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ADRENAL DISORDERS

Abstract #100

FEMINIZING ADRENAL TUMOR PRESENTING AS GYNECOMASTIA: LONG-TERM FOLLOW UP

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Objective: To report a male w/ E2-producing adrenal tumor presenting as bilateral gynecomastia (BLG).

Methods: Clinical exam, imaging, hormonal studies, histopathological, immunostaining findings & long-term FU.

Case Presentation: A 41-yrs. old man presented w/ BLG (tanner stage 5), & infertility for 4 yrs. after having fathered 7 children previously. He had atrophic testicles & was hypogonadal. Labs: serum studies: E2: 5337 pmol/L (RR: 28-156), undetectable FSH & LH, testosterone (T) 4mmol/L (RR:10-27.8), DHEA 4 ng/ml (RR: 2.3-12.8), DHEAS 1.6 umol/L (RR:2.99-11.5); 24-h UF cortisol 368 nmol/D (RR: 100-379). CT abdomen: 8.5 cm solid Rt. adrenal tumor invading IVC. Pt. had complete resection of 9 cm 300 G tumor showing pleomorphic high mitotic activity but no vascular or extra adrenal invasion. Immunostains:+ve for cytokeratin, & inhibin. Pathological Dx: Adrenal Carcinoma.

Clinical Course: 5th post op day E2 was 114 & remained normal for ensuing 7 yrs. but BLG has persisted. Postop serum “T” had returned & stayed normal (12.3-15) to-date. Testicular volume had improved to 18 ml & Pt. fathered has fathers 2 children since surgery. No additional Rx given since there was no evidence of extra adrenal invasion either intraoperatively of histologically. FU CT abdomen & pelvis for 7 yrs. have been WNL.

Discussion: A prompt resolution of abnormal E2, normalization of “T” & fertility soon after surgery occurred. Although IVC tumoral invasion & histopathological interpretation of malignancy had been concerning, yet hormonal & imaging data for 7 yrs. FU are reassuring findings. A long-term persistence of BLG indicates that once male breast tissue is exposed to chronic high levels of E2, breast tissue fails to regress. However, testicular function can return to normal. The experience w/ feminizing adrenal carcinoma producing E2 is limited because these tumors are exceptionally rare. Malignancy is reported in majority of cases w/ median survival of 1.5 yrs. BLG, decreased libido, testicular atrophy, abnormal E2 & suppressed gonadotropins w/ or w/o abnormal serum DHEAS & 17-hydroxy progesterone are hallmarks of disease. Aromatase enzyme catalyzes final stage of E2 biosynthesis from androgens. Aromatase expression is reported in E2-producing adrenal carcinoma cells. Aromatase activity of carcinoma tissue showed marked enhancement compared to surrounding normal adrenal tissue. Enhanced expression of the enzyme is responsible for overproduction of E2 in carcinoma cases.

Conclusion: Bilateral gynecomastia combined w/ abnormal E2 levels should alert to Dx of adrenal carcinoma. Our case provides evidence that complete resection of tumor can result in long term survival w/ normalization & maintenance of normal hormonal responses.

Abstract #101

GIANT RETROPERITONEAL BRONCHOGENIC CYST MIMICKING ADRENAL GLAND TUMOR

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Objective: To report a case of giant paraadrenal cyst mimicking adrenal tumor.

Methods: Clinical exam, imaging (CT/MRI), hormonal, surgical, histopathological findings & literature survey.

Case Presentation: A 45-yr. old hypertensive male had incidentaloma picked up during investigations for recurrent renal stones of 15 years duration. MRI study revealed 10 cm well defined lobulated left adrenal mass with increased signal intensity on T2 & decreased intensity on T1 weighted images with peripheral capsular & septal enhancement representing lipid-poor adenoma. Hormonal studies for the following were WNL: 24-hr. urine metanephrine (0.65 umol/day), normetanephrine (2.45 umol/D), serum cortisol AM (406 nmol/l; RR: 171-536), upright serum aldosterone AM (309 pmol/l; RR: upto 831), DHEAS 2.8 (umol/l; RR: 2.99-11.5), testosterone (15 nmol/l; RR: 9.9-27.8). At open laprotomy a large adrenal-related mass was resected. The lesion was
attached to & had ruptured thru diaphragm requiring repair of the diaphragmatic defect superiorly. Histopathology findings: 12 cm. oval cystic 312 G unilocular but septated thick pale mucoid material containing cystic lesion with normal golden yellow normal adrenal attached to the cyst. Cyst was lined by respiratory columnar ciliated epithelium & bronchial mucus glands.

**Discussion:** Bronchogenic cyst represents an anomaly during the development of the primitive foregut from which the bronchi & lungs develop. It results from aberrant budding from the ventral diverticulum, pinching off lung epithelium from primitive ventral foregut with aberrant migration into abdomen before fusion of diaphragm. Subdiaphragmatic & mediastinal locations are rare. Lung & mediastinum (subcarinal) locations are typical. Histological confirmation consists of ciliated epithelium together with cartilage or bronchial mucus glands.

**Conclusion:** Our case of giant retroperitoneal cyst in close proximity to adrenal is uncommon. Diagnostic imaging findings cannot differentiate from diverse causes of retroperitoneal tumors. It should be taken into account in differential dx of adrenal tumor, cystic teratoma, bronchopulmonary sequestration cysts of urothelial & mullerian origin, or hydatid cyst. Surgical resection is recommended for definitive diagnosis & to prevent future complications.

**Abstract #102**

**THE EVOLUTION OF NONFUNCTIONAL ADRENAL ADENOMA**

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**Objective:** The aim of study was follow up of the size and functional potential of nonfunctional adrenal adenoma after 1 year of surveillance and this paper is supported by the Sectoral Operational Programme Human Resources Development (SOP HRD) 2007-2013, financed from the European Social Fund and by the Romanian Government under the contract number POSDRU/107/1.5/S/82839.**

**Methods:** The lot of study consist of 46 patients, men and woman who were diagnosed in 2011 with nonfunctional adrenal adenoma in National Institute of Endocrinology C.I.Parhon Bucharest. They all had CT of the adrenal gland, measurement of plasma MN and NMN, Dexamethasone supression test 1 mg overnight and for patients with HTA, ionograma and aldosterone/renin ratio at the diagnosis and after 1 year of surveillance.

**Results:** Median age of woman was 49,01+/− 19,07 years old and median age of men was 51,5+/− 21,19 years old. 34 tumors (73%) were unilateral tumors: 20 (57,89%) left adrenal tumors and 14 (42,1%) right adrenal tumors. 10 ( 23% ) were bilateral tumors. Mean tumor size was: 2,71/1,64 +/- 1,63/1,28 cm for left unilateral incidentaloma, 2,81/2,11 +/- 1,32/1,17 for right unilateral incidentaloma, 1,37/1,1 +/- 0,52/1,6 cm for left bilateral incidentaloma, 2,14/3,81 +/- 1,7/1,3 cm for right bilateral incidentaloma. Just 8 patients (19,23%) had high plasma and urinary cortizol levels but they have supressed plasma cortizol after 1 mg Dexamethasone overnight test. 9 patients had surgery (laparoscopic suprarenalectomy because of the big tumor size). 36 patients had been followed at 1 year. 14 patients (41%) had tumor growth and 22 patients (59%) have been stationary regarding tumor size. Tumor growth was 0,65+/−0,12 in tumors < 2 cm and 0,59+/−0,27 cm in tumors with 2-4 cm.

**Discussion:** Data from the literature shows that most of the adrenal nonfunctional adenoma are stationary. 5-25% increase with at least 1 cm, 3-4% decrease in size. Less than 20% develop hormone-secretion, usually in the first three years. In our group of study 41% of patients had tumor growth and in 59% of patients had no increases in tumor size. None of the patients followed at 1 year had hormone secretion. If after 5 year of surveillance tumor size is stable and nonfunctional, the surveillance may not be necessary.

**Conclusion:** The majority of tumors had 2-4 cm. Tumor size was almost equal for left adrenal tumors and right adrenal tumors (p=0,012). In our lot of study 41% of patients had tumor growth and 59% of patients have been stationary regarding tumor size. There has been no bigger tumor growth for patients with bigger tumor size (p=0,015 ). None of the tumors followed at 1 year had autonomous hormonal secretion.

**Abstract #103**

**SPIRONOLACTONE INDUCED ADRENAL INSUFFICIENCY IN A PATIENT WITH ALDOSTERONE-PRODUCING ADENOMA**

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**Objective:** Primary hyperaldosteronism is an underdiagnosed cause of hypertension. Concurrent cortical adrenal hormone hypo- and hypersecretion is not common. We report a patient with concurrent primary hyperaldosteronism and adrenal insufficiency, induced by spironolactone treatment.
**Case Presentation:** A 64 year-old male with a longstanding history of hypertension for 12 years presented to endocrine clinic for evaluation of secondary hypertension. His blood pressure was poorly controlled despite multiple drug regimens (metoprolol, enalapril, amlodipine/amlodipine). In 2008, he had acute aortic dissection that required emergent sternotomy and aortic replacement with two-vessel CABG and aortic valve replacement. The patient was asymptomatic and physical examination was unremarkable. Laboratory tests were suggestive of primary hyperaldosteronism (aldosterone 13 ng/dL, plasma renin activity 0.1 ng/mL/h, aldosterone-to-renin ratio 130). Oral salt suppression test confirmed the diagnosis. An abdominal MRI revealed a 1.2 cm right adrenal adenoma. Adrenal venous sampling demonstrated lateralization to the right adrenal with ratio of 50:1 and cortisol level in the inferior vena cava was 21 mg/dL (5-23 mg/dL). Due to complicated past medical history medical management was preferred to surgery, and spironolactone was started. Six months after the treatment he complained of fatigue and found to have adrenal insufficiency confirmed by corticotrophic stimulation test (baseline cortisol 4.9 mcg/dL, 30 and 60 minutes cortisol 7.1 mcg/dL). He reported clinical improvement after hydrocortisone daily supplement.

**Discussion:** There have been several case reports of adrenal insufficiency causing by hypoxic/hypotensive injury to adrenal gland. One case was related to the rupture of abdominal aneurysm in a patient with primary hyperaldosteronism. Our patient had normal cortisol after the surgery according to the venous sampling, so we hypothesized that spironolactone might be the cause of adrenal insufficiency. Pharmacology studies in guinea pig demonstrated that spironolactone decreases the activities of several adrenal enzymes as well as induces degradation of cytochrome P-450 in adrenal microsomes resulting in decrease cortisol production. Furthermore, an in vitro study in human adrenocortical cells also showed that spironolactone caused a concentration-dependent inhibition of basal production of both cortisol and aldosterone.

**Conclusion:** Although concurrent primary hyperaldosteronism and adrenal insufficiency is very rare, routine cortisol screening should be considered in these cases, especially in patients treated with spironolactone, in order to provide appropriate replacement and to prevent adrenal crisis.

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**Abstract #104**

**THROMBOCYTOPENIA IN ECTOPIC CUSHING’S SYNDROME - A CASE SERIES**

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**Objective:** Glucocorticoids have traditionally been associated with neutrophilic leukocytosis and thrombocytosis. Pharmacological doses of these agents have been used as first line therapy in immune thrombocytopenic purpura (ITP). We describe 3 patients with Cushings syndrome (CS) due to ectopic ACTH production who were thrombocytopenia at the time of initial presentation and platelet counts normalized after correction of hypercortisolemia.

**Case Presentation:** Three Caucasian patients (2 women) with ages of 60, 75 and 80 years presented with features consistent with ectopic ACTH dependent CS. Their 24 hour urine free cortisol values were extremely elevated at 671, 2025 and 4210 mcg (normal <50) with concomitant plasma ACTH of 140, 144 and 241 pg/ml (normal 8-42). All patients were thrombocytopenic with mean (SD) platelet counts of 54 (4K), 88 (15K) and 133 (5K) per cumm (normal 150K-450K/cumm) at time of presentation. All patients underwent pituitary MRI, body CT, Octreotide scan and PET scan, none of which localized tumor source. Work up for septic foci, disseminated intravascular coagulation (DIC) and heparin induced thrombocytopenia was also negative. No patients was on medications commonly implicated in thrombocytopenia. Bone marrow biopsy in one patient showed inappropriately normal megakaryocyte numbers. Two patients underwent bilateral adrenalectomy including one with a concomitant splenectomy, while the third patient was treated with ketoconazole. Platelet counts normalized after resolution of the hypercortisolemic state in all 3 patients and were 210 (110K), 226 (116K), and 290K per cumm. The splenectomy specimen showed extra-medullary hematopoiesis.

**Discussion:** Thrombocytopenia in patients with severe CS is usually related to coexisting infection or DIC. Thrombocytopenia associated with endogenous hypercortisolism has been described as a single case report. Glucocorticoids have been used in ITP by virtue of its ability to suppress reticulo-endothelial function, inhibit production of platelet antibody and, to a lesser extent, stimulate bone marrow platelet production. There are case reports of worsening thrombocytopenia in ITP with use of extremely high doses of steroids. Although the exact mechanism(s) for glucocorticoid mediated
thrombocytopenia remain(s) conjectural, a direct suppression of megakaryopoiesis has been proposed. The presence of extra-medullary hematopoiesis in one of our patients is consistent with this concept of marrow exhaustion.

**Conclusion**: Severe endogenous hypercortisolism may cause suppression of megakaryopoiesis and consequent thrombocytopenia, which can reverse following correction of the hypercortisolism.

**Abstract #105**

**TAKOTSUBO CARDIOMYOPATHY FROM AN ADRENAL CRISIS**

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**Case Presentation**: A 38 year-old male presented to our ER with fatigue, weakness, abdominal pain, and vomiting for three days. Over the past week, he had poor appetite, decreased fluid intake, intermittent episodes of chest pain and dyspnea. On exam, BP was 84/60 mmHg, pulse 117 bpm, O2 saturation 84% on open face mask. The patient was in distress, appearing lethargic and dehydrated. Despite generous IV fluids, he required multiple vasopressors, transferred to the ICU and intubated. Lab data demonstrated hyponatremia of 123 mmol/L, hyperkalemia of 6.9 mmol/L, undetectable aldosterone, negative cardiac biomarkers, pH 7.15 on ABG. Glucose, creatinine, and tox screen were normal. Endocrinology was consulted for a random cortisol of 33 nmol/L. A subsequent 250-ug ACTH stimulation test resulted as cortisol 0.01, 40, and 38 nmol/L at 0 min, 30 min, and 60min respectively. The patient was diagnosed with adrenal insufficiency and started on hydrocortisone 100mg IV every 8 hours. Echocardiogram demonstrated severe left ventricular systolic dysfunction with akinesis of all mid-distal segments and an estimated EF of 20%. The patient responded very well to steroids and was weaned to oral replacement. Eight days after admission and prior to discharge, a repeat echocardiogram showed complete reversal of his acute severe left ventricular dysfunction. EF was estimated at 55-60%, normal cavity size and movement. A diagnosis of Takotsubo cardiomyopathy from adrenal crisis was made.

**Discussion**: Takotsubo cardiomyopathy (TTC) is a syndrome characterized by a reversible systolic dysfunction of the apical and mid-portions of the left ventricle in the absence of coronary disease. It is was named after the Japanese tako tsubo pots used to capture octupus, which, in this state, the cardiac apex resembles. Only two cases of TTC from adrenal insufficiency are found in the literature, making this a rarely described condition. Possible pathophysiology of TTC include catecholamine-mediated cardiotoxicity, myocarditis, endothelial cell dysfunction, and coronary spasm, often triggered by an emotional or physical stress. In our case, we hypothesize that the acute adrenal crisis triggered a stress cascade leading to apical ballooning and subsequent CHF. In the absence of other treatments, steroids alone rapidly reversed the stress source and resolved the cardiomyopathy.

**Conclusion**: This case is one of the few to document a Takotsubo cardiomyopathy secondary to adrenal crisis. In a diagnosed adrenal crisis, physicians should consider TTC if cardiac symptoms exist, necessitating a more complete cardiological workup in addition to steroid replacement.

**Abstract #106**

**‘THE EYE CANNOT SEE WHAT THE MIND DOES NOT KNOW’, A CASE DESCRIBING A RARE CAUSE OF ADRENAL INSUFFICIENCY**

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**Case Presentation**: A 79-year-old Caucasian male with history of diabetes mellitus and osteoarthritis was admitted with complaints of generalized weakness, nausea and lightheadedness. He had been hospitalized twice with similar complaints in the past six months. Physical examination was notable for tachycardia and orthostatic hypotension. Laboratory work revealed mild hyponatremia with serum sodium of 134 meq/dL, elevated BUN and creatinine of 31 and 1.3 mg/dL respectively. Standard ACTH stimulation test showed a low baseline cortisol of 0.9 mcg/dL with undetectable ACTH that didn’t stimulate adequately following cosyntropin administration (60 min value of 12.4 mcg/dL). Patient was treated with intravenous fluids and hydrocortisone with good clinical response. Pituitary testing disclosed low LH (1.0 mIU/mL) and total testosterone (142 ng/dL) without any mass lesions. Review of old records showed longstanding unexplained intermittent elevations of AST and ALT. The constellation of diabetes mellitus, arthropathy and liver disease in the setting of hypopituitarism raised the possibility of hemochromatosis. Iron studies were obtained and showed a serum ferritin of 1694 ng/mL with a transferrin saturation of 103%. Genetic testing confirmed the diagnosis showing the patient to be homozygous for HFE gene.

**Discussion**: The clinical presentation of adrenal
Adrenal Disorders

insufficiency can be quite variable depending on whether the onset is acute, leading to adrenal crisis or chronic, with symptoms that are more insidious and vague. The diagnosis requires a high index of clinical suspicion particularly in chronic cases. Basal plasma ACTH measurement usually helps distinguish primary from secondary and tertiary causes. An effort to identify the underlying cause should always be made as the disease process may have other ramifications and cause-specific treatment may reduce morbidity. Hemochromatosis, although uncommon, should be suspected in the clinical context of liver disease, diabetes mellitus and arthropathy. Pituitary dysfunction is an important manifestation most commonly presenting as hypogonadotropic hypogonadism. Deficiencies of TSH, GH, and ACTH have all been reported and typically occur late in the course of disease. Early treatment may lead to reversal of hypogonadism but not other endocrine deficiencies.

Conclusion: The clinical presentation of adrenal insufficiency is variable and diagnosis requires a high index of suspicion. An attempt should always be made to identify the underlying cause. Hemochromatosis is a rare cause of secondary adrenal insufficiency that should be considered in the appropriate clinical setting.

Abstract #107

SEQUENTIAL DEVELOPMENT OF SPONTANEOUS BILATERAL ADRENAL HEMORRHAGE IN A HOSPITALIZED PATIENT: CASE PRESENTATION AND LITERATURE REVIEW

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Objective: This case is about a patient who developed adrenal insufficiency secondary to sequential hemorrhage into the left and then right adrenal gland.

Methods: Case reports were identified through a computer search using Medline (1980-2012) and from bibliographies in review articles (up to 2012).

Case Presentation: A 49-year-old male with history of antiphospholipid syndrome (APS) presented with epigastric pain. He had an abdominal CT which showed normal adrenal glands. A week later, he started complaining of left upper quadrant abdominal pain for about 18 hours. His INR was 3.6 secondary to outpatient Coumadin intake. He had a CT scan of the chest to evaluate the left upper quadrant pain. It showed features suggestive of the left adrenal gland infarction. An ACTH Stimulation test was normal. Two days later, the patient developed a similar right upper quadrant pain and an MRI of the abdomen showed peripheral rim enhancement of both adrenal glands suggestive of bilateral infarction. A repeat ACTH Stimulation test showed lack of response to synthetic ACTH with a baseline of 13 and post Cosyntropin level of 14. A diagnosis of adrenocortical insufficiency was made secondary to bilateral adrenal infarction and stress-level corticosteroid replacement was started.

Discussion: Adrenal insufficiency is a rare disorder, occurring in 144 people per million population. Bilateral adrenal hemorrhage (BAH) is responsible for 1% of these cases in autopsy studies. It is associated with a 15% mortality rate. Anticoagulant therapy, thromboembolic disease, hypercoagulable state, and the postoperative state are the major risk factors. The case presented had two of these risk factors. In a review of 86 patients, adrenal insufficiency was the first clinical manifestation of APS in a third of the patients and abdominal pain was the commonest symptom. Hemorrhagic diatheses, including anticoagulant use, have been associated with approximately one third of BAH cases. However, clotting test results are usually within the therapeutic range and spontaneous bleeding elsewhere is not evident. The patient presented had normal adrenocortical function after developing unilateral adrenal hemorrhage. More than 90% of the adrenal cortex needs to be compromised before symptoms and signs of adrenal insufficiency become apparent.

Conclusion: Screening for hypoadrenalism is recommended in any APS patient who complains of abdominal pain. This case demonstrates that patients with unilateral adrenal hemorrhage are at high risk of developing bilateral disease. Such patients should be followed up with another ACTH Stimulation test if adrenal imaging indicates bilateral hemorrhage or clinical features of adrenal insufficiency develop.
Abstract #108

A RARE CASE OF VIRILIZING ADRENOCORICAL CARCINOMA IN A CHILD PRESENTED WITH PERIPHERAL PRECOCIOUS PUBERTY

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Objective: To present a rare case of adrenocortical carcinoma in a child presented with peripheral precocious puberty.

Case Presentation: A 8.5-year-old boy evaluated in our clinic for excessive pubic hair that dated back to one year ago. On examination: he looks well, normal blood pressure, the height 121 cm, weight 30 kg. Tanner stages for pubic hair, penile size and testes were 4, 3, 2 respectively. The rest of his physical examination unremarkable. The laboratory findings: FSH less than 0.10 IU/L (1.4-15.4), LH 0.15 IU/L (1.2-7.8), testosterone 8 nmol/l (0.10-1.04), 17 hydroxyprogesterone 2.1 ng/ml (0.2-3.5), cortisol 346 mMol/L (168-728), Thyroid function tests, renal function tests and serum electrolytes tests were all normal. Medical imaging data: Bone age 11 years, abdominal ultrasonography revealed a well-defined mass at right suprarenal region (49×48) mm., abdominal magnetic resonance revealed a well-defined mass at right suprarenal region measures about (5×5) cm. Dynamic computed tomography of adrenal glands revealed: right adrenal mass (5×4.4) cm well defined associated with perilesional vessels, no invasion to surrounding structures. Brain magnetic resonance imaging was normal. Scrotal ultrasonography revealed both testes slightly enlarged in size with normal echogenesity. Chest X-ray normal.

Discussion: Adrenocortical carcinoma, is an aggressive and rare cancer originating in the cortex of the adrenal gland. Incidence in United State less than 25 new cases of adrenocortical tumours (benign and malignant) are diagnosed annually (0.1-0.4 cases/million/year) and malignant adrenal tumours comprise approximately 1% of all carcinomas diagnosed prior to 20 years of age. Based on the above data, the diagnosis was adrenal androgen-secreting tumour and the patient underwent right open adrenalectomy. Histological study is consistent with adrenocortical carcinoma confirmed by Immunohistochemistry.

Conclusion: To our knowledge, this is the first case report of virilizing adrenocortical carcinoma with unique pathologic findings presented with peripheral precocious puberty in our country in this age group.

Abstract #109

WORK-UP OF BILATERAL ADRENAL NODULES IN A PATIENT WITH CONFIRMED CUSHINGS SYNDROME

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Objective: The incidental finding of bilateral adrenal nodules presents a clinical and surgical dilemma for physicians. Appropriate laboratory testing as well as adrenal venous sampling can document and lateralize autonomous functioning nodule or nodules. We present the work-up of a patient with bilateral adrenal nodules who was proven to have Cushing’s syndrome.

Case Presentation: Our patient is a 55-year-old female who presented after CT scan evaluating her aortic dissection revealed bilateral adrenal nodules; right 2.3 cm and left 3 cm. Her past medical history was significant for hypertension, controlled on 3 medications, and aortic dissection medically managed; family history was unremarkable. Her symptoms included significant weight gain, fatigue, joint aches and easy bruising. Physical exam revealed a short obese female (BMI 35.7) with a buffalo hump, supraclavicular fat pad and skin atrophy. Laboratory workup ruled out pheochromocytoma and hyperaldosteronism but confirmed the presence of Cushing’s syndrome: urine free cortisol was elevated at 53.6 mcg/day, total cortisol 14.4 mcg/dL after 1 mg DST, ACTH < 5 pg/mL and midnight salivary cortisol was elevated at 0.33 and 0.32 mcg/dL (done on 2 separate nights). However, the question remained whether this was a unilateral cortisol-secreting adenoma with a contralateral nonfunctioning cortical adenoma or bilateral cortisol-secreting adenomas. After a long discussion, it was decided to send the patient for adrenal venous sampling. Cortisol measurements were obtained from the right adrenal vein, left adrenal vein and IVC. Adrenal vein (AV) to peripheral vein (PV) cortisol ratios were then used in an attempt to establish whether or not each adrenal gland was hyperfunctioning. Finally, a cortisol ratio between adrenal glands was used in an attempt to lateralize the hyperfunctioning gland. Our patient had a right cortisol AV measurement of 435.8 mcg/dL, a left AV cortisol measurement of 169.8 mcg/dL and a PV (IVC) cortisol value of 15.5 mcg/dL. Epinephrine was used to verify proper catheter placement. AV/PV ratios were 28.1 on the right and 10.9 on the left.

Discussion: Using values proposed by Young, Jr et al (1), both adrenal nodules appear to be hyperfunctioning, but predominantly the right adrenal gland, with a cortisol
Abstract #110

NON-FUNCTIONING METASTATIC PHEOCHROMOCYTOMA

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Objective: Malignant pheochromocytoma occurs in 5-25% of cases; is incurable and 5 year survival rate is less than 50%. Presence of chromaffin cells in lungs, liver, bones and lymph nodes defines metastatic pheochromocytoma. Metastatic disease can present at the time of diagnosis or several years after surgical resection.

Case Presentation: 64 year old Caucasian male with history of well controlled hypertension on losartan and hydrochlorothiazide presented with one episode of abdominal pain after overeating. Family history was significant for bone and stomach cancer. Physical exam was unremarkable. An ultrasound of abdomen showed choledolithiasis and 5 cm right adrenal mass. A CT abdomen showed 5 cm adrenal mass with 37 Hounsfield units and delayed washout. Percutaneous biopsy of the mass was consistent with a neuroendocrine neoplasm. Lab tests done after biopsy showed normal plasma fractionated free metanephrines, normal plasma total catecholamines, normal aldosterone and renin levels. 24 hour urine normetanephrines was slightly elevated at 3753 nmol/day (ref range- 273-3548 nmol/day) and 5-hydroxyindole acetic acid at 31 (0-15 mg/day). 24 hour urine cortisol, aldosterone, homovanillic acid, 17-ketosteroids were normal. The patient was treated with phenoxybenzamine and underwent laparoscopic right adrenalectomy. Perioperative course was uneventful. Pathology showed pheochromocytoma with insular growth pattern, mitotic figures (2-5 per 10 HPF), focal periadrenal and lymphovascular extension. PET scan showed multiple bone metastases in spine, proximal humerus, liver and left lingual tonsil. Post-operative plasma fractionated free metanephrines was normal. Patient is on sunitib now and is doing well.

Discussion: Our patient was an unique case with non-functioning metastatic pheochromocytoma. Large pheochromocytomas are usually functional. A diagnosis of malignant pheochromocytoma was made based on presence of metastases. Indicies of metastatic disease in our patient were large tumor size, presence of lymphovascular invasion and numerous mitotic figures. Presence of paraganglioma and adrenal pheochromocytoma >6 cm is an indication for doing a MIBG scan preoperatively. Surgical debulking in metastatic pheochromocytoma reduces local and systemic catecholamine related symptoms. MIBG radiotherapy can be considered in patients with nonresectable metastatic disease. External radiation therapy is used to treat painful bony mets. Chemotherapy is used in radionuclide resistant metastatic disease. Most commonly used regimen is cyclophosphamide, vincristine and dacarbazine.

Conclusion: The currently available palliative therapy reduces tumor burden and prolongs survival in metastatic pheochromocytoma.

Abstract #111

17-ALPHA-HYDROXYLASE DEFICIENCY ASSOCIATED WITH MULLERIAN AGENESIS

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Case Presentation: A 16 year old female presented with primary amenorrhea and absent secondary sexual characteristics. Initial evaluation was notable for Tanner I breasts, infantile external genitalia and absent axillary and pubic hair. Blood pressure was noted to be elevated at 130/90 mm Hg which is >95th percentile for systolic blood pressure and >99th percentile for diastolic blood pressure for age and height; weight was 107 pounds (48.6 Kg) 24.8th percentile for age and height was 63.5 inches (158.8 cm) 28th percentile for age with BMI 19.3. Limited pelvic exam did not show transvaginal septum or intact hymen. Initial investigations showed normal TSH and prolactin. Further work up revealed hypokalemia, low cortisol, high ACTH, low estradiol with FSH elevated in the post-menopausal range. High progesterone level confirmed the diagnosis of Congenital Adrenal Hyperplasia due to 17-alpha-hydroxylase deficiency (17OHD). Karyotype was 46XX. Interestingly, examination under anesthesia showed the presence of a vagina ending in a blind pouch with no uterus or cervix identified. Diagnostic laparoscopy confirmed absent uterus, but streak ovaries and fallopian tubes were clearly visualized on both sides. Treatment with glucocorticoid and estrogen replacement was begun which subsequently resulted in normalization of blood pressure, resolution of hypokalemia and appropriate advancement of breast development to Tanner stage II.

