no goiter. General examination was normal. She had bilateral absent gag reflex, reduced movements of the palate and pooling of secretions in the valleculae. Possibilities were Malignancy of the hypopharynx and Brain stem stroke.

Case Presentation: CBC, blood sugar, LFT, RFT, chest x-ray, MRI brain and upper GIT endoscopy were normal. In view of weight loss, thyroid function tests were done, free T3 10.2 (Normal range 2.5 -3.9 pg/ml), free T4 3.54 (Normal range 0.6 - 1.12 ng/ml), TSH <0.01 (Normal range 0.34 -5.6 micro IU/ml), and anti TPO 140.4 (Normal up to 50 IU/ml). Thyroid scan suggested Grave’s thyrotoxicosis. Electromyography and nerve stimulation tests were normal. Nasogastric feed, beta blocker and anti thyroid drug were started. Patient also given radioiodine. Her voice improved within 2 weeks. Her dysphagia to solids improved in 3 weeks and her nasogastric tube was removed in 8 weeks. Patient had complete recovery of dysphagia and dysphonia and gained 12 kg.

Discussion: 80% of thyrotoxicosis patients have neuromuscular symptoms. Weakness is primarily of the proximal limb muscles and associated bulbar involvement is rare and found only in 21% of patients with thyrotoxic myopathy. The dysphagia is resolved rapidly with the treatment of thyrotoxicosis. The postulates include hypercalcemia and hypomagnesemia. Hypercalcemia causes dysphagia by neuromuscular effects at neuromuscular junction. Possible neuromuscular causes of dysphagia in thyrotoxicosis include bulbar or esophageal myopathy, concomitant myasthenia gravis and hypokalemic periodic paralysis. According to a report 16% of patients with thyrotoxicosis were found to develop bulbar muscle dysfunction.

Conclusion: Acute bulbar palsy as a sole manifestation of thyrotoxicosis is rare but well documented. Hyperthyroidism must be considered in unexplained dysphagia. Acute bulbar palsy is fraught with complications. Early diagnosis and treatment can be life saving. The bulbar palsy evolves rapidly and severe, but improves dramatically with treatment. Treatment is early administration of antithyroid drugs and concomitant administration of beta blocker.
Abstract #1106

ALTERNATIVES TO ORAL TREATMENT IN THYROID STORM: A RARE CHALLENGE IN AN ALREADY RARE AND EMERGENT CLINICAL CIRCUMSTANCE.

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Objective: 1) To report an interesting case of thyroid storm. 2) To highlight what happens when thionamides cannot be given orally.

Case Presentation: An 81 year old Caucasian female with history of inflammatory bowel disease presented with new onset atrial fibrillation requiring cardioversion, extreme lethargy, and recent weight loss. Physical exam revealed blood pressure of 106/59, heart rate of 135, and temperature of 101.9 F. She appeared cachectic and frail. Heart was tachycardic and regular. She had lid lag. Neurologic exam revealed generalized weakness. Lower extremities exhibited waxy pitting edema. Laboratory findings showed leukocytosis, bandemia, globally elevated liver enzymes, and abnormal thyroid studies: TSH <0.01 (.27-4.2 uIU/ml), free T3 of 5.66 (2.2-4.1 pg/ml), free T4 of 2.23 (.85-1.71 ng/dl). Urine and blood cultures were positive for Proteus mirabilis. Her Burch and Wartofsky criteria score was > 45, highly suggestive of thyroid storm. The patient later developed distributive shock and became too weak to swallow oral medication. Her medical decision maker opted against placement of feeding tubes or central lines. The patient was treated with IV crystalloid, antibiotics, hydrocortisone and oral iodine drops. IV propranolol was held due to hypotension. Methimizole (MMI) was chosen over Propylthiouricil (PTU) due to evidence of liver dysfunction. MMI requires extemporaneous conversion to IV and rectal forms. IV preparation of MMI was not possible at our facility, so rectal formulation in the form of suppository was created. The patient was switched to oral MMI as soon as she could swallow. The patient recovered and was discharged home with outpatient endocrine follow up.

Discussion: Thyroid storm is a rare and life threatening version of thyrotoxicosis that is treated with a combination of medications including thionamides. It is important to realize that the thionamides MMI and PTU are only readily available in oral form and must be converted extemporaneously for IV or rectal use. The formulation chosen will ultimately depend on the clinical situation and facility capabilities. Theoretically, necessary treatment could be delayed or rendered unavailable based on the formulation limitations of MMI and PTU.

Conclusion: We present an interesting case of thyroid storm highlighting the uncommon circumstance in which neither oral nor enteral tube administration of thionamides was an option. Given the already rare and life threatening nature of thyroid storm, we recommend that physicians not only be familiar with the various formulations of thionamides but also the capacity of their facility to promptly and effectively prepare them.

Abstract #1107

ACTIVE HYPERTHYROIDISM ASSOCIATED WITH INCREASED NON-RESPIRATORY RELATED AROUSALS FROM SLEEP AND SLEEPINESS

Roger Piepenbrink, Sleep Medicine Fellow ABIM Adult Endocrine Diabetes and Metabolism

Sleep Disorders Center; Walter Reed National Military Medical Center

Objective: Thyroid disorders have well-established associations to OSA and insomnia. Graves’ disease is associated with complaints of fatigue and sleep fragmentation, however sleepiness not commonly associated with active Graves’ Disease in the physician’s mind. Objective polysomnogram measures of sleep and sleep quality were explored in active Graves’ disease to develop extent and characteristics of excessive sleepiness.

Methods: Five consecutive active Graves’ disease patients from military endocrine practice with elevated Epworth Sleepiness Score (ESS), and fitful sleep were given in-lab overnight sleep study (PSG); performing civilian sleep center unaware of this endeavor.

Results: 5 patients included (100% female, 24.4 years ± 5.5, BMI 25.5 kg/M2 ± 5.0). One of 5 patients went to PSG 2 years after successful treatment for Graves’ disease: at PSG BMI 21.1 kg/M2, ESS 6/24 (18/24 at presentation), TSH 0.198, AHI 1.3, Arousal Index 12.5/hour. Remaining 4 patients receiving PSG within two weeks of laboratory confirmation of hyperthyroidism and medical therapy. Observations were somnolence common (ESS 15.45 ± 1.81, normal < 9), arousal index elevated 27.75/ hour ± 13.2, normal < 5), but normal AHI 2.4 (range 0 - 6.8) and normal periodic limb movement index 1.0 ± 0.5 events/hour (abnormal > 15 events/hour). These four then broke out into two groups:

Group 1. Two patients. The mean values as follows:
BMI 22.55 kg/M2 ± 0.35;
TSH < 0.01 (0.34 - 4.82 mIU/liter);
fT4: 3.66 ± 1.47 (0.6 - 1.35 ng/dcliter);
fT3: 18.65 ± 7.00 (2.0 - 4.4 pg/ml);
Thyroid stimulating immunoglobulin (TSI) 266.5% ± 88.38 (<110%);

Abstract #1106

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A 30 year old lady presented with tremors bilaterally. She had multiple bluish black bruises minute, blood pressure was 136/88 mm of Hg. She had fine on repeated questioning the couple revealed that they had a fight two days back when the husband had grasped her neck and shaken her vigorously. The symptoms had started 5-6 hours after this incident. But as her symptoms kept progressing they had sought medical help. During the consultation multiple bruises were noticed over the neck, arms, chest and head. Initially the patient attributed the bruises to an accidental fall, but on repeated questioning the couple revealed that they had had a fight two days back when the husband had grasped her neck and shaken her vigorously. The symptoms had started 5-6 hours after this incident. On examination she was agitated, pulse rate was 146 per minute, blood pressure was 136/88 mm of Hg. She had fine tremors bilaterally. She had multiple bluish black bruises on the front and sides of neck. Tenderness was elicited on palpation of the thyroid. Thyroid eye signs were absent. Systemic examination was normal. There were no fractures or other grievous injuries. A diagnosis of thyrotoxicosis due to thyroiditis was made. On investigation, ESR was 9 mm. Thyrotoxicosis was seen with a TSH = 0.010 μIU/ml (0.350-4.940), fT3=4.46 pg/ml (1.71-3.71) and fT4= 3.2 ng/dl (0.70-1.48). Ultrasound of the neck showed marked subcutaneous edema, thyroid gland showed no enlargement or nodularity. 99Tc pertechnate scan showed absent uptake and the thyroid gland could not be delineated. Based on the clinical background and laboratory results patient was diagnosed as a case of traumatic thyroiditis and started on high dose propranolol (160 mg/day). She was relieved symptomatically within one week of starting therapy.

Discussion: Excessive daytime sleepiness was common (high ESS) in active Graves’, and associated with increased nonrespiratory-related arousals. However, the etiology for this association between the cause for this sleep fragmentation leading to sleepiness in the hypermetabolic state is not known. This may have implications for patients cognitive, fine motor skill capability at work and for example driving a car. These patients may need to be protected from themselves and others.

Conclusion: To our knowledge this is the first PSG evidence, showing fragmented sleep (increase nonrespiratory event arousal) and sleepiness (increased ESS) in active Graves’ disease.

Abstract #1108

TRAUMATIC THYROIDITIS

Sachin Jain, MBBS, MD, DM, FACE1, Krishnarpan Chatterjee, MBBS2, Aditya Dutta, MBBS1, Nimisha Jain, MBBS1, Nishchint Jain, MBBS2

1. Lady Hardinge Medical College, 2. PGIMER

Objective: To present a case of thyroiditis following trauma to the neck.

Case Presentation: A 30 year old lady presented with history of palpitations & tremors for 2 days. There was no history of heat intolerance, change in appetite or voice. She had never had similar symptoms before. Initially her family members had ignored her complaints as her symptoms had started following an episode of domestic violence and they had assumed that she was malingering. But as her symptoms kept progressing they had sought medical help. During the consultation multiple bruises were noticed over the neck, arms, chest and head. Initially the patient attributed the bruises to an accidental fall, but on repeated questioning the couple revealed that they had had a fight two days back when the husband had grasped her neck and shaken her vigorously. The symptoms had started 5-6 hours after this incident. On examination she was agitated, pulse rate was 146 per minute, blood pressure was 136/88 mm of Hg. She had fine tremors bilaterally. She had multiple bluish black bruises

Radioactive iodine scan and uptake (RAIU) @ 24 hours, homogenous 73.5% ± 14.85 (< 30%).

Group 2. Two patients. Mean values as follows.

BMI 30.72 kg/M2 ± 3.35;
TSH: 0.005 ± 0.01;
fT4: 0.99 ng/dl ± 0.09;
fT3: 3.5 ± 0.7;
TSI: 118% ± 31.1; RAIU @ 24 hours, homogenous 36% ± 15.6.

Discussion: Excessive daytime sleepiness was common (high ESS) in active Graves’, and associated with increased nonrespiratory-related arousals. However, the etiology for this association between the cause for this sleep fragmentation leading to sleepiness in the hypermetabolic state is not known. This may have implications for patients cognitive, fine motor skill capability at work and for example driving a car. These patients may need to be protected from themselves and others.

Conclusion: To our knowledge this is the first PSG evidence, showing fragmented sleep (increase nonrespiratory event arousal) and sleepiness (increased ESS) in active Graves’ disease.

Abstract #1109

ANALYTICAL VALIDATION OF A GENE EXPRESSION CLASSIFIER FOR MEDULLARY THYROID CARCINOMA

Dan Pankratz, PhD1, Zhanzhi Hu, PhD1, Su Yeon Kim, PhD1, Robert Monroe, MD, PhD1, Mei Wong, BS1, James Diggans, PhD1, Tom Traweek, MD2, Jochen Kumm, PhD1, Rick Lanman, MD1, Richard Kloos, MD1, Sean Walsh, MPH1, Giulia Kennedy, PhD1

1. Veracyte, Inc., 2. Thyroid Cytopathology Partners

Objective: Early detection of medullary thyroid carcinoma (MTC), an uncommon but aggressive thyroid neoplasm, is essential for effective treatment. The preoperative detection of MTC is challenging, as cytology does not identify this tumor in over half of cases and serum calcitonin tests have a high false positive rate. Previously, a gene expression classifier for MTC (MTC classifier), part of the Afirma Gene Expression Classifier for thyroid nodules, was developed and clinically validated. The MTC
classifier identifies this aggressive thyroid neoplasm with high clinical sensitivity and specificity. Here we report the analytical verification and validation of the MTC classifier, intended for use on thyroid fine-needle aspirate biopsies (FNAB).

**Methods:** We assessed MTC classifier performance on 27 histopathologically confirmed MTC tissues. MTC tissues and FNABs were used to assess assay response to modeled mixtures of MTC samples with normal thyroid tissue, a benign thyroid nodule, a Hürthle cell adenoma and whole blood. Intra- and inter-run reproducibility and inter-laboratory accuracy of MTC classifier results were demonstrated on MTC tissues and FNABs. Limiting RNA input and genomic DNA contamination were tested on an MTC positive FNAB and tissue, respectively. An assay positive control material was produced and tested.

**Results:** The MTC classifier correctly identified 26 of 27 specimens as MTC (96.3% sensitivity). Tolerance to assay RNA input variation (5-25ng) and genomic DNA contamination (30% by mass) was demonstrated with 100% accurate classifier results under all tested conditions. Mixture modeling of MTC samples with benign thyroid tissues and blood showed detection of MTC a majority of the time at MTC sample proportions as low as 20%. Reproducibility and concordance of classifier results was demonstrated within processing runs, across processing runs, and between laboratories.

**Discussion:** We successfully demonstrated the analytical sensitivity and specificity, accuracy and reproducibility of the Afirma MTC classifier. The MTC classifier is robust to interfering substances often found in FNAB such as blood and genomic DNA, and is resistant to the effects of sample dilution.

**Conclusion:** The MTC classifier may be used to accurately assess thyroid FNAB for medullary thyroid carcinoma in nodules that are cytology indeterminate, suspicious for malignancy, or frankly malignant (Bethesda III-VI). The routine use of this test in the clinic allows endocrinologists using Afirma to avoid missing the diagnosis of medullary thyroid carcinoma pre-operatively, thus facilitating the correct surgical management of patients with this disease.

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**Abstract #1110**

**ALL-CAUSE MORTALITY AND CARDIOVASCULAR MORTALITY DUE TO FREE THYROID HORMONES ARE ASSOCIATED WITH DIFFERENT METABOLIC DYSFUNCTIONS**

Anette Merke, MD, Juergen Merke, MD PhD, Winfried März, MD PhD

1. Thyroid Center Bergstrasse, 2. Mannheim Institute of Public Health, Rupertus Carola University Heidelberg, Medical Faculty

**Objective:** The LURIC study is a large prospective cohort study. 3316 German patients were included between June 1997 and May 2001. Mean inclusion criterium was clinical stability except for acute coronary syndrome. All patients were referred to angiography. Subjects were followed up in 2010 for mortality. As published recently, high FT4 and low FT3 levels are predictors of long term all-cause mortality as well as cardiovascular mortality in LURIC.

To establish a possible relationship between morbidity and mortality we analyzed the clinical characteristics of study participants according to thyroid hormone quartiles.

**Methods:** We examined 2507 subjects with angiographic CAD and matched controls. Excluded were patients with overt thyroid disease, those receiving thyroid medication, medication with direct influence on thyroid metabolism. Patients were classified into quartiles according to TSH, fT4 and fT3 levels. Clinical and anthropometric characteristics were grouped according to quartiles, numbers and/or percentages for categorical variables and as means and standard deviations for continuous variables. Associations of categorical and continuous variables were analyzed by χ2 test and ANOVA with covariables.

**Results:** In the high risk 4th FT4 quartile (≥ 18.8 pmol/L) we saw three highly significant effects with diabetes, fasting glucose and eGFR: these patients had the most impaired kidney function, a higher fasting glucose and were more diabetic. Significant effects of FT3 levels were demonstrable in age, smoking status, coronary artery disease, cholesterol levels, triglycerides, blood pressure and kidney function. In the lowest two high risk mortality quartiles (≤ 4.7 pmol/L) patients were older and the highest numbers of NSTEMI and STEMI. Low FT3 high risk patients had the lowest Cholesterol, LDL and HDL, triglycerides as well as BP and eGFR. No significant effect of FT3 on fasting glucose and diabetes was observed.

**Discussion:** FT4 seems to have a specific lethal effect together with diabetes and kidney function. The according lab data were in a subclinical range. Elevated FT4 together with slight alterations may cause the
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Elevated mortality risk. FT3 effects can only be in part explained by the low T3 syndrome, since subjects were clinically stable and relatively young.

**Conclusion:** High FT4 and low FT3 are predictors of long term all cause and cardiovascular mortality. High FT4 takes its mortal effect together with impaired kidney function and elevated fasting glucose and/or diabetic disease. Low FT3 is associated with relatively higher age, lower lipid levels, lower blood pressure and impaired kidney function as well as severe levels of cardiovascular disease.

**Abstract #1111**

**A CASE OF GESTATIONAL THYROTOXICOSIS MANIFESTING AS WERNICKE’S ENCEPHALOPATHY**

Deep Shikha, MBBS, Bhavana Bajracharya, MBBS, Nathaniel Winer, MD

**Objective:** To present a case of gestational thyrotoxicosis and hyperemesis gravidarum (HG) manifesting as Wernicke’s encephalopathy (WE).

**Case Presentation:** A 36 year old woman, at 14 weeks of gestation, was admitted to the hospital for management of severe HG. While hospitalized, she developed low grade fever, tachycardia, hypotension and altered mentation. Labs were remarkable for TSH <0.01mIU/L, total T4 13.1 mcg/dL, total T3 177 ng/dL, T3 resin uptake 35%, free thyroxine index 4.58, and serum HCG 55,000 mIU/mL. Physical examination revealed a confused, lethargic woman with a normal sized thyroid, positive pendular nystagmus in both horizontal and vertical gaze, decreased muscle tone and no hand tremor. Thyroid storm was suspected and she was started on methimazole and propranolol. Brain MRI done later showed hyperintense abnormal signals in bilateral thalami consistent with WE. She was immediately started on intravenous thiamine and mental status improved considerably within 3-4 days. Within the two weeks thyroid function tests normalized and methimazole was discontinued. Thyroid stimulating immunoglobulin, thyroid binding inhibitory immunoglobulin and thyroid peroxidase antibodies were negative. Repeat brain MRI four days after, showed a reduction in bilateral thalamic signal intensity.

**Discussion:** Overt hyperthyroidism arising from primary thyroid disease is uncommon in pregnancy, but transient gestational thyrotoxicosis is not unusual. In gestational hyperthyroidism, beta hCG which has weak thyroid stimulating activity, may cause manifestations of thyrotoxicosis during peak serum concentrations which typically subside as hCG production falls. Women with HG have higher serum hCG levels and consequently, are subjected to greater thyroid stimulating activity. Usually hyperthyroidism is transient and does not require treatment. The association of Wernicke’s encephalopathy with gestational hyperthyroidism is a rarely reported phenomenon. Thiamine deficiency may result from increased consumption secondary to hyperthyroidism, elevated hyperemesis induced catabolism and enhanced fetal growth demand, thereby precipitating WE. Therefore, WE should be considered in hyperthyroid women with HG who develop neurological abnormalities.

**Conclusion:** Gestational thyrotoxicosis in a patient with hyperemesis gravidarum can precipitate acute Wernicke’s encephalopathy which may mimic thyroid storm and thus delay appropriate management of the neurologic disorder. Prophylactic thiamine administration may be considered in patients who present with hyperemesis gravidarum.

**Abstract #1112**

**IGG4 RELATED THYROIDITIS**

Ruchi Gaba, MD, Susan Samson, MD, PhD, FRCP, FACE, Nalini Ram, MD, James Suliburk, MD

**Objective:** We describe a unique subtype of IgG4-related disease causing Hashimoto’s thyroiditis.

**Case Presentation:** A 51 y.o. Asian female with history of hypothyroidism, presented to our clinic with a 3 month history of a painful, enlarging neck swelling with compressive symptoms. On exam, the thyroid gland was diffusely enlarged at approximately 50 g without neck lymphadenopathy. Lab testing revealed TSH 26 uIU/mL and FT4 0.7 ng/dl (0.8-1.8), with very elevated thyroperoxidase antibodies (TPO-Ab) of 21885 IU/mL. CT of the soft tissue of the neck demonstrated mass effect on the trachea and esophagus. Thyroid ultrasound showed an enlarged heterogeneous gland (right lobe 6.6 x 3.7 x 4.4 cm, left lobe 6.4 x 3.2 x 3.8 cm, isthmus 0.4 cm in size) with normal vascularity and a 2.5 cm right inferior solid nodule. FNA of the nodule and right lobe was negative but the left lobe histology was indeterminate with microfollicles. Corticosteroids provided symptomatic relief until the patient could undergo total thyroidectomy. On pathology, there was destruction of the normal thyroid parenchyma by a lymphoplasmacytic infiltrate with compressive symptoms. On exam, the thyroid gland was diffusely enlarged at approximately 50 g without neck lymphadenopathy. Lab testing revealed TSH 26 uIU/mL and FT4 0.7 ng/dl (0.8-1.8), with very elevated thyroperoxidase antibodies (TPO-Ab) of 21885 IU/mL. CT of the soft tissue of the neck demonstrated mass effect on the trachea and esophagus. Thyroid ultrasound showed an enlarged heterogeneous gland (right lobe 6.6 x 3.7 x 4.4 cm, left lobe 6.4 x 3.2 x 3.8 cm, isthmus 0.4 cm in size) with normal vascularity and a 2.5 cm right inferior solid nodule. FNA of the nodule and right lobe was negative for malignancy but the left lobe histology was indeterminate with microfollicles. Corticosteroids provided symptomatic relief until the patient could undergo total thyroidectomy. On pathology, there was destruction of the normal thyroid parenchyma by a lymphoplasmacytic infiltrate with hyperplastic lymphoid aggregates and bands of fibrous tissue and collagen. There was a predominance of plasma cells and increased kappa to lambda light chain ratio. Urine and serum electrophoresis results were normal. IgG4 was positive in > 20 plasma cells per high power field meeting
criteria for IgG4 Hashimoto’s Thyroiditis (HT). Serum IgG levels were elevated at 1789 mg/dl (700-1600 mg/dl). After surgery, patient’s compressive symptoms were relieved and she is stable on levothyroxine.

**Discussion:** There is a unique subtype of HT, termed IgG4 thyroiditis, which is characterized by lymphoplasmacytic infiltration, fibrosis, and increased IgG4 plasma cells in the thyroid and elevated IgG4 in the serum. IgG4 thyroiditis is clinically distinct from non-IgG4 thyroiditis, with rapid progression, hypothyroidism, higher levels of thyroid antibodies and low echogenicity on ultrasound. This entity has morphological similarities with Riedel’s thyroiditis and needs further study.

**Conclusion:** Our case highlights this new clinicopathological entity— IgG4 related thyroiditis distinct from non-IgG4 thyroiditis.

**Abstract #1113**

**TSH INDEPENDENT METASTATIC FOLLICULAR CANCER PRESENTING AS HOT NODULE**

*Shira Eytan, MD, David Bleich, MD, Maya Raghuwanshi, MD*

Rutgers NJMS-Newark

**Objective:** Thyroid carcinoma in a hot nodule is a rare occurrence. Thyrotropin receptor (TSHR) gene mutations have been identified in a handful of thyroid carcinomas, and to our knowledge, only one case of metastatic thyroid follicular carcinoma (Fuhrer 2003). We present a case of an autonomous functioning thyroid nodule found to be follicular thyroid cancer, which later metastasized to bone and was found to be TSH independent. We speculate that this carcinoma may have acquired a gain of function mutation in the TSHR.

**Case Presentation:** A 57 year old man originally presented to with classic symptoms of hyperthyroidism, and was found to have a suppressed TSH and elevated T3/T4. Workup revealed a hot nodule and 2 attempts at ablative therapy failed to wean him off of methimazole; eventually he required a hemithyroidectomy (2012) for compressive symptoms. The pathological specimen revealed a moderately differentiated invasive follicular thyroid carcinoma with multiple nodules ranging from 0.6 to 4 cm. Shortly thereafter he underwent completion thyroidectomy. Post operatively, thyroglobulin was 189, and post therapy I-131 scan showed uptake in midline neck, left clavicle, sternum, and left rib. Patient received 202 mCi of I-131 sodium on 8/3/2012. Most recently, whole-body I-131 scan was performed this year after withdrawing him from Synthroid for 2 months, yet his TSH remained suppressed at 0.01 (repeat on day of scan: 0.007). Thyroglobulin at this time was 2077. Despite this TSH suppression, I-131 scan demonstrated intense uptake in the sternum (11%), suspicious for skeletal metastasis (no uptake in surgical bed of thyroid). Follow-up MRI of the chest and PET CT confirmed multiple sites of osseous metastases with lytic lesions in mid and lower portions of the sternum, right sacrum, and calvarium, as well as a pathologic fracture in the left fourth rib. A decision was made to treat the patient with additional 200 mCi of I-131.

**Discussion:** Reports of functioning thyroid carcinoma within a hot nodule are very rare. Even fewer of these have been found to metastasize and be TSH independent. Different point mutations have been associated with these cases that activate TSHR, as well as activating RAS oncogene mutations.

**Conclusion:** Our patient continued to have a suppressed TSH despite levothyroxine withdrawal, with significant iodine uptake. We suspect that he has a gain of function mutation, such as TSHR or RAS gene mutation, which have rarely been described in the literature.

**Abstract #1114**

**A NOVEL RESPONSE TO TWO DIFFERENT TYROSINE KINASE INHIBITORS IN DEDIFFERENTIATED PAPILLARY THYROID CARCINOMA**

*Shuchie Jain, DO, Victor Chang, MD*

Rutgers-NJMS

**Objective:** Dedifferentiated metastatic thyroid carcinoma is a complication of thyroid carcinoma for which little treatment is available.

**Case Presentation:** A 55 year old man presented in the summer of 2012 with worsening headaches. He had been diagnosed in 2006 with papillary thyroid cancer that was resected with a near total thyroidectomy and was treated with radioactive iodine. In the spring of 2009, he developed hoarseness and was found to have a recurrent mass with undetectable thyroglobulin levels that was encasing the laryngeal nerve. It was resected and found to be thyroid carcinoma. He was then treated with 6600 cGy intensity-modulated radiation therapy. In July 2011, he was found to have destructive bone lesions in the lumbar spine that was first treated by radiation and then surgically with lumbar decompression and posterolateral fusion, followed by L5 fusion in the spring of 2012 for pain control. Workup
of the patient’s headaches showed an occipital calvarial fossa mass by Computed tomography and he underwent surgical resection with findings of metastatic thyroid carcinoma. In the fall of 2012, he had worsening of his back pain and new radiculopathy. At this point, he was started on a trial of pazopanib, and over the next few months had resolution of his pain, and stabilization of his bone metastases by CT scan. He continues to be followed in clinic.

Discussion: Papillary thyroid carcinoma is a well-differentiated cancer emerging from the follicular cells. Treatments such as TSH suppressing therapy, surgical removal and radioiodine ablation can eradicate most of these cancers, reemergence of dedifferentiated thyroid cancer occurs in about 30 percent of the patients. Until now, no treatments were available. Sorafenib has recently been shown to be effective in the treatment of these patients but was not effective in this patient. Initial treatment was with Sorafenib (TKI) without much effect in halting disease progression and with side effects of hand, foot, mouth syndrome. A trial of a different TKI; Pazopenib was initiated which not only decreased tumor burden but also was tolerated well. Pazopanib has been studied in other forms of thyroid cancer but not in dedifferentiated thyroid cancer.

Conclusion: This case indicates that if improvement with a specific TKI is not noted, patients may benefit from another drug within this class in dedifferentiated thyroid carcinoma.

Abstract #1115

INVASIVE THYMOMA POST I-131 ABLATION FOR PAPILLARY THYROID CANCER

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1. Albany Medical Center, Division of Endocrinology and Metabolism, 2. Albany Medical Center, Division of Hospitalist Medicine, 3. Albany Medical Center, Division of Pathology

Objective: We are reporting this case due to the increased awareness of the presence of secondary cancers amongst patients who have received radioactive iodine treatments for thyroid cancer. The finding of sodium-iodine symporter (NIS) expression in thymic tissue makes this organ another possible target for unwanted effects of radioactive iodine. In this patient, we report an invasive thymoma stage 3B.

Case Presentation: 39 year old patient with no previous medical history was diagnosed with multinodular goiter and treated surgically. Pathology examination revealed an incidentally found 7.5mm papillary thyroid cancer for which she was treated with 100mCi of I-131 for thyroid remnant ablation and started on levothyroxine therapy. Nine years later, she was diagnosed with invasive thymoma stage 3B.

Discussion: It is known that thymic tissue can take up radioactive iodine as reported on some post treatment scans. This uptake can be variable and may even be higher after surgical removal of the thyroid. The finding of NIS expression in the thymus explains this uptake. This may be of concern regarding risk for neoplastic transformation of thymus after exposure to radioactive iodine.

Conclusion: This case continues to reinforce the concept that clinicians need to make a careful individual evaluation of risk /benefit when deciding whether to treat a patient with radioactive iodine. Although for many years radioactive iodine has been considered as innocuous treatment, secondary cancers have been described in patients with early stage tumors who have been given this therapy. Thymomas are rare tumors, so one case report cannot establish a cause-effect relationship. However, clinician awareness of such a possibility may encourage more judicious use of radioactive iodine, especially in the younger population, and may stimulate additional studies of this possible complication of radioactive iodine therapy.

Abstract #1116

LONG-TERM SAFETY AND EFFICACY OF RECOMBINANT HUMAN PARATHYROID HORMONE, RHPTH(1-84), FOR THE TREATMENT OF ADULTS WITH HYPOPARATHYROIDISM: ONE-YEAR DATA FROM THE RACE STUDY

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1. Section of Endocrinology, University of Chicago Medicine, 2. Division of Endocrinology and Diabetes, Children’s Hospital of Philadelphia, 3. Endocrinology and Metabolism, Physicians East, PA, 4. Endocrine Research Unit, SF Department of Veterans Affairs Medical Center, University of California, 5. Division of Endocrinology, College of Physicians and Surgeons, Columbia University, 6. Endocrine Unit, Massachusetts General Hospital and Harvard Medical School, 7. NPS Pharmaceuticals, 8. Mayo Clinic Division of Endocrinology, Diabetes, Metabolism, & Nutrition

Objective: Hypoparathyroidism, the last endocrine deficiency without approved hormone replacement therapy, is a rare endocrine disorder characterized by low parathyroid hormone (PTH) levels, hypocalcemia,
hyperphosphatemia, and hypercalciuria. Current therapy with high doses of oral calcium (Ca) and activated vitamin (Vit) D does not normalize mineral homeostasis or sense of well-being and can lead to complications. The phase III placebo-controlled REPLACE study demonstrated the safety and efficacy of rhPTH(1-84) in adults with hypoparathyroidism. The primary endpoint (≥50% reduction in oral Ca and active Vit D while maintaining serum Ca in target range) was achieved in 53% of rhPTH(1-84)- vs 2% of placebo-treated patients (P<0.001). The subsequent RELAY study showed that a lower dose (25 μg) of rhPTH(1-84) achieved the same endpoint in some patients. RACE is an ongoing open-label US extension of REPLACE and RELAY designed to assess long-term safety and efficacy of rhPTH(1-84). Here we present the planned 52-week interim analysis.

Methods: All patients started on 25 or 50 μg/d rhPTH(1-84) with up-titration to 50, 75, and 100 μg/d if active Vit D and oral Ca could be further reduced. Long-term efficacy was based on the composite endpoint of ≥50% reduction in oral Ca (or ≤500 mg/d) and ≥50% reduction in active Vit D (or ≤0.25 μg/d) at Week 52 while maintaining a serum Ca level ≥7.5 mg/dL.

Results: 53 patients enrolled at 13 centers (83% female; mean age 48±10 y; BMI 31±7 kg/m2; mean duration of hypoparathyroidism 16±13 y), and 49 continued through 52 weeks. 74% (95% CI, 59-85) met the efficacy endpoint. Mean baseline Ca and active Vit D doses were 2203±1708 mg/d and 0.7±0.5 μg/d, respectively, and by Week 52 decreased by 67±34% and 73±44%, respectively. Serum phosphate decreased by a mean of 0.73±0.79 mg/dL. Over time, efficacy was maintained without any evidence for resistance. Compliance with injection was 80% or higher in 98% of patients. There were no discontinuations due to AEs. AEs were reported by 51 (96%) patients. The most common AEs were muscle spasm, hypocalcemia, paresthesia, nausea, headache, arthralgia, and constipation. Serious AEs in 4 (8%) patients were not considered to be treatment related. There were no deaths and no significant changes in cardiovascular or renal parameters. The 52-week AE profile was similar to placebo-controlled studies.

Discussion: rhPTH(1-84) was efficacious and generally well-tolerated.

Conclusion: Extended treatment of hypoparathyroidism with rhPTH(1-84) was efficacious and well tolerated over 52 weeks. Serum Ca was maintained along with reduced phosphate in the setting of substantial reductions in Ca and active Vit D doses.

Abstract #1117
THYROIDITIS - CAUGHT IN A CREEPING MANNER

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Objective: To present a case of creeping thyroiditis in a middle aged gynaecologist.

Case Presentation: 40 yr old gynaecologist presented with complaints of fever, neck pain, sore throat, odynophagia, painful cough and palpitations for the past 7 days. On examination, the patient was agitated with a pulse rate of 110/min and a blood pressure of 110/70 mm Hg. Local examination of the oral cavity and pharynx was normal. Her hands were warm and moist, tremors were noticed. On examination of the neck, a tender 1.2X2 cm tender warm swelling was noted on left side. A clinical diagnosis of thyrotoxicosis secondary to thyroiditis was made. Investigations showed an ESR=98 mm/hr (0-30). Thyroid function showed toxic state with a TSH = 0.010 μIU/ml (0.350-4.940), fT3=5.20 pg/ml (1.71-3.71) and fT4= 4.84 ng/dl (0.70-1.48). Ultrasonography of the neck revealed diffuse enlargement of the left lobe of thyroid with inhomogeneous echotexture with normal vascularity in addition to an ill defined hypoechoic mass lesion measuring 26 X 21 mm in left lobe. 99Tc Pertechnate thyroid scan revealed decreased uptake in the thyroid with a total uptake of 0.2%, right 0.2% and no uptake on the left side simulating a hemithyroidectomy on the left side. Owing to the marked tenderness of the thyroid, a possibility of a thyroid abscess was also kept, albeit lower down in the possibilities and the patient was advised an FNAC, however she refused consent. A diagnosis of thyroiditis was made and the patient was started on propanolol 20mg QID and prednisolone 40mg after breakfast. She exhibited symptom improvement over 4 weeks after start of treatment but 6 weeks after the initial presentation she came back with the development of new onset pain in the right side of the neck. Examination findings revealed tenderness on the right side of the thyroid. This time ESR was111 mm/hr (0-30), TSH < 0.004 μIU/ml (0.350-4.940), fT3=6.76 pg/ml (1.71-3.71) and fT4= 4.84 ng/dl (0.70-1.48). Repeat 99Tc Pertechnate scan revealed absent uptake throughout the gland. A diagnosis of sub acute painful creeping thyroiditis was made. On subsequent follow up at 6 months, the patient became euthyroid.

Discussion: Sub acute painful thyroiditis or de Quervain’s thyroiditis is a self limiting inflammation of the thyroid. Differential diagnoses include haemorrhage into a thyroid nodule, papillary carcinoma, hashimoto’s thyroiditis, radiation thyroiditis, palpation thyroiditis and reidel’s thyroiditis.
Conclusion: Though literature describes that thyroiditis begins in one lobe before spreading to the adjacent lobe, in the experience of the author this is only the second time in 30 years that a classical documentation of the same could be made.

Abstract #1118

SEVERE HASHIMOTO HYPOTHYROIDISM PRESENTING AS RHABDOMYOLYSIS INDUCED ACUTE RENAL FAILURE: AN UNUSUAL ASSOCIATION

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St. Francis Hospital

Objective: Hashimoto’s thyroiditis is the most frequent cause of hypothyroidism. The most common neuromuscular manifestations include myalgia, fatigue, proximal muscle weakness and hypoactive tendon reflexes. However, infrequent severe cases of rhabdomyolysis with markedly elevated levels of creatine phosphokinase (CPK) and renal disease have been reported. Association between severe hypothyroidism and acute kidney injury (AKI) is rare.

Methods: We report a case of rhabdomyolysis, acute kidney injury, and myopathy as the only manifestations of severe hypothyroidism secondary to Hashimoto’s thyroiditis.

Case Presentation: A 32 year old male was admitted to the hospital with bilateral upper and lower extremities progressive pain and swelling. Symptoms started three days prior to admission and became worse the night before admission. Pain was worse with movement. He denied any vigorous activity, trauma, previous medications, and fever. Neurological examination revealed decreased muscle strength symmetrically on lower limb (3 + / 5 +) and upper limbs (4 + / 5 +), and diminished tendon reflexes (1 + / 4 +) symmetrically. Laboratory evaluation revealed the following serum levels: CPK , 2256 IU/L (38-174), creatinine 2.6 mg/dl (0.5-1.20), free thyroxine (FT4) <0.20 ng/dl (0.93-1.70), thyroid stimulating hormone 259.70 uIU/ml (0.400- 5.40), and thyroid peroxidase antibody 452 IU/ml (<35). After ruling out adrenal insufficiency by cosyntropin stimulation test, treatment was started with 125 ug oral levothyroxine. The symptoms gradually improved. The patient was discharged from the hospital five days later, showing only mild muscle pain. CPK levels reduced significantly.

Discussion: Asymptomatic mild to moderate elevation of creatine kinase frequently develops in hypothyroidism. However,marked creatine kinase elevation with rhabdomyolysis have been reported only in a very small number of cases with undiagnosed hypothyroidism.

Conclusion: Although hypothyroidism rarely presents with AKI and rhabdomyolysis, it should be suspected in patients presenting with impaired renal function and high creatine kinase level in the absence of other causes of rhabdomyolysis.

Abstract #1119

PARATHYROID ADENOMA BIOPSY WITH 25 GAUGE NEEDLE DOES NOT LEAD TO FIBROSIS AND PROLONGED OPERATIVE TIME FOR MINIMALLY INVASIVE PARATHYROIDECTOMY

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1. Thyroid Institute of Utah, 2. Utah Valley Regional Medical Center

Objective: To determine the negative effects of 25” needle biopsy of parathyroid adenomas on fibrosis, cure rates and operative times for minimally invasive parathyroidectomy

Methods: Retrospective blinded review of surgical pathology was done for 37 patients whos parathyroid adenomas were removed surgically at a community hospital. All patients had primary hyperparathyroidism, fibrosis was graded through a scale, operative times were also compared.

Results: Out of the 15 biopsied parathyroid adenomas only 2 showed mild fibrosis compared to 4 out of the 22 controls( 13.35% vs 18.18 %). The operative times for biopsied adenomas was on average 107 minutes utilizing minimally invasive surgery vs 119 minutes for controls with other methods of pre-operative localization, controls also underwent minimally invasive surgery. Cure rates were similar.

Discussion: Pre-operative localization remains essential for minimally invasive parathyroid surgery, some papers have claimed a significant rate of fibrosis and operative morbidity if localization is done with fine needle biopsy, however ultrasound guided biopsy remains the most cost effective method of localization. This paper reports on the experience at a community hospital where a blinded review shows that u/s guided biopsy is not associated with clinically significant fibrosis or operative morbidity.

Conclusion: 25 gauge needle biopsy of parathyroid adenomas for pre-op localization does not lead to clinically significant fibrosis and does not affect surgical cure or operative time.
**Abstract #1120**

**4 DIMENSIONAL CT SCAN IS NOT SUPERIOR TO ULTRASOUND GUIDED BIOPSY OF PARATHYROID ADENOMAS IN TERMS OF CURE RATES AND OPERATIVE TIMES FOR MINIMALLY INVASIVE PARATHYROIDECTOMY**

Shahzad Ahmad, MD, FACE, ECNU1, Paul Urie, MD2, Faran Khan, MBBS, FCPS

1 Thyroid Institute of Utah , 2. Utah Valley Regional Medical Center

**Objective:** 4D-CT is an emerging technique that uses high-resolution imaging to identify parathyroid adenomas, this information is utilized in planning minimally invasive unilateral parathyroid surgery. This study attempts to compare this to the technique of ultrasound guided FNA for pre-operative localization in the context of minimally invasive parathyroid surgery.

**Methods:** this retrospective study reviews 28 patients who underwent parathyroidectomy for primary hyperparathyroidism, pre-operative localization was performed by either u/s guided fna with ipth washout or a 4-d ct scan, outcomes were compared in terms of post operative calcium and ipth and operative times.

**Results:** Pre-operative calcium and intact PTH levels were similar in both the 4-D CT localized group vs the U/S guided FNA group ( 11.2mg/dl calcium and ipth 133 ng/dl vs calcium 11.1 mg/dl and ipth 158 ng/dl). Post-operative calcium and iPTH levels were also identical at 9.6mg/dl and 48ng/dl in the 4d-ct group and calcium of 9.3 and iPTH of 55 on average in the U/S guided biopsy group.

Operative time also did not differ. 4D-CT group average operative time was 105 minutes. U/S guided biopsy localized adenomas operative time was 107 minutes.

**Discussion:** 4D-CT scanning is a high sensitivity technique for pre-operative scanning for primary hyperparathyroidism. Its clinical utility is still being evaluated. Ultrasound guided FNA is the most cost effective tool available for pre-operative utilization. This study shows that they both remain viable options in planning minimally invasive parathyroid surgery.

**Conclusion:** 4D-CT localized adenomas do not lend themselves to shorter operative times and have similar cure rates when compared to u/s guided FNA technique when minimally invasive surgery is performed for primary hyperparathyroidism.

**Abstract #1121**

**PREDICTORS OF OSTEOPOROSIS IN ACTIVE HYPERTHYROIDISM**

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**Objective:** This study determined the prevalence and analysed possible predictors of osteoporosis by correlating the Z-score, T-score for bone mineral density, measured by DXA, with some clinical and biochemical indices in patients with active hyperthyroidism.

**Methods:** This was a case-control study in which 40 active hyperthyroid patients were randomly selected and 20-age and sex matched controls who met the inclusion criteria were recruited. The exclusion criteria included patients ages < 21 or > 50, significant history of alcohol, or caffeine intake, smoking and history of chronic medical diseases like DM, chronic kidney disease, chronic liver disease etc. Clinical data was collated through interviewer-administered questionnaire, anthropometric indices measured, and biochemical and hormonal analysis done. Distal one third (1/3) radius T and Z-scores, BMD were measured by DXA. Binary logistic regression analysis (SPSS 17) and p-value < 0.05 regarded as significant.

**Results:** The mean age + SD of the hyperthyroid and Controls was comparable (p=0.37) with Female to Male ratio 4:1 and 2:1 respectively. The mean BMI was lower in hyperthyroid patients than Controls but this was not statistically significant (p=0.06). The mean BMD was significantly low compared to the Controls p=0.000 The mean duration of thyroid disease in the studied was 27.4(23.6) months.

The prevalence of osteoporosis in hyperthyroid was 45% but none in Controls. Regression analysis showed that the presence of osteoporosis was associated with duration of thyroid disease, serum 25-hydroxyvitamin D and free triiodothyronine FT3( OR 1.01, 95%CI 0.937 -1.087 p=0.05, OR 0.925, 95%CL 0.856 -1.023, p=0.049 and OR 1.425, 95%CL 0.941-2.15 P=0.05). While increasing age, urinary calcium and phosphorus excretion showed a mild but insignificant association (p=0.08,p=0.07 and 0.09 respectively). Other clinical and biochemical parameters-Gender, BMI, weight, PTH, TSH, FT4, Alkaline phosphatase, osteocalcin, corrected serum calcium and phosphate did not show any significant association p>0.05.

**Discussion:** In hyperthyroid patients, duration of thyroid disease, serum 25-hydroxyvitamin D and FT3 associated significantly with BMD as measured by DXA in the
cortical bone of radius. Therefore these parameters can reflect osteoporosis in hyperthyroidism. **Conclusion:** Hyperthyroid patients with cortical or radius osteoporosis showed a typical clinical and biochemical profile as defined by the duration of thyroid disease, reduced 25 hydroxyvitaminD and increased levels of FT3. These indices therefore, can be used to predict the occurrence of osteoporosis in hyperthyroid patients since DXA—the current gold standard for BMD measurement is not readily accessible or available in Nigeria.

**Abstract #1122**

**THE RENAL FUNCTION AND ELECTROLYTE PROFILE OF HYPERTHYROID PATIENTS (FINAL)**

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A. Ogbera, MBBS,FMCP,FACE,
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Lagos State University Teaching Hospital, Nigeria

**Objective:** Renal impairment and electrolyte imbalance occur in a wide range of diseases. The effect of hyperthyroidism on renal function and electrolyte balance of these patients is a poorly reported aspect of thyrotoxicosis. This study determined the renal function and electrolyte profile of hyperthyroid patients.

**Methods:** This is a case-control study in which 40 patients with active hyperthyroidism were randomly selected and 20 healthy age and sex matched Controls who met the inclusion and exclusion criteria were recruited. Interviewer-administered questionnaire was administered. Fasting venous blood and early morning urine were collected and analyzed for biochemical, hormonal indices and persistent proteinuria/albuminuria respectively. Data was analysed using SPSS 17 package, p value ≤ 0.05 was taken to be significant.

**Results:** The mean serum Na, K and CL, Ca, P and urinary P excretion were comparable between the hyperthyroid(HY) and Controls p>0.05 but HCO3- was significantly high p<0.05 in the hyperthyroid. The mean serum and urine creatinine(cr) of the HY was significantly low compared to the control group p=0.000 and 0.008 respectively. Urinary ca/cr excretion and eGFR were significantly elevated in the hyperthyroid compared to the Controls, p = 0.02 and 0.002 respectively. However there was no significant difference between proteinuria, mean albumin/creatinine excretion between the hyperthyroid and controls, (p = 0.8).

**Discussion:** This study showed that hyperthyroid subjects had reduced mean serum and urinary creatinine compared to the Controls. This was due to renal hemodynamics and reduced phosphocreatine while increased GFR reflected increased cardiac output, decreased renal vascular resistance and elevated renal blood flow in the hyperthyroid patients. Proteinuria has also been found to occur in hyperthyroid patients in some studies although the mechanism is not fully understood. However, our study showed that the mean albumin/creatinine ratio was < 20µg/mg. Increased renal calcium excretion reflect increased bone turnover and increased vitamin-D activity. Hyperthyroidism also showed tendency to respiratory alkalosis as shown by HCO3 level.

**Conclusion:** Hyperthyroid patients had reduced serum creatinine, hypercalciuria, increased GFR and serum bicarbonate level but a normal albumin excretion rate. Therefore thyrotoxicosis was not significantly associated with renal impairment in our study.

**Abstract #1123**

**FALSELY ELEVATED TSH LEVELS DUE TO HUMAN ANTI MOUSE ANTIBODY INTERFERING WITH THYROTROPIN ASSAY**

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1. Saint Louis University, 2. VA St Louis

**Objective:** Measurement of thyroid stimulating hormone (TSH) levels with or without Free T4 is commonly ordered by primary care physicians to evaluate the thyroid function in patients with a wide variety of clinical symptoms ranging from fatigue, weight changes to arrhythmias. We present a patient treated for hypothyroidism, it was later found that human anti mouse monoclonal antibody (HAMA) had interfered with the TSH assay.

**Case Presentation:** 63 year-old male with past medical history of osteoarthritis and hyperlipidemia presented to his primary care physician for annual physical examination. He reported symptoms of fatigue, decrease exercise tolerability. The thyroid gland was normal. A screening thyroid panel showed serum TSH level 10.90 (range 0.34-4.94) uIU/ml. He was diagnosed with hypothyroidism and started on levothyroxine 150 mcg daily. Despite the use of medication TSH level remained elevated. Gradually the dose of levothyroxine was increased to 225 mcg. He subsequently was referred to endocrinology. Repeated lab showed TSH concentration of 10.7 mU/l, with a free T4 by dialysis of 2.9 ng/dl (N 0.8-2.7), total T3: 88.3 pg/dl (N 58-159), anti microsomal antibody titer was normal <10 IU/ml (N < 35). Compliance was checked and the proper way of taking the medicine was reviewed. MRI of the head showed a normal pituitary and levothyroxine was discontinued. As part of the reevaluation the TSH was
Abstract #1124

TREATMENT OF GRAVES DISEASE UNMASKING A LIFE THREATENING MYASTHENIC CRISIS

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SUNY Downstate Medical Center

Case Presentation: 25 year old African American male presented to the Emergency Department with complaints of shortness of breath and difficulty in speaking and swallowing. Medical history included Graves’ disease, diagnosed 3 months prior, treated with Methimazole and Propranolol. Family history was positive for thyroid disease in maternal aunt. On physical exam, he was lethargic and diaphoretic; vital signs were as follows: heart rate 144/min, blood pressure 140/115mmHg, respiratory rate 32/min, temperature 100.2°F and oxygen saturation 92%. He constantly held his jaw with his hands to speak. Eye exam was notable for ptosis, proptosis and bilateral limited abduction and upward gaze. Neck exam revealed a symmetrically enlarged, smooth, firm and non-tender thyroid gland. Strength was notably reduced in the upper extremities along with generalized hyporeflexia. Lab evaluation revealed the following: TSH 0.005µU/L, free T4 5.56ng/dL, free T3 457.71ng/dL, total T4 21.5µg/dL, T3 Uptake 57%, TBII 73.5%, TSI 331% and anti TPO antibodies 129.4U/mL. With a Burch Wartofsky score of 35, suggestive of thyroid storm, patient was started on IV Hydrocortisone, Prophythiouracil, potassium iodide drops and beta blockers. However, he deteriorated and was intubated for severe respiratory distress. Additional labs revealed positive anti acetylcholine receptor antibodies. Diagnosis of myasthenia gravis was made and calcium channel blockers were substituted for beta blockers in light of worsening myasthenia. Following treatment for myasthenic crisis including plasmapheresis, high dose glucocorticoids and pyridostigmine, patient improved clinically and was successfully extubated. TFTs improved and Propylthiouracil was switched to Methimazole.

Discussion: Graves’ disease and Myasthenia Gravis are both autoimmune diseases and it is not unusual that these occur concurrently. However, there is a large body of data suggesting that antithyroid drugs have an immunomodulatory effect in addition to their thyrosuppressant action. This can unmask a myasthenic crisis in patients with Graves’ disease after initiation of antithyroid drugs. The phenomenon described as worsening of one disease while improving the other, the so-called ‘see-saw’ relationship, likely occurred in our case.

Conclusion: Muscular weakness can be the presenting symptom of both Graves’ thyrotoxicosis and myasthenia gravis. Antithyroid drugs can unmask undiagnosed myasthenia in patients with Graves’ disease and lead to a life threatening respiratory failure. Therefore, in patients with neuromuscular symptoms suspected to be secondary to thyrotoxicosis, myasthenia should be considered strongly as a differential or concurrent diagnosis.

Abstract #1125

RECTAL ADMINISTRATION OF PROPYLTHIOURACIL IN SUPPOSITORY FORM IN TREATMENT OF THYROTOXICOSIS

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1. SUNY Downstate Medical Center, 2. Veterans Affairs New York Harbor Healthcare System

Case Presentation: 66 year old man with history of recurrent diverticulitis was evaluated in clinic for abnormal thyroid function tests. He denied history of thyroid disease in the past. He denied palpitations, tremors, weight loss, and diaphoresis. He was an active smoker and drank alcohol occasionally. He denied any family history of thyroid disease. Pertinent physical exam findings were heart rate of 98/min and a nodule in the right lobe of thyroid without any regional adenopathy.

Discussion: The elevated TSH level in this patient is caused by human anti-mouse monoclonal antibodies (HAMA). Heterophile antibodies interfere with the TSH assay, HAMA, which is the most commonly encountered heterophile antibody, may be present in the serum of up to 10% of patients. The incidence increases in people who have received radiolabelled mouse monoclonal antibodies. We could attempt to block or reduce the effect of HAMA interference by preincubating the patient’s serum with increasing amounts of non immune mouse serum. Other approaches include the use of commercially available HAMA blocking reagents to counteract heterophile antibody interferences in the clinical laboratory.

Conclusion: Heterophile antibody interference with TSH immunoassay should be on the differential diagnosis of asymptomatic patients with elevated TSH. Evaluation for this condition may prevent unnecessary thyroid hormone treatment.

Abstract #1126

THE EVALUATION OF HETEROPHILE ANTIBODY INTERFERENCES IN THE TSH IMMUNOASSAY

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Lisel Loney-Hutchinson, MD, FACE,
Nathaniel Winer, MD, FACE

SUNY Downstate Medical Center

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Abstract #1127

HETEROPHILE ANTIBODY INTERFERENCES IN THE TSH IMMUNOASSAY

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Case Presentation: 66 year old man with history of recurrent diverticulitis was evaluated in clinic for abnormal thyroid function tests. He denied history of thyroid disease in the past. He denied palpitations, tremors, weight loss, and diaphoresis. He was an active smoker and drank alcohol occasionally. He denied any family history of thyroid disease. Pertinent physical exam findings were heart rate of 98/min and a nodule in the right lobe of thyroid without any regional adenopathy.

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Conclusion: Heterophile antibody interference with TSH immunoassay should be on the differential diagnosis of asymptomatic patients with elevated TSH. Evaluation for this condition may prevent unnecessary thyroid hormone treatment.
Rest of the systemic examination was normal. Labs revealed TSH 0.009 μU/ml, free T4 4.41ng/dL, free T3 17.4ng/dL, thyroglobulin antibody 12.1U/mL, TSI 417% and anti TPO antibodies 362U/mL. Patient was started on Propranolol and Methimazole. Thyroid uptake & scan and thyroid ultrasound were scheduled as outpatient. Two weeks later, patient presented with an acute abdominal pain. CT abdomen with contrast revealed extensive colonic diverticulosis and acute diverticulitis involving sigmoid colon, associated peri-colonic stranding, and an area of contained perforation. Intravenous antibiotic therapy was initiated. Patient underwent exploratory laparotomy, lysis of adhesions and Hartmann’s procedure. Postoperatively, patient was tachycardic at 140/min. In view of increased risk of thyroid storm, patient was transferred to the intensive care unit. Intravenous Propranolol was instituted for heart rate control. Oral preparations of anti-thyroid drugs (ATDs) were not an option since patient was placed on NPO status. Therefore, Propylthiouracil (PTU) 200mg rectally every 12 hours was initiated. Patient had a period of prolonged ileus and remained on rectal PTU for 3 weeks postoperatively. Repeat TFTs showed improvement. Treatment was changed to oral PTU 150mg every 8 hours after resolution of ileus.