Discussion: 17OHD is a rare clinical entity accounting for only 1% cases of Congenital Adrenal Hyperplasia.
17OHD results from mutation in the CYP17 gene encoding an enzyme with both 17-hydroxylase and 17,20-lyase activities. The classical presentation is hypertension with hypokalemia and pubertal delay. Genotypic females are sexually infantile and genotypic males have either ambiguous or female external genitalia. Here we present a case of genotypic female with the typical clinical, hormonal and metabolic characteristics of 17OHD and Mullerian agenesis. Mullerian agenesis is suggested in this case by the absence of uterus and cervix despite the presence of ovaries, fallopian tubes and vagina. To the best of our knowledge, 17OHD has not been previously reported in association with Mullerian agenesis.

**Conclusion:** 17OHD is a rare disorder of steroidogenesis that should be considered in patients presenting with hypokalemic hypertension and pubertal failure. Our case of 17OHD with concomitant Mullerian agenesis may be a unique entity. Further studies investigating the possibility of unidentified genetic links between 17OHD and Mullerian agenesis are needed for better understanding of this association and appropriate management.

**Abstract #112**

**ADRENOLEUKODYSTROPHY-A RARE DISEASE PRESENTING WITH ITS FULL BLOWN COMPLICATIONS IN AN EIGHT YEAR OLD CHILD**

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Allama Iqbal Medical College

**Objective:** ADRENOLEUKODYSTROPHY-A rare disease presenting with it’s full blown complications in an eight year old child.

**Case Presentation:** An eight year old male child presented to our endocrine clinic with complaints of mood disturbances, mute behavior, reversal of diurnal sleep rhythm, seizures and deterioration of learning abilities to the point that he had to quit school. All these symptoms started and progressed over the course of last twelve months. On examination in our clinic he was deaf, aphasic, blind with strabismus and had mental slowness as well. His vital signs were normal without any postural drop. On motor exam he had increased muscle tone and spasticity. All labs including thyroid function tests and cortisol levels were normal, though with cortisol he had reversal of his diurnal rhythm. Blood level of VLCFA could not be done because of nonavailability of test in local set up. MRI showed multiple hyper intense lesions in white matter suggesting demyelination characteristic of adrenoleukodystrophy (ALD). He was advised supportive and symptomatic treatment with physical, psychological and special education and dietary modifications.

**Discussion:** Adrenoleukodystrophy is a peroxisomal disorder of beta-oxidation that results in accumulation of very long chain fatty acids (VLCFA) in all tissues. This X-linked disorder is caused by mutations in the ATP-Binding Cassette, Subfamily D, Member 1 gene. Major categories of this disease are 1) Childhood cerebral form 2) Adrenomyelopathy and 3) Addison type. Our patient had childhood cerebral form of ALD. On investigations these patients have increased blood level of VLCFA and MRI Brain shows multiple hyper intense lesions in white matter consistent with demyelination. Treatment options include 1) supportive and symptomatic treatment with physical, psychological and special education 2) Diet low in VLCFA 3) Lorenzo’s oil, a mixture of glyceroltrioleate and glyceroltrierucate and 4) Stem cells transplantation.

**Conclusion:** Treatment for ALD is mainly supportive but family should be screened for carrier state, genetic counseling should be done and female carriers should undergo chorionic villous sampling to rule out ALD in male fetus. Secondly, this case is grim reminder of the fact that ALD should always be kept in mind when dealing with multitude of symptoms as above.

**Abstract #113**

**PHEOCHROMOCYTOMA IN NORMOTENSIVE WOMAN WITH ACUTE CARDIOMYOPATHY**

Roshni Shah, MD, Michelle Cordoba Kissee, MD, David Johnson, MD

University of Arizona

**Objective:** Pheochromocytoma is a rare endocrine neoplasm occurring in less than 0.2 % of those with hypertension. The annual incidence of pheochromocytoma is about 0.8 per 100,000 person-years. Classic symptoms are headache, diaphoresis, and tachycardia with paroxysmal hypertension. Pheochromocytomas may also present atypically as myocardial ischemia, arrhythmia, or congestive heart failure.

**Case Presentation:** A 52-year-old woman with normal blood pressure and two months of palpitations and night sweats presented with chest pain. An echocardiogram done one month previously was normal. Physical exam revealed tachycardia and hypotension. Cardiac catheterization revealed normal coronary arteries but severe systolic dysfunction, suggesting acute myocarditis. An echocardiogram done one month previously was normal. Physical exam revealed tachycardia and hypotension with no stigmata of Cushing’s syndrome.

**Discussion:** The patient’s troponin and D dimer were elevated. Cardiac catheterization revealed normal coronary arteries but severe systolic dysfunction, suggesting acute myocarditis. Echocardiogram confirmed an ejection fraction of 15%. An aortic balloon pump was inserted, and vasopressors were started. CT angiogram of
the chest did not show a pulmonary embolism but rather a 9.7cm right adrenal mass. Pheochromocytoma versus adrenal corticocarcinoma was considered. She developed respiratory, hepatic and renal failure with oliguria and cardiogenic shock, requiring mechanical ventilation and dialysis. CT chest showed no metastatic disease. Partial urine testing revealed elevated 24h levels of VMA, metanephrines and normetanephrines. Echocardiograms showed an improvement in her ejection fraction from 15% to 59% within 15 days. Blood pressure normalized, and phenoxybenzamine was started. She underwent a right open adrenalectomy. Pathology reported a 9cm pheochromocytoma with focal extension into the periadrenal adipose tissue, and malignant features, including extra-adrenal extension, profound nuclear atypia, and vascular invasion. MIBG scan showed increased activity at the site of the right adrenalectomy or in the rest of the body. Post-surgical recovery has been reassuring, with improved blood pressure, hepatic function and renal function. Plasma metanephrine and normetanephrine levels returned to normal after resection.

**Conclusion:** Pheochromocytoma with normal blood pressure is rare (less than 5% of cases). This case is unusual in that it did not feature the symptoms classically associated with this condition but rather as an acute cardiomyopathy which completely resolved prior to adrenalectomy. As a potentially reversible etiology, atypical pheochromocytoma should be considered in patients who present with acute unexplained cardiomyopathy.

Abstract #114

**FAMILIAL PARAGANGLIOMA AND CONGENITAL CYANOTIC HEART DISEASE - CASE REPORT AND REVIEW OF THE LITERATURE.**

Susanne Miedlich, Anthony diSant’Agnese, Jacob Moalem, Stephen Hammes, Runhua Hou

University of Rochester Medical Center

**Objective:** Description of a case and discussion of pitfalls of diagnosis and management.

**Case Presentation:** A 27 year old male with a history of corrected complex cyanotic heart disease (tricuspid atresia, s/p Blalock-Taussig shunt, final correction at age 7) was admitted after experiencing fatigue, nausea/vomiting, decreased appetite, shortness of breath and palpitations. For 6 months, he had also noticed occasional episodes of anxiety, tremors and palpitations lasting for 10-15 minutes. His physical exam revealed a BP of 125/82, HR of 82/min, hypoxia (oxygen saturation 92% on room air) and mild lower extremity edema but no other signs of heart failure. Diagnostic workup included an abdominal CT scan which was suggestive of three enhancing retroperitoneal lymph nodes suspicious for metastases versus lymphoma. A core biopsy of the para-aortic lymph node was consistent with a paraganglioma. Subsequent urine collection showed elevated norepinephrines 311 mcg/g (0-45) and normetanephrines 1908 mcg/mol (0-247). After MIBG scan without evidence of metastases, careful inpatient preparation with alpha and beta blockade and volume expansion he underwent resection of a 7 cm right perirenal and a 3.5 cm aortic bifurcation paraganglioma. Above symptoms completely resolved and postoperative plasma metanephrines returned to normal values. Genetic analysis revealed a germline mutation of succinate dehydrogenase B confirming familial paraganglioma. Family screening is currently under way to identify gene carriers.

**Discussion:** Chronic heart failure can mask symptoms of catecholamine excess and patients can present with normal blood pressure. Recognition and preparation of such patients for surgery can be challenging and requires a multidisciplinary approach. Of note, an autopsy study noted that congenital heart disease was more frequently found in patients with neuroendocrine tumors compared to the general population, suggesting hypoxia as a possible trigger or growth stimulus in the development of these tumors. To our knowledge this is the first report of a familial paraganglioma in the background of congenital heart disease.

**Conclusion:** This case emphasizes the importance of recognizing clinical signs and ruling out paraganglioma before proceeding with a biopsy of any retroperitoneal or mediastinal tumor that is along the path of migration of neural crest cells, since such a procedure can have life-threatening consequences. Furthermore, it is recommended that genetic screening be employed in all patients with paragangliomas, since they are often associated with dominant inheritance patterns and patients need lifelong follow up.
Abstract #115

ADRENAL INCIDENTALOMA - A SINGLE CENTER EXPERIENCE OF 413 CASES

Naykky Singh Ospina, MD, L. Fogelfeld, Evelyn Lacuesta
John Stroger Hospital at Cook County

Objective: The main objectives of this study were to determine the prevalence of adrenal incidentaloma (AI) in a tertiary care center and to assess the clinical evaluation performed.

Methods: The reports of CT scans of the chest and/or abdomen/pelvis performed between 2005-2011 were electronically screened for the keywords: adrenal mass, cyst, nodule, incidentaloma. This initial group of patients were reviewed and included if an adrenal mass was confirmed in a patient with no clinical suspicion of adrenal pathology or previous diagnosis of malignancy.

Results: The selected key words were present in 2933 of the CT scans reports screened. After exclusion of patients with malignancy, suspected adrenal pathology or no lesion a total of 413 cases of AI were identified with a prevalence of 0.63%. The mean size of the incidentalomas was 2.12 +/- 1.34 cm, with only 14 measuring more than 6 cm. A total of 108 patients (26%) underwent biochemical testing at baseline and 18 patients (4.3%) had repeat testing. A total of 99 patients were evaluated for pheochromocytoma with no abnormal results. A total of 69 patients were evaluated for primary hyperaldosteronism with 2 patients having this disorder. Hypercortisolism was evaluated in 64 patients with 2 having confirmed Cushing’s syndrome. Repeat imaging was performed in 33 patients (8%) at 3-6 months after diagnosis, in 25 patients (6%) at 12 months and in 35 patients (8.4%) at 24 months. Adrenalectomy was performed in 10 patients (2.4%) with no cases of Adrenal Carcinoma and metastatic disease found in 2 patients.

Discussion: There is a wide variation in the prevalence of AI ranging from 0.81 to 4.2%. Our prevalence of 0.63% is consistent with the lower values found in retrospective studies of clinical practice in comparison with prospective studies. The rate of adrenalectomy in our study was 2.4% which is lower than other series (6.6%). This can be explained by the fact that only 14 masses measured more than 6 cm and only 4 were functional. The rate of hormonal evaluation was 26% which is similar to previous reports of about 30%. Only 4 cases were found to be functional which is lower than previous reports of 20% of AI being hormonally active. Follow up CT scan was done in 8.4% of the patients at 2 years which is lower than previous reports of about 37%. The main limitation of our study was the incomplete hormonal evaluation and follow up which did not allow us to determine the yield of diagnostic testing.

Conclusion: This study shows that with the widespread use of technology AI has become a common clinical condition and that further efforts are needed to determine the appropriate evaluation and difficulties face by physicians while evaluating AI.

Abstract #116

LOW-DOSE DEXAMETHASONE SUPPRESSION TEST INDUCING A PHEOCHROMOCYTOMA CRISIS

Michael Tsoukas, George Tsoukas, Elliot Mitmaker, George Tsoukas, Liane Feldman, Jacques How
McGill University Health Centre

Case Presentation: A 71-year-old female patient was seen in the endocrinology clinic regarding recent diagnoses of diabetes mellitus and hypertension. The patient appeared healthy, however a detailed history revealed recurrent episodes of facial flushing associated with palpitations, diaphoresis, and headache. The patient had no stigmata of Cushing’s syndrome, but her laboratory investigations were significant for hyperglycemia, with a mildly elevated serum cortisol level of 635 nmol/L and ACTH of 6 pmol/L. 24-hour urine collection for norepinephrine and epinephrine revealed elevated levels at 1845 nmol/d and 9112 nmol/d, respectively. Subsequent abdominal ultrasound revealed a large left adrenal mass measuring 6 x 8 cm. Pheochromocytoma was diagnosed and prazosin was prescribed. However, the large size of the adrenal tumor and equivocal laboratory investigations prompted a 1 mg overnight dexamethasone suppression test (DST) to rule out a mixed corticomedullary adenoma. Sixteen hours following the administration of a single dose of dexamethasone, she developed diffuse abdominal pain with associated nausea and vomiting. Upon presentation to the emergency room, her blood pressure was 240/140 mmHg with a pulse rate of 110 bpm. Initial biochemistry revealed lactic acidosis, paradoxical hypoglycemia, markedly elevated liver enzymes and an elevated troponin. The patient was admitted to ICU and once stabilized, underwent urgent laparoscopic adrenalectomy. Final pathology confirmed the diagnosis of pheochromocytoma without areas of focal necrosis or hemorrhage.

Discussion: Glucocorticoids are widely used in the diagnostic approach to adrenal incidentalomas, with pheochromocytoma accounting for 8% of the cases. Current guidelines state that patients with incidentalomas should undergo biochemical testing for workup of...
hypercortisolism. The use of a 1 mg overnight DST subjects a large number of patients who may harbor an underlying pheochromocytoma to exogenous steroids. Steroids are known to alter catecholamine synthesis, metabolism and secretion via genomic effects. Additionally, steroid effects on vascular activity mediated by nitric oxide and prostacyclins have been described. These mechanisms may therefore offer an explanation to this patient’s sudden hypertensive crisis with hemodynamic instability in the absence of any other identifiable cause.

**Conclusion:** This is the first case documenting the potential danger of a low-dose dexamethasone suppression test to patients suspected of having pheochromocytoma. Physicians must remain cautious when performing even low-dose DST and it would be prudent to perform this test in a monitored environment.

**Abstract #117**

**COMPLETE RESOLUTION OF SEVERELY HYPERPIGMENTED TONGUE UPON TREATMENT OF ADDISON’S DISEASE**

*Bhargavi Patham, MD, Tamis Bright, MD*

Texas Tech University Health Sciences Center

**Case Presentation:** A 75 year old Latin-American male with hypothyroidism was brought to the hospital after an episode of brief loss of consciousness. He reported several episodes of vomiting, generalized weakness, fatigue, and dizziness for one week. His physical examination was notable for dark skin, noticeably darker than his family members. His palms and soles, especially over the creases, were melanotic and his tongue was striking for diffuse, black hyperpigmentation. The patient explained his tongue had been dark for as long as he could remember and had been told it was genetic. He attributed his dark skin to his yard work. Labs were remarkable for a sodium of 120mmol/L, am cortisol 1.1mcg/dL with no rise after Cosyntropin, and an elevated adrenocorticotropic hormone (ACTH) 890pg/mL. The patient was diagnosed with primary adrenal insufficiency and was managed with IV hydration and hydrocortisone. Upon investigation, the patient had received an incorrect prescription 3 weeks prior for levothyroxine 175mcg instead of his usual 75mcg. The patient was discharged with the appropriate levothyroxine, prednisone, and fludrocortisone to follow up in two weeks. The patient did not return to endocrine, but followed with a closer physician. Eight years later in 2012, he was brought to the hospital for severe fatigue, generalized weakness, loss of appetite, left testicular pain, and confusion. His vitals demonstrated severe hypotension. His physical findings were significant for a complete resolution of the hyperpigmentation with his skin tone several shades lighter. Most remarkably, his tongue was pink with no evidence of hyperpigmentation. The patient was diagnosed with an Addisonian crisis, brought on by acute epididymitis. He was managed with fluids, antibiotics, and hydrocortisone.

**Discussion:** We are reporting a rather unique case involving severe hyperpigmentation of the tongue that completely resolved upon successful treatment of Addison’s disease. A distinguishing and unique characteristic of Addison’s disease is hyperpigmentation. It is secondary to excess proopiomelanocortin that is cleaved into its active metabolites; namely ACTH and MSH (melanocyte stimulating hormone). Excess MSH results in hyperpigmentation, most commonly in the palmar creases, along the buccal mucosa, and gingiva. Diffuse hyperpigmentation of the tongue is very rare.

**Conclusion:** Our patient had undiagnosed adrenal insufficiency for years, resulting in hyperpigmentation. He however, had no other symptoms until an excessive dose of levothyroxine unmasked the Addison’s disease. After glucocorticoid replacement, the hyperpigmentation completely resolved.

**Abstract #118**

**CUSHING’S SYNDROME: DIAGNOSED A LITTLE TOO LATE!**

*Prangthip Charoenpong, Soamsiri Niwattisaiwong, Nongnooch Poowanavittayakom, Daphne O’Reilly, Maria Ferrera, Vinita Bhagia*

Advocate Illinois Masonic Medical Center

**Case Presentation:** Sixty-one year old woman who was recently diagnosed with hypertension (HTN) and diabetes (DM-2) 1 year ago presented with 4 weeks of worsening fatigue. The patient had been seeing her doctor regularly before the diagnoses of HTN and DM-2. Over the past 2 months her blood pressure (BP) and blood glucose (BG) had became very difficult to control. She also developed refractory hypokalemia, which did not improve with potassium supplement or holding off diuretics. Physical examination revealed an obese female (BMI 28) with BP of 180/90 mmHg, lower extremity bruising and purple abdominal striae. Laboratory tests showed HbA1C of 13.1%, serum potassium of 2.5 mmol/L, and serum bicarbonate of 31 mmol/L. Plasma renin and aldosterone were low normal [7.4 mU/L (8-35 mU/L) and 5.4 ng/dL (5-30 ng/dL) respectively]. The 24-hour urine free cortisol was elevated at 2895.8 mcg (<45 mcg). ACTH was suppressed to 5 pg/mL (9-52 pg/mL). Abdominal computed tomography showed left 7.1x5.3x7.8 cm...
heterogeneous adrenal mass and numerous intrahepatic lesions. Liver biopsy showed malignant neuroendocrine tissue compatible with adrenocortical carcinoma (AC).

The patient was diagnosed with Cushing’s syndrome (CS) secondary to metastatic cortisol-secreting AC. Mitotane therapy was started, along with 100 units of daily insulin and 6 different antihypertensive medications to control BG and BP. Unfortunately, the patient was admitted for osteoporotic vertebral fracture in a month and expired from hospital acquired pneumonia.

**Discussion:** CS is a clinical syndrome caused by the excess cortisol level and associated with increased morbidity and mortality. Although full-blown CS is clinically unmistakable, the diagnosis can be challenging in early disease. HTN and DM-2 are overlapping conditions found both in CS patients and general population. HTN first diagnosed in age > 55 and hypokalemia are clues for adrenal hyperfunction in our patient. Recent worsening of BG control along with HTN and hypokalemia should rise suspicion for CS. Approximately 10% of CS cases are caused by AC. AC is a rare tumor (incidence rate: 1:106 population/year) with poor prognosis, partly due to often delayed diagnosis. The only curative treatment is surgical resection in selected patients. Mitotane is an option for non-surgical candidate.

**Conclusion:** Several features of CS are common in the general population, such as DM-2 and HTN. It is important to consider CS as a secondary cause of these conditions, especially in patients with unusual presentation for age or with progressive features suggesting CS. If the possibility of CS is not considered, the diagnosis is often too delayed.

**Abstract #119**

**INTRA ARTICULAR STEROID INJECTIONS CAUSING CUSHING’S SYNDROME IN AN HIV PATIENT ON RITONAVIR**

*Divya Yogi-morren, M.D, Georgiana Dobri, M.D, Betul Hatipoglu, M.D*

Cleveland Clinic

**Case Presentation:** A 38 year old female with a history of HIV since 2003 was presented to us in January 2012 with a 9 month history of weight gain, acne, worsening HTN, worsening diabetes and hirsutism. Her HIV antiretroviral regimen included lamivudine, atazanavir and ritonavir and she had been on this regimen since 2007. She was also receiving frequent steroid injections to her ankle form 2007 to June 2011. Physical evaluation revealed acne, moon facies, scattered purpura and ecchymoses on the skin, wide purple striae in her arms and central obesity with a BMI 38.14kg/m2. Urine free cortisol levels were <1 ug/g with adequate collection. Dexamethasone suppression testing revealed cortisol <1 ug/m, ACTH <5 pg/ml with dexamethasone levels >1000. Biochemical testing was consistent with iatrogenic Cushing’s syndrome.

**Discussion:** We report a case of a patient who developed fulminant features of Cushing’s syndrome after intra-articular triamcinolone injections who was also concurrently taking ritonavir. It is a rare occurrence for iatrogenic Cushing’s syndrome to occur in a patient after intra-articular steroid injections. Putatively, significant systemic absorption of steroids from a joint may be facilitated by the rapid transit of blood through the rich arterial anastomosis supplying a joint. Ritonavir augments the activity of other protease inhibitors by prolonging their half life by inhibiting the P450 CYP (3A4). The literature suggests that ritonavir inhibits the metabolism of inhaled steroids and can cause iatrogenic Cushing’s syndrome. Recently there have been a few emerging reports of ritonavir also prolonging the duration of injected steroids such as tramecinolone.

**Conclusion:** Clinicians need to be alert to the increased susceptibility of iatrogenic Cushing’s syndrome in patients taking ritonavir when these patients are considered for intra-articular corticosteroid injections. In these vulnerable patients, other treatment options should be considered.

**Abstract #120**

**METASTATIC ADRENOCORTICAL CARCINOMA PRESENTING WITH CUSHING’S SYNDROME**

*DeAnna Henderson, MD, Edward Kilb, Andrew Goodwin*

Medical University of South Carolina

**Objective:** Adrenocortical carcinoma (ACC) is a rare cancer that is often metastatic on presentation, with liver and lung being the organs most commonly affected. It can present with Cushing’s syndrome, virilization, feminization, Conn’s syndrome, or pheochromocytoma traits.

**Case Presentation:** A 53 yo vagrant AAM with a PMH of polysubstance abuse, who presented with fever, chills, and hemoptysis. He reported feeling sick for 1 month with weight loss, blood streaked sputum, ABD pain, and constipation. He was in jail for 5 months, recently discharged. A PPD was done in jail, and was negative. Physical exam was notable for tachycardia, hypertension, thrush, decreased breath sounds, hepatomegaly, and BLE pitting edema. Lab values revealed a potassium of 1.9, chronic metabolic alkalosis, and an elevated B-D glucan. CT scans of the C/ABD/P were done and revealed cavitary lesions with air fluid levels in the lungs, lesions in the spleen and liver, pelvic ascites, bilateral pleural...
effusions, and an 11.2 cm heterogeneous left adrenal mass. Cortisol was 30.4, DHEA was 534, and ACTH was 8.1. Biopsy of the left adrenal mass and a liver lesion were performed and his hospitalization was complicated by malignant HTN and flash pulmonary edema leading to acute respiratory failure and intubation. Pathology of the adrenal mass and liver lesions revealed metastatic adrenocortical carcinoma. HTN was controlled. He was extubated, and discharged with plans to follow up with oncology. He returned two days later with a BP of 240/109 and respiratory failure again requiring intubation. With diuresis, he was again extubated. Twenty four hour urine metanephrines were WNL. The aldosterone/renin ratio was 23 with an aldosterone of 4.7 while the patient was on an ace inhibitor. He admitted to medication non-compliance and EtOH abuse for 1 day post discharge. A dexamethasone suppression test was revealed a cortisol of 29.4 and the patient was diagnosed with Cushing’s syndrome due to metastatic adrenocortical carcinoma. 

Discussion: Prognosis of metastatic ACC is poor. In early stage, disease surgery is an option, but yields an overall survival rate of only 30%. In advanced disease, chemotherapy, palliative radiation, or hospice are appropriate options. Mitotane is a steroid inhibitor and can be used with regimens including doxorubicin, cisplatin or streptozocin.

Conclusion: Oncology and endocrine were consulted. Treatment options were discussed including chemotherapy and palliative radiation, but ultimately hospice was suggested given his poor functional status and nutrition. His BP and HR were controlled with 6 medications. One week later, he presented via EMS and was found in asystolic cardiac arrest in the ED, from which he passed.

Abstract #121

LOW BACK PAIN AS THE FIRST MANIFESTATION OF MALIGNANT PHEOCHROMOCYTOMA

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Univesity of Puerto Rico

Objective: To report the case of a woman with neurofibromatosis type I (NF1) and metastatic malignant pheochromocytoma who presented with chronic low back pain as the first clinical manifestation.

Case Presentation: 37 y/o woman with NF1 and arterial hypertension (HTN), diagnosed during pregnancy, controlled with atenolol 50mg daily. Patient presented with progressive left lower back pain for the past two years, associated with bilateral leg paraesthesias and weight loss. She was admitted to our institution due to incapacitating lower back pain; appearing chronically ill, cachectic, with multiple skin neurofibromas. Vital signs were stable and laboratories unremarkable except for K+ 2.9, WBC 15.2 and a urinary tract infection. Abdominopelvic CT scan revealed a sacral soft tissue mass and a large (7.4x5.5x6.7cm) left suprarenal mass, uncertain if lesion was of renal origin or replacing adrenal gland. Metastatic renal cell carcinoma was highly suspected. FNA biopsy of soft tissue mass was done, revealing a neuroendocrine tumor. No abdominal pain, flushing, diarrhea, headaches, palpitations, skin pallor or episodes of uncontrolled HTN reported. Urine collection (24 hours) with 5-HIAA 8.3mg/24hrs (0.0-14.9), epinephrine 106ug/24hrs (0-20), norepinephrine 237ug/24hrs (0-135), dopamine 329ug/24hrs (0-510), normetanephrine 5311ug/24hrs (82-500), metanephrine 2261ug/24hrs (45-290), vanillylmandelic acid 35.5mg/24hrs (0-7.5). Plasma free metanephrines 1516pg/ml (<57), free normetanephrine 6008pg/ml (<148) and chromogranina A 2200ng/ml (1.9-15.0). Octreoscan with multiple metastatic lesions in lumbar spine, sacrum and sacroiliac joints. She was diagnosed with malignant pheochromocytoma with extensive bone metastasis, and was referred to surgery and nuclear medicine services.

Discussion: Pheochromocytomas may occur as part of genetic syndromes, but less frequently in NF1 (0.5-5.7%). Only 10% of these tumors are malignant. Diagnosis is made with 24 hour urine collection for fractioned metanephrines and catecholamines or plasma metanephrines. Malignant pheochromocytoma is diagnosed with local invasion or distant metastases. This patient never presented with hyperadrenergic spells or resistant HTN, a familial syndrome was the only risk factor. Pheochromocytoma was never suspected. Biochemical screening could have identified tumor earlier and surgical resection could have been curative.

Conclusion: Malignant pheochromocytomas are rare, with poor prognosis and limited therapeutic options. The usual clinical sings may be absent. Familial syndromes predisposing to pheochromocytoma may be enough to screen for the disease. This approach could aid in early diagnosis and surgical resection of a malignant tumor.
Abstract #122

**OPIATE ENDOCRINOPATHY: FOOD FOR THOUGHT**

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SUNY- Upstate Medical University Hospital

**Objective**: Methadone related endocrine dysfunction was recognized in the 1980s. Sexual dysfunction has long been known in heroin addicts. Opiate endocrinopathy continues to be the least diagnosed consequence of chronic narcotic therapy. These effects have been attributed to μ-receptor agonism in the hypothalamus and considered a class effect for these agents. Side effects of long term opioid therapy include decreased libido, decreased muscle mass, erectile dysfunction, anemia, depression, fatigue, menstrual irregularities, osteoporosis. These stem from sex hormone deficiency and adrenal suppression secondary to Hypothalamic-Pituitary-Adrenal Axis (HPA) and Hypothalamic-Pituitary-Gonadal-Axis (HPG) suppression. Low testosterone levels have been reported in men on chronic narcotic therapy. In women alteration of the pulsatile luteinizing hormone secretion causes menstrual problems. Decreased stress cortisol response has also been shown in animal experiments. Single dose of morphine can abruptly blunt cortisol secretion. Intrathecal opioids have shown to cause hypogonadotrophic hypogonadism. It should be considered in patients receiving opiates equivalent of 100mg of morphine. Δ and κ receptors seem to be involved in ACTH control while gonadotropin secretion seems to be modulated by ε receptors.

**Case Presentation**: 44 year old female presented with syncopal events and was found to be orthostatic in the absence of a history of dehydration. A low cortisol level was discovered at 1.9 mcg/dL. Low dose ACTH stimulation test resulted in an increase to 13.6 mcg/dL suggesting adrenal insufficiency. She was started on hydrocortisone. Labs showed a low ACTH level at <5 pg/ml, normal prolactin at 4.1 ng/ml, high FSH at 22.8 mU/ml and estradiol at 25.8 pg/ml. She was found to have oxycodone in her possession and admitted to long term abuse. Incidentally she had been evaluated 2 years ago for hyperadrenalism and suspected Cushing’s syndrome when her cortisol level was noted to be 19.5 mcg/dL. Did she over treat herself with narcotics to now result in adrenal insufficiency?