Discussion: Severe intercurrent illness or a surgical procedure may precipitate thyroid storm, a fulminant form of thyrotoxicosis, in patients with hyperthyroidism. If this condition is untreated, mortality can approach 75%. Administration of ATDs is imperative in thyrotoxicosis, even when oral intake may not be possible for various reasons. Rectal administration of ATDs is rarely used and many institutions have no experience with non-oral routes of administration. Rectal administration bypasses the liver, but absorption is slower and less extensive than with the oral form. At larger rectal dosing, serum levels of PTU have been demonstrated to reach higher levels than that achieved with oral administration.

Conclusion: Surgical procedure may precipitate thyroid storm. In such a scenario, when oral administration of anti-thyroid drugs is not possible, rectal suppository is an alternative to successfully treat thyrotoxicosis.

Abstract #1126

HYPOTHYROIDISM CAN PRECIPITATE PSEUDOINTESTINAL OBSTRUCTION IF IT OCCURS IN THE PRESENCE OF A MORE GENERALIZED DEFECT OF SYMPATHETIC HYPOFUNCTION

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Objective: To determine if the complete correction of pseudointestinal obstruction which was obtained by combined treatment with dextroamphetamine sulfate, a drug well known to improve various gastrointestinal motility disorders as well as inflammatory bowel disease, and thyroid hormone replacement for secondary hypothyroidism, could be maintained by just treating with thyroid hormone and eliminating the amphetamine therapy.

Case Presentation: Case study: A 23 year old woman developed severe pseudo-intestinal obstruction. She was treated with dextroamphetamine sulfate and her pseudo-intestinal obstruction went into complete remission. Simultaneously she was treated with 50mcg of thyroid hormone since her serum free thyroxin level was low at 0.5 ng/dL (nl = 0.8 - 1.8) and her TSH was low at <.01 mIU/L (nl = 0.4 - 4.2). Thus she was diagnosed with secondary hypothyroidism originating from a hypothalamic or pituitary defect. Because of the quick response and the knowledge that other types of gastrointestinal disorders, e.g., achalasia and gastroparesis, respond to amphetamines it was assumed that the improvement was related to sympathomimetic amine therapy. After 4 years of complete remission a decision was made to stop amphetamines to see if thyroid hormone replacement alone could maintain the remission. There has been no recurrence of the pseudointestinal obstruction in 3 years.

Discussion: The sympathetic nervous system controls cellular permeability and hypofunction is the cause of a wide variety of pain syndromes and muscle motility disorders that have been attributed to the inability to filter out harmful chemicals and toxins into specific tissues which either causes an inflammatory response with subsequent pain or adversely effects motor function leading to various pathological syndromes.

Conclusion: Since spontaneous remission from conditions caused by the sympathetic neural hyperalgesia edema syndrome are rare, it seems likely that the thyroid hormone replacement was responsible for the long-lasting remission once the dextroamphetamine sulfate
was stopped. The possibility exists that the sympathetic nervous system hypofunction was not severe enough by itself to cause the pseudo-intestinal obstruction but was precipitated by a further drop in sympathetic tone by a decrease in the thyroid hormone which is, in itself, a sympathomimetic amine.

Abstract #1127

SYMPATHETIC NERVOUS SYSTEM HYPOFUNCTION AS THE ETIOLOGIC FACTOR IN WHAT APPEARED TO BE A THYROID HORMONE RESISTANCE CONDITION

Jerome Check, MD, PhD1, Rachael Cohen, DO2, Diane Check, BS3


Objective: To determine if the standard treatment of the sympathetic neural hyperalgesia edema syndrome could improve symptomatology in a woman who appeared to have classic symptoms of hypothyroidism but perfectly normal sera thyroid function tests.

Case Presentation: A 46 year old female reported a three year history of memory impairment, constipation, fatigue, dry skin, dry eyes, brittle nails, hair loss, and weight gain despite exercise. She had a subtotal thyroidectomy due to a follicular adenoma. The patient did report taking progesterone during the luteal phase of her menstrual cycle with slight improvement in her symptoms. However the benefits were only temporary. The thyroid gland was not found to be enlarged. The patient’s heart rate was 60 beats per minute and regular. The rest of the physical exam was unremarkable. The patient’s laboratory values included: TSH = 1.96 mIU/L (0.4-5.5), free T4 - 1.3 ng/dL (0.8-1.8), Total T4 - 10.8 mcg/dL (4.5-12.5), T3 - 110 ng/dL (60-181) and PM cortisol to 3 mcg/dL (2-14). A standing and supine water load was also performed which involves ingesting 1500 mL of water over 30 minutes on two different days. The output is then measured for 4 consecutive hours and recorded. The patient’s standing output was 840 (nl >75% ingested load) and supine output 1185. The patient was started on a sympathomimetic amine (dextroamphetamine sulfate extended release 30mg) and was found to have resolution of much of her symptomatology. Her skin and hair were no longer dry, she denied exhaustion, she reported normal sleep patterns and improvement in her digestive system. She was no longer retaining any fluid.

Discussion: Possibly her symptoms could have been improved by placing her on thyroid hormone and raising her free T4 into the hyperthyroid range. However, the symptomatic improvement could be associated with muscle, heart and bone damage. Dextroamphetamine sulfate in low doses has few side effects and is a much safer option than placing a patient into a hyperthyroid state.

Conclusion: Thyroid hormone is a sympathomimetic amine. Thus it should not be surprising that a common disorder of sympathetic nervous system hypofunction could present as a thyroid hormone resistance-like syndrome and the symptoms abated by the treatment with the sympathomimetic amine dextroamphetamine sulfate which is believed to replace the defective chemical neurotransmitter.

Abstract #1128

THYROID HORMONE RESISTANCE: A CASE REPORT

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St Francis Hospital

Objective: Resistance to thyroid hormone is a rare condition caused by tissue refractoriness to the effects of circulating thyroid hormone, and may be misdiagnosed as hyperthyroidism. This syndrome is characterized by elevated circulating thyroid hormones, and unsuppressed TSH levels. Although most patients are euthyroid, rarely they may present with clinical hyperthyroidism, if the pituitary gland is more insensitive than other tissues to thyroid hormones. In this study we present a case of thyroid hormone resistance with clinical evidence of hyperthyroidism.

Methods: We present a case of 58 year old male who suffered from thyrotoxicosis for many years.

Case Presentation: A 58 year old male who suffered from thyrotoxicosis and diarrhea for many years and had been under treatment for atrial fibrillation with rate control medications. He had been tested for thyroid function in the past which revealed elevated fT3 and fT4 with slightly elevated TSH concentration. Pituitary adenoma was excluded as magnetic resonance imaging showed normal pituitary gland, alpha subunit was within normal range and TSH concentration increased after TRH administration. Sonography revealed normoechogenic, slightly enlarged thyroid gland. Methimazole had been tried in the past without any significant improvement. The diagnosis of thyroid hormone resistance was made and he was started on bromocriptine at a dose of 10 mg per day. After 2 months of treatment he achieved a state of constant euthyrosis and following next few months thyroid volume diminished.
**Discussion:** Failure to differentiate thyroid hormone resistance from primary thyrotoxicosis has resulted in the inappropriate treatment of nearly one-third of patients. Also, the diagnosis allows appropriate genetic counselling, and initiation of treatment.

**Conclusion:** In this case report we emphasize the importance of timely diagnosis of thyroid hormone resistance, which prevents many patients from being wrongly diagnosed as Graves disease and therefore various inappropriate treatments. Also, we present a successful treatment of this rare condition with bromocripten

**Abstract #1129**

**AN INTERESTING CASE OF FALSELY ELEVATED TSH LEVEL DUE TO HUMAN ANTI-MOUSE ANTIBODIES INTERFERENCE WITH THYROTROPIN ASSAY**

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**Objective:** Heterophile antibodies that interfere with the TSH assay have been described in the past. Human antimouse antibody (HAMA), which is the most commonly encountered heterophile antibody, may be present in the serum of up to 10% of patients. The incidence increases in people who have received or have been treated with radiolabeled mouse monoclonal antibodies. It has been suggested that these heterophile antibodies are natural antibodies in normal people, although they could represent autoantibodies.

**Methods:** We present a patient with falsely elevated TSH levels secondary to presence of HAMA.

**Case Presentation:** A 45 year old male presents with an incidentally found abnormal thyroid panel which showed elevated TSH levels along with normal free T3 and free T4. Patient complaints of prolonged constipation. He was started on increasing doses of levothyroxine. At 6 weeks follow up TSH did not show any significant changes. TSH was repeated at another laboratory with the addition of mouse serum to the patient’s sample, and it was normalized.

**Discussion:** A common and the first test to diagnose thyroid dysfunction is TSH measurement. HAMA is one of the multiple factors that can interfere with this test result and can result in costly diagnostic evaluation and unnecessary treatment.

**Conclusion:** It is crucial to evaluate for the interfering factors prior to initiating unnecessary and potentially harmful clinical interventions. In this case we report the presence of HAMA as the interfering substance in the TSH assay.

**Abstract #1130**

**ABSTRACT WITHDRAWN**

**Abstract #1131**

**GRAVES THYROTOXICOSIS WITH BILATERAL PARTIAL PTOSIS**

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Bangabandhu Sheikh Mujib Medical University

**Objective:** To show a rare case of Graves’ disease with myasthenia gravis.

**Case Presentation:** A 23-year-old female presented to Endocrinology Department, BSMMU with progressive swelling in the neck associated with features suggestive of thyrotoxicosis for four years. Six months after initial presentation she developed exophthalmos associated with redness, retro-orbital pain increased lacrimation and double vision; for which she was treated with high dosage of steroids for four months and significantly improved. She was on carbimazole irregularly. Two years back she developed bilateral partial ptosis which was progressive and had diurnal variation. On examination she had bilateral partial ptosis, diffusely enlarged thyroid gland with bruit and was clinically thyrotoxic. Examination of eye revealed bilateral partial ptosis with mild proptosis with complete external ophthalmoplegia. Her light reflex was intact and ice on eyes test was positive. Other systemic examination was unremarkable. Her TSH was <0.01 µIU/ml, FT4 60.64 pmol/l, FT3 30.0 pg/ml. Anti-thyroid antibodies (anti TPO & Tg) were strongly positive. Thyroid scan revealed markedly enlarged thyroid with uniform radio tracer concentration. Pre & post exercise Repetitive Nerve Stimulation (RNS) showed significant (>15%) decrease of Compound Muscle Action Potential (CMAP) in orbicularis oculi. Anti Ach receptor antibody was positive and HRCT of chest revealed enlarged thymus. She was put on carbimazole and propranolol for thyrotoxicosis and pyridostigmine for myasthenia with future plan of undertaking thymomectomy after rendering a euthyroid state.

**Discussion:** Graves disease and Myasthenia Gravis both are organ specific auto immune disease and their association is rare. A study in Japan shows prevalence of myasthenia gravis in graves disease is 0.14% and onset of graves disease in conjunction with myasthenia is earlier in this study.

**Conclusion:** Graves ophthalmopathy and ocular myasthenia gravis rarely coexist but when present can cause overlapping clinical features and diagnostic confusion. It should be distinguished clinically and by laboratory test because both the diseases have different management and prognosis.
Abstract #1132

A 40-YEAR-OLD MALE WITH FEVER, WEIGHT LOSS AND NECK PAIN

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Bangabandhu Sheikh Mujib Medical University

Objective: This case is presented to show the clinical and laboratory features of subacute thyroiditis which may present as prolonged fever and its dramatic response by steroid.

Case Presentation: A 40-year-old businessman got admitted in our department recently with the complaints of fever for one month which started as low grade with preceding upper respiratory symptoms but had become high grade for last 7 days. He noticed simultaneous painful swelling in neck in the region of thyroid initially involving left, subsequently the right side. Pain radiated to both angle of jaws, was worse on swallowing and neck movement. He had loss of appetite and weight loss of about 4 kg during this period. He gave history of excessive sweating, palpitation and restlessness. He had no previous or family history of thyroidal illness. He had taken several antibiotics prescribed by a general practitioner without any improvement. On examination patient was anxious, had warm sweaty hands with fine tremor, temperature 101°F, pulse 100/min (regular), BP 100/80 mm Hg. He had tender thyromegaly, firm in consistency, no bruit, no eye sign. All deep tendon jerks were exaggerated. Investigation showed raised ESR, suppressed level of TSH, raised FT3 and FT4. USG of thyroid gland showed bilateral enlargement with heterogenous parenchymal echotexture. Thyroid scan showed poor radiotracer concentration and poor visualization. Patient was treated symptomatically with a general practitioner without any improvement. On examination patient was anxious, had warm sweaty hands with fine tremor, temperature 101°F, pulse 100/min (regular), BP 100/80 mm Hg. He had tender thyromegaly, firm in consistency, no bruit, no eye sign. All deep tendon jerks were exaggerated. Investigation showed raised ESR, suppressed level of TSH, raised FT3 and FT4. USG of thyroid gland showed bilateral enlargement with heterogenous parenchymal echotexture. Thyroid scan showed poor radiotracer concentration and poor visualization. Patient was treated symptomatically with NSAIDs and beta blocker initially. Poor response ultimately led to the initiation of IV steroid. Within a day fever subsided and patient’s well being improved. He was discharged a few days later with oral steroid in tapering dose. On follow up after 2 months he became euthyroid.

Discussion: Sub acute thyroiditis is an inflammatory disorder of thyroid gland most likely due to viral infection. Usually it is diffuse but occasionally may present asymmetrically at first involving one lobe then the other (migratory thyroiditis). Spontaneous remission occurs in most cases with symptomatic treatment. In severe cases or in patients who do not respond to NSAIDs, glucocorticoid may be used.

Conclusion: In case of thyrotoxicosis etiological diagnosis is very important before giving any definitive therapy for thyrotoxicosis. Steroid rarely needed for subacute thyroiditis.

Abstract #1133

ABSTRACT WITHDRAWN

Abstract #1134

IMPACT OF IMPAIRED RENAL FUNCTION ON THERAPY OF DIFFERENTIATED THYROID CANCER WITH RADIOIODINE I-131.

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Objective: 1. To study rate of radioiodine removal in patients with differentiated thyroid cancer with impaired renal function compared to those with normal renal function.

2. To study and compare the effect of retained radioiodine dose on bone marrow and hospital residence time in both groups.

Methods: We studied 60 patients with differentiated thyroid cancer, admitted electively for remnant ablation radioactive iodine therapy in our hospital in last one year. We selected 30 patients with normal eGFR of 60 or more than 60 ml/min/1.73m2 and 30 patients with eGFR of less than 60ml/min/1.73m2, studied and compared the radioiodine kinetics, urinary excretion rate and its effect on hospital stay and bone marrow of both groups.

Results: We found that patients with impaired renal function have decrease excretion of radioactive iodine and there is a significant inverse relation between eGFR, hospital stay and bone marrow suppression.

Discussion: Sodium iodide I-131 is eliminated predominantly through renal clearance. Patients with renal impairment are subject to decreased excretion of sodium iodide I-131 and increased radiation exposure. Bone marrow depression can occur if larger than recommended doses of radioactive iodine are administered for treatment of thyroid cancer. Radiation exposure to bone marrow primarily depends upon rate of radioactive iodine excretion from the body. Dose reduction of I-131 for treatment of patients with differentiated thyroid cancer and renal failure is well documented. In patients with end stage renal disease, almost 5 fold decreases in I-131 administered dosages is required to avoid excessive radiation exposure to whole body and bone marrow. Therefore, we need proper guidelines to adjust the dose of radioactive iodine in patients with impaired renal function to avoid harmful effect of retained radioactive iodine on body and to decrease the hospital stay.

Conclusion: Patients with compromised renal function have delayed renal clearance of the tracer with consequent increased radiation exposure and hospital residence time.
Abstract #1135

FOLLICULAR VARIANT OF PRIMARY PAPILLARY THYROID CARCINOMA IN THYROGLOSSAL DUCT CYST: A CASE REPORT AND LITERATURE REVIEW

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Objective: Although Thyroglossal duct cyst (TDC) is one of the commonest thyroid anomalies, presenting as midline neck swelling, however, the malignant transformation is reported in only 1% of cases. The most common being papillary thyroid carcinoma (PTC) followed by its follicular variant.

Methods: We discussed a case of 42 year old Saudi female presented with 2 year history of midline neck swelling, found to have Follicular variant of Primary papillary thyroid carcinoma in DTC. In this context we reviewed the literature using Pubmed, Embase, and Medline by using following terminologies: “Papillary Thyroid Carcinoma”, and “Thyroglossal Duct Cysts”.

Case Presentation: Our patient had positive FNAB, underwent Sistrunk operation and total thyroidectomy, pathology revealed follicular variant of PTC without thyroid or lymph node involvement. We analyzed 117 patients published in major case series in last 12 years. Among 35 patients, who underwent FNAB, 77% had positive result. Among 99 patients, who had total thyroidectomy, 50% had concomitant PTC in the thyroid. Among 53 patients, who underwent neck dissection, 80% had cervical nodal involvement.

Discussion: Whether DTC arises De novo from the ectopic thyroid tissue in TDC or metastasize from thyroid gland is still debatable. Moreover, despite the risk stratification, management and follow-up plans are not clear.

Conclusion: Therefore we presented a case report with evidence based literature review to stress for the proper guidelines to be established for proper management and follow-up of these patients.

Abstract #1136

DISSEMINATED NOCARDIOSIS AFTER FNTA IN AN IMMUNOCOMPETENT PATIENT

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Case Presentation: A 41 y/o female patient with history of hypertension presented anterior neck “bump” and occasional solid dysphagia. She denied fatigue, fever, chills, changes in mental status, cough; or symptoms of hypothyroidism or hyperthyroidism. Physician evaluation revealed normal thyroid function, negative antithyroid antibodies, two large nodules on Thyroid U/S: a complex right 3 x 2.6 cm and 2.1 x 1.6 cm left solid with coarse interior calcifications and thyroid scan with heterogeneous multinodular goiter and right side hyperfunctional nodule. Results of U/S guided FNAT: right 2.1 cm nodule hyperplastic changes with cystic degeneration and left 1.6 cm nodule consistent with granulomatous thyroiditis, acid fast positive for thin acid fast filamentous bacteria, suggestive of Nocardia species. As on site adequacy smear revealed mild inflammation and few giant cells, culture was not performed. Patient started on sulfamethoxazole-trimethoprim. She was then hospitalized with pneumonia, fever, chills and productive cough. Chest CT scan with contrast showed multifocal bilateral hypoattenuating pulmonary nodules plus thyroid cystic lesions > 2 cm in right side and 1 cm in left side. Diagnosis of disseminated nocardiosis was made, although sputum, urine and blood cultures were negative and biopsy of nodules performed via bronchoscopy was negative for active nocardia infection. No evidence of immunosuppression or malignancy was found. After an uneventful hospitalization, she was discharged home on oral antibiotic therapy. Repeated FNAT after one month on antibiotics was non-diagnostic. Patient was consulted to endocrinology for evaluation of thyroid nodules. She had symptoms of neck compression, bilateral palpable nodules > 2 cm and was clinically and biochemically euthyroid. Both nodules showed in a neck U/S increase size of > 20% in all three dimensions. Due to worsening symptoms of neck compression and significant increase in nodular size, patient was referred to Endo-Surgery Services for possible total thyroidectomy. This patient lives in a rural area of Puerto Rico and has the habit of walking bare footed over the soil around her home; this is thought to be the portal of the nocardia infection.
Discussion: Nocardiosis is a life-threatening infection that may affect lungs, skin, and central nervous system, particularly in immune-compromised patients. Nocardia infection can rarely occur in patients without concurrent disease or immunosuppressive therapy. Nocardia thyroiditis is a rare clinical presentation, since thyroid gland is often resistant to infection.

Conclusion: We report a rare case of disseminated nocardiosis with pneumonia and thyroiditis, in an immunocompetent individual.

Abstract #1137

FDG-PET SCANNING IN PATIENTS WITH DIFFERENTIATED THYROID CANCERS (DTC) - INSTITUTIONAL EXPERIENCE

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Objective: Patients with detectable serum thyroglobulin (Tg) but undetectable disease on neck ultrasound and radioactive iodine whole body (RAI-WB) scan should have whole body FDG-PET scan to localize the tumor tissue. Sometimes, the scan fails to detect any pathologic accumulation of FDG. Some DTCs do not accumulate FDG or the tumor burden is too small to be detected by imaging. Studies have explored the relationship between serum Tg and results of FDG-PET scans. It is unclear if there is a certain Tg level below which PET scanning is not cost effective.

Methods: Retrospective chart review of patients with DTC who underwent FDG-PET in Cleveland Clinic in 2003-2013 for disease follow-up.

Results: We reviewed 198 PET-FDG instances, 49.5% done in women and the age was 15-85 years. 187 patients (94.5%) had papillary carcinoma, 6 follicular carcinoma (3%) and 5 Hurtle cell carcinoma (2.5%). 29 patients had PET scan while TSH was 5-24.9 uU/mL, 46 patients had TSH of 0.4-5 uU/mL and 123 patients below 0.4 uU/mL. 91 scans were considered positive and 107 negative after excluding 8 false positive scans; in six of them TG was at the lower end of detectability.

Patients with positive PET scans had Tg of 1.1-10887 ng/ml and those with negative scans, 0.2-782 ng/ml.

In the group with TSH ≥5 uU/mL and positive PET scan, Tg level ranged 7.1-885 ng/ml, and in the negative group 0.2-75.7 ng/ml.

In PET positive patients with TSH 0.4-4.9 uU/mL, Tg ranged 7.9-6367 ng/ml and with negative scan, 0.2-782 ng/ml.

Discussion: In our study all the patients with a positive PET-FDG with TSH >5 uU/mL (n=13) had TG ≥7.1 ng/ml and all the patients with normal range TSH (n=18) TG was ≥7.9 ng/ml, these levels offering 100% sensitivity.

In the suppressed TSH group (n=60), the patients with positive scan had TG ≥1.1 ng/ml, 5 patients had levels below 2 ng/ml, this cut-off yielding 96% sensitivity.

Conclusion: The results suggest that not all patients with negative RAI scan and low Tg level will benefit from PET scanning.

More data is needed to validate and refine these observations and clarify the best strategy for evaluation of these patients.

Abstract #1138

CONTINUATION OF AN OFFICE BASED EVALUATION OF GENE EXPRESSION CLASSIFIER USE IN THYROID NODULES

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Objective: To determine the ongoing usefulness and validity of a gene expression classifier technique on office based endocrine evaluation of thyroid nodule management.

Methods: Data from 272 additional thyroid nodules biopsied using UGFNA in a single location after the initial collection period previously reported were analyzed. All nodules were >1cm in size, and cytology was submitted in liquid based medium with cellular material placed in preservative for RNA analysis if needed. All cytology was interpreted by a single group of cytopathologists. Indeterminate cytology was reflexly submitted to Veracyte for GEC analysis. Benign findings were observed. Malignant cytology was referred for surgery. Indeterminate cytology with benign GEC markers were observed per ATA guidelines, and nodules with suspicious markers were referred for surgery.

Results: Benign cytology was demonstrated in 85% of nodules. Indeterminate cytology (AUS/FLUS) was reported in 13.9% of nodules. Malignant cytology was reported in 1% of nodules. Of the indeterminate nodules referred for GEC, 56% were suspicious, 41% benign, 3% inadequate RNA yield for interpretation. Of the GEC suspicious group referred for surgery, 45% had confirmed malignancy.

Discussion: Only a small percentage of thyroid nodules evaluated prove to be malignant. Between 10-30 percent of reported cytology studies show atypia that is not clearly benign or malignant. Use of this technique may help identify a subgroup of patients that can safely be observed.
if sufficient sensitivity and specificity can be demonstrated to be equal to the rate of falsely benign cytology. (5%) Collecting data from a busy single site after the previously reported data from the introduction of this technique may provide useful information to guide the individual endocrinologist in management of thyroid nodules. An observed slightly lower rate of atypia was identified in this patient population as well as a lower PPV of 45% This translates into a statistically improved implied NPV (93%) and implied risk of malignancy in this patient population of 29%.

**Conclusion:** A smaller, but significant ongoing sample set collected in one location after the initial pooled data set collection already reported demonstrated similar efficacy to the original study. Observed PPV and implied NPV are well within the confidence intervals reported in the validation studies of this technique.

**Abstract #1139**

**RARE PRESENTATION OF A HOT THYROID NODULE**

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**Objective:** Hot nodules are a common cause of hyperthyroidism. In our case, we discuss an atypical presentation of a hot nodule.

**Case Presentation:** A 25 year old female diagnosed with hyperthyroidism about 6 months ago, on Methimazole 20 mg daily came to our clinic for an initial visit. She denied any significant complaints but wanted surgery for hyperthyroidism. On exam, a palpable right thyroid nodule was noted. A prior thyroid uptake and scan reported diffuse increased uptake. Thyroid ultrasound showed a right thyroid nodule 1 X 0.5 cm.

A repeat thyroid uptake and scan at our hospital was suggestive of a hyper functioning right thyroid nodule. The TSH was 0.35 µIU/dl (0.27-4.2) with normal Total T3 and T4.

The patient insisted that she wanted to have surgery for the thyroid nodule. She was scheduled for a right lobectomy. The frozen section revealed papillary thyroid carcinoma and the patient had completion thyroidectomy.

The final pathology showed a 1.0 X 0.7 X 0.4 cm right thyroid nodule which showed cells consistent with papillary thyroid carcinoma and the margins were free of disease. The remainder of the right lobe and the left lobe of thyroid showed features of lymphocytic thyroiditis and one of the nine paratracheal lymph nodes showed features suggestive of metastatic disease. The patient was discharged and advised to review after one month.

**Discussion:** A review of literature revealed less than 80 patients diagnosed to have malignancy of thyroid in a hot nodule. This is an extremely rare presentation; physicians need to be careful not to miss this possibility.

**Conclusion:** Papillary thyroid cancer can occur in a hot nodule.

**Abstract #1140**

**RECURRENT THYROID STORM PRESENTING WITH VENTRICULAR TACHYCARDIA AND CARDIAC ARREST**

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**Objective:** Severe thyrotoxicosis is commonly associated with supraventricular tachyarrhythmias. We present a unique case of ventricular arrhythmia in the setting of hyperthyroidism.

**Case Presentation:** 43 year old male with history of untreated hyperthyroidism presented with palpitations, chest discomfort and dyspnea on exertion for 3 weeks. He also endorsed nausea, vomiting, insomnia, generalized weakness, psychomotor agitation and tremors. Vital signs and electrocardiogram (ECG) indicated atrial fibrillation with a ventricular rate of 216 bpm and blood pressure 224/176 mmHg. On exam he was tachypneic, afebrile and had a goiter with bruit and right sided nodule but no proptosis. Esmolol and heparin infusion were started and hours later the patient developed ventricular tachycardia and cardio-pulmonary arrest. Cardiopulmonary resuscitation, defibrillation and amiodarone infusion were initiated and he regained consciousness within 2 minutes. Thyroid function tests (TFTs) were: thyroid-stimulating hormone (TSH) 0.01 mIU/ml, free thyroxine (FT4) > 7.8 ng/dl and total triiodothyronine (T3) > 650 ng/dl. He was treated with methimazole (MMI), hydrocortisone, and Lugol’s solution. Coronary angiogram revealed no obstructive disease. Underlying cardiac conduction abnormalities was suspected based on family history but the patient refused an electrophysiology study and implantable cardioverter defibrillator. He was discharged home with an external defibrillator, metoprolol and MMI.

**Discussion:** A month later, the patient had recurrent symptoms and ECG revealed ventricular tachycardia at 200 bpm. He received a loading dose of amiodarone. TFTs indicated severe hyperthyroidism and Thyroid-peroxidase and TSH-receptor antibodies were positive. Thyroid ultrasound showed a right sided 2.3cm nodule,
Abstract #1141

TRANSIENT SELF-LIMITED THYROIDITIS AFTER CLINICAL REMISSION IN GRAVES’ DISEASE: A CASE SERIES.

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Objective: Graves’ disease is the most common cause of thyrotoxicosis. Antithyroid drugs are considered one of the standard treatments. Clinical remission occurs in 20-50% of patients. Recurrent hyperthyroidism has been reported in 10-30% after completion of medication. Recurrent Graves’ disease is the most common cause, however patient can have hyperthyroidism from other causes including thyroiditis. We report 3 cases of transient self-limited thyroiditis presenting as recurrence of thyrotoxicosis after clinical remission of Graves’ disease. Case Presentation: Our 3 patients had history of hyperthyroidism. The diagnosis of Graves’s disease was confirmed by the presence of Graves’ ophthalmopathy in case 1 and 2, and I-131 thyroid uptake and scan in case 3. All patients were successfully treated with anti-thyroid drugs. During follow-up after stopping medications, patient had episodes of self-limited thyroiditis with no thyroid tenderness. Case 1: 58 year-old female with prediabetes and hyperlipidemia was diagnosed with Graves’ disease at age 52. She was treated with Methimazole for 24 months and was able to achieve clinical and biochemical remission for 4 years. Patient experienced palpitations and was found to have TSH=0.01 mIU/mL. Her 24-hour thyroid uptake was decreased at 1% which was consistent with thyroiditis. Case 2: 48 year-old female was diagnosed with Graves’s disease at age 42. She was successfully treated with Methimazole for 19 months, and had been euthyroid for 2 years. She presented with weight loss and palpitations. Hyperthyroidism was consequently confirmed by blood test. Her 24-hour thyroid uptake was remarkably decreased at 0%. Case 3: 55 year-old man with diabetes type 2, and hypertension was diagnosed with Graves’ disease at age 45. He was treated with anti-thyroid drugs (Propylthiouracil then Methimazole) for 20months. His thyroid function tests showed hyperthyroidism on the follow-up visit after 5 years of clinical remission. Thyroiditis was diagnosed by decreased 24-hour thyroid uptake at 1%.

Conclusion: We present a rare case of thyroid storm with cardiac arrest from ventricular tachycardia with recurrent thyrotoxicosis despite thionamide and beta-blocker therapy with subsequent RAI induced thyroid storm. We report 3 cases of transient self-limited thyroiditis after clinical remission of Graves’ disease. Patients with Graves’ disease after clinical remission can have transient thyroiditis that can be confirmed by decreased thyroid uptake at 1% which might be subject to RAI induced thyroid storm.

Discussion: Our patients recovered and regained euthyroidism after observation and treatment with beta-blockers for 4, 3, and 5 months respectively. Conclusion: Hyperthyroidism after clinical remission of Graves’ disease can be not only from recurrence of Graves’ disease, but also from transient thyroiditis. Thyroid uptake and scan should be performed to establish the diagnosis before the definitive treatment of hyperthyroidism.
Results: The median age was 60 years-old (IQR= 41-70) and 42% of patients were female. The presence of hypertension, diabetes and cardiovascular disease were 90%, 38%, and 14%, respectively. The mean body mass index (±SD) was 24 kg/m² (±3.87), systolic blood pressure 160.64 mmHg (±30.44), and waist circumference 87.82 cm (±10.56). The median TSH was 4.1 μIU/mL (IQR= 1.9-5.8), free T4 1.01 ng/dL (±0.12), total T3 95.68 ng/dL (±25.59), and T3 reverse 0.23 ng/mL (0.15-0.34). The median IMT in the common carotid artery was 0.9 mm (IQR= 0.7-1). Twenty-five (50%) patients had significant atherosclerotic plaques in the carotid artery. In the bivariate analysis age, waist circumference, systolic blood pressure, hematocrit, PTH, total cholesterol, LDL cholesterol, and non-HDL cholesterol were related with wider IMT. HDL cholesterol was inversely related with IMT (r= - 0.53). Thyroid hormones were not associated with IMT. By multiple regression analysis, age, smoking, and hematocrit were related with IMT (p= 0.00).

Discussion: Cardiovascular disease are the most frequent cause of death in patients in hemodialysis. This excessive mortality is not only related with traditional risk factors (hypertension, diabetes, age, smoking) but also with non traditional risk factors (malnutrition, chronic inflammation). Thyroid hormones are predictors of cardiovascular mortality in this population; also, free T3 are inversely related with carotid artery IMT.

Conclusion: In our study, thyroid hormone levels were not related with carotid artery IMT or atherosclerotic plaques. Carotid artery IMT are associated with traditional risk factors.

Abstract #1143

SARCOIDOSIS OF THYROID

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Objective: To describe a case of sarcoidosis affecting the thyroid as the first manifestation of the disease.

Case Presentation: A 49-year-old woman presented with palpable left sided thyroid nodule. She had no symptoms or signs of thyroid dysfunction. Physical exam was remarkable for enlarged left thyroid lobe with no lymphadenopathy. TSH was normal. Thyroid ultrasound showed enlargement of the left thyroid lobe by a mixed solid and cystic, hypoechoic nodule measuring 2.5 x 2.0 x 3.6 cm with no increased vascularity or calcification. Right thyroid lobe was normal. Fine needle aspiration of the left thyroid nodule was performed. Cytopathology revealed a non-neoplastic thyroid nodule with prominent colloid component. Patient elected a left thyroid lobectomy as a treatment despite no obstructive symptoms. Histopathology disclosed nodular hyperplasia with non-caseating granulomas suggestive of sarcoidosis. Special stains were negative for fungal organisms and acid fast bacilli.

Discussion: Sarcoidosis is a multisystem disease that often involves the lymph nodes, lungs, eyes and skin, characterized by non-necrotizing granulomas. Thyroid gland is an uncommon site of the disease and was first described on autopsy in 1938. Isolated thyroid involvement of sarcoidosis is rare. Extrathyroidal sarcoidosis usually precedes or is diagnosed at the same time as the thyroid disease in majority of patients however there are a few cases of thyroid involvement as the first and only manifestation. Almost all patients are euthyroid, hypothyroidism is rare, and hyperthyroidism is even rarer. Sarcoidosis is thought to affect the thyroid gland by direct infiltration. Cell mediated and humoral immunity also appears to be affected. The frequency of endocrine autoimmunity in sarcoidosis showed a wide variability from 2.9% to 57%. Thyroid sarcoidosis has been associated with Hashimoto’s thyroiditis, Graves disease, De Quervain’s thyroiditis, hurthle cell hyperplasia, thyroid lymphoma and thyroid cancer. Diagnosis is made by fine needle aspiration biopsy or thyroidectomy. The histologic characteristics of sarcoidosis of the thyroid are similar to sarcoidosis elsewhere and consist of non-caseating granulomas with epithelioid cells, multinucleated giant cells and lymphocytic infiltration. Treatment depends on clinical presentation. Thyroid hormone is indicated in patients with hypothyroidism. Hyperthyroidism, if present, may require surgery since it can be resistant to antithyroid medications and radioactive iodine treatment. Thyroidectomy is indicated in patients with obstructive symptoms.

Conclusion: Thyroid involvement by sarcoidosis is rare and usually is not the initial manifestation of sarcoidosis.

Abstract #1144

HOFFMAN SYNDROME: MUSCLE STIFFNESS, PSEUDOHYPERTROPHY AND POLYMYOSITIS-LIKE MYOPATHY. A CASE REPORT OF A RARE PRESENTATION OF HYPOTHYROIDISM

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SAVAHCS

Objective: Hypothyroidism can present with neuromuscular symptoms in 30-80% of patients. Muscle stiffness, pseudohypertrophy, polymyositis-like myopathy with rhabdomyolysis tendency (Hoffman Syndrome) are not common and can be a reversible syndrome associated
with severe hypothyroidism. This case report emphasizes this rare but important presentation of hypothyroidism.

**Case Presentation:** A 65 year-old man with history of hypothyroidism after thyroidectomy in the 1990’s and non-compliant on levothyroxine for the past 2 years presented with complaints of progressive fatigue, muscle cramping, difficulty walking, muscle stiffness, cold intolerance and hoarse voice for two months. Physical examination revealed slow speech, enlargement of the thigh and calf muscles, motor weakness in both hips and knees flexor muscles with delayed relaxation of deep tendon reflexes, dry skin with excoriated red patches in the lower extremities.

The initial laboratory evaluation revealed very low free T4 (<0.07 ng/L), high TSH (280 µIU/mL), elevated Creatine Kinase (CK-10,379 IU/L) and elevated serum Creatinine (Cr- 2.1 mg/dL). The patient was given oral levothyroxine replacement and intravenous fluid hydration. Further workup showed normal urinalysis, negative ANA and Anti Jo antibodies. The acute kidney injury and elevated CK improved with Cr-1.4 and CK-2235 at discharge after 3 days of hospitalization.

The patient showed marked clinical and biochemical improvements after six months with TSH-0.75 and free T4- 1.68.

**Discussion:** The presence of typical myopathic symptoms and signs (muscle stiffness, pseudohypertrophy, and muscle weakness) in the setting of hypothyroidism is usually sufficient to make the diagnosis of Hoffman’s Syndrome. Electromyography is often normal, but might show myopathic changes. Muscle biopsy is rarely needed in this condition and if done it is to exclude other conditions. The findings are usually nonspecific, but can show mild inflammatory changes. Thyroid replacement usually leads to resolution of laboratory abnormalities and symptoms over several weeks. Weakness recovers more slowly, usually over several months, but in severely affected patients may persist even longer along with pseudohypertrophy.

**Conclusion:** Hoffman’s syndrome can be the initial presentation of severe hypothyroidism. Therefore, physicians should be aware of this uncommon yet treatable syndrome in order to initiate timely thyroid hormone replacement and to avoid unnecessary invasive testing and/or a misdiagnosis.
ABSTRACTS – Thyroid Disease

Abstract #1146

THYMIC HYPERPLASIA IN GRAVES’ DISEASE

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Objective: To report a case of thymic enlargement in a patient with Graves’ disease

Case Presentation: We report a case of a 59 year old African American woman who presented with complaints of chest pain, dyspnea on exertion, palpitations and tremor. Medical, surgical, social and family history was noncontributory and she took no medications. Physical examination was remarkable for bilateral exophthalmos, eyelid lag, proptosis, diffuse enlargement of the thyroid gland (50g) and hyperreflexia. Laboratory tests obtained (normal range in parentheses) were as follows: thyrotropin 0.005 μIU/dL (0.45 to 4.5 μIU/dL), free thyroxine 1.82 ng/dL (0.82 to 1.77 ng/dL), triiodothyronine 360 ng/dL (71 to 180 ng/dL). Serum antiperoxidase (TPO) and TSH-receptor antibody were positive. A CT scan of her chest was obtained and revealed a 3.5 cm x 1.5 cm anterior mediastinal mass. The I-123 thyroid scan showed a homogeneous uptake of 40% at 24 hours post-iodine. Thyroid scan revealed the mass anterior to the isthmus. Cytology from FNA of a left thyroid nodule, inferior to the isthmus nodule and right posterior nodule was consistent with benign thyroid nodules. The patient received radioactive iodine because of some residual thyroid tissue forming some newer nodules.

Discussion: Graves’ disease is an autoimmune disorder characterized by thyroid enlargement and hyperthyroidism. It is associated with other autoimmune diseases like myasthenia gravis, Addison’s disease, type 1 diabetes mellitus and vitiligo. The association between Graves’ disease and thymic hyperplasia is well established. However, in most cases, the enlargement is minimal and radiologically detectable thymic enlargement is uncommon. The exact pathophysiology of this thymic hyperplasia has not been determined. Thyrotropin receptor autoantibodies bind to the thyrotropin receptor (TSH-R) on the membrane of thyroid follicular cells and stimulate cell proliferation and thyroid-hormone synthesis. TSH-R has also been identified in the thymus. Histologically, the thymus enlargement associated with Graves’ disease consists of hyperplastic lymphoid follicles. It has been postulated that the thymic enlargement could be either the result or the cause of Graves’ disease. Monitoring thymic size after biochemical improvement of hyperthyroidism can prevent invasive surgical procedures.

Conclusion: Thymic hyperplasia associated with Graves’ disease can present a diagnostic challenge to the treating physician. Recognizing the benign and reversible nature of thymic hyperplasia in a patient with Graves’ disease may prevent unnecessary invasive diagnostic studies and surgical procedures.

Abstract #1147

COWDEN SYNDROME AND THYROID DISEASE

Barbara Carranza Leon, MD, Diana Dean, MD

Case Presentation: We present three patients (2 men, 1 woman) with Cowden Syndrome. All of them were referred to Thyroid Clinic for evaluation of multinodular goiter. At the time of referral two had a positive genetic test. Case 1 (woman) was diagnosed at age 40, case 2 was diagnosed at age 39 and case 3 was diagnosed at age 55. All patients’ neck ultrasound (US) showed multiple nodules on both thyroid lobes.

Case 1: largest nodule is hypoechoic located in the superior tip of the right lobe. On the last US it measured 0.8 x 0.8 x 1.5 cm. We have not been able to obtain a clear path for the needle to go through without having the carotid artery and superior thyroid artery on the way so a fine needle aspiration (FNA) has not been performed. The plan is to follow this nodule annually.

Case 2: the patient had a right thyroid lobectomy (adenomatous nodules) for compressive symptoms. This surgery was performed before the diagnosis Cowden Syndrome. About 2 years later (when the diagnosis was known) he underwent a left thyroid lobectomy (adenomatous nodules) for rapidly growing nodules. The patient received radioactive iodine because of some residual thyroid tissue forming some newer nodules.

Case 3: he had two solid indeterminate nodules on the right lobe, one nodule on the left lobe and one on the isthmus. Cytology from FNA of a left thyroid nodule, isthmus nodule and right posterior nodule was consistent with benign thyroid nodules.

The three patients continue with annual surveillance.

Discussion: Cowden Syndrome was first recognized in the 1940s. It is caused by an inactivating mutation on the PTEN gene (located on the long arm of chromosome 10) which causes uncontrolled cellular proliferation, transformation and survival. Patients have a variable age at presentation (from 4 to 74 years) and the average age at the time of diagnosis is 39 years. Muco-cutaneous lesions (facial trichilemmomas, acral keratoses, facial papules and perioral papillomatous lesions) are usually the first presenting lesion of the disease. Patients develop both benign and malignant tumors in a variety of tissues such as thyroid, breast and uterus. Approximately 50 to 70% of patients have thyroid disease. The majority develops adenomatous goiters or follicular adenomas.
The incidence of thyroid carcinoma ranges between 3 to 10% (mainly follicular thyroid cancer, occasionally papillary thyroid carcinomas) and the lifetime risk of thyroid cancer is 3 to 35%. This is a type of familial non medullary thyroid carcinoma.

**Conclusion:** Patients with Cowden Syndrome need lifelong follow up with annual thyroid US given their risk of thyroid cancer.

**Abstract #1148**

**AN UNCOMMON PRESENTATION OF FOLLICULAR THYROID CARCINOMA: WHEN CHRONIC BACK PAIN SHOULD RAISE A FLAG**

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**Case Presentation:** A 56-year-old female patient with arterial hypertension, chronic low back pain, hypothyroidism and multinodular goiter, underwent left hemithyroidectomy on March, 2006 due to left sided solid thyroid nodule measuring 1.6 x 1.3 x 1.5 cm and a corresponding fine needle aspiration (FNA) consistent with follicular lesion of thyroid. Pathology diagnosis of left thyroid lobe was reported as follicular adenoma at that time. In 2012, the patient developed a worsening left sided back pain initially believed to be herniated disk disease for which she sought multiple treatments without any pain relief. Subsequently an MRI was ordered and a spinal mass was found for which she was referred to Neurosurgery. The pain became unbearable and debilitating. Imaging study performed revealed an aggressive mass centered at T3 vertebral body with severe spinal canal stenosis causing compression of spinal cord; no evidence of lymph node enlargement. Patient underwent T3 vertebrectomy with internal fixation by Neuro-Surgery Service with final pathologic diagnosis showing thyroid tissue compatible with metastatic follicular thyroid carcinoma. Subsequent Neck Ultrasound was performed showing a solid well defined isoechoic thyroid nodule at the lower right lobe measuring 1.4cm in largest diameter; FNA was done with a cytological diagnosis of Follicular Neoplasm or Suspicious for a Follicular Neoplasm. Patient underwent completion thyroidectomy on December 18, 2013 with non-malignant results. A second review of 2006 hemithyroidectomy was performed by Pathology Service at our Institution, with new interpretation consistent with a well differentiated follicular thyroid carcinoma as it showed focal capsular invasion with indeterminate lymphovascular invasion.

**Discussion:** Follicular carcinoma is the second most common type of thyroid cancer, typically presenting as a thyroid nodule, but when it spreads it usually does via hematogenous route, with distant metastasis occurring in about 10-15% of cases. Bone metastasis is diagnosed clinically in 2%-13% of patients with differentiated thyroid cancer; nevertheless spinal cord compression complicating thyroid carcinoma is rare and only few cases have been reported in the literature.

**Conclusion:** This case illustrates a strange case of a minimally invasive follicular carcinoma that showed an aggressive behavior, and thus the importance of considering metastatic thyroid carcinoma in the differential diagnosis of chronic back pain, which may rarely, yet possibly progress to spinal cord compression which carries severe morbidity.

**Abstract #1149**

**TRIIODOTHYRONINE TOXICOSIS IN A PATIENT WITH METASTATIC THYROID CANCER**

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SUNY Downstate

**Objective:** Thyrotoxicosis due to autonomously functioning metastasis in differentiated thyroid cancer (DTC) is exceedingly rare. Functional metastases are more common with follicular carcinoma and most common sites are bone and lung. The adrenal gland is an uncommon site of metastasis from DTC and iodine avid adrenal metastatic lesions are even rarer.

**Case Presentation:** A 59-year-old woman with a history of right hemi-thyroidectomy in 1982, unknown histopathology, presented to the emergency room with left hip pain. She had been on levothyroxine (LT4) since surgery but was lost to follow up and stopped LT4 6 months prior. A pelvic computerized tomography scan demonstrated a 12cmx8.5cm lytic lesion in the left ilium with an associated acetabulum fracture. Biopsy of the iliac lesion revealed tumor cells forming nests and follicles with intra-luminal pinkcolloid material, staining positive for thyroid transcription factor 1, suggestive of a primary thyroid malignancy. Further workup revealed
pulmonary nodules and a 4 cm necrotic left adrenal mass. A bone scan revealed metastases to the ilium, bilateral sacrum, left acetabulum, ribs, T7 and lumbar spine. TSH was <0.008mIU/L (ref.: 0.55-4.78), free T4 was 0.77ng/dl (ref: 0.89-1.76) and a total T3 was 330ng/dl (ref: 60-181). Review of previous labs showed a trend of low TSH and high T3 over the last several months. Patient’s only complaint was of left hip pain. Physical examination revealed a fine tremor and minimal hyperreflexia. She was started on methimazole and propranolol for thyrotoxicosis. The patient underwent completion thyroidectomy. The pathology on completion thyroidectomy was consistent with multifocal follicular variant microcapillary thyroid carcinoma. T3 toxicosis persisted post thyroidectomy. This raised the suspicion of functional T3 metastasis. A whole body I131 scintigraphy revealed increased uptake in residual thyroid bed, left adrenal gland and left iliac region, compatible with soft tissue and bony metastasis from functional thyroid cancer metastasis. Radioactive ablation is scheduled.

**Discussion:** Thyrotoxicosis in DTC due to autonomously functioning metastasis is a rare phenomenon. Diagnosis of functioning metastases requires failure of thyrotoxicosis to resolve after thyroidectomy with low iodine uptake into the thyroid and increased uptake by metastases. Reported etiologies included excess production of deiodinase causing conversion of T4 to T3, as well as direct production of T3 by the metastases. 

**Conclusion:** As this patient does not appear to have substrate to convert T4 to T3, we conclude that the metastases may be producing T3 themselves; further investigations to identify the etiology are in process.

**Abstract #1150**

**MYXEDEMA COMA WITH HYPERNATREMIA: AN UNUSUAL PRESENTATION**

Richard Pinsker, MD, Naveen Pathak, MD, Abdier Gonzalez, MD, Armando Perez, MD, Narinder Kukar, MD, Neil Pathak

**Objective:** Myxedema is often associated with hyponatremia as a result of an inability to handle free water. Sepsis is often a precipitating factor. In this case, an elderly patient presented with severe hyponatremia. The causes of myxedema coma were multifactorial in this case and resulted in a perilous metabolic state that is seen most often in females more than males and in older individuals such as this patient.

**Case Presentation:** A 94 year old female, resident of a nursing home, was admitted with lethargy, loss of appetite, and deterioration of functional status. History included dementia and hypothyroidism for which she took levothyroxine 100 mcg daily for many years. Six months prior, TSH was noted to be 0.37 (0.47-4.7) and levothyroxine was inexplicably reduced to 25 mcg a day. On exam in ER, BP was 76/43, pulse 76, and temp 96.7 F. She was extremely drowsy, cachectic, pale, and dry. Sodium was 164, BUN 142, creatinine 2.5, WBC 9,800. U/A was positive for nitrates and bacteria with 298 WBC’s. Patient was immediately treated for septic shock, acute renal failure, dehydration, and suspected myxedema coma. Mental status improved with a regimen of IV levothyroxine, steroids, fluids, and antibiotics. TSH was eventually reported as 139, Free T4 0.30 (0.8-2.2), and Free T3 1.21 (2.77-5.27). BP, renal functions, and sodium rapidly corrected. Eventually, family decided to send patient to hospice care.

**Discussion:** Myxedema coma is a medical emergency that can be precipitated by infection. Patient became hypothyroid as a result of an unfortunate decision to lower her thyroid replacement dosage. Hypothermia (defined as less than 94.0 F) occurs in 88% of patients and indicates a worsening prognosis but was not present here. Hyponatremia was not present but the patient suffered severe hypernatremia due to dehydration. Urosepsis was caused by ESBL E Coli as seen on eventual cultures.

**Conclusion:** Even though patient did not have classical bradycardia, hyponatremia, or hypothermia, this patient was rapidly and successfully treated for myxedema coma without waiting for thyroid function test results. Reduction of a longstanding levothyroxine regimen is fraught with peril especially in an elderly individual who is a poor historian and seeing multiple health care providers.

**Abstract #1151**

**RADICAL SURGICAL APPROACH IN THE PRESENCE OF INSULAR CARCINOMA**

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**Objective:** To describe the rare case of a rapidly growing metastatic insular thyroid carcinoma in a young female Puertorrican patient.

**Case Presentation:** A 43 year old female patient was referred to our endocrine surgery clinic with the chief complaint of rapidly growing neck mass of 6 months evolution. No history of thyroid disease or familiar thyroid cancer. Symptoms included dysphagia to solids,
Abstract #1152

PREDICTION OF THYROID NODULES MALIGNANCY BY TIRADS AND BETHESDA CLASSIFICATIONS

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Objective: To evaluate the correlation between final biopsy of the thyroid nodule and their respective categorization according TIRADS and BETHESDA.

Methods: Cross-sectional study. 62 thyroid surgeries between June 2011 and January 2013 were evaluated, which corresponded to smear BETHESDA III, IV, V and VI, comparing biopsy with definitive results radiological and histological classification. We evaluated age, sex, nodule size and frequency of Hashimoto’s thyroiditis. The analysis was performed using Stata 11.1 software using chi2 statisticians and T test. Consider statistical significance p < 0.05. The results were expressed as mean and SD.

Results: Average age 41.6 ± 12.1 years, without difference between benign and malignant disease (p 0.7). The gender distribution was 85.4 and 14.6 % females and males respectively. The average size of the nodules was 15.1 ± 9.9 mm (range 4 to 52mm), 18.6 and 14 mm respectively for cancer and benign pathology (p 0.1). 32.2 % had Hashimoto’s thyroiditis. We relate nodules and biopsy according TIRADS observing cancer Category 3 : 100 % (n 3) , 4a : 57.6 % , 4b : 93 % and 5: 100 %, there being positive correlation between cancer risk and higher grade (p = 0.001). We compare the smears with final biopsy dichotomizing variables in benign (adenoma and follicular hyperplasia and thyroiditis) and differentiated carcinoma (papillary carcinoma and papillary carcinoma follicular variety) observing cancer in 63.6, 62.5, 80.9 and 100% for BETHESDA III, IV, V and VI respectively (p 0.05).

Discussion: TIRADS and BETHESDA have been developed in order to increase the accuracy of risk of malignancy of thyroid nodules in radiological and cytological diagnosis respectively. For BETHESDA categories IV, V and VI are within the average published. However, BETHESDA III is different from the statement, since the indication for surgery is not the recommendation indicated according to this classification. Our group considers risk factors, selecting the subpopulation with higher probability of malignancy. This motivates to perform monitoring BETHESDA III and assess their performance over time to confirm the published recommendations.

Conclusion: Our study show that TIRADS and BETHESDA are a good rating for predicting risk of malignancy. Our group agrees with the recommendations published today according to these scores.
Abstract #1153

HYPOTHYROIDISM WITH SYMPTOMS OF MYXEDEMA MADNESS AFTER AN EXCESSIVE AMOUNT OF IODINE SUPPLEMENT

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Albany Medical College

Objective: We present a unique case of iodine-induced hypothyroidism.

Case Presentation: In this case report, we present a patient who has taken iodine supplement (Iodoral 50mg daily) for 9 months and developed severe hypothyroidism with TSH over 120 UIU/mL and 24 hour urine iodine over 1600mcg. He was found to have pericardial effusion and symptoms of myxedema madness such as delusions and hallucinations. He did not have any previous history of thyroid disease and was found to have negative anti-thyroid peroxidase (TPO) and anti-thyroglobulin antibodies. Other than 3 hypoechoic thyroid nodules (size ranging from 1.0-1.8cm) on ultrasound, no underlying thyroid abnormality was found.

Discussion: An excessive amount of iodine can cause thyroid dysfunction. Sources of excess iodine include over-the-counter supplements, prescription medications such as amiodarone, and radiographic contrast agent. In a normal individual, the regulatory mechanism of autoregulation protects an individual from exposure to an excessive amount of iodine. This phenomenon of inhibitory mechanism is called the Wolff-Chaikoff effect. With prolonged exposure to iodine excess, iodine organification and thyroid biosynthesis resume their normal functions, and enable the thyroid to escape from the Wolff-Chaikoff effect. However, some individuals fail to escape from this inhibitory mechanism and develop hypothyroidism. Individuals at risk of hypothyroidism are those with autoimmune thyroiditis, painless thyroiditis, postpartum thyroiditis, subacute thyroiditis, and history of thyroidectomy after Graves’ disease. According to the current literature, iodine-induced hypothyroidism rarely develops in individuals without any underlying thyroid disease and without any of the aforementioned risk factors. Most of the iodine-induced hypothyroidism cases that have been reported were linked to elevated titers of anti-TPO antibodies as well as a history of thyroiditis.