**Discussion**: Diagnosis begins with knowledge and vigilance for symptoms and signs. In men with hypogonadism, testosterone levels should be obtained. In women, Dihydroepiandrosterone sulphate (DHEAS) may prove to be a good marker of adrenal activity. Low cortisol levels with an inappropriate rise with ACTH stimulation test may also be seen suggesting adrenal insufficiency.

Testosterone remains the mainstay of therapy in men with hypogonadism. Adrenal insufficiency requires hormone supplementation. Opioid rotation with different agents may prove helpful too.

Abstract #123

**COMBINED ADRENOCORTICAL AND ADRENOMEDULLARY DYSFUNCTION CAUSED BY BILATERAL ADRENAL METASTASIS OF A NON-ENDOCRINE CANCER**

Matthew Butler, Mikhail Signalov

Geisinger Medical Center

**Objective**: To present the case of a patient with adrenocortical insufficiency and elevated normetanephrine associated with metastatic squamous cell carcinoma involving the adrenal glands.

**Case Presentation**: A 70 year old male presented with new-onset of right flank pain, progressive weakness, lightheadedness, and weight loss over a 3-month period. Physical examination was remarkable for a right lateral neck mass. Laboratory evaluation revealed presence of hypoglycemia, hyperkalemia, mild hyponatremia, and acute kidney injury. CT demonstrated a 7.1 cm peripherally enhancing right adrenal mass, as well as a 4.5 cm mass-like thickening of the left adrenal gland. Serum aldosterone was low at 2 ng/dL (3-16), 24 hour urine free cortisol was 6.2 ug/dL (4-50), and a 250 mcg cosyntropin stimulation test demonstrated inadequate response with serum cortisol increased from 6.8 to 7.1 ug/dL. Urine normetanephrine was 1552 ug/24 hours (100-425). MIBG scintigraphy did not show any abnormal uptake in the adrenal glands. The patient was started on an alpha blocker and hydrocortisone. Biopsies of the right neck and right adrenal masses revealed invasive squamous cell carcinoma. Extensive imaging studies were performed, but no primary tumor was discovered. Chemotherapy was started for metastatic squamous cell carcinoma but patient died of sepsis approximately four months after his initial presentation. No autopsy was performed.

**Discussion**: Adrenocortical insufficiency is an uncommon but well-described complication of metastatic cancer involving both adrenal glands. However, biochemically significant elevation of normetanephrine associated with adrenal metastases appears to be rare. Based on one study of 33 patients with history of cancer and an isolated adrenal mass, the incidence of pheochromocytoma was 24%. While occult pheochromocytoma cannot be completely ruled out without an autopsy, the non-localizing MIBG scan does not support the initially suspected diagnosis of pheochromocytoma. The catecholamine elevation in this
case suggests that metastatic cancer exerted some local stimulatory effect on one or both adrenal medullae. There are several proposed mechanisms by which metastatic cancer could affect adrenal function: direct glandular destruction, external compression, venous or arterial compression or thrombosis, and local inflammatory effect.

Conclusion: When non-endocrine cancer metastasizes to the adrenal glands, multiple derangements of adrenal function may result. Adrenocortical insufficiency is seen most commonly, but adrenomedullary hyperfunction mimicking pheochromocytoma is also possible.

Abstract #124

NOVEL MINIMALLY INVASIVE TECHNIQUES FOR ADRENALECTOMY: A SINGLE INSTITUTION EXPERIENCE AND COMPARISON OF OUTCOMES

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Scott and White Memorial Hospital

Objective: Since the early 1990s, the most commonly performed minimally invasive technique for adrenalectomy in the United States has been a transperitoneal laparoscopic adrenalectomy (TLA). Posterior retroperitoneoscopic adrenalectomy (PRA) is a newer minimally invasive procedure for the removal of small, functioning adrenal neoplasms that is gaining increasing acceptance and preference in this country. Our group was the first to report the development of robot-assisted posterior retroperitoneoscopic adrenalectomy (RAPRA) in 2010. We evaluated our recent experience with different minimally invasive techniques for adrenalectomy, and compared outcomes for operative time, blood loss, hospital stay and safety.

Methods: Between January 2005 and October 2012, a total of 133 adrenalectomies were performed by our endocrine surgery group, at Scott & White Memorial Hospital. A retrospective chart review was undertaken to evaluate all adrenalectomies; the results were compared between the various minimally invasive techniques, as well as the standard open adrenalectomy (OA).

Results: The mean age at operation was 55.8 years (range 16-82). There were 62 men and 71 women. The mean tumor size was 3.2 cm (excluding open metastases). The resected adrenal neoplasms included 34 benign non-functional adrenocortical adenomas, 29 pheochromocytomas, 27 aldosteronomas, 9 cortisol-producing adenomas, 23 metastases, and 2 adrenocortical cancers (ACCs); additionally there were 3 myelolipomas, 3 adrenal cysts, 1 perineuroma, 1 ganglioma, and 1 hemangioma. Mean operating time was 211 min for PRA (range 135-404 min; SD 63.78), 214 min for TLA (range 120-405 min; SD 79.76), and 254 min for RAPRA (range 193-345 min; SD 59.96). Estimated blood loss was 93 ml for PRA (SD 151.53), 149 ml for TLA (SD 247), and 48 ml for RAPRA (SD 25.26). The mean postoperative hospital stay was comparable at 1.5 days for TLA, 1.2 days for PRA, and 1.3 days for RAPRA. Postoperative complications were minor and similar with both operative approaches.

Discussion: Analysis of our early experience reveals no significant differences in mean operating time or estimated blood loss for PRA, TLA, or RAPRA. Each technique has comparable complication rates and hospital stay. Novel minimally invasive approaches, including the posterior approach and robot-assisted techniques, are associated with many potential advantages for patients with bilateral adrenal tumors or previous abdominal operations.

Conclusion: Minimally invasive approaches are safe and effective for the operative removal of small, benign functional adrenal tumors. The posterior approach has become our preferred operation for the removal of adrenal neoplasms.

Abstract #125

COMPLICATIONS OF AN UNDIAGNOSED PHEOCHROMOCYTOMA

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Case Presentation: A 46-year-old male presented with newly diagnosed hypertension, abdominal pain, obstipation, and a new holosystolic murmur consistent with acute mitral regurgitation. A CT scan of the abdomen revealed dilatation of his right colon and a 5.2-cm hypervascular left adrenal mass. Because of suspected peritonitis, the patient underwent an emergent right hemicolecotomy. The operation was complicated by an intraoperative hypertensive crisis, hypoxic respiratory failure, and renal failure. Subsequent imaging and laboratory studies confirmed the diagnosis of a pheochromocytoma. After stabilization and pharmacologic adrenergic blockade, the patient underwent open adrenalectomy and intestinal diversion for treatment of a leaking ileocolonic anastomosis. The patient later underwent elective mitral valve repair.

Discussion: The manifestations of pheochromocytoma are broad and can often be puzzling. In addition to the classic presentation of hypertension, tachycardia, and headache, patients can present with heart failure, myocardial
infarction, and arrhythmias. Non-cardiovascular symptoms such as constipation, colitis, or gastrointestinal bleeding can also be the presenting complaint.

**Conclusion:** Although pheochromocytoma is rare, clinicians should have a high index of suspicion due to the potential for poor outcome if it remains undiagnosed. Patients with hypertension and an adrenal mass should undergo a prompt workup for a functional adrenal tumor and, when indicated, treat with pharmacologic adrenergic blockade to prevent subsequent complications.

**Abstract #126**

**SUPPRESSION OF CORTISOL LEVEL BY OPHTHALMIC GLUCOCORTICOID IN A PATIENT WITH A PITUITARY MASS**

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**Objective:** The potential for suppression of the hypothalamic-pituitary-adrenal (H-P-A) axis with use of corticosteroids via inhalation, intra-articular injection or application to the skin is extensively documented in the literature. The objective of this case presentation is to focus on the potential systemic effects of ophthalmic corticosteroids, which has received less attention.

**Case Presentation:** A 65 yr old white female was incidentally found to have a pituitary macroadenoma on MRI of the brain dedicated to the internal auditory canal. At that time, her physician had obtained the following laboratory studies: 8 A.M. cortisol level of 1.4 ug/dL, TSH of 1.6 uIU/mL, FT4 of 1.2 ng/dL, prolactin of 14.3 ng/mL (normal range 1.8 - 20 ng/mL), LH of 34 mIU/mL, FSH of 84 mIU/mL, IGF-1 of 122 ng/mL (normal range 75-263 ng/mL). No further diagnostic test or therapeutic interventions were pursued.

Eight months later, she presented to our Endocrinology clinic for advice on the management of the pituitary mass. Her past medical history was significant for hypertension and her only current medications were atenolol 50 mg/day and chlorthalidone 25 mg/day. She was asymptomatic and her blood pressure was 126/86 mmHg. Repeat laboratory studies showed a morning cortisol of 16.4 ug/dL, TSH of 2.4 uIU/mL, FT4 of 1.0 ng/dL, prolactin of 19 ng/mL, LH of 56 uIU/mL, FSH of 88 mIU/mL, IGF-1 of 109 ng/mL. No further diagnostic test or therapeutic interventions were pursued.

Discussion: The ability of ocular glucocorticoids to suppress the H-P-A axis is not as clearly demonstrated as the systemic effects of inhaled, cutaneous or intra-articular steroids. In fact, a recent study by Sandhu et al. of 20 patients who had been using steroid-based eye drops continuously for more than 6 months showed a normal response to a low dose ACTH stimulation test in 19 of the 20 patients. However, a small number of case reports in the literature have described development of cushingoid features caused by ocular steroids.

**Conclusion:** In our patient, we hypothesize that the suppression of cortisol levels with the use of prednisolone ophthalmic solution for one month resulted in secondary adrenal insufficiency. We suggest caution should be used in the work-up and management of patients in similar circumstances. Larger, placebo-controlled studies are needed for a better understanding of the systemic effects of these frequently used drugs.

**Abstract #127**

**CASE REPORT: IMPROVEMENT OF DIABETES AFTER SURGICAL CURE OF PHEOCHROMOCYTOMA**

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University of Kansas

**Objective:** Pheochromocytoma is known to cause secondary diabetes or worsen existing diabetes. Few case reports have shown resolution or significant improvement of diabetes after surgical cure of pheochromocytoma. In this case report we describe a 40 y/o F with a diagnosis of T2DM who was found to have Pheochromocytoma, and surgical cure of pheochromocytoma resulted in drastic improvement in glycemic control.

**Case Presentation:** 43 y/o F with PMH of T2DM, HTN presented to ER with right flank pain of one day duration, CT abdomen on admission showed 4.3 cm x 3.4 cm right adrenal mass. She reported history of episodic palpitations, anxiety, headache, sweating of 3-4 years duration. Lab work up showed significantly elevated plasma fractionated metanephrine (14 nmol/L, reference range <0.50) and mildly elevated normetanephrine (2.8 nmol/L, reference range <0.90). Pre-operatively she was prepared with phenoxybenzamine and later atenolol, and subsequently underwent successful resection of the adrenal mass. She was on multi-dose insulin (25 units levemir at night, and 12 units aspart TID with meals) prior to adrenalectomy, and when she was seen on follow up visit in the endocrinology clinic two weeks after surgery initial diagnostic work-up.

**Discussion:** The ability of ocular glucocorticoids to suppress the H-P-A axis is not as clearly demonstrated as the systemic effects of inhaled, cutaneous or intra-articular steroids. In fact, a recent study by Sandhu et al. of 20 patients who had been using steroid-based eye drops continuously for more than 6 months showed a normal response to a low dose ACTH stimulation test in 19 of the 20 patients. However, a small number of case reports in the literature have described development of cushingoid features caused by ocular steroids.

**Conclusion:** In our patient, we hypothesize that the suppression of cortisol levels with the use of prednisolone ophthalmic solution for one month resulted in secondary adrenal insufficiency. We suggest caution should be used in the work-up and management of patients in similar circumstances. Larger, placebo-controlled studies are needed for a better understanding of the systemic effects of these frequently used drugs.
she had significantly improved glycemic control and insulin requirements went down drastically. She was only requiring 8 units of levetram daily to achieve excellent glycemic control.

**Discussion:** Pheochromocytoma is a catecholamine-secreting tumor arising from chromaffin cells of the adrenal medulla. Pheochromocytoma can cause secondary diabetes or worsen preexisting diabetes. In one study of 1071 patients (191 patients with pheochromocytoma and a random sample of 880 patients with essential hypertension), diabetes was present in 35.6% of patients with pheochromocytoma and 21.8% of patients with essential hypertension (P < 0.001), while pheochromocytoma patients with or without diabetes did not differ in body mass index. For patients younger than the age of 51 years with a BMI < 25 kg/m2, the odds ratio for pheochromocytoma in hypertensive patients with diabetes was 18.9 (95% confidence interval, 5.9-58.8). Excess catecholamines results in alpha 2 receptor mediated decrease in insulin secretion and beta receptor mediated insulin resistance, which can result in diabetes.

**Conclusion:** Diagnosis of diabetes in a relatively young, non-obese, hypertensive patient is an important clue towards possibility of pheochromocytoma and warrants biochemical assessment for presence of pheochromocytoma. Surgical cure of pheochromocytoma can lead to complete resolution or significant improvement of the associated secondary diabetes.
DIABETES MELLITUS/ PREDIABETES

Abstract #200

EFFECTIVENESS OF AN INSULIN INITIATION PROTOCOL FOR TYPE 2 DIABETES MELLITUS

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Objective: To assess the effectiveness of an insulin initiation protocol in insulin naïve subjects with type 2 diabetes mellitus (T2DM).

Methods: A retrospective review of insulin naïve adults with T2DM for ≥3 months, HbA1c >8% and BMI≥30kg/m2 referred to the Diabetes Center at an academic acute care facility for teaching on insulin therapy, dose titration and counseling were included in the study. Subjects were classified as Treatment Group (TG) versus Standard Group (SG) based on the number of encounters with certified diabetes educator (CDE), nurse practitioner (NP) and physician (MD). Data points measured at 0, 3 and 6 months included A1c, body weight, number of encounters (CDE, NP, MD), hypoglycemic events, blood pressure, estimated GFR, and lipid profile. Patients without known history of diabetes, current use of corticosteroids, liver disease, serum creatinine ≥3.0 mg/dl and pregnancy were excluded.

Results: A total of 784 subjects were identified; of 384 patients, 51 met criteria for the TG and 41 of 400 qualified for the SG. In the TG, HbA1c at 3 months dropped by 1.7% (p<0.001), and by 2% at 6 months (p<0.001). In the SG, HbA1c at 3 and 6 months dropped by 0.14% (p=0.23) and 0.17% respectively (p=0.23). No significant changes in body weight, hypoglycemic episodes, lipid panel or systolic blood pressure were noted in either group. Hypoglycemic events were 5 in TG and 7 in SG. Diastolic blood pressure (BP) in the IG showed a mean drop at 3 months by 4 mmHg (p=0.03) and the SG showed a mean drop of Systolic BP by 5 mmHg (p=0.48) at 3 months.

Discussion: Pharmacological management of T2DM typically begins with lifestyle modification and oral agents, to achieve and maintain A1C levels of 6.5%-7%. However, long-term, the majority of patients require insulin therapy. Our study shows that intensifying patient education by increasing clinical encounters improves glycemic control as compared to the standard treatment. These results suggest that standardizing early intense insulin initiation protocols could optimize HbA1c, prevent short-term complications, minimize chronic hyperglycemia, weight gain, and ultimately reduce long-term morbidity and mortality.

Conclusion: These results suggest that standardizing early intense insulin initiation protocols could optimize HbA1c, prevent short-term complications, minimize chronic hyperglycemia, weight gain, and ultimately reduce long-term morbidity and mortality.

Abstract #201

IMPACT OF NURSE-LED DIABETES MEDICATION MANAGEMENT CLINIC ON GLYCEMIC CONTROL

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Objective: To determine the effect of a nurse-led Diabetes Medication Management Clinic (DMMC) on glycemic control in diabetic patients.

Methods: This longitudinal retrospective cohort study was conducted at a community outpatient clinic. The study period was from 10/2010 to 9/2011 for one year. Non-pregnant adult diabetic patients who attended DMMC at least twice were included. HbA1C, fasting and all home blood glucose (HBG) levels at baseline and at their last visit were recorded.

Results: A total of 133 patients were identified. 40 patients had only 1 DMMC visit and 9 had incomplete data and therefore they were excluded. 84 patients with at least 2 DMMC visits were included in the study. Mean A1c level decreased from 10.6% to 8.9% (P<0.0001), mean fasting HBG results decreased from 196 to 146 mg/dL (P < 0.0001) and mean all HBG results decreased from 203 to 171 mg/dL (P = 0.0084). There was a positive correlation between age and change in the baseline HbA1c (r= +0.337, P=0.0091) whereas there was a negative correlation between baseline A1c and change in A1c (r = -0.646, P<0.0001).

Discussion: The DMMC was set up in a community outpatient clinic historically associated with lengthy delays in obtaining physician appointments, as a resource to provide timely and improved diabetic care for those with poorly-controlled diabetes mellitus. Traditionally, Certified
Diabetic Nurse Educators (CDEs) provide DSMT only. In DMMC, CDEs initiate and adjust the insulin dose under supervision of the internists over a maximum period of 3 months. DSMT provided by CDEs has been shown to improve the glycemic control in several studies. However, the impact of a nurse-led medication clinic on glycemic control was previously unknown. Our study demonstrated that a nurse-led DMMC may be an effective resource to help improve glycemic control at least in short term.

**Conclusion:** Nurse-led medication management clinic significantly improved short-term glycemic control. Younger patients and those with higher baseline HbA1c were associated with the higher reduction in HbA1c. The reduction of HbA1c was 2.5 times higher in the patients who received simultaneous DSMT than those who did not. All patients in medication management clinic should therefore undergo simultaneous DSMT to get the maximum benefit of the clinic.

**Abstract #202**

**COMPARATIVE EFFECTIVENESS OF ORAL DIABETES MEDICATIONS WHEN ADDED TO METFORMIN: AN OBSERVATIONAL STUDY**

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**Objective:** Physicians commonly must choose a second-line drug to add to metformin in diabetics who are not controlled on metformin alone. Evidence to guide this choice is lacking and professional guidelines are inconsistent. We sought to inform this clinical decision by using a large observational dataset to compare the effects of sulfonlyureas (SU’s), thiazolidinediones (TZD’s), and dipeptidyl peptidase 4 inhibitors (DPP-4’s) when added to metformin.

**Methods:** A longitudinal retrospective cohort study was done in the Health Information Network (THIN) database, with exposure to diabetes medications as the exposure of interest and change in glycosylated hemoglobin(HbA1c) from baseline as the outcome of interest. Patients were eligible for inclusion if they were on metformin monotherapy for at least 6 months, with serial HbA1c’s measured during that time. Cohort entry was then defined as the point where a second agent was added to metformin, as long as the second drug was a SU (glibenclamide, gliclazide, glimepiride, or glipizide), TZD (rosiglitazone or pioglitazone), or DPP-4 inhibitor (sitagliptin or vildagliptin). Patients were followed until metformin or the second drug were stopped, or another drug was added. Change in HbA1c was entered in a multivariable model which included the drug used, along with all covariates and interaction terms between all drugs and all covariates.

**Results:** During the first 6 months of followup, SU’s were associated with the greatest adjusted improvement, about 1.2%. The TZD’s and DPP-4 inhibitors were associated with statistically significantly smaller improvements of 0.86-1.09%. TZD’s were statistically significantly more effective at higher BMIs and in women, while SU’s were less effective in these groups. Over long-term followup, the effectiveness of SU’s diminished while DPP-4 inhibitors and TZD’s had a more stable response; at one year the advantage of SU was largely eliminated, particularly in women and in obese patients.

**Discussion:** In these observational data, the comparative duration of effectiveness of SU versus TZD versus DPP-4 inhibitor added to metformin varies. SU performance is relatively poor over the long term, especially in obese patients and in women.

**Conclusion:** SU may not be the best choice for routine add-on therapy to metformin in obese patients and women. In those patients, a DPP-4 inhibitor may be the optimal choice of second-line therapy. TZDs should also be considered in obese and female patients where injectable medications cannot be used and the goal is a durable significant reduction in HbA1c.

**Abstract #203**

**MANAGING POSTURAL HYPOTENSION IN DIABETIC AUTONOMIC DYSFUNCTION WHEN ADRENERGIC DRUGS ARE CONTRAINDICATED**

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Allama Iqbal Medical College

**Objective:** To report the use of alternate treatment option in patient with severe postural hypotension secondary to diabetes-related autonomic neuropathy when adrenergic drugs are contraindicated. **Case Presentation:** 48 year old male with history of Type 2 Diabetes for 20 years with relatively poor control. Patient had gastroparesis, retinopathy, nephropathy, neuropathy and CAD. Presenting complaints were dizziness for 2 months with progressive inability to stand without support. On examination his lying BP was 150/90 with significant postural drop measuring up to 80/60 after two minutes of standing. Neuropathic features of symmetrical distal sensory neuropathy with absent sense of vibration were noted. Fundoscopy revealed scattered hard exudates, dot and dot blot haemorrhages. ECG findings suggestive of dysautonomia were: abnormal heart rate response to deep breathing was 1.0(normal-E:I ratio ≥1.17), abnormal valsalva ratio was 1.03 (normal-longest to shortest R-R
ratio >1.2), abnormal 30:15 R-R ratio was 0.99 (30th to 15th R-R ratio on standing > 1.03). These three tests along with significant postural drop were suggestive of marked cardiac dysautonomia in this patient. Lab data showed complete blood count, serum electrolytes, renal function tests, liver function tests, serum cortisol, ATCH and thyroid function tests to be within normal limits. Midodrine in this patient could not be used because of history of significant CAD. Patient did not have any response to fludrocortisones. So as a final resort he was started on low dose atenolol. Patient had dramatic clinical improvement with this therapy. Orthostatic BP changes improved and he was able to ambulate without significant difficulty.

Discussion: Diabetic autonomic neuropathy can be quite challenging and difficult to treat. Although medications cannot cure dysautonomic neuropathy, they can help with symptoms. Even though adrenergic drugs like midodrine are the first line choice in patients with orthostatic hypotension from diabetic autonomic neuropathy but in select patients where those are contraindicated other options can be used. Nonselective Beta-blockers, particularly those with intrinsic sympathomimetic activity, have been used in several trials in the treatment of orthostatic hypotension with variable results. The suggested mechanism of action of these agents is the blockade of beta-2 receptors allowing unopposed adrenoreceptor mediated vasoconstriction. Moreover, Beta-blockers can help regulate heart rate and rhythm.

Conclusion: Beta Blockers may be considered in the treatment of postural hypotension due to diabetic autonomic dysfunction in situations where adrenergic drugs are contraindicated.

Abstract #204

ILEAL INTERPOSITION WITH DIVERTED SLEEVE GASTRECTOMY FOR TREATMENT OF TYPE 2 DIABETES

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Objective: To prospectively evaluate the results of laparoscopic ileal interposition (II) with diverted sleeve gastrectomy (DSG) for control of type 2 diabetes mellitus (T2DM) and related metabolic abnormalities.

Methods: All patients underwent II + DSG. They had T2DM ≥ 5 years with poor glycemic control despite adequate dosage of oral hypoglycemic agents (OHAs)+insulin. The primary outcome was remission of diabetes (HbA1C <6.5% without OHAs/insulin). Secondary outcomes were reduction in antidiabetic agent requirement and components of metabolic syndrome.

Results: We report the postoperative follow-up data of 13.1 ± 5.3 months (range: 3-26 months). There were 32 patients (Male: female= 21:11) with mean age of 48.7± 7.8 (range, 34-66 years), duration of diabetes of 13.1 ± 5.8 years (range, 5-30 years) and preoperative body mass index of 29.1 ± 6.9 kg/ m2(range: 22.4-39.5 kg/m2). They had poorly controlled diabetes with mean FBS: 236.52 ± 88.4 mg/dl, PLBS: 305.1 ± 124.3 mg/dl and HbA1C: 9.8 ± 1.8%. Sixteen patients (50%) had hypertension, while dyslipidemia and microalbuminuria was present in 12 patients (39%) each. The mean operative time was 387.7± 84.3 minutes and the mean postoperative hospital stay was 8.8±5.4 days. Intraoperative complications were noted in 4 patients (12.5%). Nausea and loss of appetite was observed in 3 patients (10%), which improved over a period of 2 weeks. At 3 months postoperative follow up, none of these patients had any complications with regards to the intraoperative and immediate postoperative events. Twenty two patients (70.5%) had diabetes remission. Fifteen/ sixteen (93%) patients had remission in hypertension. All participants had weight loss ranging between 15% and 25%. Postoperatively statistically significant decline was observed in the glycemic and lipid parameters, microalbuminuria at all intervals (p< 0.05). Patients with duration of follow up more than 6 months demonstrated to have better improvement in terms of reduction in glycemic, lipid parameters and microalbuminuria. Three patients had vitamin B12 deficiency 1 year after surgery.

Discussion: The surgery addresses the foregut and hindgut mechanisms for DM control. The DSG component restricts calorie intake and induces ghrelin (orexin) loss. It also excludes the duodenal loop, thereby negating the effect of insulin resistance promoting Rubino’s factor. II leads to earlier and rapid stimulation of interposed ileal segment by ingested food resulting in augmented GLP-1 secretion. Accompanying improvement in hypertension, lipid profile and microalbuminuria justify its metabolic beneficial effects.

Conclusion: II+DSG seem to be promising procedures for control of type 2 DM and associated metabolic abnormalities.
Abstract #205

PELVIC PAIN IN A TYPE 2 DIABETES PATIENT

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Objective: To present a type 2 diabetes patient complaining of chronic pelvic pain due to bilateral vas calcification.

Methods: Clinical, laboratory and radiographic data are reported on a 62 year old diabetic presenting with chronic pelvic pain.

Case Presentation: A 62 year old man, a known diabetic for 17 years presented with chronic dull aching, non radiating pain in the pelvis and sacal sulcus below 5th lumbar vertebra. There was no history of fever with chills and sweats, dysuria, urgency, frequency of urination. Pain was not aggravated during intercourse. There was no past history of sexually transmitted disease, frequent and extramarital sexual encounters, chronic kidney disease. Complete blood picture and routine urine examination did not reveal any evidence of infection or proteinuria. Fasting and post prandial blood sugars were 104 mg/dl and 136 mg/dl with Hba1C at 6.7%. Other blood parameters including lipid profile, renal and liver function tests, serum calcium, phosphorous were all within normal limits. X Ray showing anteroposterior view of pelvis revealed bilateral serpentine structures with symmetric and regular vas deferens calcification involving vas calcification.

Discussion: Bilateral vas calcification can be due to degenerative changes due to ageing, diabetes mellitus, end stage renal disease with secondary hyperparathyroidism. They give rise to regular calcifications within the muscular components of the vas with preservation of luminal patency. Causes of unilateral vas calcification include inflammatory conditions like tuberculosis, gonorrhea, syphilis, schistosomiasis, and chronic non-specific urinary tract infections. The calcifications are intraluminal and irregular leading to partial or complete occlusion of the lumen. Vasa differentia may calcify after relatively short duration of diabetes if the disease starts after the age of 40, whereas if the disease occurs before the age of 40, it has usually been present for at least 15 years before calcification is noted. Diabetes accelerates the process of senescent calcification of the vas deferens by augmented expression of several bone-associated proteins (e.g., osteopontin, bone sialoprotein, alkaline phosphatase, type 1 collagen, osteocalcin) that facilitate or regulate the calcification process. In addition uremic serum upregulates osteoblast transcription factor Cbfa 1 and osteopontin expression.

Diabetic patients with vasal wall calcification may also develop failure of emission, where no sperm reach the posterior urethra due to aperistalsis of the vas deferens.

Conclusion: Type 2 diabetic subjects with long standing pelvic pain and without any elicitable cause should be evaluated for this uncommon etiology of vas calcification.

Abstract #206

SAFETY AND EFFICACY OF LINAGLIPTIN IN ELDERLY PATIENTS (≥65 YEARS) WITH TYPE 2 DIABETES (T2D)

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Objective: Treating T2D in the elderly can be complicated by associated co-morbidities and high risk of treatment-related issues, including hypoglycemia and gastrointestinal (GI) side-effects. Using pooled Phase 3 trial data, we assessed safety and efficacy of linagliptin in these patients.

Methods: This post-hoc analysis identified all patients ≥65 years from 7 randomized, double-blind, placebo-controlled trials of linagliptin 5mg/day as monotherapy or add-on to various glucose-lowering therapies. All 7 trials were at least 24 weeks; safety and efficacy in this analysis were assessed up to week 24.

Results: Of 1331 patients ≥65 years, 841 patients received linagliptin and 490 placebo. Mean ±SD baseline characteristics were similar in linagliptin and placebo groups: age, 71.1 ±4.5 v 70.9 ±4.7 years; BMI, 29.5 ±5.0 v 30.0 ±4.9 kg/m2; HbA1c, 8.0% ±0.8 v 8.1% ±0.8. Overall, 21% of patients had moderate or severe renal impairment (eGFR <60mL/min), more than 80% had diabetes for >5 years and more than 60% were receiving ≥2 glucose-lowering drugs. Median exposure to linagliptin and placebo was 173.0 and 176.5 days, respectively. The linagliptin group had significantly greater reductions from baseline to week 24 in HbA1c (placebo-adjusted mean [95% CI]: −0.62% (−0.73, −0.51; P<0.0001) and fasting plasma glucose (placebo-adjusted mean [95% CI] change: −14.8mg/dL [−20.7, −8.9]; P<0.0001). Adverse events (AEs) occurred in 71.3% and 73.3% of the linagliptin and placebo groups, respectively. Fewer patients receiving linagliptin had drug-related AEs (18.1% v 19.8% with placebo). The incidence of hypoglycemia was slightly lower in patients receiving linagliptin (21.4%) compared with placebo (25.7%), and severe hypoglycemic events
Abstract #207

SIMILARITIES AND DIFFERENCES BETWEEN PATIENTS INCLUDED AND EXCLUDED FROM A RANDOMIZED CLINICAL TRIAL OF VITAMIN D SUPPLEMENTATION FOR IMPROVING GLUCOSE TOLERANCE IN PREDIABETES

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Objective: To compare African American men (AAM) excluded to those included into RCT of vitamin D supplementation for prediabetes.

Methods: We performed retrospective chart review to compare the subjects excluded (OUT) to those included (IN) in RCT. The main inclusion criteria were hemoglobin A1C (A1C) 5.7-6.9%, body mass index (BMI) 28-39 kg/m2, circulating 25-hydroxyvitamin D (25OHD) 5-29 ng/mL, and the main exclusions were known T2DM, and serious disease that may interfere with participation or increase the risk of side effects.

Results: The subjects (n=245) had the same demographics (mean [SD]): AAM, Age 59 [10] years old. The OUT (n=118) vs IN (n=127) group had lower BMI (kg/m2) (30.4 [4.7] vs 31.9 [4.7], p=0.007) and A1C (%) (5.9 [0.5] vs 6.1 [0.2], p=0.008). The level of 25(OH)D was similar (ng/mL) 15.2 [6.5] vs 15.1 [6.5], p=0.88. The odds ratios (OR) and 95% confidence intervals [CI] after adjustment for BMI and A1C were significantly different for serum LDL (0.990 [0.981 - 0.998], p=0.02) and HDL (1.033 [1.014 - 1.053], p=0.001), hyperlipidemia (1.033 [1.014 - 1.053], p=0.001), and serious disease (2.207 [1.300 - 3.745], p=0.003). There was a trend for differences for AST (1.015 [0.999 - 1.031], p=0.07), ALT (1.012 [1.000 - 1.025], p=0.05), and vitamin D supplement use (1.705 [0.952 - 3.054], p=0.07). There were no differences for other measured parameters: eGFR, cholesterol, triglycerides, proportion of hypertension, degenerative joint disease, cardiovascular disease (including myocardial infarction, stroke, peripheral vascular disease, and congestive heart failure), cancer (all combined), and psychiatric problems (including post-traumatic stress disorder, depression, schizophrenia, and substance abuse). Subgroup analysis of subjects with A1C 5.7-6.5% (OUT n=49, IN n=113) showed significant differences for serious disease (2.340 [1.166 - 4.697], p=0.02).

Discussion: Our analysis shows that RCT, an accepted gold standard for evidence-based advice, has clinically relevant limitations. Although the notion exists that a RCT involves highly selected patients the comparison of included and excluded subjects is rarely done or reported in the literature. It is important for physicians to have this evidence and to understand limitations of generalizing results of RCT to patients seen in clinical practice.

Conclusion: Patients included and excluded from this RCT differ by several important clinical characteristics. Advice based on the evidence from RCT may not be applicable to a patient with the same demographics and disease seen in a clinical practice.

Abstract #208

PRECIPITATION OF NEW ONSET DIABETES BY H1N1 INFECTION

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Objective: Infectious diseases in type 2 diabetes can complicate diabetic ketoacidosis, derange hyperglycemia or precipitate new onset diabetes. Novel pandemic influenza virus H1N1 strain needs to be kept in mind when dealing with new onset diabetes with co-existing infectious agent, which if present has high mortality if not treated.

Case Presentation: A 63 yr old female, with no known chronic illness, was hospitalized in August 2010 with fatigue, breathlessness on exertion, productive cough with scanty sputum, and high grade fever for a duration of 4 days. Quick emergency assessment had shown to have temp 101 F, tachycardia, tachypnoea, p02:90% at room air and normotensive. Clinical chest examination was unremarkable. Further evaluation revealed NHO in both lung fields on chest x-ray, hyperglycemia 325 mg/dl, detected for first time. There was no ketonuria, no leucocytosis. Her symptoms and oxygen desaturation...
were out of proportion to clinical finding and chest x-ray findings. The patient was managed with insulin infusion and empirical broad spectrum antibiotic coverage in ICU. As her condition worsened over next 12 hours, infection with novel influenza virus was thought and empirically started on oseltamavir after taking throat swab for H1N1 test and later the sample was tested positive for H1N1 influenza RT-PCR. Clinical course in the hospital was complicated by oxygen dependence requiring 10-12lt/hour of oxygen administration by nasal mask. Oseltamavir was continued for 02 weeks with broad spectrum antibiotics for super added bacterial infection. Her blood sugar was well controlled. She made an uneventful recovery and was discharged on biphasic insulin @ 35 units/day with well controlled blood sugar levels. 

**Discussion:** People with diabetes and influenza are three times more likely to die from complications than without diabetes. Immunological research found high levels of a molecule called interleukin 17 in the blood of severe H1N1 patients, and low levels in patients with the mild form of the disease. Interleukin 17 can produce inflammation and autoimmune diseases.

Our case was complicated by precipitation of new onset hyperglycemia and occurrence of pneumonia with rapid decline in general condition. High flow oxygen was required to be delivered by face mask to maintain oxygen saturation. 

**Conclusion:** Recognition of an existing infectious process in a new onset diabetes mellitus, H1N1 infection and prompt institution of oseltamavir to retard the progression of disease and decrease the mortality associated with it. Vaccination offers better advantage for diabetic patients.

**Abstract #209**

**BARRIERS TO INSULIN INITIATION IN TYPE 2 DIABETES MELLITUS - A SINGLE INSTITUTION STUDY AMONG THE PHYSICIANS**

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**Objective:** Diabetes is a growing health problem, incurring cost of $170 billion in US in 2007. The benefits of good glycemic control have been demonstrated extensively. However, insulin use among patients with poorly-controlled Type 2 Diabetes Mellitus (T2DM) is still inadequate despite massive evidence-based studies. This lack of insulin use is likely attributed to the patients and/or their physicians.

**Methods:** In this study, we retrieved the data regarding glycemic control among T2DM patients in our institution through the Electronic Medical Record system. We then conducted a survey among our primary care physicians (PCPs) to investigate the barriers in insulin initiation and to develop solutions to improve it.

**Results:** A total of 1226 patients were identified, 273 of whom had a Hemoglobin A1C greater than 8.5%. Among these 273 patients, 119 were not on insulin. A survey was conducted among 71 PCPs to study insulin-, resource-, physician-, and patient-related issues contributing to the lack of insulin use, with responding rate of 45%. Greater than 80% believed that insulin is efficacious and that resource is unlikely a limiting factor. Over 90% disagreed that decision regarding insulin initiation should be made exclusively by endocrinologists. Most of the PCPs believed that patient would be more willing to use insulin if no injection was involved. Experienced PCPs were more aware of guidelines and were more comfortable with insulin initiation. Those who were less comfortable with insulin therapy believed that education was needed, and many of them disagreed with the necessity of maintaining tight glycemic control.

**Discussion:** Our study shows that educating the PCPs of T2DM management and insulin usage may improve insulin initiation. Additionally, PCPs could increase the insulin utilization through open discussion with their patients. This provides us evidence to guide our practice as well as to improve glycemic control.

**Conclusion:** Our study suggests that education is the key to improving glycemic control and insulin usage among patients managed by their PCPs.

**Abstract #211**

**AWARENESS OF DIETARY RISK FACTORS FOR DIABETES AND CARDIOVASCULAR DISEASE AMONG MIGRANT ASIAN INDIANS**

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**Objective:** A survey was conducted among Asian Indians living in Houston, Texas to examine prevalence and assess knowledge, attitudes and beliefs regarding dietary factors that can affect risk for development of diabetes and cardiovascular disease.

**Methods:** A health and disease survey was collected during a major festival at the Hindu temple. All the participants were migrants from India. Demographic information including age, gender, duration of stay in the US, education, employment and marital status was collected. Self reported height and weight were used to calculate body mass index. Survey included questions to assess dietary factors and current health status.
Results: Total 199 Asian Indians (Male: 116, Female: 83) completed the survey. 51% of participants have been living in the US for > 10 years. 92% of participants reported at least Graduate level of education. Majority of participants were < 45 years of age (63%), were married (78%) and were employed (66%). 58% of participants agreed that it is important to cut down saturated fat intake. > 80% of participants were able to make healthy food choices (healthy bread, curry and dessert). 71% of participants believed that lack of physical activity and increased stress can increase risk for obesity, diabetes and heart disease. Top six responses for risk factors for development of diabetes were being overweight, family history of diabetes, eating too much fat and sugar, age more than 40 years and ethnic origin. When asked about complications of diabetes, top three responses were kidney failure, heart attack and blindness. > 70% of participants believed that lack of physical activity and increased stress can increase risk for obesity, diabetes and heart disease. When asked about preventive measures for diabetes, top three responses were healthy diet, exercise, and weight control.

Discussion: Asian Indians are the second fastest growing racial and ethnic subgroup in the US. They carry relatively higher risk for metabolic syndrome, diabetes mellitus, and cardiovascular disease compared to other ethnic groups. Previous studies have reported poor knowledge of lifestyle risk factors among Asian Indians. However, in our study we did not find significant knowledge gaps with regards to dietary risk factors. In spite being aware of dietary risk factors and preventive measures, prevalence of overweight, obesity and self reported diabetes was 41.7%, 17.1% and 12.5% respectively.

Conclusion: Migrant Asian Indians may differ in their knowledge of dietary risk factors. High prevalence of obesity and diabetes among local migrant Asian Indians warrants development of targeted prevention programs.

Abstract #212

ACARBOSE REDUCE GLYCEMIC VARIABILITY IN TYPE 2 DIABETIC PATIENTS

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Objective: Present study was aimed to evaluate and compare the glycemic variability in AGI (Alpha Glucosidase Inhibitor) and Non-AGI treated type 2 diabetic patient (T2D).

Methods: This retrospective study was conducted in 65 T2D patients for the duration of ≥5 years. Patient were included if their HbA1c level ≥ 8-9 and baseline characteristic of patients were noted at first visit. Patients were divided into 2 Group, Non-AGI treatment (OHA or Gliptine or Glitazone or Sulfonyl urea) was given to first group and AGI treatment (Acarbose combination with OHA or Gliptine or Glitazone or Sulfonyl urea) was given to second group. Parameters such as fasting blood sugar (FBS), postprandial blood sugar (PPBS), body weight and HbA1c level was estimated and compared. The 8 point Self Monitoring of Blood Glucose (SMBG) was performed to determine glycemic variability in both treatment groups. The level of HbA1c was estimated at every 3 month during study (24 months).

Results: The study showed that the AGI treatment caused less glycemic variability compared to Non-AGI treated group and gives desired control in postprandial sugar level. Reduction in level of HbA1c in Non-AGI treated group was 0.33%, whereas 1.08% reduction in level of HbA1c was noted in AGI treating group at 9 month after treatment. After 9 month of treatment AGI was added to Non-AGI treated group and it’s caused significant reduction in HbA1c level (7.12±0.5 Vs 8.8±0.41; P<0.01) with 1.68% difference compared to baseline after 24 months of treatment. Furthermore, the AGI treatment caused significant reduction in HbA1c level (6.88±0.23 Vs 8.86±0.15; P<0.01) at 24 month with 1.98% difference compared to baseline. Results of present study shown that the AGI treatment improve the SMBG and AGI treated group showed better PPBS control compared to Non-AGI treated group. Reduction in body weight was higher in AGI treated group than Non-AGI treated group compared to baseline (P<0.05).

Conclusion: Present study revealed that the AGI treatment decreases glycemic variability and also help to reduce PPBS and body weight of T2D compared to Non-AGI treatment.
**Abstract #213**

**EFFECT OF GLP-1 AGONIST ON GLYCEMIC CONTROL IN UNCONTROLLED TYPE 2 DIABETIC PATIENTS BEING TREATED WITH INSULIN**

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**Objective:** Present study was aimed to evaluate the combining effect of GLP-1 agonist (Liraglutide) with Insulin on glycemic control in type 2 diabetic patient (T2D).

**Methods:** A 52-week retrospective study was performed in 52 T2D patients, all of whom were currently on Insulin and oral antidiabetic with HbA1c level more than 8.5% were included in study. Epidemiological parameters such as age, gender, BMI, waist circumstance, blood pressure, fasting (FBS) and postprandial blood sugar level (PPBS), HbA1c (Before and after GLP-1 agonist combining with insulin), family history and medical history were included in study. Baseline HbA1c level noted at baseline visit and then patient shifted on GLP-1 agonist combining with Insulin. Effect of GLP-1 agonist and Insulin combination was evaluated by measuring HbA1c level at 3, 6, 9 and 12 months after the treatment.

**Results:** The combining effect of GLP-1 agonist and Insulin were evaluated in adult type 2 diabetic (n=40, mean age 54.7±8.6 years). The combination of GLP-1 agonist and Insulin cause significant improvement in glycemic control. The HbA1c level was significantly (P<0.01) decreased at 3 months (8.33±0.9 Vs 9.12±2.2; **P<0.001) and continuous reduction was observed at 6 months (7.92±1.2 Vs 9.12±2.2; **P<0.001), 9 months (7.47±1.3 Vs 9.12±2.2; *P<0.05) and 12 months (7.2±0.9 Vs 9.12±2.2; **P<0.001) after the treatment of GLP-1 agonist and Insulin combination as compared to baseline HbA1c level. The level of FBS and PPBS was significantly decreased at 3 months and continuous reduction was observed at 6 months, 9 months and 12 months after the treatment as compared to baseline value. More over the results also suggest that the GLP-1 agonist does not cause weight gain and reduced insulin requirement.

**Conclusion:** Data of present study revealed that the combining of GLP-1 agonist with insulin improve glycemic control without weight gain and decreases the insulin requirement in type 2 diabetic patients.

**Abstract #214**

**DIABETIC AMYOTROPHY PRESENTING WITHIN FIVE YEARS OF DIAGNOSIS OF TYPE 1 DIABETES MELLITUS**

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**Objective:** To report a case of profound diabetic amyotrophy presenting within five years after onset of type 1 diabetes in a twenty five years old male.

**Case Presentation:** 25 year-old male with type1 diabetes mellitus for last five years presented to us with complaints of pain in the back and thigh for six months and difficulty in walking and standing from sitting position. On examination asymmetrical quadriceps wasting with absent deep-tendon reflexes in the right leg and diminished sense of vibration and proprioception was noted in both lower limbs. X-ray lumbar spine and Doppler of the lower extremities were normal. Labs revealed HBA1c of 8.5% with complete blood count, serum electrolytes, renal function tests and liver function tests within normal limit. Serum CPK, aldolase, LDH, calcium, vitamin D, vitamin B12 and cortisol levels were also normal. An electromyogram (EMG) showed denervation changes involving both femoral nerves. The diagnosis of diabetic amyotrophy was thereby established based on above test results. Patient was advised about better control of diabetes and muscle strengthening exercises.

**Discussion:** Diabetic amyotrophy usually occurs in patients with poorly controlled diabetes. It is characterized by subacute onset of severe proximal leg and hip pain involving Iliopsoas, quadriceps, hip abductors, and adductors. The findings may be either unilateral or bilateral. Nerve conduction studies generally demonstrate evidence of a typical diabetic sensorimotor axonal polyneuropathy and EMG reveals abnormalities of ongoing denervation in proximal limb musculature. The mechanism of diabetic amyotrophy is uncertain, although perivascular inflammation and secondary nerve infarction are thought responsible. It is more commonly observed in elderly men, several years after diagnosis of type 2 diabetes mellitus. However, we have noticed this condition in a young patient within 5 years of diagnosis of his type 1 diabetes mellitus.

**Conclusion:** Diabetic amyotrophy is more often seen in type 2 diabetics over 50 years of age but it should not be overlooked in young type 1 diabetics even during their early years of diabetes.
Abstract #215

SURVEY OF DIABETES RISK FACTORS IN URUGUAIAN POSTMENOPAUSAL WOMEN

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Objective: The aim of this study was to analyze risk factors for DM2 in a population of uruguaian postmenopausal women

Methods: This is a case - control study, we included 300 posmenopausal women older than 55 years from general practice and endocrinology clinics assisted by the authors in Uruguay. We interviewed our population between 06/01/2011 - 06/30/2012. They were asked about: obesity or diabetes familial history; personal history of menarche age (MA), acne, facial hair, irregular menses before perimenopause, contraceptive pill use (CPU), spontaneous abortion (SA), number of pregnancies, macrosomic siblings, gestational diabetes (GDM) and menopause age. The waist circumference (WC) was measured. The body mass index (BMI) was calculated. We divided the group in 2: Group 1: those with DM2 diagnosed by a physician (n=125); and Group 2: without DM2 history (n=175) and compared them statistically. The association is expressed with OR and its 95% confidence interval. It was used X2 test or T test as needed. Significance was determined by p < 0.05.

Results: It was found statistic significance as risk factors for DM2: diabetes or obesity mother's history (OR 3.21, 95% IC: 1.92 - 5.34, p < 0.01 and OR 1.57, 95% IC: 1.01 - 2.58, p < 0.05 respectively), birth weight >4 Kg (OR 3.20, 95% IC: 1.05 - 9.81, p 0.04), MA < 11 years old (OR 3.21, 95% IC: 1.92 - 5.34, p < 0.01), CPU (OR 1.61, 95% IC: 1.01 - 2.55, p < 0.05), three or more pregnancies (OR 1.09, 95% IC: 1.01 - 2.58, p < 0.05), macrosomic siblings (OR 1.82, 95% IC: 1.09 - 3.1, p < 0.05) and GDM (OR 4.36, 95% IC: 1.21 - 2.38, p < 0.05). It was found an inverse lineal association with DM2 risk by MA (p <0,05), and direct linear association with WC and BMI (p <0,05). We found a not statistically significant trend with spontaneous abortion (OR 1.38, 95% IC: 0.85 - 2.24, p 0.18), acne (OR 1.26, 95% IC: 0.71 - 2.27, p 0.42), facial hair (OR 1.11, 95% IC: 0.57 - 2.16, p 0.75), and irregular menses before perimenopause (OR 1.14, 95% IC: 0.65 - 2.00, p 0.63). There was not a clear cut off menopausal age related with higher DM2 risk.

Discussion: Some risks factors are known and others have little evidence, our results are according to the literature.

Conclusion: We recommend to add routinely as part of the medical record questionnaire this DM2 risk factors: body weight at birth, menarche age, contraceptive pills use; mother's history of diabetes or obesity and number of pregnancies, to the traditional known risk factors as: macrosomic siblings, gestational diabetes and DM general family history.

Abstract #216

FIBRINOGEN LEVEL AND METABOLIC SYNDROME'S RISK FACTORS IN STABLE CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS

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Objective: This study was undertaken to evaluate the relation of fibrinogen level and metabolic syndrome’s risk factors in stable chronic obstructive pulmonary disease (COPD) patients.

Methods: In this observational cross sectional study, we measured the characteristic of metabolic syndrome and plasma fibrinogen levels in 43 stable COPD patients. The criteria for identification of metabolic syndrome includes 3 or more of the following features : abdominal obesity (waist circumference ≥ 90 cm in men, ≥ 80 cm in women), triglycerides ≥ 150 mg/dL, HDL cholesterol : 40 mg/dL in men and < 50 mg/dL in women, blood pressure ≥130/85 mmHg, and FPG ≥ 110 mg/dL.

Results: There were 43 stable COPD patients. The mean of age in stable COPD patients was 63.28±5.595 years, FEV1 1238,14±481,3, 54,30±13,9% predicted. Fibrinogen level was increased (mean 364,51±70,09 mg/dl). Fibrinogen level were related to predicted FEV1 (r=-0,312;p<0,05) and frequency of exacerbations. Metabolic syndrome presence in 34,9% stable COPD patients. The frequencies of metabolic syndrome in stable COPD patients GOLD II, III and IV were 53%, 33,3% and 13,3%. Fibrinogen level were increased progressively from 316.83±59.36 mg/dl to 375.30±72.52 mg/dl in COPD patients with metabolic syndrome (p<0,05).

Discussion: Fibrinogen level is considered as a part of the metabolic syndrome. This study showed a mean fibrinogen level of 70 091 ± 364.51 mg/dl. Fibrinogen level in the range of 330 mg - 370 mg/dl is considered increasing the risk of heart disease. The mean level of fibrinogen in subjects with no MetS risk factors was 316.83 ± 59.36 mg/dl. This level was much lower than the mean level of fibrinogen in subjects with MetS, i.e. 375.3 ± 72.5 mg/dl. Metabolic syndrome is associated with proinflammatory
and prothrombosis states. Proinflammatory state is characterized by elevated CRP level, while prothrombosis state is characterized by elevated fibrinogen an PAI-1 level. This study revealed no significant association between fibrinogen level and MetS (p = 0.085).

**Conclusion:** These study found that fibrinogen level was increased in stable COPD patients and 34.9% stable COPD patients had coexisting with metabolic syndrome with more frequent in moderate COPD patients.

**Abstract #217**

**ASSOCIATION BETWEEN GLYCEMIC STATE IN TYPE 2 DM AND REDUCED LUNG FUNCTION**

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**Objective:** To examine the relationship between pulmonary function (ventilation disturbance/derangement) with glycemic state in type 2 DM.

**Methods:** Design : cross sectional analytic study subjects of DM patients without history of or not under therapy for pulmonary disorders that visit the ambulatory clinic from June 2008 to August 2008. informed consent was delivered and then subjects filled the agreement paper for further examination: physical diagnosis, chest x ray, blood sampling and pulmonary function test (spirometry).

**Results:** There were 28 subjects with HbA1c < 6.5 (controlled) and 32 people > 6.5 (uncontrolled). Pulmonary function test showed that forced vital capacity (FVC) in controlled group has mean 90.6 + 7.5 % predicted or 2350 + 412 ml, in uncontrolled subjects 82.5 + 10.7 % predicted or 2051 + 366 ml with T test (P = 0.001). Forced Expiration Volume in first second (FEV1) showed 88.6 + 8.3 % predicted or 1881 + 8 ml in controlled subjects, and FEV1 was 87.6 + 13.3 % predicted or 1795 + 13 ml in uncontrolled subjects with T test (P = 0.728).

**Discussion:** There is significant association between uncontrolled DM with decreasing PVC predicted but no association between FEV1 and uncontrolled DM. There was association between hyperglycemia and PVC but not with FEV1, this may be the result of hyperglycemia effect not too affect to airway obstruction. The result of the study stated that there was decreasing mean pulmonary function each year higher in DM patients than non DM. Value of FVC in DM subjects decreasing to 64 mL each year comparing to non DM 58 mL each year and value of FEV1 in DM patients decreasing 2 mL each year as resulted in 47 mL in non DM subjects and 49 mL in DM subjects each years. This study reflected that DM is a progressive disease and has greater effect on FVC than FEV1. It actually can be stated that the effect of hyperglycemia on the lung precisely destroy lung parenchym eventhough there is influence to bronchus but statistically not significant.

**Conclusion:** There is a significance correlation between decrease in FVC and uncontrolled DM (power = 80%), but no relationship between decreased in FEV1 among controlled and uncontrolled DM.

**Abstract #218**

**RELATIONSHIP OF RESISTIN AND VISFATIN WITH COAGULATIVE ACTIVATION IN TYPE 2 DIABETIC PATIENTS**

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**Objective:** The purpose of this study was to investigate the potential roles of resistin and visfatin in patients with type 2 diabetes mellitus and to evaluate the correlation between the adipocytokines and markers of coagulative activation.

**Methods:** We consecutively evaluated 187 patients, who presented with a type 2 diabetes. Baseline concentrations of circulating levels of resistin, visfatin, von Willebrand Factor (VWF), factor (F)VIIa, prothrombin fragment 1 + 2 (F1+2), 11-dehydro-thromboxane B2 (TXM), activated protein C, and soluble thrombomodulin (TM) were determined by enzyme-linked immunosorbent assay (ELISA).

**Results:** Type 2 diabetic patients had significantly higher levels of resistin, visfatin, VWF, FVIIa, F1+2 compared with healthy men. Likewise, both TXM and prothrombin F1+2 levels were higher in diabetics (P < 0.05). By contrast, anticoagulant markers, such as activated protein C, and TM were depressed in type 2 diabetes (P < 0.05). Plasma levels of resistin and visfatin positively correlated with TXM (resistin: r = 0.268; P = 0.001; visfatin: r = 0.254; P = 0.001) and prothrombin F1+2 (resistin: r = 0.221; P = 0.001; visfatin: r = 0.206; P = 0.025). Plasma levels of both adipokines have shown an inverse correlation with markers of anticoagulation such as activated protein C (resistin: r = -0.132; P = 0.045; visfatin: r = -0.216; P = 0.035) and soluble thrombomodulin (resistin: r = -0.165; P = 0.035; visfatin: r = -0.195; P = 0.038). A multiple linear regression analysis, performed to quantify further the relationship between resistin and visfatin levels and the above-mentioned variables as well as the inflammatory marker C-reactive protein (CRP) and including age, body mass index (BMI), waist-hip ratio (WHR) and lipid parameters as potential confounders, revealed that only FVIIa and VWF were independently related to resistin levels as well as VWF to visfatin level.

**Discussion:** Proteins secreted from adipocytes - so-called adipocytokines - influence metabolic and vascular
function. Resistin and visfatin have 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**: Increased concentrations of resistin and visfatin were associated with type 2 diabetes mellitus. Intriguingly, high plasma levels of both adipokines seem to modulate platelet activation and coagulative activation. These results suggest that increased resistin and visfatin levels in diabetes mellitus may be novel biochemical risk factors for atherothrombotic complications, promoting to procoagulant reactions.

**Abstract #219**

**EUGLYCEMIC DIABETIC KETOACIDOSIS WITH ACUTE PANCREATITIS IN A PATIENT NOT KNOWN TO HAVE DIABETES**

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**Objective**: Diabetic Ketoacidosis (DKA) is a serious acute metabolic complication of DM. A triad of uncontrolled hyperglycemia, metabolic acidosis and increased total body ketones characterizes it. Euglycemic DKA is a less known entity and can go unrecognized at initial presentation. It has been described mainly in type 1 DM. We report a case of euglycemic DKA precipitated by starvation and severe pancreatitis in a patient with chronic alcoholism and no known underlying DM.

**Case Presentation**: A 36 years old lady presented with acute pancreatitis. She had not been eating for a week and admitted to heavy drinking, her last drink was 3 days prior to admission. Her vitals were normal except for RR of 24 per minute. BMI was 20 kg/m2. She was in mild distress, lethargic, easily arousable, followed commands. Abdominal exam revealed hypoactive bowel sounds and moderate tenderness in the epigastric area. Her laboratory tests were pertinent for mild anemia, bicarbonate level of 10 mmol/L, glucose of 86 mg/dL, amylase of 208 U/L, lipase more than 10,000 u/l and negative blood alcohol level. She had severe metabolic acidosis (pH 7.21, pCO2 19 and anion gap 27 mmol/L), large serum acetone and normal lactic acid level. CT scan of the abdomen revealed severe pancreatitis. Patient was kept NPO. Normal saline followed by 5% dextrose in normal saline was initiated. 18 hours after intensive fluid resuscitation, she continued to have low bicarbonate at 9 mmol/L and elevated anion gap at 22 mmol/L, her glucose increased to 315 mg/dL, glucosuria developed and ketoacidosis remained. Euglycemic DKA was suspected and low-dose intravenous insulin was initiated with continuation of 5% dextrose in normal saline. 7 hours later bicarbonate level increased to 16 mmol/L, anion gap normalized to 11 mmol/L, ketonuria and ketoacidosis resolved. Her HbA1C was 4%.

**Discussion**: Euglycemic DKA is thought to be due to a combination of factors: exogenous insulin injection, food restriction and starvation, and inhibition of gluconeogenesis. The fact that ketoacidosis in this patient did not resolve until intravenous insulin was initiated supports acute depletion of pancreatic beta cells reserve due to acute pancreatitis and possible underlying unrecognized DM. Severe acute on top of chronic destruction of beta cells would have lead to acute decompensation and resultant insulin deficiency. Decreased glycogen reserve secondary to chronic alcoholism with prolonged fasting would lead to the euglycemic state.

**Conclusion**: Euglycemic DKA should be considered in the differential diagnosis of ketoacidosis since intravenous insulin and dextrose infusion is the mainstay of therapy to correct electrolyte abnormalities and re-establish carbohydrate metabolism.
Abstract #220

ELEVATED C-REACTIVE PROTEIN IS ASSOCIATED WITH PERIPHERAL ARTERIAL DISEASE IN NIGERIANS WITH TYPE 2 DIABETES

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Objective: This study determined the prevalence of peripheral arterial disease using history, palpation method and ankle brachial index (ABI) and the association between traditional / non-traditional inflammatory risk factors and peripheral arterial disease in Nigerians living with Diabetes.