Conclusion: Iodine-induced hypothyroidism with symptoms of severe psychosis can be caused in individual with negative anti-TPO antibodies and without any history of thyroiditis or thyroidectomy. It would be important to recognize the possibility of thyroid dysfunction, both hyper- and hypothyroidism in individuals with high iodine intake.

Abstract #1154

MARINE–LENHART SYNDROME - A CASE OF SUCCESSFUL TREATMENT FOLLOWED BY RECURRENCE

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Objective: To report a case of recurrent hyperthyroidism secondary to Graves’ disease and co-existing functioning thyroid nodule (Marine-Lenhart syndrome).

Case Presentation: A 78-year-old woman presented with weight loss, tremors and palpitations. Thyroid profile was consistent with hyperthyroidism; TSH <0.02 uIU/ml (0.35-5.00uIU/ml), fT4 of 4.5 ng/dl (0.8-1.8 ng/dl). Thyrotropin receptor antibody was elevated at 82 IU/L (<=1.75 IU/L), consistent with the diagnosis of Graves’ disease. Anti-TPO antibody was reported negative at <10 IU/mL. Physical examination was consistent with diffuse thyroid enlargement, palpable right sided thyroid nodule and orbitopathy. Thyroid ultrasound confirmed a 2.5 cm solid nodule in the right lobe, hypervascular on Doppler color flow. FNA biopsy showed benign cells. Thyroid scan showed diffuse homogenous increased uptake throughout the gland, right hyper-metabolic nodule (20.5% uptake at 24 hours). She was treated with 29.5 mCi of I-131. Post therapy, she was euthyroid at 6 weeks and hypothyroid at 6 months. Low dose Levothyroxine replacement therapy was started to maintain TSH between 0.4-3.5 uIU/mL. Follow up thyroid ultrasound in 1 year showed decrease in the size of the right thyroid nodule and no hypervascularity. After 2.5 years, she presented with recurrence of her symptoms. Repeat thyroid horonnes showed, low TSH <0.02 uIU/ml, high fT4 1.9 ng/dL. Levothyroxine was stopped but lab abnormalities and symptoms persisted. She was then started on Methimazole. Repeat thyroid ultrasound showed shrunken left thyroid lobe, persistent right thyroid nodule with moderate vascularity on Doppler color flow. Repeat Thyroid scan showed right thyroid nodule, replacing right lobe, with markedly increased radioactive iodine activity (66.1% at 24 hours). As definitive treatment, she was again treated with 29.6 mCi of I-131 this time. Her clinical outcome was good, became hypothyroid at 8 weeks and was started on Levothyroxine.

Discussion: Marine-Lenhart syndrome is rare with prevalence of only 2.7 - 4.1%. Coexistence of both Graves’ disease and functioning nodule cause thyrotoxicosis by different pathophysiological mechanisms. Toxic thyroid
nODULES ARE A POWERFUL DIAGNOSTIC TOOL FOR DIFFERENTIAL DIAGNOSIS OF THYROID NODULES

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**Objective:** Although thyroid nodules are extremely common, thyroid cancer is a relatively rare condition. In some cases the correct diagnosis of a thyroid nodule can be very challenging. Many of these difficult cases are diagnosed as indeterminate, and often result in thyroidectomy. Therefore new tools for accurate diagnosis are essential to accurately identify malignant nodules and to potentially avoid unnecessary surgical procedures. MicroRNA expression profiling has been shown to be a reliable method for cancer subtype classification. In the present study, we used several microRNA profiling platforms and screened over 1000 microRNAs to identify microRNAs to stratify thyroid lesions into benign or malignant neoplasms. Additionally, this study was aimed to investigate the feasibility of extracting microRNA from stained FNA smears and cell blocks for the detection of tumor-specific microRNAs.

**Methods:** Our proprietary protocols for extraction and profiling of high quality microRNA from archival FFPE samples were adapted for the processing of thyroid FNA cell blocks and smears. Over 200 thyroid FFPE samples representing various histological subtypes and dozens of FNA cytological samples were hybridized to proprietary microarrays in order to measure the expression of more than 1000 microRNAs. Potential microRNA biomarkers that differentiate benign from malignant tumors were identified and were further validated on a proprietary qRT-PCR platform.

**Results:** We found that the expression of a small number of specific microRNAs can be used as biomarkers for differentiating benign from malignant lesions, and to further sub-classify the specific histologic subtype of the tumor. Moreover, we were able to extract RNA from both stained FNA smears and cell blocks, which enabled us to identify the aforementioned thyroid-specific microRNA biomarkers.

**Discussion:** The data presented here demonstrate the feasibility of extracting and profiling microRNAs from thyroid FNA smears and cell blocks. We identified microRNAs that represent excellent biomarkers for the classification of thyroid tumors. This study adds to the accumulating evidence on the specificity of microRNA expression in tissues and tumor types. Most importantly, a combination of a small number of microRNAs can successfully provide specific differential diagnosis of morphologically-similar thyroid nodules.

**Conclusion:** These findings form the basis for the development of a simple and reliable diagnostic assay, which will offer an accurate tool for surgical and preoperative thyroid FNA samples, including those that presently fail cytological evaluation.
residual disease. Neck CT showed tumor in the L thyroid and erosion of thyroid cartilage. Trachea was deviated to the right, but without evidence of endoluminal extension. There was L vocal cord paralysis and level 3-4 nodes. On TSH suppressive therapy, thyroglobulin (Tg) was 5.1ng/ml without antibodies. The tumor was BRAFV600E mutated by DNA analysis. Pt was started on NEO VEM. A Tg measured 1 week prior to surgery was 449ng/ml (possibly due to tumor lysis) and CT scan showed reduction in size of infiltrative mass and adenopathy. A radical L lobectomy with sacrifice of the L recurrent laryngeal nerve, partial laryngectomy with removal of thyroid cartilage ala and L esophageal/cricopharyngeal musculature, L paratracheal and pretracheal dissection, and L lateral neck dissection was performed. In preparation for the need of postoperative EBRT, a pectoralis major muscle flap was also performed. Pt recovered well from surgery and did not require tracheostomy. Post-operative Tg was 1ng/ml 1 week later. Details of the follow up will be presented at the meeting.

Discussion: Here we present a case of a pt who underwent NEO VEM for locally advanced, infiltrative, BRAF mutated PTC. A successful surgery was performed, preserving her larynx and esophagus. Our case illustrates 2 points: 1. Pts should undergo comprehensive imaging of the neck prior to surgical intervention and 2. NEO chemotherapy with non-anti-angiogenic drugs, such as VEM, may benefit pts with locally advanced, BRAF mutant PTC.

Conclusion: NEO approach may result in less mutilating surgery and potentially preserve vital structures. A clinical trial with NEO VEM is underway.

Abstract #1157

HOW HIGH IS TSH IN CENTRAL HYPTOHYROIDISM?

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Objective: Our objective was to describe an inappropriately high level of TSH that would still merit a diagnosis of central hypothyroidism

Methods: We describe a 28 year old male with panhypopituitarism with an inappropriately elevated TSH of 19 miu/ml.

Case Presentation: 28 year old male presented with primary infertility. He was diagnosed as a case of panhypopituitarism in 2000 and was treated with growth hormone, thyroxine and testosterone from 2000 to 2004 and discontinued later. He had complains of easy fatiguability, and myalgia. There was no change in weight or appetite. There was no development of facial hair and no progression of pubic hair after 2004. He denied symptoms of decreased libido or erectile dysfunction. His weight, height and BMI were respectively 70kg, 163cm and 26.34 kg/cm2. His blood pressure was 96/62 mmHg and pulse rate was 76/min. There was no goitre or gynecomastia. Genital examination showed stretched penile length of 10cm, pubic hair in Tanner’s stage 2, and testicular volume were 1ml each. Hormonal work-up showed: His hormonal profile showed: TSH 19.18 (0.27-4.2 mIU/ml), T4 2.79 (5.1-14.1mcg/dl), cortisol 0.717(6.2-19.4µg/dl), and ACTH 17.54(7.2-63.3 pg/ml), total testosterone <0.025(2.4-8.3 ng/ml), LH <0.1(1.7-8.6mIU/ml), and FSH 0.58(1.5-12.4miu/ml)(assayed by electro-chemiluminescent method). His repeat TSH was 18.53 miu/ml. Thyroid peroxidase antibody was negative. MRI sella showed a partially empty sella. He was restarted on thyroxine, prednisolone and testoviron. Follow up of his thyroid functions showed normalisation of TSH to 2.25 miu/ml when T4 had normalised.

Discussion: Central hypothyroidism is often associated with low, normal or high TSH levels. The level of TSH in the normal or high range is considered inappropriate to the level of low thyroxine levels in central hypothyroidism. Available literature do not clearly define the upper limit of TSH in central hypothyroidism. The normalisation of TSH on thyroxine supplementation could be intact TRH and dysfunctional TSH in this patient. The intact TRH response in the presence of low T4 levels can stimulate TSH to rise. Since the TSH is dysfunctional, thyroxine levels were low. When thyroxine supplementation was started, the negative feedback to TRH and TSH is lost, and hence TSH had normalised.

Conclusion: The only evidence available in our literature search was from Williams Textbook of Endocrinology which mentions that TSH could be as high as 20 miu/ml although there are no literature online to support this. Our case would serve as a reference data for supporting such a statement.

Abstract #1158

ATYPICAL PRESENTATIONS OF THYROTOXIC PERIODIC PARALYSIS (TPP): REVIEW OF 4 CASES

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Case Presentation: We aim to describe such less common TPP cases, presenting with lower extremity paralysis: 2 White men, 1 White woman and also 1 Asian man, age 34±7 y (mean±SD). Patients were clinically thyrotoxic on presentation: presence of palpitations, heat intolerance, hyperdefecation and tremor. Heart rate was 130±33 beats/min: 1 patient had atrial fibrillation, another patient had
supraventricular tachycardia. TSH and free T4 were 0.06±0.05 (0.4-5µIU/mL) and 4.6±1.8 (0.6-1.2ng/dL), respectively. Supporting the hypothesis of a channelopathy as the defect for paralysis, and no evidence of muscle damage, creatinine (Cr) and creatine kinase levels were normal: 0.6±0.2 (0.5-1.18mg/dL) and 34±21 (30-285U/L), respectively. One patient had an electromyogram, which was normal. All the patients had low a potassium (K) and magnesium: 2.5±0.45 (3.7-5.2mEq/L) and 1.5±0.2 (1.8-2.4mg/dL), respectively; a normal phosphate: 3.7±1.6 (2.5-4.5mg/dL); and a normal-to-high calcium: 9.4±0.96 (8.9-10.2mg/dL). Precipitant factors included: carbohydrate-rich meal in 2 of them and interestingly, fasting in the other 2. Two patients had a known history of Graves’ disease, were smokers and they developed ophthalmonapathy. One patient had recurrent TPP with normal K: 3.9mEq/L. They all responded to non-selective β-blockers and treatment of thyrotoxicosis.

Discussion: The presentation of episodic hypokalemia with weakness in the setting of hyperthyroidism is pathognomonic for a condition known as thyrotoxic periodic paralysis (TPP). TPP is described to occur mainly in young Asian men, affecting predominantly the proximal muscles. The described underlying pathophysiology, a K channel defect, causes intermittent intracellular K shifts in a hyperadrenergic state caused by thyrotoxicosis. Precipitated by additional factors that move K into cells, such as large meals, exercise, and stress from increased catecholamines, typically the weakness is self-limited but recurrent if hyperthyroidism persists. TPP has not been widely described in Whites or women.

Conclusion: In conclusion, TPP, a potentially fatal paralytic syndrome, can present with normal K, in women, ethnicities other than Asian and precipitated by fasting. These atypical TPP cases stress the importance of maintaining a high level of suspicion upon encountering muscle paralysis and thyrotoxic symptoms. A normal K level in TPP should be interpreted with caution. The catabolism of hyperthyroidism causes a low Cr due to its increased excretion, potentially masking underlying chronic kidney disease, an important clinical consideration upon replacing K and/or other electrolytes safely, as K is overall not depleted but rather shifted intracellularly.

Abstract #1159

WHEN CLOSE MONITORING IS NOT ENOUGH

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Objective: Among the several histological types of thyroid cancer, the anaplastic thyroid carcinoma (ATC) type is the least common (<1%), yet the most aggressive and fatal. We report a case of a patient that developed a neck mass diagnosis elusive by sonographic monitoring, FNA, and core biopsy. However after repeated core needle biopsy ATC was diagnosed.

Case Presentation: A 77 year old male with history of multinodular goiter, benign prostate hyperplasia, arterial hypertension, hyperthyroidism and right neck well differentiated liposarcoma treated with complete excision (2010). Seen (9/17/2012) at the emergency room (ER) due to a right neck mass progressively increasing in size for the last 15 days. Accompanying symptoms included hoarseness, dyspnea, cough, and dysphagia. During the last two years patient was evaluated by thyroid ultrasound (US) that showed right sided heterogeneous nodule 2.1cm larger dimension (8/13/2010). Fine needle aspiration and core biopsy were negative for malignancy (11/24/10). One year later, repeated thyroid US reported no significant changes and MRI of the neck revealed no detectable neck mass (9/30/2012). One month prior to admission (8/10/2012) thyroid US showed large mass which occupies the middle of the right thyroid lobe measuring 1.7x1.9x1.7cm, complex pattern, faint calcifications at the margins; but not abnormal vascularity. Due to the progressive rapid growth of the right neck mass, repeated CT of neck (9/16/2012) showed a confluent nodular soft tissue compatible with enlarged lymph node and the already described thyroid nodule findings. Core needle biopsy of right neck mass and thyroid nodule demonstrated poorly differentiated carcinoma consistent with ATC and positive for epithelial markers, and thyroglobulin.

Because of the advancement of radiological and clinical neck tissue involvement, the appropriate management was palliative radiotherapy. However, patient did not respond to the above therapy and died three months afterwards.

Discussion: An interesting feature of this case is the elusive to confirm the diagnosis in spite of FNA and core biopsy done by experience pathologist. This case reaffirms reported in the literature about the abrupt development of ATC, which makes it with grade mortality and poor prognosis at time of diagnosis.

Conclusion: Early diagnosis modes are urgently required to develop a treatment plan for this rapidly progressive tumor.

Abstract #1160

BEHAVIOR OF THYROID CANCER IN PATIENTS SURROUNDING THE THREE MILE ISLAND NUCLEAR POWER PLANT

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Pinnacle Health

Objective: The prevalence of thyroid cancer in the US has increased to over 8% in the last decade but the mortality rate has remained unchanged. This has led societies to propose a less aggressive approach in the treatment of thyroid cancer. Radiation exposure remains a major risk
factor associated with an increased incidence and severity of thyroid cancer. Three Mile Island (TMI) is a nuclear plant in Harrisburg, PA that suffered the largest nuclear accident in US history in 1979. We elected to study the incidence and behavior of thyroid cancer including effects of treatment, recurrence, and the quality of life in these patients in the greater Harrisburg area.

Methods: We conducted a retrospective study of 293 patients selected from a private endocrinology practice in Harrisburg, PA. Data was collected by review of medical records. Demographics, type of cancer, treatment, follow up, and history of recurrence were collected. The second part of the study included the SF-20 questionnaire survey done by phone to measure the quality of life in these patients. Statistical analysis was done using SAS software 9.2.

Results: Of the 293 patients studied, Hurthle cell cancer was prevalent in 10.24%, above the national average of 5%. Papillary with mixed follicular variant accounted for 22.5%, and papillary alone for 54%. 72% were treated with RAI ablation. 20 patients (6.8%) had a recurrence, national average is 3-21%. Patients with recurrence had an average age at diagnosis of 42 yrs. SF-20 results showed that patients with advanced cancer had a worsened quality of life compared to low risk cancer.

Discussion: TMI did not contribute to the severity or recurrence of thyroid cancer but prevalence of Hurthle cell increased patients were a younger age at diagnosis compared to national averages. No correlation was found between recurrence and multiple factors analyzed i.e. family history, BMI, etc. It was confirmed that patients with advanced cancer have a decrease in quality of life and RAI treatment did not seem to affect this concluding the SF-20 score.

Conclusion: The recurrence rate in our study is statistically similar to the national average indicating there is no increased severity of thyroid cancer in the Harrisburg (TMI) area. However, in patients with recurrence, there was an increased incidence of Hurthle cell carcinoma. The average age at diagnosis was below the national average and quality of life is affected in patients with recurrent disease. To our knowledge this has not been studied before.

Abstract #1161

ACUTE SUPPURATIVE THYROIDITIS CAUSED BY METHICILLIN- RESISTANT STAPHYLOCOCCUS AUREUS

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Objective: Methicillin-resistant staphylococcus aureus (MRSA) is a rare cause of acute suppurative thyroiditis. We describe a patient with MRSA-associated thyroiditis and review its management.

Case Presentation: A 50-year-old man without known thyroid disease presented to the emergency room with four weeks of sore throat, dysphagia and generalized weakness. On physical examination he was afebrile, though tachycardic, and was noted to have an enlarged thyroid that was firm and tender. He had palpable cervical lymphadenopathy and a positive Pemberton’s sign. Neck CT demonstrated a 6 cm right thyroid lobe mass with multiple cystic areas. There was right vocal fold paralysis, and the mass was noted to surround the right common carotid artery. Laboratory testing demonstrated a leukocytosis (WBC 18.9 K/uL; ref. 4-11 K/uL), a suppressed TSH (0.03 mcu/mL, ref 0.27-4.2 mcu/mL), and a free T4 that was greater than 7.7 ng/dL (ref. 0.9-1.8 ng/dL).

Thyroid ultrasound demonstrated a thickened, abnormal appearing isthmus, as well as an enlarged right thyroid lobe with three poorly-defined hypoechoic areas, with the largest measuring almost 5 cm. Fine-needle aspiration of the right lobe was performed, as well as a core needle biopsy of the isthmus. Though peripheral blood cultures were negative, fluid cultured from the thyroid was positive for MRSA. Cytology demonstrated inflammatory and necrotic debris.

Prednisone, methimazole, and vancomycin were started. His antibiotic was changed to oral sulfamethoxazole/trimethoprim for a three-week course. His methimazole was discontinued given the inflammatory nature of his thyroiditis, and his steroids were continued for the duration of his hospitalization.

He was euthyroid within two weeks of discharge and over the next month his symptoms resolved. Repeat thyroid ultrasound three weeks after initiation of therapy showed normal thyroid but persistent cervical lymphadenopathy. The etiology of his MRSA-associated thyroiditis remains unclear.

Discussion: Acute infectious thyroiditis can result from bacterium including Staphylococcus, Pneumococcus, Salmonella, or Myobacterium tuberculosis. Thus far there are very few reported cases of MRSA in the literature. Factors that predispose to infectious thyroiditis include underlying autoimmune disease, congenital abnormalities of the piriform sinus, and being immunocompromised; however none of these risk factors were present in our patient.

Conclusion: We present a unique case of MRSA-associated acute suppurative thyroiditis. This case presents an opportunity to review this rare entity, and to discuss its presentation and management.
Abstract #1162

A PATIENT WITH A PITUITARY MICROADENOMA AND ELEVATED TSH AND THYROID HORMONE LEVELS FOUND TO HAVE THYROID HORMONE RESISTANCE: CHANCE ASSOCIATION OR CAUSE AND EFFECT?

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Objective: To describe a case of thyroid hormone resistance in a patient referred for elevated TSH and a concomitant pituitary adenoma.

Case Presentation: A 44 y.o. male was referred to the Pituitary Center for assessment of a pituitary microadenoma (0.8 x 0.6 x 0.5 cm) found on brain MRI performed for headaches. He had experienced temperature intolerance and palpitations over 2 years, now controlled by a beta blocker. He had similar symptoms in college which had resolved. He had a deceased brother who had hyperthyroidism, without known details. On physical exam, there was an enlarged thyroid without nodules and he was clinically euthyroid. Lab results revealed TSH 0.95 uIU/ml with elevated Free T4 2.49 ng/dl (0.8-1.8), free T3 5.63 pg/ml (2.3-4.2). A thyroid scan showed diffusely increased radio-iodide uptake (58% 24 h).

Thyroid stimulating immunoglobulin and thyroperoxidase antibodies were negative. To differentiate between a TSH secreting pituitary adenoma and thyroid hormone resistance (THR), additional tests were performed. Alpha subunit was 0.3 mg/ml (<0.5) and sex hormone binding globulin was low at 14 nmol/l (16-94). Reverse T3 was elevated at 41.8 ng/dl (0.8 x 0.6 x 0.5 cm) found on brain MRI performed for headaches. He had experienced temperature intolerance and palpitations over 2 years, now controlled by a beta blocker. He had similar symptoms in college which had resolved. He had a deceased brother who had hyperthyroidism, without known details. On physical exam, there was an enlarged thyroid without nodules and he was clinically euthyroid. Lab results revealed TSH 0.95 uIU/ml with elevated Free T4 2.49 ng/dl (0.8-1.8), free T3 5.63 pg/ml (2.3-4.2). A thyroid scan showed diffusely increased radio-iodide uptake (58% 24 h).

Thyroid stimulating immunoglobulin and thyroperoxidase antibodies were negative. To differentiate between a TSH secreting pituitary adenoma and thyroid hormone resistance (THR), additional tests were performed. Alpha subunit was 0.3 mg/ml (<0.5) and sex hormone binding globulin was low at 14 nmol/l (16-94). Reverse T3 was elevated at 41.8 ng/dl (9-27). Finally human anti-mouse antibodies and heterophile antibodies were negative ruling out interference with the TSH assay. These results were suggestive of THR and he was referred to genetics. Sequence analysis of his thyroid hormone receptor beta (THRβ) gene revealed that the patient was heterozygous for Ala279Glu mutation, shown previously in vitro to abolish T3 binding, and consistent with inherited THR. Notably, octreotide administration did decrease TSH and T4 levels but whether this was due to suppression of normal pituitary thyrotropes or a putative TSHoma is not clear. At this juncture, the microadenoma is being monitored.

Discussion: THR is caused by reduced target tissue response to thyroid hormone and ineffective feedback on the pituitary thyrotropes resulting in inappropriately normal or elevated TSH with elevated thyroid hormone. A frequent cause of THR is a mutation in the gene for THRβ subunit, altering hormone binding. The mutant receptor may still bind DNA but interferes with hormone regulated transcription so that it presents in an autosomal dominant fashion.

Conclusion: Both TSH-secreting pituitary adenomas and THR are rare entities, while pituitary microadenomas are common. When faced with elevated TSH and thyroid hormone levels in combination with a pituitary adenoma, it is important to determine whether there could be THR. Without a tissue diagnosis for the microadenoma, we cannot rule out that THR has promoted TSHoma formation in this patient.

Abstract #1163

ABSTRACT WITHDRAWN

Abstract #1164

PREOPERATIVE IDENTIFICATION OF PARATHYROID TISSUE BY AN MRNA CLASSIFIER ON PROSPECTIVELY COLLECTED THYROID NODULE FINE-NEEDLE ASPIRATION BIOPSIES

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Objective: The parathyroid glands are located adjacent to the thyroid and occasionally within it. Enlarged parathyroid glands can be mistaken as thyroid nodules. On fine needle aspiration biopsy (FNAB) of such lesions, cytology is most often indeterminate and fails to identify its parathyroid origin, typically resulting in unnecessary thyroid surgery. The Afirma Gene Expression Classifier (GEC) identifies genomically benign thyroid nodules amongst those with indeterminate FNABs to prevent unnecessary diagnostic surgery. Here we report the clinical performance of a parathyroid mRNA classifier used with the GEC.

Methods: The parathyroid classifier was performed, along with the GEC, on prospectively collected FNAB samples with indeterminate cytopathology or upon physician request, as part of the Veracyte clinical stream. Clinical details were obtained in 15 cases where the classifier suggested parathyroid tissue.

Results: Eight patients with FNAB samples identified by the classifier as suspicious for parathyroid tissue underwent surgery. A false positive parathyroid call was identified in none. Parathyroid adenoma or hyperplasia was identified in 7 cases (1 intrathyroidal). Cytology in 5 was AUS/FLUS, 1 cellular parathyroid tissue, and 1 malignant (consistent with parathyroid carcinoma). Three had concomitant primary hyperparathyroidism
(HPT), 3 did not, and 1 was unknown. An 8th patient had primary HPT and poorly differentiated malignant cytology from a mass posterior to the thyroid that was not resected. A synchronous resected brain lesion was compatible with metastatic neuroendocrine carcinoma, although a primary parathyroid origin was not entirely excluded. The brain lesion had negative PTH immunostaining, although it is possible that this expression was lost in the metastasis.

HPT (2 primary + 2 secondary with chronic renal failure) was diagnosed in 4 additional patients, but they did not have histological diagnoses available. All had AUS/FLUS cytology.

Surgery was deferred based on the classifier suspicion of parathyroid tissue combined with clinical factors in 5 cases. Two mentioned above had secondary HPT. Of the remaining 3, cytology was AUS/FLUS (2) or SFN.

Discussion: Parathyroid disease was present or suspected in all 15 cases identified by the parathyroid classifier. HPT was absent in 3 of 8 operated parathyroid cases. Cytology from academic and centralized cytopathology missed the parathyroid origin in 10 of 12 cases (83%).

Conclusion: The preoperative genomic identification of parathyroid tissue allows appropriate management of parathyroid disorders to replace unnecessary thyroid surgery, an impact likely to reduce complications such as hypoparathyroidism.

Abstract #1165

COMPLIANCE WITH CLINICAL GUIDELINES FOR MANAGEMENT OF THYROID NODES

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Objective: The objective of this study was to examine the discrepancy between daily practice and clinical guidelines for management of thyroid nodules.

Methods: This was a retrospective chart review study. There were 833 ultrasound guided fine-needle aspiration (FNA) cases performed at the midwest academic medical center from January 2010 to January 2012. We randomly selected 200 patients among the 833 cases for the chart review. The clinical measures were selected according to the guidelines, including family history of thyroid cancer, history of neck radiation, PET positivity, neck symptoms, TSH values, ultrasound characteristics, and other measures.

Results: Most patients were female (82%), Caucasian race (71%), and had no significant co-morbidities. Among 200 subjects, family history of thyroid cancer was asked in 59%. History of neck radiation was addressed in 61%. 7% had documented PET positivity. Neck symptoms were assessed in most subjects, including dysphonia (58%), dysphagia (70%), and dyspnea (39%). TSH value was documented in 75%. Majority of subjects had ultrasound performed prior to biopsy (88%). Regarding ultrasound description of the nodules, 50% described nodules consistency, but only 36% described their echogenicity. Presence of microcalcification was documented in 19% and increased vascularity was noted in 17%. Margin of nodules was described in 41% and nodule taller than wide was noted in 71%. 54% described presences of cervical lymph nodes. Radioactive iodide scans were performed in 10% of subjects. 81% of nodules had benign cytology. Indeterminate cytology, suspicious for malignancy, and malignancy were found in 8%, 6%, and 1% accordingly. 78 subjects underwent surgery, of those, 7% were confirmed to have thyroid cancer.

Discussion: FNA biopsy is the standard of care for management of thyroid nodules. Few studies reported how patients with thyroid nodules are managed according to the clinical guidelines. It appears from our study that there is a gap between current patients care and clinical practice guidelines for management of thyroid nodules. Clinical history and US features for risk stratification of FNA were lacking which could reflect physicians’ unfamiliarity with clinical practice guidelines.