Methods: This case-control study involved 150 Nigerian Type 2 diabetic patients and 150 apparently healthy adults, age and sex matched. Relevant clinical information was obtained and physical examination was carried out. PAD was determined using hand-held Doppler and defined as ABI less than 0.9 in at least one limb. Venous blood was collected to measure fasting plasma glucose, serum total cholesterol, low-density lipoprotein, high-density lipoprotein, triglycerides, white blood cell count and C-reactive protein. Glycated haemoglobin level was also determined among the diabetic population. Regression analysis was done and results interpreted with confidence interval (CI) and odds ratio (OR).

Results: Of the 150 diabetics and 150 controls that participated in the study, 66(44.0%) diabetics and 68 (45.3%) controls were males, and 84 (56.0%) diabetics and 82 (54.7%) controls were females. Mean ± SD age of the diabetic and control groups were 56.12 ± 7.65 years and 55.76 ± 7.49 years respectively (p = 0.681). Prevalence of PAD, using ankle-brachial index was 22% in diabetics and 8% in control. Regression analysis showed that the presence of PAD was associated with age (OR 0.908, 95% CI: 0.829 - 0.994, p = 0.036), male gender (OR 0.224, 95% CI 0.064 - 0.787, p = 0.020), waist circumference (OR 0.829, 95% CI: 0.015 - 0.530, p = 0.008), and serum CRP (OR 0.701, 95% CI: 0.498 - 0.986, p = 0.041). There was an inverse relationship between glycated haemoglobin level and presence of PAD (r = -0.191, p = 0.019).

Discussion: Increased prevalence of PAD with advancing age may be explained by the fact that other risk factors for atherosclerosis also increases with age. CRP is a marker of inflammation, but previous reports indicate that it may also influence vascular vulnerability. Central obesity has been associated with atherogenic lipid profile and release of cytokines that mediate atherogenesis.

Conclusion: The study further confirms the high prevalence of PAD in Nigerian diabetics. Peripheral arterial disease was associated with central adiposity and CRP. Our Type 2 Diabetes patients should be screened for PAD, and efforts should be intensified in preventing and managing associated risk factors such as obesity.

Abstract #221

HEALTHCARE COSTS AND ADHERENCE ASSOCIATED WITH HUMAN REGULAR U-500 VERSUS HIGH-DOSE U-100 INSULIN IN PATIENTS WITH DIABETES IN THE UNITED STATES

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Objective: Describe real-world healthcare costs and adherence of patients treated with concentrated human regular insulin U-500 (U-500R) versus high-dose U-100 insulin (U-100) regimens for diabetes.

Methods: Data from Thomson Reuters MarketScan Databases (July 1, 2008 through December 31, 2010) were used. The U-100 cohort had received ≥150 units/day of U-100 insulin therapy for ≥31 days during the first 60 days after index date; the U-500R cohort had received ≥2 prescriptions of U-500R post-index date. Patients were required to have continuous coverage for 6 months pre- and 12 months post-index and be aged ≥18years. All analyses were performed on propensity-matched cohorts. The changes in annualized costs, from the pre- to post-period, were compared between the two cohorts using paired t-tests and non-parametric bootstrapping methods were used to compute confidence intervals (CIs). Insulin pump utilization and hypoglycemia (hypo) incidence during the post-period were compared using a chi-square
test; hypo rates and associated costs were compared using Wilcoxon rank-sum test. Adherence was assessed by the proportion of days covered (PDC) measuring the proportion of days U-500R was available for U-500R cohort and the proportion of days when a minimum of each patient’s index daily dose of insulin was available for the U-100 cohort. PDC was compared using a two-sample t-test. Glycemic efficacy data were not available in this database.

Results: There were 1,044 U-500R patients (19.1% type 1) and 11,520 U-100 patients (23.8 % type 1) identified, and 1039 matched pairs were obtained. A total of 30.5% of U-500R (off-label) and 28.0% of U-100 patients utilized an insulin pump (p=NS) in the post-period. The mean decrease of $1,290 in annual pharmacy costs for the U-500R cohort was significantly different than the mean increase of $2586 for the U-100 cohort (p<0.001, 95% CI [-$4345, -$3422]). The between-cohort differences on diabetes-related medical, non-diabetes related medical, total medical, and overall cost changes were not significant. Significantly more U-500R patients experienced hypo (17.3% vs. 11.8%, p<0.0001) but the hypo rate and hypo-related costs were not significantly different between cohorts. Finally, the mean 12-month PDC was 65.0% for U-500R patients and 47.6% for U-100 patients (p<0.0001).

Conclusion: For patients with diabetes requiring ≥150 units/day of insulin, treatment with U-500R was associated with a decrease in pharmacy costs, a higher proportion of patients experiencing hypo, no difference in hypo rate or costs, and greater treatment adherence, as compared to U-100 therapy.

Abstract #222

A CASE OF HYPERGLYCEMIC CHOREOATHETOSIS: A CURIOUS NEUROLOGIC MANIFESTATION OF HYPEROSMOLAR NONKETOTIC HYPERGLYCEMIA

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Objective: To present a case of hyperglycemic choreoathetosis and raise awareness of its existence.

Case Presentation: A 57 year old man with Hypertension, chronic kidney disease, Hep. C, and a CVA 3 years ago with no significant deficits presented with 1 week of uncontrollable right sided facial twitching and grimacing with right arm twitching and uncontrollable jerking movements. Vitals were BP 90/61, repeat 115/88 after 1 L of normal saline (NS). P 64, R 18, Sat 94%. Significant exam findings included right sided facial twitching, dysarthria and right upper extremity choreiform movements. Strength was normal except 4/5 strength in right upper limb. Labs revealed: WBC 6.1 Kmmm3 (4.4-11), Hb 9.5 g/dl (13.9-17.2), plt 133 K/mm3 (140-440), meter glucose >500mg/dl (70-100), Troponin I 0.032 ng/ml (0-0.25). Urine glucose >1000mg/dl and ketones negative. Serum glucose 712 mg/dl (70-100), A1C >17.5, BUN 7.9 mg/dl (10-26), AGAP 11mEq/L (3-25), Cr. 7.89 mg.dl (0.6-1.4), baseline Cr. 4.3, Na 124 mEq/L (135-150), Corrected Na 133.8mEq/L, Serm osmolality 310 mmol/kg (285-295), K 4.3 mEq/L (3.5-5.3), CO2 25 mEq/L (23-32), Ca 9.7 mg/dl (8.5-10.4). He was given IV normal saline and Q4 hourly insulin sliding scale. CXR was normal, EKG unchanged from previous, Head CT showed dystrophic calcification form prior left internal capsule infarct, multiple lacunar infarcts, cortical atrophy and no acute process. He was assessed by neurology as having hyperglycemia induced hemichorea-hemiballismus (HIHH). MRI showed bilateral changes of multiple old infarcts, generalized cortical atrophy, intrinsich bright T1 signal along the left internal capsule and no evidence of acute ischemia. Carotid Dopplers were normal. He was placed on a basal bolus insulin regimen. In the next 24 hours his glucose decreased form > 500’s to 232-255. Creatinine returned to baseline and he had cessation of the choreiform movements. He was discharged on day 5. At his two month clinic visit, he was asymptomatic.

Discussion: Diabetes can present with acute neurologic manifestations. Chart review revealed an A1C of 6.9 two years ago and 9.1 one year ago but no prior diabetes management. Patients with HHH typically have T1 hyperintensity and CT hyperattenuation in the contralateral basal ganglia which is reversible. The mechanism of HHH is not well understood but contributing factors are thought to include hyperviscosity, impairment of GABAergic or cholinergic neurons, impairment of cerebrovascular self-regulation, petechial hemorrhage and myelinolysis.

Conclusion: HHH is typically reversible with normalization of glucose in most cases. Medical management with antipsychotics, benzodiazepines and topiramate is sometimes warranted.
Abstract #223

METABOLIC CONTROL IN TYPE 2 DIABETES MELLITUS PATIENTS ATTENDING A TERTIARY DIABETES CLINIC IN NIGERIA

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Objective: The purpose of the study was to determine the percentage of patients who had their HbA1c, BP and Lipids treated to target.

Methods: Type 2 Diabetes Mellitus (T2DM) patients attending Lagos University Teaching Hospital (a tertiary hospital) Diabetes Clinic, Lagos, Nigeria were recruited. Information such as; age, sex, duration of DM, HbA1c, blood pressure, fasting lipids values were obtained from case notes and clinical examination. Data collected was analyzed using SPSS version 17.

Results: 218 subjects (41.3% males, 58.7% females) seen in the diabetes clinic in July and August 2012 were recruited for the study. Mean age of the cohort was 59.08 ± 11.02 years. Mean DM duration was 8.51 ± 7.37 years. Mean HbA1c was 7.56 ± 2.42. Of the 218 subjects, 47.7% of patients had good glycemic control using HbA1c of <7%, 40.8% of patients had good BP control of < 130/80mmHg and 80.7% had dyslipidemia. 78.9% had central obesity. 1.8% of subjects were under weight, 21.6% had normal weight, 43.6 % overweight, 23.4% had obesity class 1, 7.8% had obesity class 2 while 1.4% had obesity class 3.

Discussion: Diabetes Mellitus is a burden on the healthcare system, which is already under strain due to other chronic diseases. Diabetes is associated with other comorbidities like hypertension, dyslipidemia and obesity. Uncontrolled diabetes has led to increased rate of complications, and thus increased the cost of treatment. These complications of diabetes can be prevented or progression delayed by tight glycemic, blood pressure and lipid control. The United Kingdom Prospective Diabetes Study has shown that retinopathy, nephropathy and neuropathy were improved by lowering the blood glucose levels with intensive therapy in which a mean HbA1c of 7.0% was achieved. In our study, we found that 47.7% of our study population had HbA1c <7%. Mean HbA1c was 7.56 ± 2.42. This is similar to another study done by Unadike et al in Benin, Nigeria (2010), which reported poor glycemic control in 46% of subjects. Probable reasons for poor control in that study included; poor health seeking behavior, low level of literacy, poverty, poor adherence with follow up visits and medications amongst others. Coker and Fasanmade (2006) also documented poor glycemic control in their study amongst persons with diabetes in Lagos, Nigeria with a mean HbA1c level of 10.5%.

Conclusion: Metabolic control in T2DM patients attending our tertiary health centers in Nigeria remains sub-optimal and dyslipidemia seems to be the least well controlled. Concerted efforts need to be put in place to address metabolic control especially dyslipidemia.

Abstract #224

RISK FACTORS OF UNCONTROLLED HYPERGLYCEMIA IN A SURGICAL SERVICE

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Objective: To identify modifiable risk factors associated with uncontrolled hyperglycemia in surgical patients.

Methods: Retrospective review of all patients admitted to the surgical service of Harborview Medical Center (Seattle, WA) in 2010. Medical records reviewed of patients who met the following criteria: 1.Hyperglycemia defined as any hospital day with a blood glucose above 180mg/dl 2.Administration of insulin during hospital stay 3.ICD-9 code 249 or 250 defining a pre-existing diagnosis of diabetes documented up to one year prior to admission 4.HbA1c measured 3 months prior to or up to 1 day after admission 5.Administration of tube feeding during admission. Demographics and information about the unit prior to surgical service admission was obtained on all patients.

Results: The number of patients admitted to the surgical service was 1,316 in 2010. 18.8% (n=247) had 2 blood glucose measures above 180mg/dl on one or more hospital days. Among these patients, 52.6% (n=130) had a pre-existing diagnosis of diabetes of which 26% (n=65) had a measured HbA1c within 3 months prior to admission. Mean HbA1c was 8.2+/-.23% among patients with hyperglycemia whereas those with diabetes who remained euglycemic had a mean HbA1c of 6.2+/-.5%. 40% (n=98) of patients with hyperglycemia were on tube feeds and 40% (n=100) were admitted from the ICU. Interestingly, 15% (n=36) of hyperglycemic patients did not get insulin during their hospital stay and of those with a history of diabetes, 3% (n=4) were never given insulin. There was no difference between males and females, however hyperglycemia was significantly higher in older people (mean age: 55.3+/17.5 years, mode: 61 years).

Discussion: Inpatient hyperglycemia is a serious problem affecting up to 38% of patients in community hospitals. Approximately 33% of hyperglycemia in acute care patients do not have a history of diabetes. Hyperglycemia
is associated with increased length of stay, incidence of infections, and disability after hospital discharge. This study identifies use of tube feeds, previous stay in an ICU, and older age to be significant risk factors for hyperglycemia in addition to suboptimal controlled diabetes. Furthermore, some high risk patients with hyperglycemia do not get insulin, suggesting the need for greater awareness among surgical services about these patients.

**Conclusion**: In addition to suboptimal controlled diabetes, use of tube feeds, previous stay in an ICU, older age are significant risk factors for uncontrolled hyperglycemia in the surgical service. Early detection of these risk factors may improve glycemic control and avoid unnecessary complications among surgical patients.

**Abstract #225**

**CELL PHONE TEXT MESSAGING TO SUPPORT DIABETES MELLITUS SELF-MANAGEMENT (CELL TECH DM)**

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St. Joseph’s Hospital

**Objective**: Determines if daily text messaging can significantly change lifestyle practices and improve clinical outcomes in patients with uncontrolled diabetes mellitus.

**Methods**: Community dwelling patients (ages 18+) with poorly managed or uncontrolled diabetes mellitus (HgA1c > 9.0) are being recruited from the St. Joseph’s Hospital and Medical Center clinics’ diabetic registry (N=50). Study participants with cell texting capabilities receive a daily message asking for information on health practices (e.g., vegetable servings, amount of exercise or fasting blood sugar levels). They respond with a numerical answer and receive an immediate text back, based on their answer. The 162-character message prompts an appropriate intervention or provides a message to reinforce good behaviors or suggest better choices. Data is collected three times over 12 months (i.e., surveys, vital signs and satisfaction measures) and is combined with extracted EMR data. No direct medical intervention is provided.

**Results**: Preliminary HgA1c measures on 25 patients show that 14 have decreased HgA1c levels by an average of 1.64% (μ=1.64, range 0.2 - 4.3). Only three (n=3) show slightly increased levels for HgA1c levels (μ=0.67, range 0.4 - 1.1). No repeat measures are available on the reminder of patients at this time (n=8). Complete analysis of data will begin in January 2013 with comparisons of key outcomes between pre- and mid-study data. Data analysis includes descriptive statistics, logic regression and analysis of covariance.

**Discussion**: Traditional group or one-on-one education sessions are costly and time intensive interventions. Getting patients to attend several sessions is equally challenging so patient education classes may be poorly attended and, thus, not very effective. In locations where public transportation is minimal, and the patient population lacking in personal transportation, attending group visits and regular classes becomes difficult if not impossible. Cell Tec DM, a text messaging system to the patient’s cell phone, is an easy-to-use, affordable method for keeping healthy lifestyle practices and behaviors on patients’ minds on a daily basis. The study identifies attitudinal, behavioral and medical outcomes from a low-cost text messaging educational intervention and profiles characteristics of patients for whom the intervention is most highly effective.

**Conclusion**: Widespread use of cell phone technology begs for applications that offer cheaper, faster and more effective patient education methods. Cell Tech DM shows great promise as a low-cost, high-efficacy method for improving diabetic self-care practices among patients with diverse backgrounds.

**Abstract #226**

**ADHERENCE TO DIABETES TREATMENT: DO CERTAIN BEHAVIORS AND CHARACTERISTICS IMPACT ADHERENCE?**

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**Objective**: Adherence is crucial in diabetes management. There are; however, many challenges in helping patients achieve optimal adherence: concerns about side effects and how to take medication, difficulty following lifestyle approaches, costs, psychological issues. We evaluated the extent to which these factors relate to adherence.

**Methods**: Between April 30 and May 7, 2012, an internet survey was offered to patients with diabetes visiting WebMD. It was answered by 807 respondents, including adults with type 1 & type 2 diabetes.

**Results**: Adherence (misses per week as proportion of units prescribed) was highly correlated with self-reported medication adherence. Younger, more recently diagnosed persons with type 2 diabetes had lower adherence. The most frequently cited cause of missing medications was “I forget”; expense, side effects, and the complexity of care plan were less frequently mentioned. Self-reported
adherence was lower with insulin than with oral agents. 61% of respondents reported side effects, which were associated with reduced medication adherence. Self-monitoring of blood glucose (SMBG) was associated with adherence, with medication dose adjustment based on SMBG associated with even greater adherence. Carb counting and carb knowledge also were associated with improved adherence. Respondents who received information/material related to diabetes from their clinicians also had greater adherence. Of side effects, upset stomach was strongly associated with decreased adherence. Respondents expressing more worry about medications, expense, and side effects reported lower adherence.

Discussion: Those with many “adherence issues” were more likely to report worry that the medications could harm, make them feel worse, and produce side effects, possibly signaling an underlying negative perception of their treatment. Respondents with more “non-adherence issues” appeared more self-conscious about their treatment (i.e., interferes with lifestyle, embarrassment, afraid of needles). Those with fewer “non-adherent issues,” curiously, were more likely to indicate that their clinician did not have time to talk to them. Those having the fewest issues with adherence were more likely to report receiving information, having discussions, and engaging in nutritional and diabetic programs.

Conclusion: Some targeted interventions may track with greater adherence. Adherence has complex relationships to self-reported variables. The extent to which the associations reflect causal relationships between clinician-patient interactions, rather than reflecting underlying patient characteristics, is not known.

Abstract #227

IMPACT OF DIABETES EDUCATION AND PEER SUPPORT GROUP ON THE METABOLIC PARAMETERS OF PATIENTS WITH DIABETES MELLITUS (DM) (TYPE 1 & TYPE 2)

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Objective: Participation in diabetes education and/or diabetes peer support groups has been recommended in the American Diabetes Association DM guidelines as an indispensable tool for managing DM. However, there are few studies that examine the effect of diabetes education alone versus diabetes education plus a peer support group on various metabolic parameters. Hence, this study was done to investigate the effect of such strategies in controlling metabolic parameters.

Methods: Study subjects were obtained from an electronic chart review of DM patients seen at the Diabetes and Primary Care clinics at Queens Hospital Center, Jamaica, New York between January 1, 2007 and June 1, 2011. A total of 188 subjects were included in the study. The patients were categorized into 3 main groups: (1) control group (n=62), which received primary care only, (2) diabetes education group (n=63), which received primary care plus diabetes teaching from a certified diabetes nurse educator and (3) patients who were seen in Primary Care clinic who also received diabetes education and who also joined a peer support group for at least two sessions (n=63). The mean change from baseline in hemoglobin (Hb) A1C, weight, body mass index (BMI), systolic blood pressure, total cholesterol (TC), HDL cholesterol (HDL-C), LDL cholesterol (LDL-C) and triglycerides (TG) was calculated after 3 follow up visits.

Results: Statistically significant improvements in HbA1C (mean change: -0.78%, p=0.013), TC (mean change: -16.89 mg/dL, p=0.01) and LDL-C (mean change: -11.75 mg/dL, p=0.04) from baseline to final follow up were observed in the diabetes education group alone. Patients in the diabetes education group also exhibited consistently significant reductions in HbA1C and LDL-C throughout from the 3rd month to the 13th month of follow up. Though not statistically significant, moderate improvements in glycemic control, weight loss, systolic blood pressure, TC and TG and HDL-C were noted in the combined diabetes education and peer support group in the final follow up.

Discussion: The average change in HbA1C and LDL-C levels recorded in our study is consistent with a previous study, demonstrating the benefit of diabetes education on certain metabolic parameters. The lack of benefit seen in group # 3 may be attributed to the small sample size, the retrospective nature of the study and the possibility of non-compliant patient group.

Conclusion: Participation in diabetes education could help optimize control of metabolic parameters of diabetic patients in terms of HbA1C, TC and LDL-C levels, and this benefit may perpetuate through time, but additional peer support group participation may have no additional benefit.
INFLAMMATORY MARKERS IN DIABETIC FOOT AND IMPACT OF VITAMIN D DEFICIENCY.

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Objective: 1. To evaluate plasma levels of IL-6, adiponectin and resistin in subjects with diabetic foot in comparison with subjects without foot complications. 2. To assess the impact of vitamin D status on the levels of above inflammatory markers.

Methods: A total 100 diabetic foot cases and 100 diabetic controls were recruited in the study. Serum level of 25OH vitamin D was estimated from the cases & controls by RIA. Serum IL6, adiponectin and resistin were assayed by ELISA. Data were analyzed using online graphpad quickcalc software and P < 0.05 was considered statistically significant.

Results: Mean age of the study population was 54.3 ± 12.4 years (Male: Female= 68: 32). Mean age of the controls was 52.5 ± 13.6 (Male: Female= 60: 40). Glycated hemoglobin was comparable (10.3% Vs 10.9%). Diabetic foot cases were having lower vitamin D status (16.1±16.0ng/ml) than the diabetic controls (19.8±14.1ng/ml). Prevalence of vitamin D deficiency was higher in cases than controls (62% vs 57%). Females outnumbered males in terms of prevalence of vitamin D deficiency [22/ 32 females (68%) vs 40/68 (58%) males in cases and 25/ 40 females (62%) vs 32/60 (53%) males in control group]. Severity of vitamin D deficiency (<10ng/ml) was higher in cases (48.2%) than controls (26.2%). IL6 level was higher in cases (128.3pg/ml) than the controls (63.8pg/ml) (p<0.01). Similarly lower median plasma levels of adiponectin (7.7 vs 8.4 µg/ml) and higher median plasma levels of resistin (3.8 vs 3.6 ng/ml) were observed in cases (p<0.05). No significant difference was observed in the levels of these markers between male and female study participants in both the groups. Patients under vitamin D deficient group (<30ng/ml) demonstrated higher IL6 (130.8 pg/ml Vs 100.0 pg/ml), higher resistin (3.9 vs 3.6 ng/ml) and lower adiponectin (7.6 vs 8.3 µg/ml) levels compared to vitamin D sufficient (≥ 30ng/ml) group in diabetic foot (p< 0.05).

Discussion: Immunoregulatory role of vitamin D is well established. Diabetic foot infections reflect the immune compromised state of the patients. Therefore it is speculative that vitamin D deficiency is more common and severe in diabetic foot. Our study demonstrated that diabetic subjects with diabetic foot showed in comparison with diabetics without diabetic foot higher IL-6 and resistin levels and lower adiponectin levels in plasma. Hypovitaminosis D is more prevalent in patients with diabetic foot and Vitamin D deficiency is more severe in patients with diabetic foot infections. The levels of the above markers are more in diabetic foot patients with vitamin D deficiency.

Conclusion: Assumption is made that Vitamin D deficiency enhances inflammatory response in addition to hyperglycemia, in diabetic foot.

METABOLIC SURGERY ASSESSMENT SCORE: TOOL TO PREDICT DIABETES REMISSION AFTER MODIFIED BARIATRIC SURGERY

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Objective: Laparoscopic ileal interposition (II) with sleeve gastrectomy (SG) / diverted sleeve gastrectomy (DSG) are modified bariatric surgeries for treatment of type 2 diabetes (T2DM). DSG is preferred over SG in patients with less favorable metabolic profile. Due to variable remission response in our patients, retrospectively we devised a novel score metabolic surgery assessment score (MSAS). It helps to select the type of procedure and to predict the diabetes remission before surgery.

Methods: Forty six patients underwent II + SG and II + DSG was performed on 29 patients. MSAS was calculated based on preoperative parameters. MSAS of the subjects with and without remission (maintaining HbA1C < 6.5% without any medication) were compared.

Results: Patients subjected to II+SG had mean age of 48.3 ± 8.1 years, duration of T2DM 9.8 ± 7.6 years and body mass index (BMI) 32.1 ± 6.9 Kg/m2. All patients had poorly controlled diabetes with HbA1C 9.5 ± 2.2 %. Mean MSAS in patients who underwent II + SG (n=46) was 9.2±1.4. Twenty one (46%) had remission in diabetes. In the same group, patients with BMI ≥35 kg/m2, MSAS was 8.9 ± 1.7 and remission rate was 85%. MSAS was significantly lower in patients with remission than patients without remission (8.1±0.8 versus 10.2 ±0.9, p=0.0001). Patients subjected to II+DSG had mean age of 48.7 ± 7.8 years, DM duration of 13.1 ± 5.8 years and BMI 29.1 ± 6.7 Kg/m2. All patients had poorly controlled diabetes with HbA1C 9.8 ± 1.8 %. Mean MSAS was 10.4±1.3 (significantly higher than II+SG group, p = 0.0004). Twenty one (72%) had remission in diabetes.
significantly lower in patients with remission than patients without remission (9.7±0.8 versus 12.0 ±0.5, p<0.0001). Patients with MSAS ≥ 10 in II+SG group and MSAS ≥ 12 in II+DSG group did not get remission. MSAS was not significantly different (p = 0.1468) in patients without remission in II+SG (10.2 ±0.9) versus patients with remission in II+DSG (9.7±0.8). This indirectly suggests that DSG instead of SG would have helped them in achieving remission.

Discussion: The surgery addresses the foregut and hindgut mechanisms leading to remission in diabetes. The SG component restricts calorie intake and induces ghrelin (orexin) loss. II leads to rapid stimulation of interposed ileal segment by ingested food leads resulting in augmented GLP-1 secretion. DSG leads to better remission rates by exclusion of Rubino’s factor and GIP from duodenum, abolition of hedonic effect of food, earlier stimulation of ileum leading to better incretin response.

Conclusion: Preoperative MSAS can be a useful tool to select the type of surgical procedure and to predict the post operative diabetes remission.

Abstract #230

PEG-ASPARAGINASE (PEG-ASP) INDUCED HYPERGLYCEMIA IN A PATIENT WITH ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)

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Case Presentation: A 22 y/o Hispanic male with acute lymphoblastic leukemia (ALL) diagnosed in NOV 2011 with complex karyotype on treatment protocol AALL0232 was admitted after new onset witnessed tonic clonic seizure with postictal state. His blood glucose on arrival was 359 mg/dL (65-99 mg/dL) with an anion gap of 18, and negative urine and serum ketones. By family’s report, patient had poor appetite since being on chemotherapy and was surprised by his blood glucose level. Patient was started on intensive basal bolus with correction insulin therapy with glargine and aspart at 1 unit/kg and despite titration of insulin dosage, close monitoring of oral food intake, and no exogenous dextrose IV solution, patient’s blood glucose remained labile between high 200’s to low 400’s and refractory to therapy. Subsequently, endocrinology was consulted. It was noted that five days prior to admission, patient had received vincristine 2mg IV x 1 and PEG-Asparaginase (PEG-Asp) 5,375 units IV x 1 as part of delayed intensification treatment per protocol. No steroids were used as part of protocol for this treatment. After an in-depth review of patient’s outpatient and inpatient medications including his chemotherapy regimen, it was concluded that patient’s glycemic control was influenced by the biological effects of PEG-Asp on insulin production. Patient’s insulin therapy was further intensified with increased dosages and temporarily placed on IV insulin with gradual resolution of hyperglycemia.

Discussion: ALL leukemic cells are dependent on host asparagine for survival since it cannot synthesize asparagine. Asparaginase is an enzyme which catalyzes the conversion of asparagine to aspartic acid and ammonium. Depriving leukemic cells of asparagine results in apoptosis. However, insulin biosynthesis is impaired since asparagine is a vital amino acid which resides in the 18th and 21st position of the A chain and 3rd position of the B chain. Synthetic pegylated asparaginase has a prolonged half life (t½=5.73 days) compared to biologic asparaginase ((t½=0.65-1.35 days) and when combined with vincristine which decreases clearance of PEG-Asp, its hyperglycemic effects are magnified.

Conclusion: Patient with acute lymphoblastic leukemia (ALL) being treated with PEG-Asparaginase should be closely monitored for severe hyperglycemia and potential for diabetic ketoacidosis due to the chemotherapy’s biological effects on insulin biosynthesis. Treatment of hyperglycemia may require aggressive and high doses of insulin along with cessation of PEG-Asparaginase initially with rapid taper of insulin once the biological effects of PEG-Asparaginase decline over time in about 5-10 half lives.

Abstract #231

TRUE STARVATION INDUCED EUGLYCEMIC DIABETIC KETOACIDOSIS IN A PATIENT WITH TYPE 2 DIABETES MELLITUS

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Objective: To present a complex case of euglycemic diabetic ketoacidosis in a patient with DM-2.

Case Presentation: A 56-year-old Caucasian male veteran was admitted with 2 week history of nausea, vomiting and diarrhea. He was found to have MSSA bacteremia, cellulitis, pyomyositis and multiple abscesses. Past medical history was significant for DM-2, HTN, depression, and alcohol abuse. His diabetes had been managed with metformin for 15yrs and he was recently transitioned to a basal-bolus insulin regimen alone. During hospitalization, his diabetes was well managed with NPH and Regular insulin alone but due to frequent NPO diets from daily imaging studies or I&D procedures, his insulin doses were frequently held or
reduced. Hospital course was complicated by acute kidney injury secondary to contrast and nafcillin. Despite gradual improving renal function with removal of offending agents and normal saline hydration, the patient was noted to have progressive metabolic acidosis eventually necessitating transfer to the MICU. Electrolytes revealed sodium 140 mmol/L, chloride 106 mmol/L, bicarbonate 9 mmol/L, creatinine 177 mg/dL, Agap 25 mmol/L and negative osmolar gap. Albumin was 2.0 and C-peptide 0.7. Further work-up confirmed 2+ ketonuria, positive serum acetones, and negative lactic acid. Serum alcohol, ethylene glycol, and salicylates were undetectable while urine drug screen was negative. The patient was diagnosed with euglycemic DKA, started on IV hydration with D5 NS, IV insulin and increased caloric diet. His ketoacidosis soon resolved.