Conclusion: Thyroid nodules are extremely common, therefore, improvement of knowledge of the current guidelines could be highly beneficial. Further studies are needed to examine factors associated with compliance with clinical guidelines in management of thyroid nodules.

Abstract #1166

WEIGH TOO MUCH FOR ROBOTIC THYROID SURGERY?

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Objective: Currently, the majority of practices in the United States that perform robotic thyroid surgeries are reluctant to include the obese patient population. This study aims to examine the feasibility and safety of robotic thyroid surgery in obese patients with similar morbidity scores.

Methods: From September 2009 to June 2013, 135 consecutive patients underwent outpatient robotic thyroid surgery by the same surgeon at our institution. We performed a retrospective analysis of 45 consecutive obese patients, and then compared them to another
90 patients that were either overweight or of average weight. Obesity was defined as body mass index (BMI) ≥30, overweight was defined as BMI 25-29.9, and fit was defined as BMI 18.5 - 24.9, as per NIH criteria. All patients met predetermined morbidity scores based on the Charlon index score. Clinical variables including patient demographics, and surgical outcomes were obtained and analyzed. Principle outcome measures were thyroid volume, length of operation, length of hospital stay, incidence of complications, and estimated blood loss (EBL). Clinical characteristics of patients and operative data were compared between the groups using Fisher’s exact test and ANOVA.

Results: The obese, overweight, and fit groups were similar in age (45.29 ± 10.67 vs. 47.15 ± 12.12 vs. 43.65 ± 13.05 years, p=.38), gender (93.3% vs. 86.7% vs. 88.9% females, p=.68), thyroid volume (24.69 ± 19.24 vs. 16.97 ± 16.50 vs. 18.89 ± 16.43 cm³, p=.08), and Charlon index score (1.17 ± 1.09 vs. 1.35 ± 1.95 vs. .71 ± .97, p=.08). Post-operative complications were 15.9% in the obese group, 17.8% in the overweight group, and 9.09% in the fit group (p=.55). EBL was similar between the groups (16.64 ± 10.45 vs. 14.48 ± 11.83 vs. 16.11 ± 10.97 mL, p=.73). No significant difference was found between the groups in total operative time (139.2 ± 44.32 vs. 144.4 ± 45.35 vs. 144 ± 33.54 min p=.85).

Discussion: This retrospective study examined the feasibility and safety of robotic thyroid surgery in obese patients with similar morbidity scores.

Conclusion: In a select patient population with a similar Charlson index score of 3 or less, robotic thyroid surgery had comparable surgical outcomes between obese, overweight and fit patients.

Abstract #1167

INTERPRETATION OF THYROID FUNCTION TESTS IN THE SETTING OF GERM CELL TUMOR

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Objective: Review the association of elevated βhCG levels and hyperthyroidism

Case Presentation: A 35-year-old male with metastatic carcinoma presented to the hospital with hemoptysis and shortness of breath for two days. A recent supraclavicular lymph node biopsy showed poorly differentiated carcinoma. He underwent chemotherapy and radiation with no improvement. Meanwhile the tissue obtained at biopsy revealed βhCG expression indicating germ cell origin. On admission patient denied anxiety, palpitations, tremors, hyper-defecation or muscle weakness. Physical exam was significant for tachycardia, supraclavicular lymphadenopathy, decreased breath sounds, and a large dark papule on the right nares. Pertinent medications included dexamethasone for brain metastases. At admission, serum βhCG was 133,683 MIU/ML (nl 0-5). Thyroid function tests were drawn for evaluation of his tachycardia. TSH was 0.01 MCU/ML (nl 0.27-4.20), free T4 1.9 ng/dl (nl 0.9-1.8) and free T3 2.7 pg/ml (nl 2.3-4.2). TSI was 41% (nl 0-139%) and thyrotropin receptor Ab <0.51 IU/L (nl 0.00-1.75). Thyroid ultrasound was normal. Propanolol was started at 10 mg three times daily. Thionamide therapy was held due to lack of significant thyrotoxic symptoms. Nares biopsy demonstrated βhCG expression consistent with choriocarcinoma. Scrotal ultrasound showed a left sided hypoechoic area. The patient was started on a germ cell tumor chemotherapy of bleomycin, etoposide and cisplatin. A week later, his βhCG level improved to 92,848 MIU/ML. After another 9 days of chemotherapy, his level improved to 9489 MIU/ml. Repeat thyroid indices were drawn at this time and showed a TSH of 0.84 MCU/ML and free T4 of 1.4 ng/dl. At the time of discharge, βhCG was 1991 MIU/ML.

Discussion: When hCG levels are very high as in our patient with a germ cell tumor, the hCG can bind to the TSH receptor and induce a hyperthyroid state. This association must be interpreted in the clinical context. As in our case, the patient was on dexamethasone which can potentially alter thyroid function tests. Antithyroid drugs may not be needed unless overt signs of thyrotoxicosis are present and chemotherapeutic agents may be enough to treat. The improvement in TSH corresponding to decreasing levels of hCG needs to be interpreted with caution since patient was no longer receiving dexamethasone. Furthermore no rise in free T3 was seen which is a hallmark of true hyperthyroid state.

Conclusion: Although it is important to recognize the association between high hCG levels and hyperthyroidism, thyroid indices must be consistent with symptom score and concordant. Aberrations in TSH alone should not dictate intervention.
Abstract #1168

PRE-OPERATIVE IDENTIFICATION OF BRAF V600E MUTATIONAL STATUS IN THYROID NODULES USING A NOVEL GENE EXPRESSION CLASSIFIER

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Veracyte, Inc.

Objective: The BRAF V600E mutation has low sensitivity for detecting cancer in thyroid nodules but its high specificity may help guide a decision to perform total thyroidectomy at the outset instead of lobectomy (risking a need for completion thyroidectomy). Microarray-based molecular evaluation of thyroid nodules using the Afirma Gene Expression Classifier (GEC) provides accurate detection of benign gene expression signatures in nodules with Bethesda III and IV cytological diagnoses but could also address additional clinical questions, e.g., gene mutation status, in a single combined assay. Here we present the performance of a pre-operative molecular test for the identification of the V600E mutation in thyroid fine needle aspirate biopsies (FNABs) using mRNA to detect downstream expression perturbations. FNABs were obtained from 716 nodules comprising Bethesda cytopathology categories II-VI.

Methods: Gene expression of more than 3,000 genes was measured on a custom microarray and BRAF V600E-positive or -negative labels for training (n=181) and test (n=535) sets were established using castPCR (Life Technologies). We specified a minimum detection of 2.5% mutant allele frequency by castPCR to designate a sample as V600E-positive. These data were used to train (via 10-fold cross-validation) a linear support vector machine classifier using 128 genes. Performance was then evaluated on an independent test set.

Results: Overall false positive rate was 1% (99.0% specificity, 95% confidence interval (CI) 97.5%-99.7%) while maintaining high sensitivity (86.0%, 95% CI 78.5%-91.6%). Analytical verification studies indicate classifier performance is maintained across laboratories, operators and critical reagent lots. The classifier is robust to the presence of up to 60% blood or 30% genomic DNA.

Discussion: The novel classifier was able to accurately determine the presence or absence of the BRAF V600E mutation in FNABs using changes in gene expression.

Conclusion: Pre-operative knowledge of BRAF mutational status may reduce completion thyroidectomy and intra-operative frozen section review and may eventually allow for mutation-targeted chemotherapeutics.

Abstract #1169

GRAVES’ DISEASE FOLLOWING HASHIMOTO’S THYROIDITIS: A CASE REPORT

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Objective: Development of Graves’ disease (GD) following Hashimoto’s thyroiditis (HT) in adults were described as rare events and sporadically reported, and the underlying mechanism(s) were not elucidated well.

Case Presentation: A 37 year old female with history of SLE, myopic degeneration, axial ocular muscle myopathies, prediabetes, and Hashimoto’s thyroiditis (was put on levothyroxine treatment, and then later discontinued after resolution in 5 years). 2 years later, she presented to ED with 2 month history of worsening intermittent palpitation, shortness of breath, tremor, hair loss, skin flushing, nausea, vomiting, myalgia, arthralgia, and swelling in the lower extremities. In the ED, patient was noted to have heart rate of 140 bpm, ophthalmopathy, diffusely enlarged thyroid gland with bruit, lower extremity edema, and tremor. Laboratory revealed: TRAB: 96.2 (<16%), TSH: <0.03 (0.55-4.78 mIU/mL), Thyroglobulin: 25.4 (0.73-84 ng/dL), FT4: 4.65 (0.86-1.76 ng/dL), T4: 20.4 (5.7-11.4 ug/dL), FT3: 15.6 (2.3-4.2 pg/mL), T3: 400.8 (60-181 ng/dL). Thyroid scan showed homogeneous uptake in a diffusely enlarged gland. 24 hour Iodine-123 uptake was 77% (10-30%), consistent with GD. Ten mCi of Iodine-131 was administered for treatment of hyperthyroidism.

Discussion: The continuum between HT and GD can occur within the scope of autoimmune thyroid disease (AITD). In a study of eight cases of GD following HT, one proposed mechanism was that the alterations in the thyroid state are related to the balance between the activities of Thyroid stimulating Antibody (TSAb) and Thyroid stimulation blocking antibody (TSBAb), and the responsiveness of the thyroid gland to these antibodies. The balance between TSBAb and TSAb changes in rare cases after Levothyroxine therapy for HT or anti-thyroid drug treatment for GD. These alterations involve differences in TSAb versus TSBAb concentrations.
and their effect(s) on the thyroid gland. De-novo TSAb synthesis can occur converting the long-standing HT to GD. The variable effects of TSH receptor mutations on Thyrotropin receptor antibody (TRAb) and M22 (TSHR-stimulating human monoclonal antibody) functions can cause these alterations as well. A significantly higher prevalence of clinical hypothyroidism and GD, and higher mean values of TSH and anti-TPO Ab were observed in female SLE patients than in controls. We are curious if this may play any role in the HT to GD transition.

Conclusion: GD following HT might not be uncommon in the adult population. Increased awareness of this entity will facilitate in early diagnosis and appropriate treatment in these patients, and may also lead to further research.

Abstract #1170

THYROID DYSFUNCTION DURING INTERFERON β-1A TREATMENT

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Objective: To report a case of thyroiditis in a patient after beginning therapy with interferon β-1a for multiple sclerosis.

Case Presentation: A 40-year-old male with no prior thyroid dysfunction presented for evaluation of abnormal thyroid function tests (TFTs) on routine blood work. He started Rebif (Interferon β-1a, IFN) six months prior for recently diagnosed multiple sclerosis. He was generally asymptomatic denying tremors, palpitations, heat intolerance, fatigue, nausea and vomiting. His physical exam including thyroid exam was unremarkable except for dry mucous membranes. An EKG showed sinus tachycardia. Laboratory evaluation revealed a positive serum pregnancy test with 10 weeks twin gestation on ultrasound. Her serum hGC was >225000 mIU/mL, TSH was <0.0100 (0.350-4.940 uIU/mL), FT4 was 2.82 (0.70-
ABSTRACTS – Thyroid Disease

1.48 mg/dl), and FT3 was 6.6 (1.7-3.7 pg/ml). Because of the severity of her symptoms she was started on propylthiouracil (PTU). Thyroid stimulating immunoglobulin (TSI) and anti thyroid peroxidase (anti-TPO) antibodies were later found to be within normal limits. The patient was discharged on PTU and followed up with a high-risk obstetrician. She required treatment with PTU to maintain normal thyroid function throughout her pregnancy and after delivery.

Discussion: Untreated overt hyperthyroidism during pregnancy can result in adverse maternal and fetal outcomes. Conversely, gestational hyperthyroidism resulting from hCG stimulation of the TSH receptors in early pregnancy is self-limiting and usually does not require treatment. The finding of hyperthyroidism, hyperemesis gravidarum, and negative thyroid antibodies in the first trimester of a twin pregnancy, especially in a patient with no past history of thyroid dysfunction, is highly suggestive of gestational hyperthyroidism. However, when symptoms are severe and the patient is found to have a significantly elevated free T3, consideration should be made for treatment with antithyroid medication with close patient follow up.

Conclusion: Applying clinical judgment based on severity of symptoms at the time of presentation and close monitoring after stabilization is important in the management of a patient with hyperthyroidism during pregnancy in order to determine the appropriate diagnosis and treatment.

Abstract #1172

A CASE OF METASTATIC PAPILLARY MICROCARCINOMA DISCOVERED INCIDENTALLY FOLLOWING PARATHYROIDECTOMY IN A PATIENT WITH RADIATION EXPOSURE

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Objective: Herein, we present a case of a patient with a history of radiation treatment to the head and neck during childhood. Close to thirty years later, she was found to have incidental papillary microcarcinoma detected within a lymph node near a parathyroid adenoma that was excised for primary hyperparathyroidism.

Case Presentation: The patient is a 61 year-old female with a four year history of hypercalcemia initially referred to surgery for primary hyperparathyroidism. During her initial neck exploration an enlarged left upper parathyroid adenoma was resected. Post-operatively a node within the resected specimen demonstrated metastatic papillary carcinoma. A total thyroidectomy was performed two weeks after initial operation. At the time of this second surgery a subcentimeter tumor was identified adjacent to the recurrent laryngeal nerve on the same side as the metastatic node. Post-operative pathology revealed this to be a 5mm focus of papillary thyroid carcinoma without evidence of malignancy in the remainder of the thyroid gland. The patient subsequently received 102mCi of I-131 due to the metastatic disease and adherence of the primary tumor to the nerve. There was no evidence of residual disease on post-therapy scan.

Discussion: Low-dose radiation therapy is recognized as a risk factor in both thyroid carcinoma and primary hyperparathyroidism. The concomitant finding of parathyroid pathology with thyroid carcinoma can exist in up to 25% of cases and requires thoughtful preoperative planning, operative intervention, and long-term follow-up. Thyroid carcinoma within this subset of patients is papillary carcinoma 80% of the time. Furthermore, papillary microcarcinoma, defined as tumors ≤1 cm, accounts for 10% of all papillary thyroid carcinomas and is found in up to 36% of thyroid glands at autopsy. The natural history of this cancer is indolent with mortality <1%; however, it presents an interesting clinical challenge due to recurrence rates of up to 7% after initial surgery. This is a rare presentation of metastatic papillary microcarcinoma found incidentally after parathyroidectomy and has only been reported once previously.

Conclusion: This is a novel case of metastatic papillary microcarcinoma identified during surgery performed initially for primary hyperparathyroidism in a patient with a remote history of radiation therapy.

Abstract #1173

SEVERE REFRACTORY HYPERTHYROIDISM IN PREGNANT WOMAN WITH GRAVE’S DISEASE COMPLICATED BY FETAL GOITER.

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Case Presentation: We present a 32 year old female with a history of Grave’s disease on anti-thyroid drugs (ATDs) who developed severe hyperthyroidism during pregnancy. In the first trimester, in spite of treatment with propylthiouracil (PTU), patient had worsening symptoms of thyrotoxicosis and significant enlargement of goiter. Laboratory analysis revealed elevated anti-thyroid antibodies (TSHrAB 79.1 (n <16%)), TSI 533 (n <140%), suppressed TSH (<0.03 (0.55-4.78 mIU/mL)), and elevated thyroid hormones levels (FT3 11.3 (2.3-4.2 pg/mL), FT4 3.4 (0.8-2.7 ng/dL)).
As pregnancy progressed in the second trimester, no clinical or biochemical improvement was noted. The patient gained some weight. However, her palpitations, weakness, and dyspnea worsened, and her goiter continued to enlarge. All attempts to reduce the daily dose of PTU resulted in increase of thyroid hormone levels and worsening of symptoms. At 21 weeks, fetal goiter developed. Patient was advised to proceed with total thyroidectomy; however she elected treatment with transplacental LT4 infusions.

**Discussion:** Hyperthyroidism complicates less than 1% of pregnancies. Grave’s disease, in most cases exacerbates in the first trimester but improves in the second and third trimesters. However, worsening thyrotoxicosis has been reported as well.

Treatment for pregnant patients with Grave’s disease includes ATDs and beta blockers. Beta blockers have been associated with fetal growth retardation. ATDs can cross the placenta and cause fetal goiter development and iatrogenic fetal hypothyroidism, therefore lowest dose should be used. Methimazole may be teratogenic, and therefore is not recommended for use in the first trimester. The management of fetal goiter is not well studied. Fetal goiter is detected by ultrasound, and confirmed by MRI. It can be associated with hyper and hypothyroidism in the fetus and biochemical analysis via percutaneous umbilical blood sampling is necessary. The treatment of fetal hyperthyroidism is administration of ATDs to the mother. Fetal hypothyroidism requires tapering of ATDs to the lowest tolerated dose. If that is not possible, maternal thyroidectomy is recommended. If surgery is contraindicated, then transplacental replacement of LT4 has been reported.

**Conclusion:** We present a case of pregnancy complicated by severe refractory maternal thyrotoxicosis secondary to Grave’s disease, complicated by development of fetal goiter. Both maternal thyroidectomy and transplacental replacement of LT4 represents significant risk. It is not clear at this time what the best management is. Thyroidectomy is indicated for severe refractory hyperthyroidism and best done in the second trimester.

**Abstract #1174**

**VITAMIN D DEFICIENCY IN HYPOTHYROIDISM**

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**Objective:** To study the prevalence of Vitamin D deficiency and its correlation with Parathyroid Hormone (PTH) levels in Hypothyroid Asian Indians in a tertiary care referral center in India.

**Methods:** 239 consecutive patients with hypothyroidism were screened for 25-hydroxycholecalciferol [25(OH) D] and Parathyroid Hormone (PTH) along with Serum calcium, phosphorus and alkaline phosphatase levels. Bone density DEXA scan was done in 168 cases with hypothyroidism. All (239) cases were newly diagnosed cases (6 month to 2 years of diagnosis) and were on thyroid hormone replacement therapy.

**Results:** 61 cases had 25(OH)D levels below 10 ng (Group I) and 105 cases had 25(OH)D levels between 11 ng and 30 ng (Group II). 35 subjects in Group I had elevated PTH, while no subject in group II had elevated PTH. Of the 35 cases with elevated PTH in Group I, all of them had 25(OH)D levels below 4 ng.

**Discussion:** Vitamin D deficiency is currently based on 25(OH)D level cut-offs. A large subset of hypothyroid population have low 25(OH)D levels below 30ng and below 10ng. But a low 25(OH)D level, below 30ng or below 10 ng does not necessarily correlate with poor bone health. For true vitamin D deficiency, 25(OH)D must be correlated with PTH due to this inverse relation. Therefore, true vitamin D deficiency needs reworking of normal values of 25(OH)D in Indian population taking into consideration PTH values. Current study indicates that 1 in 7 hypothyroid patients may have true vitamin D deficiency, which itself is a significant finding and merits a screening protocol.

**Conclusion:** The prevalence of Vitamin D level abnormality in hypothyroid cases is high among Asian Indians, with most cases having Vitamin D insufficiency. Among the deficient group, a much lower number had true vitamin D deficiency with a PTH elevation. The norms of vitamin D normal levels need to be reworked especially with PTH.

**Abstract #1175**

**SCLEROSING MUCOEPIDERMOID CARCINOMA WITH EOSINOPHILIA : AN UNUSUAL TUMOR OF THE THYROID.**

*Racha Dermesropian, MD1, John Mihailidis, MD1, Manmeet Kaur, MD2*


**Case Presentation:** 51-year-old woman with history of hypothyroidism who presented with a painless thyroid mass associated with voice changes and difficulty swallowing. Thyroid ultrasound was done showing a 4.2 cm nodule in the midpole of the right lower lobe. Fine needle aspiration was done and cytology was consistent with a follicular lesion of indeterminate significance. The thyroid gland was removed and the pathology showed a 2cm Sclerosing Mucopidermoid Carcinoma with Eosinophilia tumor of the right thyroid lobe on a background of Hashimoto’s thyroiditis. Margins were free of involvement without any blood vessel invasion. Patient has been followed for nine years with yearly bone density DEXA scan.
ABSTRACTS – Thyroid Disease

We present a 68 year-old man who presented to his primary care physician with symptoms of generalized weakness only. He denied weight loss, diarrhea, or heat intolerance. He had a medical history of type 2 diabetes, chronic kidney disease, coronary artery disease, abdominal aortic aneurysm, peripheral vascular disease, hyperlipidemia, and congestive heart failure. TSH was found at that time to be 4.67 mciu/ml (0.30-5.00 mciu/ml), free T3 was 6.0 pg/ml (2.0-4.4 pg/ml) and free t4 was >7.77 ng/ml (0.80-1.80 ng/ml). Soon after this, the patient was started on propylthiouracil (unclear about dose) for presumed hyperthyroidism by his primary care physician and monitored periodically with thyroid function tests. We were consulted when patient was found to have a TSH of 108.23 mcu/ml and free t4>8.0 ng/dl when he was admitted to our hospital for elective coronary artery bypass graft. During interview with the patient, he mentioned that he had been tapering his dose of propylthiouracil as he had not been finding any improvement in his anxiety symptoms. On examination, he did not exhibit any signs or symptoms of hyperthyroidism including exophthalmos. Patient underwent coronary artery bypass grafting without any complications and was extubated successfully with no complications of respiratory acidosis. Paucity of clinical findings caused us to explore other causes for the abnormal thyroid function tests. Differential included thyroid hormone resistance, even though this is considered to be a rare occurrence. There was no family history of similar thyroid hormone abnormalities. An uncle had recently been diagnosed with papillary thyroid cancer. We measured the alpha subunit of TSH and determined the alpha subunit to TSH molar ratio to be 0.23 (a value >1 is suggestive of a TSH-secreting tumor). We ordered human anti-mouse antibodies which were pending at the time of submission of this abstract and free T4 by equilibrium dialysis. This was low at 0.4 ng/dl (1.1-2.4 ng/dl).

Discussion: This patient, who was most likely euthyroid at initial presentation, was subjected to a potentially hepatotoxic medication because of a misinterpretation of thyroid function tests. We would have not been able to determine this if we had not requested the previous medical records.

Conclusion: This case illustrates the importance of past history in timely diagnosis and avoidance of potentially harmful treatments.

Abstract #1177

GREY-SCALE ANALYSIS IN THE ULTRASONOGRAPHIC EVALUATION OF THYROID NODULES

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Objective: Subjective analysis of ultrasonography (US) images is the first-line method to assess thyroid nodules, although it is limited by inter-observer variability and experience. The purpose of this study is to perform a quantitative measurement of echogenicity and echopattern, obtaining an objective estimate of the degree of hypoechogenicity and homogeneity, associated with risk of malignancy.
Methods: From January 2010 to October 2012, 839 consecutive patients (908 nodules) underwent US-guided FNA. In a single US image, three regions of interest (ROIs) were drawn: the first including the nodule; the second included a portion of the adjacent thyroid parenchyma; the third, the strap muscle. Histogram analysis was performed, obtaining the median, mean and SD of the pixels comprising each ROI. Echogenicity was expressed as a ratio: the nodule/parenchyma and parenchyma/muscle median grey ratios were calculated. The heterogeneity index was calculated as the coefficient of variation of grey histogram for each of the three ROIs.

Results: Nodule/parenchyma median grey ratio was significantly lower (more hypoechoic) in nodules found to be suspicious for cancer, according to the cytology report (p=0.006) and in confirmed malignant nodules (p=0.02). A nodule/parenchyma median grey ratio <0.46 has a sensitivity of 53.6% and specificity of 71.1% in predicting malignancy (OR 2.84; p=0.01). It can also be used as a continuous measure of hypoechogenicity and risk of malignancy (OR 0.20; p=0.02).

Discussion: US is a widely available and harmless method. It nonetheless is operator-dependent. The inter-observer agreement seems to be relatively good; however, a merely slight agreement was reported for echogenicity and echotexture. We developed a method to perform a quantitative measurement of thyroid echogenicity, avoiding the need for fixed US operating conditions.

Conclusion: Evaluation of nodule echogenicity according to the nodule/parenchyma median grey ratio allows for an objective stratification of thyroid nodule structure and risk of malignancy.

Abstract #1178

DANGEROUS WEIGHT LOSS: A CASE REPORT

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Case Presentation: 62 y.o. man presented with his wife, to the Emergency Department (ED) with complaints of altered mental status, fever and tachycardia. He had been in his usual state of health and only has a history of hypertension; no history of substance abuse. He initially developed generalized malaise with accompanying 101 fevers. Physical exam showed altered mental status, tachycardia and hypotension. EKG showed sinus tachycardia; MRI and CT of the head where unremarkable. Lumbar puncture was negative. Labs: CBC/CMP unremarkable, Cortisol 16.8 UG/DL, TSH 0.099 UIU/ML, FT4 0.99 NG/DL, FT3 20.45 PG/ML, TT4 6.94 UG/DL, TT3 5.99 NG/ML, thyroglobulin 1.34 NG/ML and Ab <3.0 IU/ML. In the ED, he was treated with IV fluids and antibiotics for a possible infection. He was started on Hydrocortisone, Esmolol drip and PTU. Patient was seen by endocrinology and PTU was switched to Methimazole. After 2 days, the patient was alert and oriented and confirmed he had been taking thyroid hormone in an effort to lose weight. He was taking a “thyroid booster” called Thyroid PX for approximately 4 months. Labs prior to discharge: TSH 0.07 UIU/ML, FT3 3.15 PG/ML and FT4 0.66 NG/DL. At discharge, fever and hypotension had resolved. Methimazole and antibiotics where stopped, steroids tapered and he followed up with endocrinology. The patient was diagnosed with “Thyrotoxicosis factitia” caused by taking too much thyroid medication.

Discussion: Exogenous hyperthyroidism describes hyperthyroidism caused by ingestion of excessive amounts of thyroid hormone. Surreptitious ingestion of thyroid hormone is termed thyrotoxicosis factitia. Some of the symptoms include: weight loss, palpitations, anxiety, heat intolerance or tremors. The diagnosis of exogenous hyperthyroidism is based upon clinical manifestations, laboratory findings, and 24-hour radioiodine uptake. Laboratory findings are: Decreased TSH, elevated free T4 and/or elevated total T3. Discontinuation or reduction in the dose is usually the only treatment needed. Thyrotoxicosis factitia has been seen in patients taking thyroid hormone to promote weight loss.

Conclusion: Thyroid PX is a dietary supplement for “thyroid support” which has Iodine, Selenium and 3,5-Diiodotyrosine in each capsule. 3,5-Diiodotyrosine is a precursor of thyroid hormone which increases conversion of T4 to T3 and Selenium is a cofactor for 5′-deiodinase, the enzyme that converts T4 to T3. Thyroid hormone should not be used for weight loss in patients who do not have a thyroid condition since it may cause life-threatening side effects. There are multiple dietary supplements available that claim to benefit thyroid levels but we recommend caution before starting any new medications.

Abstract #1179

ABSTRACT WITHDRAWN
Abstract #1180

CONSUMPTIVE HYPOTHYROIDISM IN A BOY WITH MESENCHYMAL HAMARTOMA OF THE LIVER: RESOLUTION SHORTLY AFTER COMPLETE TUMOR REMOVAL

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Case Presentation: Consumptive hypothyroidism is a rare form of thyroid hormone disturbance due to excessive levels of type 3 iodothyronine deiodinase enzyme (D3). This enzyme removes iodine from the inner ring of thyroxine (T4) to form reverse triiodothyronine (rT3), which is physiologically inactive. Several case reports have described tumors, usually hemangiomias, with elevated D3 levels that cause consumptive hypothyroidism. These patients typically require large doses of levothyroxine to maintain normal TSH and free T4, up to 70 mcg/kg/day (usual dosing is 5-10 mcg/kg/day in children). Patients require treatment with levothyroxine until tumor involution, but due to the nature of these tumors, they are usually not completely resected. There have been no published cases with consumptive hypothyroidism and complete tumor removal.

We present the case of an 18 month old boy with 1 month of abdominal distension and hepatomegaly, found to have a tumor of the left lobe of the liver (13.9 x 6.8 x 11.4 cm). Preoperatively, he was diagnosed with mild compensated hypothyroidism (TSH 25.8 mIU/ml and free T4 1.42 ng/dL). Anti-TPO and anti-thyroglobulin antibodies were negative. His reverse T3 was elevated (165 ng/mL). MRI imaging suggested the tumor to be a hemangiomia or hemangioendothelioma. The surgeons determined that his tumor was amenable to a complete resection. Levothyroxine was not started due to his adequate free T4. One day after successful tumor resection, his thyroid levels were normal (TSH 4.18 mIU/ml, fT4 1.56 ng/dL) with decreased rT3 (68 ng/mL). His labs remained normal through the next two weeks. Pathology ultimately revealed the tumor to be a benign mesenchymal hamartoma. The tumor expressed high levels of D3 activity, as determined by a competitive assay with 6n-propylthiouracil.

Discussion: This is the first case of consumptive hypothyroidism occurring with a mesenchymal hamartoma, which is a rare benign tumor in infants and young children. Another novel feature of this case is that the tumor was fully removed with surgery, and the patient never required levothyroxine treatment. In cases of tumor-associated consumptive hypothyroidism where a full resection is anticipated, thyroid hormone replacement may not be necessary.

Conclusion: Consumptive hypothyroidism can occur with a mesenchymal hamartoma and may rapidly resolve after tumor resection.

Abstract #1181

ASSOCIATIONS BETWEEN INSULIN SENSITIVITY, BETACELL FUNCTION, ADIPOKINES AND THYROID FUNCTION IN OBESE ADOLESCENTS

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Objective: Increasing serum TSH concentration, even within normal range, is associated with worsening insulin sensitivity (Si) in adults. It is not known if this relationship exists in children.

Methods: A total of 36 euthyroid, obese adolescents (BMI ≥ 95th percentile) aged 12-18 years without Type 1 or type 2 diabetes mellitus or receiving glycemic agents were studied. Each subject underwent a 7-sample 75 g oral glucose tolerance test (OGTT) with glucose, insulin and C peptide used to calculate Insulin sensitivity (Si) and Disposition index (DI) using the oral minimal model. DI estimates β-cell function, calculated as product of β-cell responsivity and Si. Lipid profile and adipokines [Interleukin-6 (IL-6), total and high molecular weight (HMW) adiponectin and retinol binding protein 4 (RBP-4)] were also measured. Associations between measures of thyroid function and Si, DI, lipid profile and adipokines were summarized using Pearson correlation coefficient and multiple regression analysis.

Results: The study population was 97% Caucasian with 47% subjects being male. Mean age of subjects was 14.3 ± 1.88 years, mean BMI 32.5 ± 4.65 (kg)/m2 and mean TSH 2.7 ± 1.2 mIU/L. Males and females did not differ in mean age, BMI or thyroid function. Increasing serum TSH was correlated with decreasing Si (log Si) (p= 0.024). TSH concentration was not correlated with disposition index (p-value 0.48). TSH correlated positively with LDL (p-value 0.04) and IL-6 (p-value 0.031), but when adjusted for BMI the association was no longer significant (LDL p-value 0.44, IL-6 p-value 0.07). There was no correlation between TSH and total and HMW adiponectin or RBP-4. Levels of free T4 and TPO antibodies did not correlate with Si, DI, lipids, IL-6, total and HMW adiponectin or RBP-4.
ABSTRACTS – Thyroid Disease

**Discussion:** We report for the first time an inverse association between TSH and insulin sensitivity in obese adolescents. This relationship was based on assessment of Si using a dynamic study and persisted after adjustment for BMI suggesting an independent relationship between thyroid function and insulin sensitivity.

**Conclusion:** In obese adolescents, increasing TSH even within the normal range is associated with decreased insulin sensitivity. Additionally, thyroid function may impact adipokine profiles in obesity.

**Abstract #1182**

**SIZE DISTRIBUTION OF METASTATIC LYMPH NODES WITH EXTRANODAL EXTENSION IN PATIENTS WITH PAPILLARY THYROID CANCER: REDEFINING CLINICALLY RELEVANT NODES**

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**Objective:** Understanding of the prognostic implications of positive metastatic lymph nodes in well differentiated papillary thyroid cancer (PTC) has evolved. Growing evidence has shown that all lymph node metastases in PTC do not have equal prognostic significance. A recent meta-analysis by Randolph et al. stratified lymph node metastases based on several parameters including if nodes were clinically evident on preoperative and/or intraoperative evaluation, number of positive nodes, size of the largest lymph node and presence of extranodal extension (ENE). This stratification scheme presumed that all small and/or clinically nonevident lymph nodes are not prognostically significant. That study reported that macroscopic, clinically apparent nodal metastases pose a greater risk of recurrence than small volume, subclinical, nodal metastases. Small lymph nodes were sized at 0.2 <1.0cm. Ito et al. identified a higher risk of recurrence in nodes greater than 1.5cm. ENE represents an aggressive phenotype of well differentiated PTC leading to an increased risk of recurrence and the development of distant metastases, and a worse disease free survival. However, to date, no study has attempted to correlate lymph node size with the presence of ENE.

This study evaluated the size of metastatic lymph nodes manifesting ENE to determine if lymph node size correlates with the ability of a cancer to break through the overlying capsule and to examine the size distribution of lymph nodes with ENE in patients with PTC.

**Methods:** This was an IRB approved retrospective review of 77 lymph nodes demonstrating ENE removed from 53 patients, treated for well differentiated PTC from 2004 to 2013 by a single surgeon. All patients in whom the pathology report indicated ENE were included in this study. The main outcome measure was analysis of the size of all lymph nodes with ENE. Pathology slides and reports were reviewed by a senior pathologist. Extranodal extension was defined as invasion into fat, skeletal muscle, nerve, and/or thick walled vascular structures.

**Results:** Lymph nodes manifesting ENE ranged from 1.6mm to 4.1cm. 39% (30) of lymph nodes with ENE were <1cm and 74% (57) of lymph nodes were 2cm or smaller.

**Discussion:** The results indicate that clinically nonevident, small lymph nodes are at risk of harboring aggressive disease biology reflected in ENE. 39% of all nodes fell within Randolph’s characterization of being “small”, while 56% of the nodes were less than 1.5cm, deemed by Ito to be the clinically significant size criteria.

**Conclusion:** This study suggests that the previous presumption that nodes with ENE only appear in clinically evident, macroscopic nodes is flawed.

**Abstract #1183**

**A TAKATSUBO CARDIOMYOPATHY PRESENTING WITH THYROTOXICOSIS**

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**Objective:** Takatsubo cardiomyopathy is a rare stress induced cardiomyopathy which is characterized by transient left ventricular apical ballooning. This syndrome was first described in Japan in the early 1900’s. In rare instances, takatsubo cardiomyopathy can occur as a rare complication of an acute hyperthyroid state. There exist only 13 described cases in the literature. Here we report a case of takatsubo cardiomyopathy which presented with thyrotoxicosis.

**Case Presentation:** A 71 year old Caucasian female presented to our hospital with an acute episode of chest pain and dyspnea. She had recently been told by her endocrinologist that she was hyperthyroid and was scheduled to have a thyroid uptake scan, however she had not started any medication and was asymptomatic prior to the admission. Physical exam included a blood pressure of 105/43mm Hg, heart rate of 123bpm, respiratory rate of 16 bpm, and temperature of 98.9 degrees F. Her neck was significant for a thyroid nodule measuring 1 centimeter on the right. She had tachycardia, crackles, trace pedal
edema, +2 deep tendon reflexes, no tremors, and was neurologically intact. Serum concentrations of thyroid stimulating hormone, free thyroxine, and triiodothyronine were <0.002mIU/L (normal 0.35-4.7), 292 ng/dL (normal 79-149), and 3.4 ng/dL (normal 0.7-1.0), respectively. Treatment included propriothiouricil, hydrocortisone, propranolol, supersaturated potassium iodide, Lasix, and anticoagulants. Her echocardiogram revealed hypokinesis and an ejection fraction of 42%. A cardiac catheterization revealed hemodynamically nonsignificant stenosis and apical left ventricular hypokinesis with ballooning characteristic of Takatsubo cardiomyopathy. Her repeat echocardiogram two weeks later revealed a normal ejection fraction and normal wall motion.

Discussion: The most common symptom of Takatsubo cardiomyopathy is acute chest pain mimicking myocardial infarction, however patients may also present with dyspnea, pulmonary edema and, more rarely, cardiogenic shock. It is often misdiagnosed and usually reversible. The etiology and relationship to the hyperthyroid state is not completely clear, however many theories have been elucidated. It has been proposed that an increase of thyroid hormones result in an acute activation of the adrenergic system. Other theories take into account multivessel epicardial spasms. The management is supportive and not evidence based. The prognosis is good.

Conclusion: Takatsubo cardiomyopathy can be a presenting symptom of hyperthyroidism, although rare. Thyrotoxicosis can be associated with life threatening complications in patients who were previously asymptomatic.

Abstract #1184

CHRONIC LYMPHOCYTIC THYROIDITIS INCREASES THE RISK OF INCIDENTAL THYROID CANCER IN PATIENTS WITH NODULES OF INDETERMINATE CYTOLOGY

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Objective: Thyroid nodules with indeterminate cytology on fine needle aspiration (FNA) present a management dilemma. The decision to operate and the choice of operation are based largely on the surgeon’s calculation of cancer risk, both within the nodule and within the entire gland. We sought to determine whether the presence of chronic lymphocytic thyroiditis (CLT) influenced the rate of malignancy in patients with indeterminate nodules.

Methods: We retrospectively reviewed all patients having thyroidectomy for thyroid nodules with indeterminate cytology on FNA between 2007 and 2011 at our institution. Indeterminate cytology included atypia or follicular lesion of undetermined significance (AUS/FLUS), suspicious for follicular neoplasm (FN), and suspicious for papillary carcinoma (PTC). We recorded patient risk factors, preoperative laboratory results, ultrasonographic features, cytologic findings, and final pathological results. Logistic regression analysis quantified the effect of CLT and other factors on the risk of malignancy.

Results: Indeterminate cytology was present in 132 nodules in 127 patients. Sixty-two (47%) were categorized as AUS/FLUS, 28 (21%) suspicious for FN, 40 (30%) suspicious for PTC, and 2 other indeterminate. Cancer was found on final pathology in 42% of the nodules; 91% were PTC. Incidental cancer, or a focus separate from the nodule in question, was found in 35% of patients. CLT was found in 38% of thyroid, and was correlated with elevated TPO antibodies (r 0.66, p<0.001) and a preoperative history of CLT (r 0.28, p<0.001). Although presence of CLT did not change the risk of malignancy within the indeterminate nodule, it did increase the risk of incidental malignancy within the gland (OR 2.5, 95% CI 1.2-5.4, p=0.01). Incidental cancer was present in 49% of patients with CLT, and 24% of patients without CLT. In half of the patients with CLT and incidental cancer, the indeterminate nodule was benign; the only cancer was the incidental lesion.

Discussion: In patients with cytologically indeterminate nodules, CLT was associated with an increased risk of incidental thyroid cancer, even if the nodules in question were benign. Nearly half of the patients with CLT had an incidental cancer not associated with the indeterminate nodule. Thus a lobectomy may be an inadequate operation for many of these patients.

Conclusion: In patients with an indeterminate nodule and CLT, a total thyroidectomy should be considered as the initial operation, given the risk of malignancy elsewhere in the thyroid.

Abstract #1185

DNA METHYLATION MARKERS FOR EARLY DETECTION OF THYROID CANCER

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Objective: Thyroid cancer (TC) has the fastest rising incidence rates in women, and the second fastest in men with an annual percentage change of approximately 5%, making TC the sixth most common cancer in women. There are four main types of which the papillary and follicular types (PTC and FTC, respectively) together
account for >90% followed by medullary cancers (3%-5%) and anaplastic carcinomas (<3%). PTC is the most common and has the best prognosis. FTC has a slightly worse prognosis than PTC. The cells in FTC can accumulate radioactive iodine, which can be used in its treatment. Hurthle cell carcinoma, a variant of FTC, has a worse outcome. It is less likely to concentrate radioactive iodine making it harder to detect and treat. For individuals who present with early stage disease of either PTC or FTC, there is no accurate marker(s) to predict whether they will develop metastatic or recurrent disease. Our immediate and long term goals are to identify DNA methylation markers for early detection of TC, to molecularly differentiate TC subtypes for enhanced classification, and as potential therapeutic targets.

Methods: Promoter methylation status of CASP8, CDKN2A, DAPK1, ESR1, NIS, RASSF1 and TIMP3, genes with reported associations in thyroid cancer, were examined in a cohort comprising of 26 FTC-Hurthle and 27 FTC-Classic subtypes utilizing quantitative methylation-specific PCR (QMSP).

Results: RASSF1 demonstrated significant differences in methylation between FTC-Hurthle and FTC-Classic tumor tissues (p<0.001). For CASP8 and CDKN2A, QMSP values of 0 were noted. The other 4 genes demonstrated methylation (>0) but were not statistically significant.

Discussion: Our data suggests that aberrant methylation of RASSF1 maybe useful as a marker to distinguish FTC-Classic cancer from FTC-Hurthle. Classification based on promoter methylation profiling may well be a more promising approach than expression profiling since these DNA-based techniques are not subject to the problems of tissue preservation, potential pitfalls of tissue heterogeneity, and easily detected by PCR-based methods. The potential reversibility of DNA methylation holds promise for these markers as potential targets for novel alternative demethylating treatments.

Conclusion: DNA methylation of RASSF1 maybe a useful marker to distinguish FTC subtypes, specifically FTC-Classic from FTC-Hurthle.

Abstract #1186

INCIDENCE OF HYPOTHYROIDISM AFTER UNILATERAL THYROID LOBECTOMY AND PREDISPOSING RISK FACTORS

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Objective: To determine the incidence and identification of pre-operative risk factors for the development of hypothyroidism after lobectomy.

Methods: 109 patients were selected after a retrospective chart review of 453 patients who underwent thyroid lobectomy between January 2000 and February 2013 at Thomas Jefferson Hospital. All study patients had indeterminate thyroid nodules per FNA. Exclusion criteria included prior use of thyroid suppressive medications, previous hemithyroidectomy, use of thyroid hormone replacement therapy prior to lobectomy or post-lobectomy for suppressive purposes, or lack of patient follow up within two years post-lobectomy or had incomplete medical records. Patients were diagnosed with hypothyroidism and were prescribed thyroid replacement therapy if their TSH was > 5.0 mIU/mL with symptoms of fatigue, weight gain, hair loss, and cold intolerance. All patients were followed for 2 years post-thyroid lobectomy and observed for clinical and laboratory signs or symptoms of hypothyroidism.

Results: In our study of 109 patients, 41% of patients developed hypothyroidism and required thyroid hormone replacement. Predisposing factors for developing hypothyroidism included; 1) a higher mean pre-operative TSH (2 vs. 1.17 mIU/mL); 2) older age (51 vs. 49yrs). Side of lobectomy or gender had no effect on the development of hypothyroidism. On the basis of pathologic subtypes, multinodular goiter (MNG) was more represented in the euthyroid group. Patients with evidence for lymphocytic infiltration and with papillary thyroid carcinoma were equally represented in each group, but follicular neoplasms were greater represented in the hypothyroid group.

Discussion: Following unilateral thyroid lobectomy, 41% of patients developed symptomatic and biochemical hypothyroidism and required thyroid hormone replacement. Patients who developed hypothyroidism were older and had a higher pre-operative TSH level than patients who remained euthyroid following lobectomy, while gender, and side of lobectomy did not appear to be significant risk factors. There was no specific pathologic subtype that appeared to increase the risk of hypothyroidism following lobectomy, however, multinodular goiter and follicular adenoma were more represented in the euthyroid group.

Conclusion: 41% of post thyroid lobectomy patients developed biochemical and clinical hypothyroidism. Higher pre-operative TSH and age appear to be risk factors, while no differences were found among side of lobectomy, gender, or pathology.
Abstract #1187

**THYROTOXIC PERIODIC PARALYSIS AND SEVERE HYPOKALEMIA COMPLICATED BY CARDIAC ARREST DUE TO VENTRICULAR FIBRILLATION**

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**Objective:** To report a case with thyrotoxic periodic paralysis (TPP) who presented with cardiac arrest and ventricular fibrillation

**Case Presentation:** A 23-year-old Hispanic male presented to ED with 9 hours of progressive generalized muscle weakness. He had 4 similar episodes within the past 5 months but he did not seek medical attention. His only significant past medical history was vitiligo. Initial vitals were BP 139/79 mmHg, HR 85/minute, Temp 36.3°C, and RR 16. Within an hour after his arrival, he developed ventricular tachycardia and Torsade de Pointes followed by ventricular fibrillation. He was defibrillated one time with 200J and he received cardiopulmonary resuscitation for several seconds. Serum potassium level came back immediately after resuscitation and it was 1.3 mEq/L. He was immediately and aggressively given intravenous and oral potassium supplementation (totally 100 mEq) over 2 - 3 hours. The serum potassium level was normal when checked at 4 hours and remained normal afterwards, without further replacement. His generalized weakness completely resolved within 24 hours after admission. The results of thyroid studies were consistent with Graves’ hyperthyroidism: TSH <0.008 (NR 0.35-5.5 mU/L), Free T4 2.8 (NR 0.89-1.76 ng/dL), Free T3 6.6 (NR 2.3-4.2 pg/mL), thyroid stimulating immunoglobulin 480 (NR <140%). He was therefore started on methimazole and propranolol. He did not have any further episode of paralysis. At 4 weeks after the hospital discharge, he was clinically and biochemically euthyroid and serum potassium level was normal at 4.8 mEq/L.

**Discussion:** TPP predominantly occurs in Asian male populations. But it has been reported in other races including Caucasians, Hispanics and African Americans. Most patients were not diagnosed with hyperthyroidism prior to the acute attack of TPP. They could easily be misdiagnosed if the thyroid function studies were not obtained. The symptoms of TPP range from muscle cramps and mild weakness to complete paralysis. It occurs as a result of rapid, massive shift of potassium from the extracellular into the intracellular compartment. Hypokalemia can cause EKG abnormalities. Arrhythmia including ventricular tachycardia has been described in patients with TPP. However, cardiac arrest and ventricular fibrillation in patients with TPP are extremely rare.

**Conclusion:** This case highlights the fact that cardiac arrest and ventricular fibrillation may be the presenting features of thyrotoxic periodic paralysis. Therefore, TPP should be considered as one of the possible causes in patients with severe hypokalemia and ventricular arrhythmia.

Abstract #1188

**ABSTRACT WITHDRAWN**

Abstract #1189

**RECURRENT SILENT THYROIDITIS AS A SEQUELA OF POSTPARTUM THYROIDITIS**

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**Objective:** Thyroiditis encompasses a group of disorders characterized by thyroid inflammation. Though clinically indistinguishable from silent thyroiditis, postpartum thyroiditis occurs in women within 12 months after delivery. Recurrent postpartum thyroiditis in subsequent pregnancies is common, but recurrent silent thyroiditis is rare. We reported a case of patient with recurrent episodes of thyroiditis, unrelated to pregnancy, after an episode of postpartum thyroiditis.

**Case Presentation:** A 31-year-old pregnant woman visited the Thyroid clinic for routine follow up of previously diagnosed hyperthyroidism. She remained clinically and biochemically euthyroid during the pregnancy while on methimazole which was discontinued postpartum. Five months after, she was diagnosed with postpartum thyroiditis manifesting with palpitations and tremors. Neck exam was essentially normal. Thyroid panel revealed severely suppressed TSH (0 mIU/mL), elevated free T4 (2.09 ng/dL) and T3 (212.6 ng/dL). Scintigraphic thyroid imaging was notable for decreased thyroid uptake (0.6%). Antibodies to thyroglobulin were positive. In two months she became euthyroid which persisted for the next eleven months until she developed the first episode of recurrent thyroiditis. The second episode of silent thyroiditis occurred fourteen months after the previous one. She became euthyroid 2 months later. She was offered thyroidectomy or radioablative iodine treatment to which the patient declined at the present. She remains clinically and biochemically euthyroid at this time.

**Discussion:** The prevalence of postpartum thyroiditis varies widely from 1.1 to 21.1%. Risk factors that may
predispose the development of postpartum thyroiditis are the presence of thyroid peroxidase antibodies, past history of thyroid disease, family history of thyroid disease, and type 1 diabetes mellitus. After first episode of postpartum thyroiditis, there is a 70% chance of recurrence with subsequent pregnancies in women with positive thyroid peroxidase antibodies. Even though the clinical features of silent thyroiditis are similar to postpartum thyroiditis, the recurrence rate is less than 10%. The largest number of recurrences in a single patient is nine. Yamamoto et al. reported a patient with 7 episodes of silent thyroiditis within 4 year period, between 2 episodes of postpartum thyroiditis. We reported the second case of recurrent silent thyroiditis (2 episodes) following postpartum thyroiditis. 

Conclusion: It is of interest that postpartum thyroiditis and silent thyroiditis might be overlapping disorders. This report is to remind physicians of the possibility of recurrent silent thyroiditis in women with history of postpartum thyroiditis.

Abstract #1190

THYROTOXICOSIS- INDUCED HYPERTENSIVE EMERGENCY AND SYSTOLIC HEART FAILURE

Bill Flatley, DO

Geisinger

Case Presentation: A 28 year old female with no significant known medical history presented with severe dyspnea on exertion for the last 2-4 weeks. She had been treated for anxiety and panic attacks for several months prior to this. Physical Exam: BP 189/130 mmHg, Pulse 142 /min, Temperature 37.1 °C, Respiration 32/min. Patient was anxious and distressed. She was found to have jugular vein distension, tachycardia, basilar crackles, and moderate pitting edema on lower extremities. Her thyroid was mildly enlarged. EKG showed sinus tachycardia with nonspecific ST-T changes. CXR showed bilateral interstitial edema with small pleural effusions. Echocardiogram showed severely reduced left ventricular ejection fraction (LVEF) (20-24%) with diffuse hypokinesis, moderate enlarged left atrium, no ventricular hypertrophy or dilatation. Patient was diagnosed with hypertensive emergency and acute heart failure. Subsequent lab showed negative cardiac enzyme, Coxsackie, Echovirus, Adenovirus antibody panels. TSH <0.01 uIU/ml, Free T3 of 26.2 pg/ml, Free T4 of 6.59ng/dl, TSI 221%. Patient was diagnosed with thyroid storm. Treatment with methimazole and propranolol. On eight week follow up, patient denied symptoms of heart failuer or hypertension. A repeat echocardiogram showed LVEF of 56% with no hypokinesis. Plan to have thyroidectomy as a definitive treatment.

Discussion: This is a young patient with no risk factors for CAD, no preexisting HTN or heart disease who presented with hypertensive emergency and CHF. Her clinical presentation can be well explained by the unique hemodynamic changes caused by hyperthyroidism. Firstly, hyperthyroidism increases cardiac output and blood volume, and causes hypervolemic status and hypertension. Secondly, hyperthyroidism causes tachycardia, which decreases ventricular filling time and impairs left ventricular contractility without causing ventricular dilation. Retrospectively, the patient could have had untreated hyperthyroidism for several months prior to admission.

Conclusion: Thyrotoxicosis can cause hypervolemic status and tachycardia, which precipitates hypertensive emergency and CHF. Early recognition and appropriate treatment can rapidly reverse its clinical course.

Abstract #1191

TSH REFERENCE RANGE AMONG SAUDI ARABIA ADULT POPULATION

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1. King Saud University, 2. King Fahad Medical City

Objective: The aim of the present study is to establish new reference intervals for serum TSH levels in Saudi adults (13-60) years old living in Riyadh.

Methods: A Prospective study included healthy males and females Saudis aged between age 13 and 60 years. We obtained history, physical examination and laboratory investigations including TSH, Free T4, Anti-thyroperoxidase antibodies (TPO-Ab) and Anti-thyroglobulin T antibodies (T-Ab). We excluded all volunteer with the history of thyroid disorders, family history of thyroid diseases, taking medications affect the thyroid function test, pregnant or lactating women, and who has clinical goiter.

Results: Out of 337 subjects 132 were candidates for final analysis (52 males, 80 females), the mean, median, minimum and maximum values of TSH were 1.95mIU/L, 1.73mIU/L, 0.42µIU/mL, and 4.74µIU/mL respectively. FT4 mean, median, minimum, and maximum values
were 15.46 pmol/L, 15.30 pmol/L, 11.40 pmol/L, and 19.77 pmol/L, respectively. The 95% reference interval (2.5th - 97.5th percentile) of serum TSH in the total population was 0.59-4.37 mIU/L.

Conclusion: The upper limit of TSH in this study was close to the currently used reference range, however we advise for more studies with larger sample size that may shows narrower range.

Discussion: There are no previous studies conducted in Saudi Arabia documenting the reference range of TSH. Our study is considered the first study to establish the reference range of TSH and discuss lowering its upper limit in adult. TSH reference values corresponding to the 97.5th percentile showed an upper limit of 4.37 mIU/L. This value was not significantly different from customary upper reference limit of 5.00 mIU/L. Most of the studies done in different countries to determine the TSH reference range had similar results. However, fewer studies supported the lowering of the range to 2.5 mIU.

FT4 analysis was performed and the values were not significantly different from the currently used reference range.

Conclusion: Based on the results of our current study, the TSH reference range corresponding to the 95% reference interval (2.5th, 97.5th percentile) is 0.59-4.37 mIU/L. The upper limit is close to the currently used reference range in our institution. However, we recommend conducting a similar study involving a larger sample which is more representative of general population to establish normal reference values of TSH and FT4 for Saudis.

Abstract #1192

INITIAL PRESENTATION OF WELL DIFFERENTIATED PAPILLARY THYROID CANCER AS A SCALP LESION AND REVIEW OF THE LITERATURE ON SCALP METASTASES OF WELL DIFFERENTIATED THYROID CANCER

Eliza Dewey, BA1, Henry Su, BA1, Erin Alpert, BA1, Laura Dos Reis, BA1, Mark Weisen, MD2, Michael Tuttle, MD, FACS3, Mark Urken, MD, FACS2

1. Thyroid Head and Neck Cancer (THANC) Foundation, 2. Beth Israel Medical Center, Department of Otolaryngology, 3. Hackensack University Medical Center, 4. Memorial Sloan Kettering Cancer Center

Objective: The most common clinical presentations of papillary thyroid carcinoma (PTC) are the detection of a solitary thyroid nodule on physical examination, a dominant nodule in a multinodular goiter, cervical lymphadenopathy or the incidental finding of a thyroid nodule based on other imaging studies. Initial presentation of PTC as distant metastases is extremely rare, especially those manifesting as a cutaneous metastasis. Only five other cases have been reported in the literature of a patient presenting initially with a scalp lesion, which, upon further examination, led to the diagnosis of a thyroid carcinoma. We present a 50 year-old female whose initial presentation of papillary thyroid cancer was cutaneous involvement of the scalp.