Discussion: Our patient’s history and poor caloric intake suggests a starvation state while his inappropriately low C-peptide indicates insulin deficiency. Catabolic stresses associated with trauma, surgery, starvation and other acute illness may predispose to DKA. During starvation, glycogenolysis provides 75% of the total body glucose requirements followed by gluconeogenesis and eventually ketone body formation ensues. These processes are accelerated by insulin deficiency and may subsequently result in euglycemic ketosis. Other possible contributors of ketoacidosis such as alcohol or isopropanol intoxication were ruled out. Starvation on its own typically maintains a bicarbonate level ≥18 mmol/L. Management of euglycemic DKA consists of increasing carbohydrate intake and insulin.

Conclusion: True starvation induced euglycemic (BG ≤180 mg/dL) DKA occurring in a DM-2 patient is infrequently reported in the literature. One must be cognizant of caloric intake in an insulin dependent diabetic patient under stressful conditions. A thorough work-up is needed to rule out other etiologies.

Abstract #232

A PILOT PROGRAM TO COORDINATE FOOD DELIVERY AND MEALTIME INSULIN ADMINISTRATION IN THE HOSPITAL IMPROVES ON TIME INSULIN DOSING AND GLYCEMIC CONTROL

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Objective: Multiple studies have demonstrated basal/bolus insulin superior to sliding scale insulin for management of hospitalized patients with diabetes mellitus. However, failure to coordinate meals and administration of prandial insulin may limit the effectiveness of basal/bolus insulin regimens. The SIU School of Medicine Hospital Diabetes Team observed frequent poor coordination between meals and prandial insulin dosing and helped St. John’s Hospital Food Services implement a pilot program to link delivery of food and mealtime insulin.

Methods: A prospective trial comparing two internal medicine floors was conducted. On the intervention floor, food service personnel were required to hand cards to unit secretaries identifying patients with diabetes who had received food. Unit secretaries notified Registered Nurses that patients were ready to eat. Trays were delivered to the control floor according to usual Food Services policy (no notification of food delivery). Primary end point was the frequency of on time administration of insulin lispro, defined as within ± 20 minutes of meal delivery. Secondary end point was glycemic control measured by comparisons of mean capillary blood glucose (CBG) and categorical distributions of CBG for each floor. Data were collected June through September 2012, and all study patients were managed by the SIU Hospital Diabetes Team under the supervision of faculty endocrinologists.

Results: A total of 131 insulin doses were evaluated on the intervention floor, and 152 insulin doses were evaluated on the control floor. Frequency of on time prandial insulin was increased on the intervention floor compared to the control floor (50.4% vs. 35.5%, P = 0.016). Median time deviance between delivery of food and insulin lispro was 20 min on the intervention floor and 43 min on the control floor (P = 0.006), with proportion of prandial insulin doses more than 30 min from meals decreased to 42% from 56.6% (P = 0.033). Mean of CBG measurements recorded before lunch, dinner, and bedtime was significantly lower on the intervention floor than the control floor (157 ± 54 mg/dL vs. 185 ± 85 mg/dL, P = 0.02). Improved glycemic
control was achieved without an increase in hypoglycemia, defined as CBG < 70 mg/dL (2.5% vs. 1.4%, P = 0.66).

Discussion: A pilot program yielding 50% on time dosing of insulin lispro resulted in better glycemic control on the intervention floor without increased hypoglycemia. Median time between food delivery and prandial insulin was reduced significantly due to fewer extreme deviations in insulin administration.

Conclusion: These results should encourage additional work to better coordinate meals and prandial insulin dosing in the hospital.

Abstract #233

INSULIN RESISTANCE AND DIETARY MACRONUTRIENT INTAKE IN YOUNG NON-OBESE ASIAN INDIAN MEN

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Objective: To compare dietary macronutrients and insulin sensitivity between healthy young non-obese Asian Indian (AI) and White men of similar body mass index (BMI).

Methods: Twenty seven AI and 29 White men of similar age and BMI without diabetes were evaluated with anthropometric measurements, underwater weighing for percentage of total body fat mass, and euglycemic-hyperinsulinemic clamp study for measurement of insulin sensitivity. A quantitative Food Frequency Questionnaire (FFQ) which included Asian Indian foods was administered by clinical coordinator. A seven day estimation of total calories, percentage of carbohydrate, protein and fat were calculated by Nutribase software. The FFQ was validated by seven day food recall both in Asian Indians and Whites.

Results: There were no differences in age, BMI and waist circumference between AI and White men (age: 26±4 vs. 25±3; BMI: 24±4 vs 24±4; Waist circumference: 86±10 vs 87±9; mean ± SD in AI and Whites respectively). AI men had higher total body fat (21±7 vs. 18±6; p-value=0.04, mean ± SD; AI and Whites) and lower peripheral glucose disposal rate (Rd) during hyperinsulinemic-euglycemic clamp (6.4±2.6 vs. 8.5±2.5; p-value=0.03 adjusted for total body fat, mean ± SD; AI and Whites respectively). AI and Whites had similar total caloric and fat intake. However, AI had significantly lower protein intake (16.7±3.2 vs. 19±4; p-value=0.003, mean ± SD; AI and Whites respectively) and higher carbohydrate intake (54.4±8 vs. 47±10; p-value=0.001, mean ± SD; AI and Whites respectively) compared to White men. When adjusted for carbohydrate and protein intake, besides total body fat, ethnic difference in glucose disposal was attenuated with adjusted p-value of 0.01. The self reported exercise was similar in the two groups.

Discussion: We and others in the past have reported increased insulin resistance and type 2 diabetes in migrant AI men compared to White men independent of total body fat and regional fat distribution. However, role of dietary macronutrients and physical activity level in ethnic difference in insulin resistance still remains unclear. Our study demonstrated that AI had similar total caloric and fat intake as in Whites, however had significantly lower protein intake and higher carbohydrate intake and higher insulin resistance with similar self reported exercise.

Conclusion: In conclusion, we demonstrate that Asian Indian men have significantly lower protein intake and higher carbohydrate intake and higher insulin resistance compared to age and BMI matched White men of European descent. Self reported exercise level did not explain the difference in insulin resistance.
the uncontrolled patients at referral had never shown a single controlled value (HbA1c ≤ 7%) for available HbA1c records up to 6 years prior to referral. At 6-months and 12-months post-referral, HbA1c levels were reduced to 7.8% (p<0.05) for each, a 1.0% reduction compared to baseline HbA1c. Among patients who attended the diabetes education program (DEP) at LMC, a 1.1% reduction in HbA1c was observed compared to a 0.7% reduction among patients who did not attend the LMC DEP. Mean LDL cholesterol reduced from 2.30 mmol/L pre-referral to a value of 2.04 mmol/L at 6 months and further to 1.78 mmol/L at 12 months post-referral (both p <0.05). Prescription for evidence-based medications were increased post-referral for the cohort: 1. Metformin : 82% usage pre-referral was increased to 85% at 6 months and 91% at 12 months. 2. RAAS (Renin-Angiotensin-Aldosterone System) medications : 67% usage pre-referral was increased to 73% at 6 months and 79% at 12 months. 3. Statin medications : 74% usage pre-referral was increased to 86% at 6 months and 91% at 12 months.

Discussion: In this observational cohort study: Significant improvements were observed in both mean HbA1c and LDL cholesterol levels after referral to LMC. Among a primary care provider population that does seek consultant care, and where consultant availability is NOT restricted, there is a significant delay to referral. LMC DEP attendance was associated with a significant reduction in HbA1c. Evidence based medications usage for cardiometabolic risk reduction was higher post-referral compared to prior to referral.

Conclusion: Patient referral to a specialist-run, multidisciplinary program should be considered early in diabetes to optimize patient glycemia and CV risk factor management.

Abstract #235

PREVALENCE AND CHARACTERISTICS OF PAINFUL DIABETIC NEUROPATHY IN A COMMUNITY-BASED DIABETIC POPULATION ATTENDING A TERTIARY CARE SETTING

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Objective: We assessed the prevalence of painful neuropathic symptoms and their relationship with clinical severity in patients with diabetes. We also determined the gender distribution, type and duration of diabetes in patients with peripheral neuropathy.

Methods: This observational study included diabetic patients attending tertiary care centre (n = 5617, M: 3480, F: 2137). A detailed clinical history and examination was done on all the patients. Painful Diabetic Neuropathy (PDN) was assessed using Neuropathy Symptom Score (NSS) and Neuropathy Disability Score (NDS). Statistical analysis was done using the SPSS version 16.

Results: Prevalence of painful symptoms (NSS ≥5) and PDN (NSS ≥5 and NDS ≥3) was 42% and 29%, respectively. Painful symptoms occurred in 28% of patients without neuropathy (NDS ≤2) and 70% of patients with severe neuropathy (NDS >8). Adjusted risk of painful neuropathic symptoms in type 2 diabetes was double that of type 1 diabetes [odds ratio (OR) = 2.1 (95% CI 1.2-2.1), P < 0.001] and was not affected by severity of neuropathy, insulin use, foot deformities, smoking, or alcohol. Women had 50% increased adjusted risk of painful symptoms compared with men [OR = 1.3 (1.5-1.7), P < 0.0001]. The duration of diabetes correlated positively with severity of symptoms but the symptoms were not attributed to neuropathy.

Discussion: We have shown in our study that one-third of all patients with diabetes have painful neuropathic symptoms, regardless of whether they have clinical neuropathy. Another quarter of our patients without clinical neuropathy had significant painful neuropathic symptoms, indicating the large variation between signs and symptoms. This reemphasizes the need to enquire all patients about the occurrence of painful neuropathic symptoms. The major strength of this study is that it is community-based and therefore reflects the magnitude of the problem in nonselected diabetics. We did not identify pain from a different origin or enquired about the use of medications for the treatment of neuropathic pain.

Conclusion: Only one-third of diabetic patients in the study had painful neuropathic symptoms, regardless of their neuropathic deficit. PDN was more prevalent in patients with long standing type 2 diabetes and in women. This highlights large proportion of asymptomatic neuropathy and identified key groups which warrant screening for PDN.
Abstract #236

PREVALENCE OF DIAGNOSED AND UNDIAGNOSED DIABETES MELLITUS IN PEOPLE AGE 19 YEARS OR OLDER IN BASRAH, IRAQ

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Objective: Of the top ten countries with highest prevalence of diabetes, six of them were from Middle East. The objective of this investigation is to describe the prevalence of diabetes mellitus in Basrah, Southern Iraq.

Methods: A population-based, cross-sectional, simple random study was carried out, with target population being the entire Basrah population.

Results: Out of 5445 persons screened, the age range was 19-94 years. The method of screening was by HbA1c in 88.3% followed by fasting plasma glucose in 18.7%. New diabetes discovered in 11% and known diabetes was seen in 8.7%, leading to an age adjusted prevalence of diabetes of 19.7%. Of those with diabetes, 55.7% were undiagnosed before. Over all diabetics seen in 29.1%. This mean that dysglycemia was present in 48.8%, with only 51.2% were having normal glycemia. The peak age of diabetes in both gender was in the age range 46-60 years. Diabetes was slightly more prevalent in females than in males. About 70.3% of our diabetic patients have BMI of 25 and above.

Conclusion: Unprecedented increase in diabetic epidemic in Iraq seen (one in five adults from all Iraqi society will be affected with diabetes). The implication of these results means shortening lives and straining the financial resources of health care systems.

Abstract #237

SURGICAL EVALUATION OF PREOPERATIVE DIABETES CONTROL

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Objective: Preoperative control of diabetes can affect surgical outcomes. We evaluated preoperative through postoperative management of patients with diabetes (DM) who underwent elective surgery. We hypothesized that those with better preoperative diabetes control would have fewer complications compared to those with less optimal hemoglobin A1c (A1c) measurements.

Methods: Retrospective chart-review study using data from two VA hospitals from 2002 to 2009. Thirteen elective procedure categories were evaluated including urology, cardiovascular, respiratory, gastrointestinal, amputations, and total joint replacements (TJR).

Results: Procedures were analyzed among 179 patients with DM. Most patients had severe systemic disease by anesthesia evaluation (ASA class 3 or 4 = 88.8%). Thirty-one percent of patients were on insulin. Only 10% of patients had A1c recorded in preoperative surgical or anesthesia notes, only 8% had referral for diabetes management, 11% with uncontrolled DM (A1c > 7.9), and 53% of patients had a specific recommendation for changes in insulin or in oral medications on the day of or prior to surgery. Nineteen percent had TJR procedures, 17% had cardiovascular, 16% had genito-urinary, 7% had fracture repair, 7% had amputation, and 6% had gastrointestinal procedures. During hospitalization, 47% of patients had sliding scale insulin given, 9% had basal (long-acting) insulin, and 5% had prandial insulin administered. Mean (SD) BMI was 30.3 (6.1), mean (SD) 72-hour postoperative glucose was 190 (56) mg/dl, and mean (SD) A1c was 7.5 (1.3). Postoperative complications occurred in 32 patients (18%). Preoperative ASA class and A1c did not predict complications (p=0.68, 0.83, respectively). However, greater age predicted greater risk of complications (p=0.04), as did nephrectomy procedures (p=0.016) in univariate analyses. Acute kidney injury was underreported; 24 patients experienced AKI by review of laboratory data with only 2 reports of AKI in postoperative evaluations. These notes recorded changes in diabetes medications or insulin in only 4% of patients.

Discussion: Diabetes remains a morbid condition for those undergoing most elective procedures and is associated with increased complication rates. Older patients and those with renal procedures should be especially well-evaluated for diabetes control prior to elective procedures.

Conclusion: Patients with DM experienced high rates of complications during hospitalization following elective procedures, specifically renal complications. Preoperative evaluations did not account for prior uncontrolled diabetes, while post-operative evaluations underreported complications and did not sufficiently modify DM control.
Abstract #238

THE METHODOLOGY OF DIABETES FORWARD: A DIABETES-FOCUSED PRACTICE-BASED RESEARCH NETWORK

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Objective: Although randomized controlled clinical trials help provide conclusions to guide treatment recommendations for patients with type 2 diabetes (T2DM), data on actual management of diabetes outside a research setting is necessary to provide insight into real-world diabetes care. The mass movement towards Electronic Health Records (EHR) across North America provides a unique opportunity for data collection and is the premise behind Diabetes FORWARD (Foundation of Real-World Assessment and Research in Diabetes). Here we describe a unique, rapid, in-depth, real-world observational data collection, which will help to establish a research platform focused on comparative effectiveness research (CER) and health care decision-making in diabetes care.

Methods: Diabetes FORWARD is a North-American research platform being organized to conduct longitudinal, noninterventional investigations of approximately 10,000 T2DM patients on active treatment over 18 to 48 months. Recruitment will focus on patients and practice settings not typically studied, focusing on community-based primary care and referring endocrinology practices, with the goal of enrolling 350 to 400 practice sites. By using data from the EHR and periodic electronic surveys, the burden of study participation is reduced and data collection made simpler and more streamlined for researchers.

Results: Physician data will include baseline demographic and practice information. Patient data information will include demographics, T2DM characteristics and treatment, resource utilization, and patient-level outcomes (including adherence, satisfaction and productivity). Effects of diabetes management practice patterns on the following outcomes will be monitored over time: (1) glycemic control; (2) titration and dose of antidiabetic medication; (3) delivery mode of antidiabetic medication (oral, pen, vial and syringe, pumps, etc.); (4) persistence with and adherence to antidiabetic medication; and (5) discontinuation of and switching from antidiabetic medication.

Discussion: Diabetes FORWARD is expected to provide important data allowing real-world CER on how differing clinical management of T2DM impacts glycemic control, treatment adherence and persistence, and clinical outcomes, as well as help identify the effect of diabetes management on onset and progression of diabetes complications at 6-month intervals.

Conclusion: To our knowledge, Diabetes FORWARD is the first diabetes-focused practice-based research network in the United States and Canada. Diabetes FORWARD is expected to provide robust data using a large sample across a broad population that should reflect typical T2DM clinical practice in North America.

Abstract #239

DIABETES MELLITUS AND PREGNANCY IN A TERTIARY CARE CENTRE: PATTERNS AND OUTCOMES

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Objective: To report the pattern of presentation, treatment modality and outcomes amongst persons managed for diabetes in pregnancy.

Methods: 46 persons with diabetes in pregnancy were recruited consecutively into the study at diagnosis, either by the ADA or WHO criteria from March 2010 to February 2012. A short history was obtained which included anthropometric measurements before pregnancy. Patients were followed up till delivery and maternal and neonatal outcomes noted. Data was analyzed using SPSS version 16.

Results: The mean age (SD) of the study population was 33(4.32) years. Out of these, 65.2%( 30) had GDM, 30.4%( 14) had type 2 DM while 4.3% (2) had type 1 DM with 43.5% being nulliparous. 71.9% were managed with diet, insulin and exercise, 15.6% had diet & exercise alone while 12.5% were on dietary management alone. Amongst 60.9% (28) of these subjects who knew their pre-pregnancy weight, the mean (SD) pre-pregnancy BMI was 30.1(5.89) Kg/m² with 86.2% being overweight or obese. 44.2% had a history of DM in a first degree relative. 87.5% & 72% had GDM diagnosed by WHO & ADA criteria respectively. Only 10.9% had HbA1c done at any time in pregnancy. Most of the patients had caesarean delivery (92%) with 66% of these being emergencies. 63.8% of all deliveries were at term. There was no maternal mortality but there were 2 perinatal deaths. 22.7% of the babies had hyperbilirubinaemia while hypoglycaemia was reported.
in 9.1%. Only 4 of the women reported back OGTT done 6 weeks post partum despite counseling in pregnancy.

**Discussion:** Gestational diabetes mellitus (GDM) is defined as impaired glucose tolerance with onset or first recognition during pregnancy. This requires careful monitoring and treatment for best maternal and neonatal outcomes. Pre-gestational diabetes is also a growing concern due to the increasing incidence of type 2 diabetes mellitus (type 2 DM) in the younger age group and the rising average age of pregnant women. Being overweight or obese prior to conception and family history of DM were important risk factors for GDM identified. About 70%, required insulin therapy in addition to dietary management and exercise. This contrasts with other studies, which have reported much lower rates of insulin use in GDM. We observed a high incidence of operative deliveries in persons with diabetes in pregnancy, and this has been reported in other studies.

**Conclusion:** Diabetes in pregnancy requires close collaboration between obstetricians and endocrinologists for better outcomes. Lifestyle modification aimed at weight reduction may help to reduce the risk of GDM.

**Abstract #240**

AN INFANT WITH AN UNUSUAL INSULIN REQUIREMENT

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**Objective:** Rabson-Mendenhall syndrome (RMS) is a rare insulin receptor disorder characterized by growth retardation, lack of subcutaneous fat, acanthosis nigricans, enlarged genitalia, hirsutism, coarse facial features, paradoxical fasting hypoglycemia and post-prandial hyperglycemia, extreme hyperinsulinenia and pineal hyperplasia. It is Autosomal recessive disorder associated with Mutations in insulin receptor gene. Mutant receptors retain a bit of residual activity. We describe a 6 month male child with physical and biochemical features suggestive of RMS.

**Case Presentation:** A 6 month old boy was referred to our centre with Acute bronchopneumonia and newly detected Diabetes. He had normal developmental milestones with incomplete immunization. His Weight was 3 kg (<50th centile)& Length 53 cm (<80th centile). He had dysmorphic facial features with large ears, prominent eyes & fleshy nose. There was hypertrichosis of face, bushy eyebrows, hairy pinna and hairy upper back. We also noted loss of gluteal, axillary & abdominal pad of fat. Random blood sugar of 508 mg/dl with HbA1c (HPLC) of 16.8%. Chest X-ray confirmed B/L bronchopneumonia. USG Abdomen showed normal Pancreas. The patient was started on supportive management and Insulin infusion (via an insulin pump) at rate of 0.1 unit/kg/hr with no change in CBG values. Insulin infusion rate was increased to 0.2 to 0.4 to 0.8 to 1.5 to 3.0 to 5.0 to 10 units/kg/hr with no improvement in CBGs. Soluble insulin was continued for 4 days with good improvement in patients condition and then gradually changed over to Glargine BD along with Regular Insulin TDS without significant changes in the CBS. The C-Peptide assay was significantly high at 17.3 ng/ml (0.4 - 2.2 ng/ml). Mutation screening for Kir 6.2 , SUR, INS was done which were negative. Other Endocrine Assay were Cortisol of 16.42 µg/dl , FSH - 3.03 mIU/ml , LH - 4.12 mIU/ml and Testosterone of 135 ng/dl. The patient was started on Pioglitazone 15 mg OD. However the blood sugars remained over 300 mg/dl on last follow up visit. The Genetic analysis of insulin receptor mutations is awaited.

**Discussion:** We considered a diagnosis of RMS due to detection of Diabetes in first 6 months of age. Growth retardation, Facial Dysmorphisms, Hypertrichosis, Features of insulin resistance and biochemical evidence of Precocious puberty (Elevated LH, FSH) and very high C-peptide. However the patient had no Paradoxical hypoglycemia and inability to control Sugars with such high doses of insulin was perplexing.

**Conclusion:** We present a case of Rabson-Mendenhall syndrome with poor glycemic control inspite of receiving about 240 U/kg/day of Insulin.

**Abstract #241**

EFFECTIVENESS OF V-GO® FOR PATIENTS WITH DIABETES IN A REAL-WORLD SETTING: A LONG-TERM, PROSPECTIVE, OBSERVATIONAL REGISTRY (SIMPLE)

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**Objective:** The V-Go is an easy to use disposable 24-hour non-electronic device that delivers both a continuous preset basal rate of insulin and on-demand bolus dosing. The purpose of this study is to observe glycemic control, insulin dose requirements, and possible adverse effects and weight changes, as well as to compare these parameters to prior treatment when patients with Type 2 diabetes are treated using the V-Go during circumstances as close to
normal clinical practice as possible. The primary objective is to compare change of average glycemic control as measured by A1C from baseline to endpoint.

**Methods:** A prospective, observational, open-label, multicenter study is being conducted in patients with Type 2 diabetes with baseline A1C >7.0% treated with any of the 5 following baseline treatments: oral antidiabetic medications (OADs) only; OADs plus exenatide, pramlintide, or liraglutide and without insulin; once- or twice-daily injection of an intermediate or long-acting insulin (LAI) +/- OADs; premixed insulin regimen +/- OADs; insulin therapy with 3 or more insulin injections a day (MDI) +/- OADs. The patients were followed on their previous therapy for 4-6 weeks before starting the V-Go. The study is observational in nature with no protocol-mandated instructions to guide therapy. Patients are treated as standard practice by their healthcare providers. A planned interim analysis was conducted to evaluate safety and efficacy.

**Results:** To date, 47 patients had continuous V-Go use for a minimum of 3 months. Most were men (61%) with an average age of 60 yrs. Average diabetes duration was 13 yrs. Mean baseline A1C was 8.6%, FPG 177 mg/dl, and weight 225.2 lbs. Most patients were previously on LAI (34%) or MDI (55%) +/- OADs. During the 4-6 week pre-randomization phase A1C was reduced by 0.4% (9.0 to 8.6%) reflecting a clinical study effect pre-V-Go initiation. After V-Go initiation A1C further improved; the mean (SD) change from month 0 to month 3 was 8.6 (1.54) to 7.8 (1.16) %; P<0.05. Total daily insulin dose (TDD) was reduced by 18% (12 Units). There was a modest mean weight gain of 1.4 lbs. Five patients reported AE’s probably related to V-Go (primarily rash or skin irritation). Six patients reported hypoglycemia <70 mg/dl with no severe hypoglycemic events.

**Discussion:** The interim analysis results suggest improved glucose control in patients on the V-Go in combination with OADs after 3-months of treatment.

**Conclusion:** In real-world practice setting, without forced titration protocols, the interim results suggest improved glycemic control and a reduction in total daily insulin dose in patients switching to the V-Go.

**Abstract #242**

**REDUCTION IN HEMOGLOBIN A1C WITH 72 HOUR CONTINUOUS GLUCOSE MONITORING: A RETROSPECTIVE STUDY**

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**Objective:** To determine if the use of 72 hour continuous glucose sensor improved metabolic control in patients with diabetes mellitus.

**Methods:** A total of 45 records were reviewed from patients who underwent a 72 hour Continuous Glucose Monitoring (CGM) from 2008 to 2012. Patients presented for insertion of the CGM sensor by a trained nurse and returned on day three for removal. Patents returned for their endocrine follow up appointment and changes were made to their insulin regimen after reviewing the CGM data. HbA1c and number of hypoglycemic events before and after 3 months of CGM were evaluated. Other factors reviewed included race, gender, and age. Patients with incomplete data were excluded.

**Results:** Thirty-six patients were included in the final study with an average age of 36 years. 71% of the patients were African American with an equal distribution of men and women. The mean HbA1c before CGM was 9.07% and the mean HbA1c after CGM was 8.57% (p=0.00). The average number of hypoglycemic events before CGM was 17.06 and the average after CGM was 14.69 (p=0.00).

**Discussion:** Frequent monitoring of blood glucose is an important component of management in patients with diabetes. Standard use of glucose meters for SMBG provides only intermittent single blood glucose levels, hence missing on the glucose variability during the 24 h. Recent data has also shown that the number of hypoglycemic events is equally important in decreasing mortality. Therefore, the use of CGM can help patients and physicians optimize glycemic control. These devices have the potential to increase the number of patients who are able to achieve target HbA1c goals, decrease glucose excursions, and decrease the risk of severe hypoglycemia.

**Conclusion:** Hypoglycemia is often a barrier to the achievement of tight glycemic control. CGM may represent a valuable tool to detect asymptomatic hypoglycemic episodes and optimize the therapeutic regimen in patients with diabetes. Our study showed that 72 hour CGM represents a safe and effective intervention to improve glycemic control in patients with diabetes.
Abstract #243

TREATMENT OF TYPE 2 DIABETES MELLITUS IN A GENERAL HOSPITAL IN LIMA PERU

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Objective: To determine the treatment of patients with diagnosis of type 2 diabetes mellitus in a general hospital in Lima Peru. To evaluate glycemic control in patients with diagnosis of type 2 diabetes mellitus in a general hospital in Lima Peru.

Methods: Mean age was 63 years old (DE 11.8), (MIN 26, MAX 93). 538 were female (58%), 384 were male (42%). Just 552 patients had data for Glycated Hemoglobin. Mean value were 7.88 (DE 2.13) (MIN 4.4, MAX 14.9).

298 patients used glibenclamide (32%), 736 patients used metformin (80%), 319 patients used nph insulin (35%), 28 patients used glargine insulin (3%), 16 patients used regular insulin (1.7%), 11 patients used lispro insulin (1.2%).

Results: Mean age was 63 years old (DE 11.8), (MIN 26, MAX 93). 538 were female (58%), 384 were male (42%). Just 552 patients had data for Glycated Hemoglobin. Mean value were 7.88 (DE 2.13) (MIN 4.4, MAX 14.9).

298 patients used glibenclamide (32%), 736 patients used metformin (80%), 319 patients used nph insulin (35%), 28 patients used glargine insulin (3%), 16 patients used regular insulin (1.7%), 11 patients used lispro insulin (1.2%).

Discussion: Metformin is the main drug to use in diabetic guidelines. In our institution most patients use Metformin as expected. The use of insulin is increasing to obtain adequate glycemic control. Recommended value to Glycated Hemoglobin is variable according to main guidelines. The mean age of our patients was 63 years old. Mean HBA1C value is 7.88%. Recommended level for patients in this age group is 7 TO 7.5%. However we do not have the data of hypoglycemic episodes.

Conclusion: Metformin is the main drug used in these patients. 38% of patients used insulin of intermediate or long action. Mean HBA1C value was 7.88%

Abstract #244

EMPGALIFLOZIN, A SODIUM GLUTOSE COTRANSPORTER 2 (SGLT2) INHIBITOR, LOWERS BLOOD PRESSURE IN PATIENTS WITH TYPE 2 DIABETES

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Objective: Empagliflozin (EMPA) improved glycemic control, weight, and blood pressure (BP) in Phase II studies in patients with type 2 diabetes (T2DM). The effects of the EMPA doses tested in Phase III trials (10 mg qd and 25 mg qd) on BP were analyzed using pooled data from two Phase II trials.

Methods: Data were pooled from two randomized, placebo (PBO)-controlled 12-week trials that examined EMPA as monotherapy (N=408) or as add-on to metformin (N=495) in patients with T2DM. Changes from baseline to week 12 in BP (last observation carried forward) measured as a safety assessment were analyzed using ANCOVA with study, treatment, and baseline BP as fixed effects and country as a random effect in patients receiving PBO (n=153), EMPA 10 mg (n=152), or EMPA 25 mg (n=152). Data from patients with systolic BP (SBP)>140 mmHg at baseline were analyzed as a sub-group (PBO: n=33; EMPA 10 mg: n=27; EMPA 25 mg: n=38).

Results: Median age (years) and mean±SD BMI (kg/m²) for PBO, EMPA 10 mg and 25 mg were 59.0, 59.5 and 58.0 and 30.3±4.8, 29.9±4.4 and 30.1±5.0, respectively. The majority (67.8%) took antihypertensive medication at baseline. Baseline mean±SD SBP was 134.3±15.9 mmHg, 131.3±13.8 mmHg and 132.5±14.6 mmHg for PBO, EMPA 10 mg and 25 mg, respectively. Adjusted mean±SE changes from baseline in SBP were -1.2±1.0 mmHg for PBO vs -3.8±1.0 mmHg and -4.5±1.0 mmHg for EMPA 10 mg and 25 mg, respectively (both p<0.05 vs PBO). Reductions from baseline to week 12 in DBP were not significantly different from placebo in either EMPA group (adjusted mean±SE changes: -1.8±0.6 mmHg for PBO, -2.3±0.6 mmHg for EMPA 10 mg, -2.7±0.6 mmHg for EMPA 25 mg). In patients with baseline SBP >140 mmHg, baseline mean± SD SBP was 157.2±13.6 mmHg, 152.8±8.9 mmHg, and 151.1±8.7 mmHg for PBO, EMPA 10 mg and 25 mg, respectively and adjusted mean (SE) changes from baseline were -10.4±2.4 mmHg, -17.0±2.6 mmHg, and -13.4±2.3 mmHg, respectively (p=NS). Including the number of antihypertensive medications at
baseline in the ANCOVA did not alter the effect of EMPA on BP versus placebo. Blood pressure changes did not correlate with pulse rate changes. The number of patients with AEs was comparable across groups (34.6% for PBO, 34.2% for EMPA 10 mg, 31.6% for EMPA 25 mg).

**Discussion**: Treatment with EMPA was well tolerated and provided statistically significant and clinically meaningful reductions in SBP. Reductions in SBP were more pronounced in patients with SBP >140 mmHg, but due to the small sample size, the differences in this sub-group did not reach statistical significance.

**Conclusion**: EMPA 10 mg or 25 mg for 12 weeks provided statistically significant and clinically meaningful reductions in SBP without increases in pulse rate.

**Abstract #245**

**EFFICACY & TOLERABILITY OF GLICLAZIDE MODIFIED RELEASE AT THE DOSAGE OF 90 TO 120 MG OVER BANGLADESHI TYPE 2 DIABETIC PATIENTS DURING RAMADAN**

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**Objective**: There are more than 3 million Diabetic patients in Bangladesh. 90% of them are of type 2 diabetic patients. A big portion of these type 2 diabetic patients observes fast during Ramadan as the majority of Bangladeshi people are Muslim. Among the oral hypoglycemic drugs sulfonylureas are the most widely used agent here in Bangladesh. In Ramadan physicians prefer oral antidiabetic drugs cause less hypoglycemia. In case of sulfonylureas they usually prefer once daily formulations for better compliance and low risk of hypoglycemia. Glimepiride modified release formulation is one the most widely used once daily agents. Therefore, a phase IV study was conducted to observe the efficacy and tolerability of glimepiride modified release formulation at high dosage of 90 to 120 mg over Bangladeshi type 2 diabetic patients during Ramadan. The study was named as FACT- Efficacy & tolerability of DiamiCron MR 60 (research brand of glimepiride modified release formulation) at the dosage of 90 to 120 mg over Bangladeshi Type 2 diabetic patients during Ramadan.

**Methods**: It was an open level, non-comparative, observational study. Total duration was 180 days (6 months including one month of Ramadan). Patients uncontrolled with 160 or 240 mg of glimepiride 80 mg; 60 or 90 mg of glimepiride modified release and 2 or 3 mg of glimepiride were switched to 90 or 120 mg of gliclazide modified release formulation respectively. Total number of study population was 359 patients, comprises of 46% males and 54% females having a mean age of 51 years and mean BMI of 26 kg/m2. At the 1st visit 92% of the patients were prescribed 90 mg and 8% were given 120 mg of gliclazide modified release formulation.

**Results**: The reduction in mean value of HbA1c, FPG, SGPT and weight of respondents from 1st visit to final visit was highly significant (p<.001). Out of 359 respondents only 4 had hypoglycemic episodes (3 had 1 episode and 1 had 2 episodes) during the study period.

**Discussion**: According to this study gliclazide modified release formulation at the dosage of 90 to 120 mg significantly reduces HbA1c by -1.9% in 6 months with very low episodes of hypoglycemia and without weight gain.

**Conclusion**: Thereby gliclazide modified release formulation confirmed its efficacy and tolerability at a high dosage of 90 to 120 mg over Bangladeshi type 2 diabetic patients in Ramadan.

**Abstract #246**

**SEVERE HYPERTRIGLYCERIDEMIA IN DIABETIC KETOACIDOSIS COMPLICATED BY ACUTE PANCREATITIS**

Quang Ton, Jorge Vivar, Catherine Jonnakuty

Mt. Sinai School of Medicine (Englewood)

**Objective**: To report a rare case of severe hypertriglyceridemia in diabetic ketoadidosis accompanied by acute pancreatitis.

**Case Presentation**: A 50 year old Caucasian male with past medical history of diet controlled type 2 diabetes mellitus and hyperlipidemia presented with acute onset of severe abdominal pain associated with projectile vomiting. Patient also endorsed thirty pound weight loss in last month and large ingestion of free water per day. Examination reveals a somnolent patient with dry mucous membranes and distended diffuse tender abdomen. On blood draw serum sample was turbid and milky. Laboratory findings significant for triglyceride 4425 mg/dl, cholesterol 1015 mg/dl, sodium 117 mmol/l, chloride 77 mmol/l, ABG (pH 7.24, pCO2 19 mmHg, pO2 101 mmHg, HCO3 8 mEQ/L), hemoglobin A1c 15.0%, lipase 2551 u/l, amylase 1482 u/l, serum osmolality 307 mosm/kg and urine osmolality 759 mosm/kg. CT scan revealed diffuse peripancreatic stranding surrounding entire pancreas and acute inflammatory change. Patient was aggressively hydrated with normal saline infusion and treated with intravenous insulin in the medical intensive care unit.
Patient’s symptoms resolved with medical management and triglyceride levels decreased to 559 mg/dl. Following hospital course was uneventful and on post-admission day 5 patient was discharged on fibrate medication and subcutaneous insulin injection. Outpatient investigation for familial hypertriglyceridemia was initiated.

**Discussion**: Severe hypertriglyceridemia is an uncommon cause of acute pancreatitis occurring in 1-4% of cases. Diabetic ketoacidosis accompanied by hypertriglyceridemia induced pancreatitis has rarely been previously reported. The insulin deficiency in diabetic ketoacidosis activates adipose tissue lipolysis resulting in increased free fatty acids accelerating the formation of very low-density lipoprotein in the liver. In addition, peripheral tissue reduction of lipoprotein lipase leads to hypertriglyceridemia. Overtreatment with hypertonic saline was avoided as pseudohyponatremia was caused by hyperglycemia and hyperlipidemia. Plasmapheresis was considered but not started due to concurrent hyperglycemia. Free radical damage to pancreatic capillaries occurs when free fatty acid release causes activation of trypsinogen.

**Conclusion**: Few cases have been reported where severe hypertriglyceridemia resulted from DKA associated with acute pancreatitis. When triglyceride level exceeds 1,000 mg/dl, clinicians should consider the consequences of acute pancreatitis and treat accordingly.

Abstract #247

**RISK FACTORS FOR A NEW AMPUTATION IN DIABETIC SUBJECTS HOSPITALIZED FOR FOOT ULCERATION**

Harold Torres, Hugo Arbañil, Rosa Pando, Jaime Pajuelo, Rosa Agüero, Dante Gamarra

Dos de Mayo Hospital

**Objective**: To estimate incidence and identify risk factors for a new amputation in diabetic subjects hospitalized because of foot ulceration.

**Methods**: We included diabetic patients hospitalized for foot ulceration from 2006 to 2008 in Dos de Mayo Hospital, Lima -Perú. The predictors for new amputation were determined using Cox regression (proportional hazards) multivariate analysis.

**Results**: We evaluated a cohort of 96 diabetic patients, 22 women and 74 men. Mean age 60.9 ± 10.8 years. At the first admission, 64 patients (66.7%) underwent amputation (22 minor and 42 major). On the cohort of 96 patients, 90 (93.8%) had sensorimotor diabetic neuropathy and 49 (51.0%) had peripheral arterial disease. The average follow-up was 2.2 ± 1.6 years. Overall, 10 homolateral and 19 contralateral episodes of new amputation occurred (9 minor amputations and 20 mayor amputations). They were performed within a mean of 1.7 ± 1.4 years, with an incidence of 15.9 per 100 person-years. In the adjusted Cox regression analysis, age (1.05 [95% CI 1.01-1.08]), smoking (3.76 [95% CI 1.44-9.83]) and previous ulcer (5.28 [95% CI 1.70-16.38]) were the major risk factors identified.

**Discussion**: The lack of significant association between new amputation and some traditional risk factors surprised us. Most of patients were men; however sex was not a statistically significant risk factor. Similar to other studies, diabetic neuropathy was present in almost all patients. Nor neuropathy nor peripheral arterial disease were predictors for amputation. We believe the lack of use of therapeutic shoes could increase incidence of amputation in our patients.

**Conclusion**: The most important risk factors for a new amputation were history of previous ulceration, smoking and age. Patients with the above-mentioned profile should be considered at very high risk and followed closely.

Abstract #248

**MODY MASQUERADING AS DIABETES TYPE 1**

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University of Buffalo, State University of New York

**Objective**: To present a case of MODY 3 (Maturity onset Diabetes of the young).

**Case Presentation**: A 23 year old woman presented for evaluation of Diabetes. She was diagnosed with Diabetes type 1 at the age of 12 when hyperglycemia without ketoacidosis was found. She was reluctant to medical therapy; hence was only on dietary modifications for four years after diagnosis. Later, due to progressive hyperglycemia, Lantus and Humalog insulin were started. Her great grandmother had diabetes type 2. Home blood glucose readings were 80-120 mg/dl with hypoglycemias once to twice weekly. C-peptide was 0.5 ng/ml (0.8-3.1) with plasma glucose of 67mg/dl and negative GAD-65, IA-2 and Insulin Antibody. HbA1c ranged between 5.1%-6%. Humalog was discontinued and she was started on Glipizide 5mg daily. Her hypoglycemias persisted, hence Lantus was stopped and Glipizide was halved. She was suspected to have MODY and genetic testing revealed a mutation in the HNF-1 genes.

**Discussion**: MODY 3 is caused by mutations of HNF1-α gene (Hepatocyte nuclear factor 1). It is located on chromosome 12 and highly expressed in the liver. It is a transcription factor (TCF1) important for differentiation
of beta cells, mutations of which lead to qualitative and quantitative beta cell dysfunction. Overall prevalence of MODY is 1-5% cases of diabetes. MODY is often initially misdiagnosed as type 1 or type 2 Diabetes. Its distinction is important to determine treatment. It is differentiated from them by absence of ketoacidosis and obesity. Genes have autosomal dominant inheritance. Mutations in HNF-4α and HNF-1β cause MODY 1 and 5 respectively. Mutations in Glucokinase gene (MODY2) causes permanent neonatal DM-2. Patients usually have low insulin requirements and a strong family history of diabetes. It usually presents in childhood or adolescence. MODY 5 has progressive hyperglycemia, renal abnormalities, genital malformations and premature risk for microvascular complications. MODY 1, 3 and 4 respond to sulfonylureas but over time insulin may be required. MODY 2 can be managed by diet and exercise alone. Relatives should be screened for mutations and if present, monitored for development of diabetes.

**Conclusion:** Younger adults presenting with hyperglycemia should be evaluated with genetic testing for MODY if reasonable suspicion exists in the setting of minimal insulin requirements and a strong family history of Diabetes. MODY usually affects each generation in the family due to its autosomal dominant inheritance. Our case however is unique since three generations were skipped prior to the patient being diagnosed with MODY.

**Abstract #249**

**NISSEN FUNDOPICATION: NOVEL TREATMENT FOR POORLY CONTROLLED TYPE 2 DIABETES**

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University of Utah

**Objective:** Nissen fundoplication is the most common procedure to treat gastroesophageal reflux. Obesity predisposes people to reflux and type 2 diabetes. Post-operative hypoglycemia has been described following fundoplication among patients without diabetes. Resolution of hyperglycemia and type 2 diabetes has been described following roux-en-y gastric bypass surgery but not following Nissen fundoplication.

**Case Presentation:** A 59-year-old female with a 12-year history of poor glycemic control (HbA1c 9.6%) and large insulin requirements (1.6-2 units/kg/day) returned for management of type 2 diabetes. She had a Nissen fundoplication two months prior and noted dramatic improvement in self-monitored blood glucose (SMBG) values. Glucometer download revealed abrupt change in mean SMBG from 250 to 150 mg/dl the day after surgery. Two months post-op, her HbA1c improved to 7.4% and she lost 9 lbs. Four months later, she had lost an additional 17 lbs with HbA1c down to 6.4%. Her insulin requirement decreased (1.08-1.25 unit/kg/day), as did her mean SMBG (100 mg/dl). She reported no GI complaints or hypoglycemia.

**Discussion:** Dumping syndrome, a frequent complication of gastric surgery, is thought to be related to rapid gastric emptying leading to delivery of undigested solid food to the small intestine. Early symptoms of dumping syndrome are primarily gastrointestinal complaints, including pain, borborygmi, and nausea. Late symptoms occur 1-3 hours after food intake and have been ascribed to reactive hypoglycemia mediated by excessive insulin release in response to glucose in the jejunum. Dumping syndrome is more common in children following Nissen fundoplication. Weight gain is expected following surgery due to intake of previously reflux-precipitating foods. Case series have described post-operative weight loss attributed to post-operative dietary modification, early satiety, and altered gastric emptying. Additionally, intestinal L cells secrete GLP-1, stimulating glucose-dependent insulin release and inhibiting glucagon release/gastric emptying. Augmented secretion of GLP-1 has been proposed as the mechanism underlying resolution of hyperglycemia following gastric bypass surgery. Increased secretion of GLP-1 following fundoplication procedures has also been described in case series.

**Conclusion:** This case illustrates the impact that Nissen fundoplication can have on hyperglycemia, weight and diabetes in some patients. Glycemic improvements cannot be ascribed solely to weight loss as the trending toward euglycemia preceded weight loss by weeks to months. The resolution of hyperglycemia seen in this patient may have been mediated by accelerated gastric emptying, which led to increased GLP-1.
Abstract #250

PREVALENCE OF CHRONIC COMPLICATIONS OF TYPE 2 DIABETES MELLITUS AT THE TIME OF DIAGNOSIS

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Objective: To study the prevalence of micro and macrovascular complications in newly detected type 2 diabetes mellitus and evaluate fasting blood glucose, HbA1c, Insulin levels, urine microalbumin, homocysteine levels and correlate these with clinical profile of type 2 diabetes mellitus patients

Methods: All patients who were presented to clinic for the first time either for symptoms of diabetes mellitus or found to have hyperglycemia on routine examination/work up for other ailments as per WHO criteria. Detailed history and work up done to identify micro and macrovascular complications at onset

Results: 75 subjects were diagnosed to have new onset diabetes at presentation in a limited study conducted to ascertain the prevalence of chronic complications of type 2 diabetes mellitus. Of them 53.3% were detected incidentally and younger group was found to have osmotic symptoms at presentation. Diabetes in elderly patient was found incidentally and have more macrovascular complications. Microvascular complications like incipient nephropathy and retinopathy were found to have 11.8% and 4% respectively. 26.6% had hypertension already at the time detection and 17.3% presented for the first time at diagnosis of new onset diabetes. 15%,4%,1.3% subjects were found to have ischaemic heart disease, peripheral vascular disease and cerebrovascular disease at presentation. In addition 44% of all subjects were found to be insulopenic at diagnosis.

Discussion: The analysis has shown that diagnosis of diabetes was more incidental than presentation with osmotic symptoms and it was evident more in elderly diabetics who also have more macrovascular complications. Microvascular complications like incipient nephropathy and retinopathy were found to have 11.8% and 4% respectively. 26.6% had hypertension already at the time detection and 17.3% presented for the first time at diagnosis of new onset diabetes. 15%,4%,1.3% subjects were found to have ischaemic heart disease, peripheral vascular disease and cerebrovascular disease at presentation. In addition 44% of all subjects were found to be insulopenic at diagnosis.

Conclusion: Chronic complications were detected at time of diagnosis of type 2 diabetes mellitus and the high prevalence necessitate to incorporate screening methods during clinical examination at the time of diagnosis. Contrary to western countries, lean and normal weight diabetics were more common. Normal weight diabetics are insulopenic. Chronic insulin insufficiency and asymptomatic hyperglycemia state exists before the diagnosis. In this limited study, the prevalence of hyperhomocystenemia and hyperglycemia at diagnosis may serve as a marker for development of chronic complications, possibly due to the mechanism of injury to vascular endothelium by homocysteine.

Abstract #251

AWARENESS AND USE OF CONTINUOUS SUBCUTANEOUS INSULIN INFUSION THERAPY AMONG PATIENTS WITH DIABETES IN NORTH INDIA

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Objective: To find out the awareness, knowledge and acceptance of continuous subcutaneous Insulin infusion (CSII) therapy among patients with diabetes in rural and urban North India.

Methods: This is a cross-sectional study over a period of one month from an Endocrine clinic. 34 Diabetic patients, 17-males (M) & 17-females (F) on MSI (Multiple Subcutaneous Insulin) were included in the study. Data was collected using uniform questionnaire regarding the awareness, knowledge and acceptance of CSII. There were 13 Type 1 Diabetes (T1D) & 21 Type 2 uncontrolled brittle Diabetes (T2D) in the study. 13 patients belonged to the urban areas of north India, while others were from the surrounding rural areas. Patient’s detailed clinical history, physical examination, BMI, Lab biochemistry, HbA1C, history of hypoglycemic episodes, diabetes complications, history of hospitalization & its frequency, treatment history, economic status, education status of the patients & parents in case of children and their internet usage was also recorded and analyzed during the study.

Results: Only 1 out of 34 (3%, T1D, F) patients was aware and had knowledge of CSII therapy for Diabetes management. 8 out of 34 (24%) patients started using CSII therapy (T1D-13% & T2D-87%; M-25% & F-75%). 6 out of 34 (18%) patients planned to use CSII therapy (T1D-83% & T2D-17%; M-50% & F-50%) within 4-12 weeks and 20 (59%) patients refused to use CSII therapy.
ABSTRACTS – Diabetes Mellitus/PreDiabetes

(T1D-25% & T2D-75%; M-60% & F-40%). The user group included patients with recurrent hypoglycemia (n=1), diabetic amyotrophy (n=1) and females planning for pregnancy (n=2).

Discussion: Despite India being labeled as the Diabetes capital of the world, insulin usage particularly CSII therapy is less than 1% and is much less in North India. CSII is the most physiological mode of Insulin delivery to the body. CSII has the ability to program changes in basal insulin dosage to maintain normal glycemic control before meals, during exercise and fasting. The bolus delivery significantly lowers the postprandial rise of glucose levels. In patients with recurrent hypoglycemia, hypoglycemic unawareness, gestational diabetes and chronic complications, CSII with sensor/CGM has proven to be a boon. Despite this, the usage is almost negligible in this part of the country. Our study attempts to find out the reason for the underusage of CSII.

Conclusion: Despite the poor knowledge of CSII (3%), the acceptance of CSII was comparatively high (42%). The barriers identified for acceptance of CSII during this study are - lack of awareness (100%), cost (50%), and inconvenience to use the device (50%). There was no difference in the acceptance of the CSII therapy among Diabetes patients from rural and urban area.

Abstract #252

CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF PATIENTS HOSPITALIZED FOR DIABETIC FOOT IN DOS DE MAYO HOSPITAL, LIMA-PERU

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Dos de Mayo Hospital

Objective: In a previous study developed between 1989 and 1997, it was found that 61.17% out of 206 patients (mean age 61.4 years) underwent amputation. It was perceived that the characteristics of diabetic foot patients and the therapy received have changed over the past few years. The objective of this study was to describe epidemiological and clinical characteristics of patients hospitalized due to diabetic foot in Dos de Mayo Hospital between January 2006 and July 2010.

Methods: Cross-sectional study. We reviewed the medical records of patients hospitalized for diabetic foot from January 2006 to July 2010, requesting information on the type of surgical treatment received, the presence of peripheral neuropathy, peripheral arterial disease and other clinical and epidemiological history. The review covered the registration data of the variables in record for three months prior to hospitalization, during hospitalization and three months after hospitalization. Means, standard deviations and frequencies were described. Z-test and t-test were used to assess statistical significance.

Results: We evaluated 290 patients, 216 males (74.5%). Mean age was 58.4±11.7 years. The mean length of illness of diabetes was 12.2±8.1 years. 35.9% had a history of hypertension and 24.6% of dyslipidemia. 97 patients (33.7%) had a history of previous foot ulcer. 95.5% had diabetic neuropathy and 59.5% peripheral arterial disease (PAD). 89.7% had HbA1c above 7%. According to Wagner classification: 51.9% had grade 4 lesions, 30.9% in grade 3, 15.1 grade 2 and 1.1% in grade 5. The location of the lesion was 64.3% in the fingers, followed by 14.3% in the sole. 31.7% received only medical treatment, 19.5% required surgical scrub, the same percentage was minor amputation and 29.3% for major amputation. The mean hospital stay was 29.62 ± 17.7 days.

Discussion: We found that our diabetic foot patients were younger (mean age 58.4 years; 95% IC 57.2-59.9) compared to the previous study (mean age 61.4 years) (p<0.001). Additionally, 48.7% of patients underwent amputation (95% CI 42.8-54.7) which is significantly lower than the 61.17 % previously found (p<0.001)

Conclusion: Most patients hospitalized for diabetic foot were male. They were younger compared to the previous study. One quarter and one third of the patients had a history of hypertension and dyslipidemia, respectively. Furthermore, one third of the patients had a history of prior ulcer. The major component was neuropathy. More than half of the patients had lesions with areas of necrosis. About half of the patients required some type of amputation, a lower value to that described in previous studies.
Abstract #253

VALIDITY OF HBA1C TEST FOR DIAGNOSIS OF DIABETES AND PRE DIABETES AMONG BANGLADESHI PEOPLE

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Objective: Diabetes is an increasing epidemic in Bangladesh with more than 12% of the adult population affected by diabetes or pre diabetes. Early detection of diabetes and pre diabetes is the mainstay of prevention and control of the disease and it’s complication. There was no study to test the validity and performance of HbA1c test for diagnosis of diabetes and pre diabetes among Bangladeshi people. Objective of this study was to determine the accuracy, sensitivity and specificity of using HbA1c measurement as a diagnostic method for diabetes and pre diabetes in Bangladesh.

Methods: HbA1c test was done in total 878 subjects not previously diagnosed as diabetes or pre diabetes, by systemic random sampling method, who reported at tertiary care hospital (research center) for oral glucose tolerance test. The test was done by high performance liquid chromatography method in BIo-Rad D 10 system, France. The performance of HbA1c test was done with cut off value ≥6.5% for diabetes and 5.7 to <6.5% for pre diabetes.

Results: With oral glucose tolerance test, among the 878 subjects 48.7% was diagnosed as DM, 17.1% was diagnosed as Pre DM and 34.2% was diagnosed as normal. The performance of HbA1c test for diagnosis of DM with cut off value ≥6.5% showed the sensitivity of the test 85.52%, specificity 88.44%, positive predictive value 87.53%, negative predictive value 86.33% and accuracy 86.90%. The performance of HbA1c test for diagnosis of pr DM with cut off value 5.7 to <6.5% showed the sensitivity of the test 41.33%, specificity 79.67%, positive predictive value 29.52%, negative predictive value 86.82% and accuracy 73.12%.

Discussion: HbA1c has few advantages over oral glucose tolerance test. It does not require overnight fasting, can be done with a single sample and at any time of day and reduces the time of stay in hospital. It reflects chronic blood glucose values, has important role in initiating and guiding therapy during diagnosis and is used in monitoring glycemic control. But there is still limited availability of the test through out Bangladesh and lack of standardization in different laboratories. Moreover, the cut off point of HbA1c varied in different ethnic population. HbA1c also may be misleading in some conditions, such as hemoglobinopathies, hemolysis that alters erythrocyte life span.

Conclusion: HbA1c test has less sensitivity and specificity in labeling DM and pre DM with the current recommended cut off value so might not be able to replace OGTT at present. Further investigation of the validity of both tests in detecting and predicting diabetes and pre diabetes is needed to draw firm conclusions on the best diagnostic test in Bangladesh.

Abstract #254

AUDIT OF DIABETES CARE OF PATIENTS WITH END STAGE RENAL DISEASE ON MAINTENANCE HAEMODIALYSIS

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Objective: We sought to assess the quality of diabetes care of patients with end stage renal disease receiving haemodialysis at our hospital. The objectives included the assessment of glycaemic control, screening and management of diabetic complications and follow up.

Methods: This is a retrospective study of prevalent haemodialysis patients with diabetes at the Renal Unit of Luton and Dunstable Hospital. United Kingdom (n = 57). Patient data was collected from our diabetes database, clinic letters and laboratory data from electronic patient record. The measured variables included patients age, type of diabetes, treatment, HbA1c and fructosamine levels, Lipid and Blood pressure control, blood glucose monitoring, number of patients screened for foot problems and number of contacts with a diabetes educator in the last year.

Results: The mean age of patients was 62 years with a range of 32-80 years.16 % had Type 1 DM and 84 % had Type 2 DM.84 % of patients were on Insulin.92 % had their HbA1c checked in the last 6 months.12 % had both their HbA1c and fructosamine checked. The mean HbA1C was 61 mmol/mol (7.7 %) with a range of 34 -96 mmol/mol (5.3 - 10.9 %). 36 % of patients had an acceptable control with an HbA1c of less than 58 mmol/mol (7.5 %). 12 % had poor control with an HbA1c of >75 mmol/mol(9 %). 36 % of patients had an acceptable control with an HbA1c of less than 58 mmol/mol (7.5 %). 12 % had poor control with an HbA1c of >75 mmol/mol(9 %). 36 % were doing SMBG and 32% reported to have regular hypoglycaemic episodes usually during the dialysis days.28% did not have their feet examined in the last one year. The mean number of patient contact(s) with a diabetes educator for each patient was 1 (Range 0 -4).

Discussion: Despite the limitations associated with
HbA1c in patients on haemodialysis, it is still considered a reasonable measure of glycaemic control. We recommend that patients who have a normal serum albumin should have fructosamine checked at least 3 monthly along with an HbA1c to assess their glycaemic control, patients with altered albumin levels should continue to have their control assessed with an HbA1c. Foot lesions are the single most commonly mismanaged problem in patients with DM and associated renal disease. We emphasize that foot care should form an integral part of diabetes care of haemodialysis patients and patients with high risk feet should be regularly followed up by community podiatry team.

**Conclusion:** Diabetic patients with ESRD on haemodialysis have special needs and are at an increased risk of co-morbidities and complications that can lead to increased hospital admissions. We suggest that they are best managed in a multidisciplinary diabetic-renal clinic setting, using the skills of diabetologists, nephrologists, clinical nurse specialists in diabetes and nephrology along with dietitians and podiatrists.

Abstract #255

**A GROWING TREND BY PATIENTS WITH DIABETES TO RESORTING TO TATTOOS AS MEDICAL ALERTS**

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**Objective:** We recently reported case studies and review articles on several patients with diabetes who elected to replace wearable metal medical alerts with permanent tattoos. Despite the scarcity of similar cases published in the medical literature, an internet search indicates a growing trend towards this medical alert alternative amongst patient with diabetes. No practice guidelines have been published to educate patients and clinicians about this personal option. Such guidelines are warranted in view of health risks associated with tattooing. We present an additional case of medical tattooing in the hopes of drawing more attention to this growing trend.

**Methods:** A case presentation.

**Case Presentation:** A 26 year old healthcare professional student with type 1 diabetes, followed in our diabetes center, decided on his own to have a permanent tattoo on his wrist, depicting a traditional medical alert with the six-pointed “Star of Life”, the “Snake-Staff” and the words “Type 1 Diabetes”. Elaborating on the motivation behind getting the tattoo, he cited frustration having broken numerous metal necklaces and bracelets, with the accruing cost of the metal alerts, especially the jewelry types. His diabetes control was optimal prior to getting the tattoo, he used a licensed tattoo parlor, and he had no complications from the tattooing.

**Discussion:** This is an additional case we report on patients with diabetes resorting to medical alert tattoos, in addition to few other cases we encountered that have not been published or presented. Furthermore, the internet is full of discussions about medical alert tattooing amongst patients with diabetes and their families. Despite papers we published about this issue to attract attention of medical organizations to this growing trend, no clinical practice guidelines addressing this piece in diabetes management have been published. Due to health risks related to tattooing, it is prudent that diabetes organizations address this emerging phenomenon. Tattooing is a minor surgical procedure, and patients with diabetes are vulnerable to infection and poor healing if their sugars are not optimally controlled. Standardization of the technique is also prudent so emergency personnel and first responders can be familiarized with these emerging medical alerts (e.g., location of the tattoo). Furthermore, regulation of tattooing is mandatory in view of the risk of transmission communicable diseases if proper hygiene practice is not applied.

**Conclusion:** In view of the growing trend of patients with diabetes to resorting to medical alert tattooing, diabetes organizations should address this practice, in terms of regulation and standardization.

Abstract #256

**A BRIEF EDUCATIONAL INTERVENTION TO IMPROVE MEDICAL INTERNS’ KNOWLEDGE OF MANAGEMENT OF HOSPITALIZED DIABETIC PATIENTS**

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**Objective:** To assess medical interns’ knowledge of current approaches to management of diabetes mellitus (DM) and general medicine in hospitalized patients. We evaluated the impact of an educational intervention on interns’ knowledge of inpatient DM management.