Methods: We reviewed all surgical and pathological reports as well as all imaging studies associated with this case and completed a thorough review of the literature using the search terms cutaneous metastases, metastatic thyroid carcinoma, papillary thyroid cancer, scalp metastases.

Case Presentation: At the time of detection of the scalp lesion, the patient had undergone several prior thyroid biopsies, none of which identified a malignant process. A subtotal thyroidectomy and excision of the scalp lesion were performed. The patient underwent post-operative radioactive iodine therapy but had persistent uptake in the anterior mediastinum from a mass that was not removed at the time of the initial surgery. One year following initial surgery, the patient developed metastases in her sternum and in her lungs leading to surgical resection of the locoregional disease followed by external beam radiotherapy. In addition, the patient developed a second cutaneous metastasis to the scalp, which was resected and then also treated with external beam radiation. The patient is scheduled to undergo further radioactive iodine therapy for her persistent, slowly progressive lung disease.

Discussion: In a review of the literature, only 13 cases of patients with differentiated thyroid cancer metastasizing to the scalp region have been reported, seven of which exhibited pure PTC histology. The other six cases reported in the literature demonstrated either a follicular thyroid carcinoma (FTC) histology or a mixed PTC and FTC histology. Only two cases of those patients with a pure PTC histology, presented initially with a scalp metastasis, demonstrating the rarity of this case.

Conclusion: PTC is most commonly associated with lymphatic spread, thus PTC which metastasizes to the scalp region via vascular dissemination represents an aggressive disease that leads to poor survival rates.
Abstract #1193

INSULAR THYROID CARCINOMA WITH UNDETECTED METASTASES ON POST I-131 THERAPY WHOLE BODY SCAN.

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McLaren Macomb

Case Presentation: A 6-year-old female was referred to exclude pulmonary embolus which delayed the post-thyroidectomy I-131 whole body scan (WBS) analysis. 1.5 months after total thyroidectomy, the patient developed pain in the left lower back. Thyroglobulin was 729 ng/ml with negative anti-thyroglobulin antibody titers and TSH was 83.28 uIU/ml. Pre-therapy WBS demonstrated a 24-hour I-131 uptake of 2.2% in the anterior neck. Two focal areas of activity were noted in the region of the thyroid surgical bed, consistent with residual thyroid tissue. There was no apparent scintigraphic evidence of metastatic disease. The patient was treated with 125 mCi of I-131 2 months post total thyroidectomy. The post therapy scan was deemed negative for metastatic disease and physiologic uptake was noted in the bladder.

One day after the post-therapy whole body scan, the patient presented to the hospital with left leg weakness and paresthesias. CT of the lumbar spine without IV contrast revealed a “new 2.1 cm lytic lesion in the upper left sacral wing and new 1 cm focus of subtle altered density in the upper aspect of the L3 vertebral body”. Biopsy of the L3 lesion was positive for metastatic thyroid cancer. She underwent vertebroplasty to “prevent further collapse and potential disability”.

 Palliative radiation with 30-35 Gy in 10-14 fractions over 2-3 weeks is planned. After the first radiation treatment (1.5 month after I-131 therapy) the thyroglobulin declined to 681 ng/ml with a TSH of 0.23 uIU/ml on thyroid hormone replacement therapy.

Discussion: Thyroid cancer accounts for 2% of all newly diagnosed cancers in the United States. Insular carcinoma in turn accounts for approximately 2% of all thyroid cancers. Most common sites of the metastases are lung and bone. Approximately 25% of insular thyroid carcinoma cases are responsive to I-131 radioactive iodine and make thyroglobulin. Thus, our case is of a rare form of thyroid cancer, metastases of which can be overlooked on post-131 therapy whole body imaging especially when obstructed by the usual sites of normal physiological uptake.

Conclusion: It remains essential to be vigilant of a patient’s symptomatic concerns and correlate the clinical presentation in full context of the pathological diagnosis.

Abstract #1194

LANGERHANS CELL HISTIOCYTOSIS (LCH): A UNIQUE PEDIATRIC PRESENTATION OF A RARE DISEASE

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University of Florida

Case Presentation: A 62-year-old female presented with compressive goiter. She was having dysphagia and dyspnea. Thyroid function studies were normal. Total thyroidectomy was performed revealing a poorly differentiated carcinoma of insular pattern (multi-focal, 6.8 cm at its greatest dimension, with extensive lympho-vascular invasion, no tumor capsule, and negative margins).

Nine days after the total thyroidectomy, chest CT with contrast was obtained to exclude pulmonary embolus which delayed the post-thyroidectomy I-131 whole body scan (WBS) analysis. 1.5 months after total thyroidectomy, the patient developed pain in the left lower back. Thyroglobulin was 729 ng/ml with negative anti-thyroglobulin antibody titers and TSH was 83.28 uIU/ml. Pre-therapy WBS demonstrated a 24-hour I-131 uptake of 2.2% in the anterior neck. Two focal areas of activity were noted in the region of the thyroid surgical bed, consistent with residual thyroid tissue. There was no apparent scintigraphic evidence of metastatic disease. The patient was treated with 125 mCi of I-131 2 months post total thyroidectomy. The post therapy scan was deemed negative for metastatic disease and physiologic uptake was noted in the bladder.

One day after the post-therapy whole body scan, the patient presented to the hospital with left leg weakness and paresthesias. CT of the lumbar spine without IV contrast revealed a “new 2.1 cm lytic lesion in the upper left sacral wing and new 1 cm focus of subtle altered density in the upper aspect of the L3 vertebral body”. Biopsy of the L3 lesion was positive for metastatic thyroid cancer. She underwent vertebroplasty to “prevent further collapse and potential disability”.

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Discussion: Thyroid cancer accounts for 2% of all newly diagnosed cancers in the United States. Insular carcinoma in turn accounts for approximately 2% of all thyroid cancers. Most common sites of the metastases are lung and bone. Approximately 25% of insular thyroid carcinoma cases are responsive to I-131 radioactive iodine and make thyroglobulin. Thus, our case is of a rare form of thyroid cancer, metastases of which can be overlooked on post-131 therapy whole body imaging especially when obstructed by the usual sites of normal physiological uptake.

Conclusion: It remains essential to be vigilant of a patient’s symptomatic concerns and correlate the clinical presentation in full context of the pathological diagnosis.
- Group 1 - Treatment Arm A. She had a mixed response to vinblastine and prednisone, with improvement of her CNS and thyroid disease, but progression of her lung disease. Subsequently, she was treated with high dose cytarabine with further progression of her lung disease, and finally with cladribine to which she has responded.

**Discussion:** LCH is a rare disorder with variable presentations and can be a formidable diagnostic challenge. Our patient is unique in that she presented with diabetes insipidus, thyroid and lung involvement at such a young age. Thyroid and lung disease are rare in children.

**Conclusion:** Lung involvement in LCH is most often seen in young adults that smoke. We hypothesize that the significant second hand smoke exposure may have accelerated her lung disease and caused a presentation that is rarely seen in children.

**Abstract #1195**

**VITAMIN D DEFICIENCY IS HIGHLY PREVALENT IN GRAVES’ DISEASE: EFFECT OF PREOPERATIVE HIGH DOSE VITAMIN D SUPPLEMENTATION ON POSTOPERATIVE HYPOCALCEMIA**

_Cara Govednik, MD, Samuel Snyder, MD, FACS, Courtney Quinn, MD, Saurabh Saxena, BS, Daniel Jupiter, PhD, Mathew Tillman, MD, Jesse Conner, BS_

Texas A&M/ Baylor Scott and White

**Objective:** Postoperative hypocalcemia, a known complication of thyroid surgery, can be a significant burden, necessitating more laboratory testing, medications, hospital stays and follow up. Vitamin D deficiency prevents proper intestinal calcium absorption, potentially leading to worsening of hypocalcemic symptoms even with calcium supplementation. It is thought that Graves’ disease (GD) patients have a higher incidence of vitamin D deficiency and therefore preoperative treatment may decrease the prevalence of postoperative symptomatic hypocalcemia.

**Methods:** From February 2013 to October 2013, all Graves’ patients that required thyroid surgery had preoperative testing for vitamin D deficiency (Group 1). Patients diagnosed with vitamin D deficiency were preoperatively treated with high dose vitamin D, and data was prospectively collected on postoperative outcomes. Surgical outcomes were compared to a historical cohort of GD patients from March 2004 to January 2013 with no preoperative vitamin D testing (Group 2).

**Results:** Of 36 patients tested, 68.6% were found to be deficient in vitamin D. These patients were treated with high dose vitamin D for an average length of 3+/−5.4 weeks preoperatively. There was no statistically significant difference between Groups 1 (n=36) and 2 (n=226) in terms of age, gender, BMI, procedure type, preoperative calcium level or requirement for parathyroid autotransplantation. Although the occurrence of postoperative hypocalcemia was slightly lower in Group 1 than 2 (8 (22.2)% vs. 75 (33.6%), p=0.17), the difference was not significant, as was the occurrence of symptomatic hypocalcemia (3 (8.3%) vs. 24 (10.6%), p=1), requirement for intravenous calcium (2 (5.6%) vs. 14 (6.2%), p=1), emergency room visits (0 vs. 9 (3.9%), p=0.62) or extension of hospitalization (0 vs. 4 (1.8%), p=1). No patients in the treatment group developed carpopedal spasm compared with 7 (3.1%) in the untested group, but the majority of patients in both groups required only oral calcium supplementation.

**Discussion:** The prevalence of vitamin D deficiency in GD was significantly higher than the national estimate of 40%, but preoperative treatment did not appear to lessen the postoperative complications. Extending the length of treatment preoperatively may potentially decrease the occurrence of postoperative hypocalcemia, although vitamin D deficient patients did not demonstrate a higher occurrence of symptomatic hypocalcemia when compared directly to patients who had a normal level preoperatively.

**Conclusion:** Despite the high prevalence of vitamin D deficiency in GD, treatment with high dose vitamin D does not appear to significantly decrease the occurrence of postoperative hypocalcemia and its sequelae.

**Abstract #1196**

**PSAMOMMA BODIES AND SARCOID REACTION IN OCCULT PAPILLARY CARCINOMA: A CASE REPORT**

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Dalhousie University

**Objective:** Thyroid cancer incidence is on the rise. While most cases are identified through evaluation of thyroid nodules, other histologic findings are important clues and should raise suspicion for occult malignancy. This case report is the first to describes two of such findings as they occurred in a single, unique case.

**Case Presentation:** A 43 year-old male of African descent was evaluated for intractable hiccups associated with vomiting and 40lbs of weight loss. Investigations revealed bilateral hilar and mediastinal adenopathy with partial collapse of the left lower lobe and slight reduction in diffusion capacity. Bronchoscopy and mediastinoscopy identified non-caseating granulomas and psamomma bodies. A short course of prednisone for presumed sarcoidosis completely resolved the lung abnormalities
and pulmonary function testing with no improvement of the primary complaint. The finding of psamomma bodies prompted further evaluation of the thyroid gland in light of the known association with papillary thyroid carcinoma. Subsequent surgical pathology showed multifocal micropapillary carcinoma with locoregional lymph node involvement. He is awaiting iodine ablation.

**Discussion:** Psamomma bodies (PB) are round, dark, glassy appearing structures that form by concentric lamellated calcification. PB are most commonly associated with papillary thyroid carcinoma (PTC) where they have been seen in up to 50% of cases. It has been suggested that this is an adaptive process that leads to apoptosis, preventing the growth and spread of neoplastic cells. PB are seen in one quarter of thyroid fine needle aspiration biopsies and can be detected on thyroid ultrasound. When identified, their presence is positively correlated with gross lymph node metastases and higher TNM staging and a tendency towards extrathyroidal extension.

The term sarcoid reaction refers to lymphadenopathy with non-caseating granuloma in the absence of systemic findings of sarcoidosis. There have been several case reports documenting sarcoid reaction in the lymph nodes in the setting of PTC, typically in regional lymph nodes. This may be a local tissue response and defense mechanism against carcinoma.

**Conclusion:** This case highlights the diagnostic and prognostic value of psamomma bodies in the setting of papillary thyroid carcinoma. We provide some guidance for properly investigating this finding when noted outside the context and location of suspected malignancy. Clinicians should also be familiar with the rare presentation of sarcoid reaction in the setting of malignancy. This is the first case in the literature that describes these findings in combination.

**Abstract #1197**

**EXOPHTHALMOS AS AN INITIAL MANIFESTATION OF HYPOTHYROIDISM**

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**Objective:** To report a case of a 53 year old woman with hypothyroidism and coexisting exophthalmos.

**Case Presentation:** A 53 year old lady presenting with 18 months history of bulging of both eyes. Additionally patient noted excessive tearing of the eyes for several years. There was no history of anterior neck swelling, palpitations, weight loss or gain, nor tremors of the hands. There was no history of menstrual irregularities or alteration insleep pattern. Significant examination findings revealed BMI 26.81, (weight- 73kg, height- 1.655m) and truncal obesity (waist circumference-93cm). Eye examination findings included bilateral proptosis with peri-orbital hyperpigmentation, lower lid lag, chemosis and soft tissue fullness. There was no goiter but she had elevated blood pressure of 146/104mmHg. Investigations revealed FT4-5.1pmol/l(12 to 20), FT3-3.2pmol/l(3.9 to 6.7), TSH - 71.5mIU/L(0.27 to 4.2). Thyroidperoxidase antibody- 70.7iu/ml(0 to 9),thyroglobulin antibody-0.6iu/ml(0 to 4). Full blood count was normal. She was treated with Levothyroxine tablets. Repeat Thyroid Function Test 2 months later showed reduction of TSH to 18.92mIU/L (0.37 to 3.50) but the eye signs remained the same.

**Discussion:** Only infiltrative ophthalmopathy but no dermopathy or diffuse goitre was present in our patient. Exophthalmos is usually associated with Graves’ disease and may occur before or after its diagnosis. It is however an unusual initial presentation of autoimmune hypothyroidism. The markedly elevated TPO confirms that there was autoimmune destruction of the thyroid gland resulting in hypothyroidism.

**Conclusion:** Exophthalmos is a common finding in Graves’ disease but a rare occurrence in hypothyroidism. Appropriate biochemical tests are important to make accurate diagnosis even in resource constrained settings like ours.

**Abstract #1198**

**A RARE CASE OF PAPILLARY THYROID CANCER ARISING IN STRUMA OVARI**

Maali Milhem, MD, Christine Oakley, MD

Marshall University

**Objective:** Struma ovarii is a tumor of the ovaries in which thyroid tissue comprises over 50% of the overall tissue. Most cases are asymptomatic from a thyroid standpoint. Hyperthyroidism is seen in about 8% of patients. Malignant transformation comprising only 0.5-5%.

**Case Presentation:** A 35 year-old Caucasian female without significant past medical history was incidentally found to have right ovarian mass on MRI done for evaluation of back pain. Pelvic ultrasound showed a 12cm complex appearing right ovarian cystic mass near the bladder with no invasion. Endometrial biopsy revealed hyperplasia with atypia. She subsequently underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy. Pathology showed struma ovarii with a 2-cm well-differentiated papillary carcinoma of the thyroid, follicular variant, confined to the ovary. Tissue testing for
BRAF V600E mutation was negative. She was referred to the endocrine clinic, and denied symptoms suggestive of thyroid dysfunction. On exam there was mild enlargement of the thyroid gland and laboratory testing revealed low serum thyroid stimulating hormone (TSH) level 0.318uIU/ml (0.35-5.5uIU/ml) with normal thyroxine (T4) and triiodothyronine (T3) levels, consistent with subclinical hyperthyroidism. Ultrasound of the thyroid showed an enlarged heterogeneous gland with several small nodules. Fine needle aspiration of the dominant right-sided nodule was benign. She underwent total thyroidectomy which revealed benign findings. Her post-operative course was complicated by transient hypoparathyroidism. Recently she received I-131 radioablation.

**Discussion:** Malignant struma ovarii are an exceedingly rare entity, comprising 0.5-5% of all struma ovarii cases. Due to its rarity, there are no standardized treatment guidelines. In cases of malignant struma ovarii with distant metastasis, aggressive treatment including total thyroidectomy to facilitate adjuvant I-131 radioablation is less controversial. In patient without metastases, though, the indication for thyroidectomy and RAI is less clear.

**Conclusion:** Malignant transformation of struma ovarii is exceedingly rare, thus no standardized treatment guidelines exist. Review of literatures suggests that subsequent total thyroidectomy and I-131 radioablation may decrease rates of metastasis and recurrence.

**Abstract #1199**

**THYROID STORM AND ACUTE STROKE: THE CHICKEN OR THE EGG**

Mehreen Husain, MD, Suja Shenoy, MD, Gail Nunlee-Bland, MD, FACE,
Rabia Cherqaoui, MD, Yassin Mustafa, MD, Sujay Madduri, MD, Wolali Odonkor, MD, Vijaya Ganta, MD

Howard University Hospital

**Objective:** To identify and treat thyroid storm presenting with acute stroke.

**Case Presentation:** 48 year old African American woman with hypertension, diabetes mellitus and tobacco use presented to the ED with sudden inability to speak. She was afebrile, had sinus tachycardia with blood pressure of 160/68 mmHg. Neurological examination showed right facial nerve palsy with normal motor strength and brisk reflexes. Babinski sign was negative. Other systems were normal. Head CT showed an acute infarct in the right anterior cerebral artery (ACA) territory. Over the next few hours, she deteriorated and became quadriplegic and aphasic. Subsequent evaluation revealed a history of hyperthyroidism and non compliance with therapy. Endocrine evaluation revealed a diffuse goiter without exophthalmos. Free T4 was greater than 6.15 (0.8-1.9 ng/dL) with TSH of 0.01 (0.4-4.0 uIU/mL). Total T4 was 27.36 (4.5-12.5 mg/dL), total T3 was 647 (82-179 ng/dL). Hemoglobin A1C was 5.5%. Later, blood pressure worsened and she developed high grade fevers without any apparent focus of infection. Burch and Wartofsky score was 60, suggestive of thyroid storm. She was treated with propylthiouracil, propranolol, hydrocortisone and potassium iodide. The infarcts later worsened to involve the entire ACA territories bilaterally with hemorrhagic transformation. She was diagnosed with akinetic mutism. Echocardiogram showed mild tricuspid regurgitation and moderate pulmonic regurgitation with a normal ejection fraction. Carotid doppler showed no significant stenosis. With treatment for thyroid storm, her neurological status improved. She was able to answer questions with a delayed response and able to move her lower extremities before transfer to a skilled nursing facility.

**Discussion:** Our patient had a rare presentation of stroke with thyroid storm. It is unclear whether the thyroid storm precipitated the stroke or the reverse. Thyroid storm is a rare endocrine emergency. It occurs in 1% to 2% of hospital admissions with mortality rates between 10% and 75%. Thromboembolic complications are responsible for 18% of deaths in thyrotoxicosis. Hyperthyroidism is associated with hypercoagulability caused by increased concentrations of prothrombotic factors and increase in red cell mass due to up regulation of erythropoietin and augmented platelet plug formation.

**Conclusion:** Stroke represents a rare manifestation of thyroid storm. Hyperthyroidism is associated with thromboembolic phenomena with or without evidence of cardiac dysrhythmias. In patients who present with thyrotoxicosis and neurological deficits, the possibility of thyroid storm must be considered.

**Abstract #1200**

**RAPIDLY ENLARGING THYROID MASS: A CASE OF AMYLOID GOITER**

Manivel Eswaran, MD, MS, Shwetha Thukuntla, MD

University of Texas Medical Branch

**Objective:** To emphasize the clinical recognition of amyloid goiter in patients with rapidly enlarging thyroid mass and rule out systemic amyloidosis in these patients.

**Case Presentation:** 21 year old south Asian female presented to ER with rapid neck swelling for the last 8 weeks and compressive symptoms. She had no significant past medical history. She had diffusely enlarged thyroid with no nodules, right side measuring more than the left. CT showed heterogeneous thymomally, right > left, with posterior extension around the trachea and the esophagus resulting in compression of the laryngeal inlet.
The right lobe measured 4.6 x 5.2 x 9.3 cm and the left lobe measured 3.6 x 3.0 x 7.4 cm. FNAC showed unusual benign appearing thyroid follicular cells, some colloid and abundant amorphous material, fibroblast-like, benign-appearing spindle cells and capillary blood vessels. She eventually got total thyroidectomy for her symptoms. Her biopsy was positive for amyloid goiter with extensive fatty infiltration. Immunohistochemical staining for the type of amyloid protein is pending at this time.

Discussion: Although amyloid deposits can be commonly seen in patients with systemic amyloidosis and medullary thyroid carcinoma, clinically recognized thyroid enlargement due to amyloid deposition is rare. It is seen in only 0.04% of patients with primary amyloidosis. Amyloid goiter from localized amyloidosis is also rare. Amyloid goiter usually presents as a gradual, painless, diffuse, firm enlargement of the thyroid. However it can also present as a rapidly enlarging mass as in our patient and can appear as a possible case of anaplastic thyroid carcinoma or lymphoma. Diagnosis is by histopathological evaluation as FNA cannot distinguish between amyloid goiter, non goitrous amyloid of the thyroid, and medullary carcinoma. Microscopic sections show eosinophilic amorphous deposits in the inter and parafollicular areas that stain intensely with Congo red and apple green under polarized light. Immunohistochemical tests can differentiate between the type of amyloid protein. Further evaluation includes work-up to rule out systemic amyloidosis and if negative, the goiter can be considered as a manifestation of localized amyloidosis. Treatment involves thyroidectomy in patients with obstructive symptoms and treatment of underlying systemic amyloidosis if found.

Conclusion: In patients with a rapidly enlarging thyroid mass appearing as a malignancy, amyloid goiter should be suspected even when features of systemic amyloidosis are not clinically apparent.

Abstract #1201

EVALUATION OF THYROID DISFUNCTION AND OBESITY IN CHILDREN WITH ALL, NHL TREATED WITH CHEMOTHERAPY ALONE OR PLUS RADIOThERAPY

Saghi Elmi, MD, Reza Erfani Sayyar, MD, Sam Elmi, MD

Mashhad University of Medical Sciences

Objective: In most children with Acute Lymphoblastic Leukemia (ALL) and Non Hodgkin’s Lymphoma (NHL) who undergone chemotherapy with and without radiotherapy, some late effects due to treatment may occur such as endocrinopathies like impairment in growth and puberty, changes in Body Mass Index (BMI) and thyroid dysfunction.

Methods: We evaluated growth criteria (include short stature, obesity) and thyroid test function in 50 children with ALL (n=25), NHL (n=25) 3-17 year-old in remission period who randomly received chemotherapy with (n=25) or without (n=25) radiation as our treatment groups. The values for height, weight and BMI in less than 5th percentile or more than 95th percentile considers abnormal. We used T-test, Man-Whitney, regression, Pierson and Spearman correlations as statistical tests.

Results: 6 (12%) patients were in less than 5th percentile height (short stature), 2 patients (4.0%) had over weight and 48 (96%) were in normal range of BMI. 6 (12%) patients were in less than 5th and 3 (6%) were in more than 95th percentile weight. There was no significant difference between 2 different treatment groups for TSH (P= 0.662) but there was significant difference between these 2 groups for T4 (P= 0.049). Mean and SD for T4 in patients with chemotherapy alone was less than in whom received chemotherapy plus radiotherapy. There was no significant difference between ALL, NHL groups for TSH, T4 (P= 0.567, 0.528 respectively). 2 boys with ALL without history of radiation had hypothyroidism based on their laboratory data.

Discussion: It seems that hypothyroidism as an important factor in short stature and endocrinopathies during treatment in children with malignancies should be considered.

Conclusion: Regarding to effects of thyroid dysfunction on short stature and obesity in adolescent with ALL, NHL it is suggested to pay attention more to growth in them for improving their quality of life.

Abstract #1202

SCREENING STUDY OF IODINE DEFICIENCY STATUS AND THYROID DISEASES IN CAUCASIAN CHILDREN

Shota Janjgava, MD, PhD Student1, Elene Giorgadze, Professor1, Lasha Uchava, MD, PhD Student1, Marina Lomidze, Professor1, Ketevan Mikadze, Professor2, Ketevan Asatiani, Professor1, Tamar Zerekidze, MD, PhD Student1

1. National Institute of Endocrinology, 2. Enmedic

Objective: Thyroid disorders are the second commonly encountered disorders in endocrine clinics and are significant causes of medical morbidity and mortality. Thyroid disorders are widely recognized as an important public health problem; its prevalence has increased substantially in the recent decades. Routine screenings for thyroid disorders are not performed universally. The objective of this pilot study to determine the prevalence of thyroid diseases associated with iodine deficiency in
Caucasian (Georgian population) children.

**Methods:** 21,118 children with age range 6-16 years were included in the study. Screening for thyroid disorders involved palpation and ultrasonography of the thyroid gland, and serum TSH and anti-TPO measurements.

**Results:** Based on these information we divided the patients into five groups: 1) children with normal thyroid examinations and normal TSH and TPO antibodies, (n=15301) 2) children with hypothyroidism (n=4578),, 3) children with hyperthyroidism (n=285) 4) children with nodular goiter (n=43) and 5) children with autoimmune thyroiditis (n=911). Thus our screening has revealed 27.5% of children in our study have thyroid disorders.

**Discussion:** Thyroid gland diseases in children are an important medical and epidemiologic entity, as its deleterious effects on patients is firmly established. Attention to thyroid disorder evaluation is an important part of health screening in children.

**Conclusion:** Our study demonstrated routine screening for thyroid gland diseases in Georgian children provides valuable information and tools for proper intervention.

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**Abstract #1203**

**UNABLE TO EXTUBATE: THINK THYROID**

Arundeep Kahlon, MBBS, Arunpreet Kahlon, MBBS, Amrita Dhillon, MBBS, Nidhi Bansal, MBBS, Gaganjot Singh, MBBS

SUNY Upstate Medical University

**Case Presentation:** A 60 years old male with past medical history of coronary artery disease, diabetes mellitus type 2, hypertension and hypothyroidism was brought in to E.D. by EMS when his friend found him lying on the floor at home. Patient fell two days ago and was unable to get up since then due to pain and weakness over right hip. Imaging studies done revealed right femur fracture and patient was scheduled for surgery. Basic lab tests including a comprehensive metabolic panel (CMP), CBC and coagulation panel were within normal range prior to surgery. Patient underwent open reduction and internal fixation for right femur fracture under general anesthesia next day. He was transferred to intensive care unit for close monitoring as he was still intubated. Multiple attempts for extubation failed due to poor respiratory effort and hypoxia. Repeat lab tests including CMP and CBC did not show any abnormality. Thyroid function tests (TFTs) showed TSH of 84.06 (normal: 0.270-4.200 µU/ml) and a free thyroxine (FT4) level of 0.22 (normal: 0.90-1.70 ng/dl). Patient was immediately started on IV levothyroxine and subsequent improvement in his respiratory effort and oxygenation was noticed which led to successful extubation next day. Repeat TFTs showed marked improvement with levothyroxine therapy.

**Discussion:** Hypothyroidism affects many bodily systems that might influence perioperative outcome and course including respiratory system as it can cause hypoventilation secondary to respiratory muscle weakness and decreased pulmonary response to hypoxia and hypercapnia.

**Conclusion:** Hypothyroidism should be considered as one of the potential causes for delayed extubation as it may cause delay in recovery from general anesthesia due to respiratory depression and slowed drug metabolism.
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