**Methods:** We developed a 19 item questionnaire and administered it to interns as a pretest at the beginning of their internal medicine residency. Eleven questions tested inpatient diabetes management and 8 questions tested general medical conditions frequently encountered in hospitalized patients. In addition to routine teaching rounds on the wards, two didactic lectures on DM management
in hospitalized patients were presented during the first 4 months of training. The same questionnaire was administered 5 months later as a post test. A two-tailed t-test was used for statistical analysis.

**Results:** A total of 33 interns participated in the study. In the pretest, mean DM test scores were significantly lower than general medicine test scores [46% vs 81.75%, p<0.0001; 95% CI -2.40 to -0.86]. In the post test there was significant improvement in the DM test scores [60% vs 46%, p <0.0001; 95% CI 1.10 to 2.35] but no change in the general medicine test scores [81.75% vs 84%, p =0.46; 95% CI -0.36 to 0.79]. There was no significant difference between international and American medical graduates’ performance in both pre and post tests.

**Discussion:** DM in hospitalized patients is frequently a secondary diagnosis and poor glycemic control is associated with increased morbidity and mortality. In teaching hospitals, house staffs commonly bear primary responsibility for implementing DM management. In our study, medical interns’ knowledge of inpatient diabetes care improved by 14% with educational intervention. Improved diabetes control in hospitalized patients results in substantial cost savings. A major limitation of this study is that this is a single center study involving only medical interns.

**Conclusion:** The results demonstrated greater gaps in new interns’ knowledge in several major areas of inpatient diabetes management compared to general medicine. We have found that developing a brief set of lectures has provided significant improvements in the knowledge of diabetes care. Whether this would correlate with actual improvement in clinical practice of DM in hospitalized patients has not been studied.

**Abstract #257**

**IMPAIRED FASTING GLUCOSE (IFG) AS A RISK FACTOR FOR CORONARY ARTERY DISEASE (CAD) COMPARED TO DIABETES MELLITUS (DM) AND NORMAL BLOOD SUGAR IN ASSOCIATION WITH OTHER CAD RISKS**

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**Objective:** To identify the contribution of IFG as a risk for CAD compared to DM and normal blood sugar patients in association with other CAD risk factors.

**Methods:** In a descriptive analysis study, 85 patients’ charts were reviewed for adults who had elective PCI. We identified the age, number, gender, and number of risk factors associated with impaired fasting glucose in those patients. Out of 85 patients, we calculated the percentage of association of normal blood sugar, DM and IFG with HPL, HTN, and family history of CAD and smoking.

**Results:** 19 (22%) of them have normal blood sugar, 29 of them have impaired fasting glucose (34%) and 35 of them have diabetes (41%). The mean age for normal blood sugar patients is 65, for IFG patients it is 66 and for DM patients it is 68. Those who have HPL have an association with normal blood sugar of 20(20%), with IFG is 31(36%) and with DM of 32 (37%). In HTN patients, 15 (17%) have normal blood sugar, 25 (29%) have IFG and 29 (34%) have DM. In the family history of ACS patients, 7(8%) have normal blood sugar, 11(12%) have IFG and 9(10%) have DM. In patients with a history of smoking, 10(11%) have normal blood sugar, 11(12%) have IFG and 15(17%) have DM. The risk of CAD increases with increasing blood sugar. Double the number of patients with IFG and DM have CAD compared to normal blood sugar. The risk of CAD with HPL increases significantly with both IFG and DM compared to normal blood sugar patients. The risk of CAD with HTN doubled with both IFG and DM patients compared to normal blood sugar patients. The risk of CAD with family history of CAD increases with increasing blood sugar. Double the number of patients with IFG and DM have CAD compared to normal blood sugar. The risk of CAD with smokers increases with increasing blood sugar.

**Discussion:** Impaired fasting glucose has been described to be a risk factor for CAD. Glucose levels in non diabetics have been linked to the prognosis of CAD. IFG have been noted to cause extensive CAD. Our study is aiming at evaluating the impact of IFG as a risk factor for CAD compared to normal blood sugar and diabetic patients in association with other CAD risk factors. This study looks at how CAD risk changes with adding IFG and DM to other risk factors.

**Conclusion:** It is recommended to aggressively treat impaired fasting glucose patients since it has comparable risk factors for CAD compared to DM, which is double the risk compared to normal blood sugar patients especially in association with HPL and HTN.
Abstract #258

DIABETES FORWARD: A COMPARISON OF SOURCES OF REAL-WORLD DATA ON TYPE 2 DIABETES IN PRIMARY CARE

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Objective: Patients with type 2 diabetes (T2DM) receive the majority of their treatment within primary care; however, there is a lack of focused real-world data from this setting. Diabetes FORWARD (Foundation of Real-World Assessment and Research in Diabeties) is a large practice-based research network (PBRN) wherein the dataset is currently being compiled using Electronic Health Records (EHR) throughout North America. Here, we aim to establish whether the current dataset is a representative sample by comparing it with previous studies.

Methods: Demographic and clinical characteristics were compared descriptively between the Diabetes FORWARD (DF) dataset (March 2012 to October 2012) and 3 other studies containing data on T2DM in the US primary care setting: the Diabetes Outcome Study (DOS; February 2001 to April 2002); the National Interdisciplinary Primary Care (NIPC) PBRN (January 1, to June 30, 2008); and the National Health and Nutrition Examination Survey (NHANES) 2003 to 2006.

Results: A total of 935 patients were enrolled in DF as of September 2012, compared with 822 for DOS, 1,309 for NIPC, and 889 for NHANES. The race distribution of study participants was similar between studies (77.9%, 71.4%, 68.1%, and 68.3% Caucasian, respectively). Proportions of coverage from either private insurance (47.4% vs 30.6%) or Medicare (39.8% vs 31.5%) were higher in DF than NHANES, likely due to more individuals with no coverage in NHANES. Mean age [SD] was similar in the DF, DOS, NIPC and NHANES studies (59.8 [12.0], 59.5 [13.1], 58.3 [13.5], and 60.6 [not available] years, respectively). Approximately 45% of patients in all studies were male (43.6%, 44.5%, 44.2%, and 46.2%, respectively). More patients in DF were obese than in DOS and NHANES (69.7%, 53.4%, and 56.9%, respectively, ≥ 30kg/m²). Mean duration [SD] of T2DM was higher in the DF study than in the DOS study (10.9 [8.6] vs 9.1 [8.7] years). Approximately 20% of patients used insulin in the DF, DOS, and NHANES studies (18.6%, 22.7%, and 22.9%, respectively).

Discussion: At this early stage of recruitment, the DF PBRN data show good comparability with data from primary care sources. The increase in diabetes duration and level of obesity seen in the DF population, in comparison with earlier studies, may be explained by changing demographics over time.

Conclusion: DF shows similar demographic and clinical characteristics to T2DM subsets taken from previous primary care data sources. DF is likely to provide a representative data source for future real-world comparative effectiveness research into T2DM.

Abstract #259

SUCCESS OF A COMMUNITY BASED SCREENING AND INTERVENTION PROGRAM FOR TYPE 2 DIABETES

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EVMS

Objective: The burden of Type 2 Diabetes (T2DM) is increasing in the United States at an alarming rate; fueled by the concomitant epidemics of obesity and sedentary lifestyle. Within Virginia, the prevalence of T2DM in the Western Tidewater health service area (WTSA) approaches 20%, far exceeding both state and national averages (8%). Mortality from diabetes is also overrepresented in the WTSA. Lessons from the Diabetes Prevention Program suggest small changes in weight, activity and food choices can result in a significant decline in the progression from prediabetes to T2DM. In an effort to slow the expanding pool of patients with T2DM, a community-based diabetes screening program was designed to identify persons at risk for T2DM and cardiovascular disease and then enroll them into a telephone lifestyle management program (TLMP).

Methods: Individuals received general diabetes education and were assisted in selecting a personal goal (e.g. decrease in carbohydrates, increase in walking). On average each participant was contacted 3 times over 6 months.

Results: 1100 persons age > 18 years were offered screening for prediabetes or T2DM with point of care HbA1c tests (Afinion™) and cardiovascular risk assessed by measurement of blood pressure, body mass index, and lipids (Cholestech LDX®). Screenings were offered at community events, churches, schools and similar venues. Persons identified with an HbA1c > 6% where then invited to participate in a telephonic lifestyle management intervention conducted by a certified diabetes educator (CDE). The participants were primarily African-american (60%) with genders equally represented. The majority of participants were either overweight or obese (68%) with...
almost half (44%) found to have either prediabetes or T2DM as stratified by HbA1c. Approximately 50% of the identified subjects at risk participated in the TLMP. Self-efficacy scores regarding general knowledge of diabetes were obtained at the beginning and conclusion of the TLMP. Participants uniformly improved their efficacy scores.

Discussion: Screening for T2DM in communities at high risk for cardiovascular mortality identifies and engages persons with prediabetes in adoption of therapeutic lifestyle change.

Conclusion: In a community, with a known high prevalence of T2DM and cardiovascular mortality, a screening program coupled with an efficient phone management intervention was able to empower individuals at risk for cardiovascular disease to be successful in lifestyle interventions. TLMP was well accepted by participants and delivered at a low cost. Analysis of participants enrolled in the TLMP in improving HbA1c, lipids and blood pressure are ongoing.

Abstract #260

COMPARISON OF VARIOUS METHODS FOR EVALUATION OF DIABETIC PERIPHERAL NEUROPATHY

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Objective: To evaluate the discriminative power of the symptom screening questionnaire [Michigan Neuropathy Screening Instrument (MNSI)], monofilament test and tuning fork examination as compared with the vibration perception threshold testing in the assessment of Diabetic Peripheral Neuropathy (DPN).

Methods: All consecutive patients with Type 2 Diabetes Mellitus (DM) seen over a 6-month period in the University of Benin Teaching Hospital, Benin City, Nigeria were recruited for the study. Questionnaires were administered to the subjects to obtain socio-demographic and clinical and laboratory information. The Michigan Neuropathy Screening Instrument was used for symptom screening of diabetic peripheral neuropathy, while the Biothesiometer was used as the Gold standard for diagnosing diabetic peripheral neuropathy, against which other methods (Monofilament, 128Hz tuning fork and Symptoms) were compared.

Results: A total of 609 persons with Diabetes Mellitus were screened during the 6-month period. The prevalence of DPN was 52.5% with VPT. The symptoms of neuropathy were present in 71.3% of subjects while 45% and 42.8% of the subjects studied had impaired sensation to light touch using the 10g monofilament and impaired tuning fork tests respectively. When compared to the VPT, the 10-g monofilament had the highest specificity of 84.2% while symptoms had the highest sensitivity of 94.1% with the lowest specificity of 53.3%. Tuning fork on the other hand had a sensitivity and specificity of 63.7% and 80.3% respectively.

Discussion: Diabetic neuropathy is the most common long term complication of diabetes mellitus while DPN is the most common form of diabetic neuropathy. Screening for DPN is therefore very important the management of persons with DM, which makes selecting in-expensive, quick and accurate instruments essential in very busy diabetic clinics. Biothesiometry was used as gold standard in his study against which other methods were compared. The sensitivity and specificity of the 10-g monofilament as well as the tuning fork were high and comparable to other studies.

Conclusion: The use of monofilament and the tuning fork to examine for DPN are strongly recommended as simple and cheap bedside tests in clinical practice particularly in resource challenged countries.

Abstract #261

ASSESSING A NOVEL DIABETES NURSING PRE-VISIT IN A COMMUNITY HEALTH CENTER

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Objective: To assess effects of a novel electronic medical record (EMR) based Diabetes Nursing Pre-visit on clinical data collection in a Federally Qualified Community Health Center (FQHC).

Methods: We developed EMR based visit templates, electronic order sets and referrals to include: instruction in home glucose monitoring (HGM) and nutrition, bundled labs (HbA1c, creatinine, urine microalbumin, lipids), eye exam referrals, and immunization status. During a seven-month pilot (4/12-11/12), 116 diabetics (ages 18-75) were selected by diagnosis, with preference for those with HbA1c > 9%, or those who had no HbA1c measured in > 1 year. Patients in this group had a no-fee visit with a nurse (Pre-visit) about 1-2 weeks before seeing their primary care clinician to address diabetes management. The percentage of patients with the standard diabetes
measures completed was calculated and compared to the diabetes population with no pre-visit during the same time period.

**Results:** In the pilot group, 91% (vs 69% control) of patients had HbA1c performed, 84% (vs 48%) urine microalbumin, and 77% (vs 33%) referral for eye exam. All patients with a Diabetes Pre-visit were instructed in HGM and nutrition. Every measure (additional data to be discussed) was higher in the Pre-visit group compared with control. Clinicians indicated that the Pre-visit improved point of care diabetes management and could promote patient connection to the healthcare system by using the team care approach.

**Discussion:** Our novel EMR integrated Diabetes Pre-visit shows promise in improving acquisition of standard measures of diabetes care in our population. Diabetics at FQHCs often have significant care barriers and don’t consistently engage healthcare resources. Our Pre-visit, part of an overall Diabetes Quality Improvement Program, focuses on testing, referrals and immunizations and utilizes electronic resources for data collection. Having relevant clinical data available may aid point-of-care clinical diabetes management by primary care clinicians.

**Conclusion:** Diabetes Nursing Pre-visits (with EMR integrated templates, order sets and referrals) increased the availability of patient data for review by primary care clinicians at the point of care.

**Abstract #262**

**DETERMINANTS OF GLUCOREGULATORY PARAMETERS IN NORMOGLYCEMIC OFFSPRING OF DIABETIC OR NON-DIABETIC PARENTS**

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**Objective:** Progression from prediabetes (PD) to diabetes has been studied, but the trigger for escape from normoglycemia to PD remains unclear. Offspring of diabetic parents and ethnic minority groups have unexplained predilection to T2DM and the mechanism for progression to PD remains unclear. Therefore, we investigated glucoregulation in African-Americans (AA) and Caucasians (C) with or without parental diabetes; hypothesizing that heredity would permit detection of early defects in euglycemic subjects.

**Methods:** A hundred offspring of non-diabetic parents were matched for age, gender, race and BMI with offspring of diabetic parents. Subjects underwent 75 g OGTT, with blood sampling at 0, 30 and 120 minutes after ingestion of glucose. Glucose and insulin levels were measured. Insulin resistance (IR) was assessed by HOMA-IR (H-IR), QUICKI (QI) and Matsuda Index (MI). Insulin secretion (IS) was evaluated by HOMA-B (H-B) and insulinogenic index (II). Data were analyzed using t-test, Chi square and logistic regression.

**Results:** Offspring of diabetic parents had higher IR: H-IR (1.46 ± 0.09 vs 1.0 ± 0.14, P<0.01); QI (5.19 ± 0.03 vs 5.57 ± 0.04, P<0.0001) and MI (8.03 ± 0.56 vs 11.72 ± 0.72, P<0.0001) and increased basal and dynamic IS: fasting insulin (6.5 ± 0.4 vs 4.6 ± 0.6, P<0.01); H-B (87.5 ± 4.9 vs 63.2 ± 7.5, P<0.01); II (1.5 ± 0.2 vs1.0 ± 0.1, P<0.05). Obesity and parental diabetes conferred higher IR and IS. Compared with non-obese offspring of non-diabetic parents, non-obese offspring of diabetic parents had 1.84-fold increase in IR; obese offspring of non-diabetic parents had 2.2-fold increase in IR, while obese offspring of diabetic parents showed 2.7-fold higher IR. BMI was a stronger predictor of IR and IS than parental diabetes P<0.0001 vs P<0.01. Race predicted FPG with AA having lower FPG than C (88.4 ± 6.4 vs 90.8 ± 5.5 mg/dl, P<0.001).

**Discussion:** Offspring of diabetic parents had higher IR with compensated IS and normal DI. Elevated IR and defective IS has been reported in T2DM; but we have shown that defects in insulin action and secretion are evident in the normoglycemic phase in high risk subjects. Obesity exerted a stronger influence on glucoregulation than parental diabetes, indicating early influence of environmental factors in the pathogenesis of T2DM. Lower FPG in AA was unexpected; its etiology is unclear and deserves further study.

**Conclusion:** Normoglycemic offspring of diabetic parents exhibit diminished insulin action and compensatory insulin secretion. These may represent the earliest demonstrable defects in the evolution of dysglycemia in high risk subjects. Obesity and heredity affect glucoregulation in euglycemic subjects.
Abstract #263

CORRELATION BETWEEN ENDOTHELIAL DYSFUNCTION MARKERS AND ADIPOCYTOKINES IN TYPE 2 DIABETIC PATIENTS

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Objective: We hypothesized there may exist a correlation between the plasma levels of von Willebrand factor, thrombomodulin, and tissue plasminogen activator antigen (tPAag) as markers of endothelial cell dysfunction and the adipocytokines, visfatin and resistin in patients with type 2 diabetes.

Methods: Patients (n=212) with type 2 diabetes and matched controls (n=211) were included. Patients differentiated by age and diabetes duration time with normal blood pressure and hypertension were included into the research.

Results: The concentrations of von Willebrand factor, thrombomodulin and tPAag in plasma were significantly higher in type 2 diabetic patients as compared to healthy subjects (p<0.001, p<0.05 and p<0.01, respectively). The patients also had significantly higher concentrations of visfatin and resistin compared to healthy controls (p < 0.01 for both comparisons). There were strong correlations between the concentration of visfatin and von Willebrand factor in patients with type 2 diabetes (r=0.51, p<0.01), between the concentration of thrombomodulin and resistin (r=0.61, p<0.001), and between tPAag and visfatin (r=0.57, p<0.05). Furthermore, a negative correlation was observed between the concentration of thrombomodulin and the cell surface expression of CD11b on monocytes and granulocytes in the peripheral circulation (p<0.05 in both cases).

Discussion: Diabetes causes the development of atherosclerotic vascular changes. Inflammatory mediators released by the adipose tissue can lead to local insulin resistance and endothelial dysfunction.

Conclusion: The strong correlation between markers of endothelial dysfunction and adipocytokines in type 2 diabetic patients strengthen the view that an ongoing stress on endothelial cells is present in these patients. These results suggest that increased resistin and visfatin levels in diabetes mellitus may be novel biochemical risk factors for cardiovascular complications, providing a pathophysiological link between inflammation from adipose tissue and early vascular alterations.

Abstract #264

IMPACT OF TIME TO TREATMENT INTENSIFICATION WITH ORAL ADD-ON DRUG ON GLYCEMIC GOAL ATTAINMENT AMONG DIABETIC PATIENTS FAILING METFORMIN THERAPY

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Objective: Patients with type 2 diabetes on metformin monotherapy frequently require treatment intensification with another anti-hyperglycemic drug over time. Previous studies have indicated that a high proportion of patients with diabetes have a significant delay in the initiation of oral add-on therapy after metformin alone fails to achieve targeted glycemic control. In this study, we evaluated the impact of the timing of treatment intensification with oral add-on drug on glycemic goal attainment among diabetic patients failing metformin monotherapy.

Methods: Using the General Electric (GE) Centricity Electronic Medical Record database (January 2004 through December 2009), we identified 8,663 patients with type 2 diabetes with treatment failure on metformin monotherapy - defined by a glycosylated hemoglobin of ≥7.5% (index date). This cut-off of ≥7.5% (trigger HbA1c) was chosen rather than that of >7.0% to ensure that selected patients were more likely to be indicated for a treatment intensification with add-on drug. Continuous enrollment of one year prior and two years after index date was required to be included in the study. Add-on treatment was defined as prescription of 2nd oral agent from any available therapeutic classes while continuing metformin. Early treatment intensification was defined as initiation of oral add-on therapy within 3 months (n=1,251) of index date while late intensification was defined as add-on initiation between 10-15 months after index date (n=505). The study outcome was defined as glycemic goal attainment (HbA1c<7%) which was evaluated between 18-24 months after index date.

Results: Our results suggested that at the end of follow-up period, 46% of patients in early add-on group were at glycemic goal compared to 40% in the late add-on group (p=0.039). In a multivariable logistic regression model that accounted for age, gender, trigger HbA1c level, Charlson comorbidity score, anti-hypertensive and anti-hyperlipidemic drug use and history of cardiovascular disease, the adjusted odds ratio (OR) for glycemic goal attainment was 1.37 (95% confidence intervals [CI]: 1.11-1.71) comparing early add-on to late add-on treatment. This association was stronger among patients with higher
trigger HbA1c at baseline; ORs of 1.49 (95% CI: 1.07-2.09) for HbA1c ≥8% and 2.34 (95% CI: 1.28-4.54) for HbA1c ≥9%.

Discussion: Future studies should evaluate whether earlier treatment intensification is also associated with longer term health outcomes such as risk of microvascular and macrovascular complications.

Conclusion: These results suggest that earlier use of oral add-on drug in treatment regimen helps achieve better glycemic goal attainment in patients with metformin failure.

Abstract #265

ATTENUATION OF INCIDENTAL AND INDUCED HYPOGLYCEMIA BY MEANS OF INSULIN SUSPENSION: REVIEW OF PUBLISHED STUDIES

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Objective: Several published studies suggest that automatic suspension of insulin delivery in the face of sensor-detected hypoglycemia (Threshold Suspend) is safe and can lessen the incidence, severity, and duration of hypoglycemia.

Methods: Three prospective studies (Ly 2011, Danne 2011, Choudhary 2011) and one retrospective study (Agrawal 2011) of Threshold Suspend’s effects on incidental hypoglycemia and one prospective study of its effects on clinically-induced hypoglycemia (Garg 2012) were identified. Results of these studies are summarized.

Case Presentation: Of the prospective studies, Ly studied 24 adults and children (mean age 17.4 years) for 6 months; Danne studied 21 children and youth (mean age 10.8 years) for 6 weeks, Choudhary studied 31 adults (mean age 41.9 years) for 3 weeks, and Garg studied 50 adults for 2 episodes of clinically-induced hypoglycemia. Agrawal retrospectively studied data from 935 patients, 278 of whom used the pump for ≥3 months. The pump suspension threshold was set anywhere from 43 mg/dL (Choudhary) to 70 mg/dL (Danne) but most commonly between 50-60 mg/dL (Agrawal). Suspension event rates were between 1.9/week (Choudhary) to 1.3/day (Ly). Most pump suspension events lasted for <10 min in the studies of incidental hypoglycemia. Significant reductions in the number and/or duration of hypoglycemia (SG<70 mg/dL) with threshold suspend use were noted by Danne, Agrawal, and Garg (all P<0.05); Choudhary noted significant reduction in nocturnal hypoglycemia in those at greatest risk (P=0.02).

Discussion: In published reports to date, Threshold Suspend significantly reduced the number, severity, and/or duration of hypoglycemic excursions, whether measured by sensor glucose values or a reference instrument. The risk of severe rebound hyperglycemia resulting from long-duration pump suspensions appeared negligible. The observed attenuation of severe hyperglycemia (Agrawal) may have been attributable to fewer episodes of excessive carbohydrate intake prompted by symptomatic hypoglycemia.

Conclusion: Threshold Suspend is an important step towards a closed-loop diabetes management system and decreases the burden of hypoglycemia in type 1 diabetes.

Abstract #266

DIETARY HABITS AND FREQUENCY OF HYPOGLYCAEMIA IN DIABETIC PATIENTS ON SULPHONYLUREAS

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Objective: This was a cross-sectional study carried out in patients with type 2 diabetes treated with sulphonylureas. The aim was to assess the frequency of hypoglycaemia in them and its relationship with their dietary habits.

Methods: Patients with type 2 diabetes on follow-up at a tertiary facility in Enugu SE Nigeria and another hospital in Abuja Nigeria who had been on sulphonylureas for at least 6 months were recruited. Patients on insulin treatment were excluded. Interviewer-administered questionnaires were used to obtain demographic data and other information on their meal patterns including type and use of snacks and the frequency of episodes of hypoglycaemia.

Results: There were 33 males and 43 females with a mean age of 56.9 ± 9.3 years and mean duration of diabetes of 7.6 ± 7.0 years. The most common sulphonylurea used was Glibenclamide (80%) followed by Glimepiride (16.9%)
and Gliclazide (3.1%). Metformin was used concomitantly in 90.8%. Twice daily dosing of sulphonylureas was more common (64.9%). Only one patient on Glibenclamide was on maximal dose (20mg) and the most common total daily dose was 10mg (40.4%). Majority (89.1%) took their drugs half an hour before their meal. Sixty (78.9%) of the patients took 3 main meals daily while the rest took at least two meals regularly. The heaviest meal of the day was lunch in 44% followed by dinner in 34.7%. Between-meal snacks were taken in 52.6% of patients, mostly once a day before lunch. Though 26.3% of the patients reported having had at least one episode of hypoglycaemia, the frequency was mostly < 2-3x a week in 85% of them. Only 10 (1.3%) of the patients had been admitted in hospital for severe hypoglycaemia.

**Discussion:** Hypoglycaemia is the major limitation to the maximal use of drugs to achieve proper control of blood glucose in patients with diabetes. Sulphonylureas which are insulin secretagogues are reported to have high rates of hypoglycaemia. In developing countries, sulphonylureas are still widely used because they are cheaper and more readily available than the other oral agents. The frequency of hypoglycaemia in this study appears to be low. The habits of eating regular meals, having a heavy lunch after a morning dose of drugs and taking drugs with meals in majority of the patients may be responsible for this. In addition, twice daily dosing was more common and may have contributed to fewer episodes of hypoglycaemia.

**Conclusion:** The frequency of hypoglycaemia was low and may be due to good dietary habits and frequency of drug administration.

**Abstract #267**

**RATIO BETWEEN CYTOKINES WITH PRO-INFLAMMATORY ACTIVITY AND ANTI-INFLAMMATORY ACTIVITY IN SERUM OF PATIENTS WITH CHRONIC HEPATITIS C COMORBID WITH INSULIN RESISTANCE**

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**Objective:** To determine the pathogenic role in changes in the ratio of concentrations of tumor necrosis factor - alpha (TNF-alpha) and interleukin - 4 (IL-4) in the serum of HCV patients with the presence of the IR.

**Methods:** We observed 48 patients with chronic hepatitis C (39 men and 9 women) aged 24 to 40 years, with the presence of IR (Group 1 - 19 patients) and in absence of IR (group 2 - 29 patients). In addition to conventional clinical and laboratory findings of HCV, patients surveyed levels of TNF-alpha and IL-4 in serum using sets (UkrMedDon) by enzyme immunoassay analyzer STAT FAX 2100 (USA). Statistical processing of results was performed using the statistical software package «Statistica 8.0», and Microsoft Excel 2010.

**Case Presentation:** In the analysis of the level of TNF-alpha, we found that in group 1, there was significantly higher values than that of the control group by 6.1 times (90,4 ± 1,7 pg / ml: 14,9 ± 0,8 pg / ml, respectively; P <0.001 by Mann-Whitney), and significantly higher than in patients without insulin resistance (76,4 ± 2,1 pg / ml; P <0,001). Analyzing the level of IL-4, we found that in the presence of IR, level of this cytokine increases by only a factor of 2 (61,2 ± 2,9 pg / ml) relative to that of the control group (30,2 ± 1,7 pg / ml; P <0.001). In the second group, the level of IL-4 (101,4 ± 3,3 pg / ml) was significantly higher than in group 1 patients (P <0,001) and exceeded the performance of control group by 3.4 times (P <0,001). Analyzing the ratio of the level of TNF-alpha and IL-4, we have detected a significant increase in the coefficient TNF-alfa/IL-4 in group 1 (1,48 ± 0,12) compared with group 2 patients (0,76 ± 0,09). That is, IR in CHC patients with a significant shift in the balance of cytokines toward pro-inflammatory interleukins, which can be documented by increasing the TNF-alfa/IL-4 over 1.37.

**Discussion:** Significant prevalence of diabetes is not only medical but also a social problem in many countries. The epidemic of chronic hepatitis C (CHC) has led to an increase in not only the frequency of fibrotic liver damage but also extra-hepatic manifestations of HCV infection, including lesions of the endocrine system. Search for pathogenic mechanism of progression of insulin resistance (IR), including patients with chronic liver disease has developed to a new algorithm of prognosis and methods of treatment.

**Conclusion:** Progression of IR in patients with CHC accompanied by an increase in the ratio TNF-alfa/IL-4 serum. Beyond the value of 1.37, CHC patients will an require in-depth study for the state of carbohydrate metabolism.
Abstract #268

**BETTER HYPOGLYCEMIA DETECTION RATING SCALE**

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**Objective:** Hypoglycemia (HYPO) is underreported and/or poorly documented. Its risk factors are incompletely identified. Avoiding this major barrier to attaining control of diabetes requires better screening methods and characterization. The objective of this project was to determine the prevalence of HYPO between clinic visits based on patient history and to develop screening tools to improve detection of HYPO.

**Methods:** Using data from a detailed interview by PharmD/Certified Diabetes Educator, patient surveys, medical chart, 4 EXPERTS (2 endocrinologists and 2 PharmD's with diabetes clinic experience) adjudicated the likelihood of HYPO for 141 patients with diabetes as “definite”, “probable”, “possible”, “doubtful” or “none”. If ≥3 EXPERTS rated the probability as probable or definite, HYPO was rated as “yes.” If ≥3 EXPERTS rated the probability as doubtful or no, HYPO was rated as “no.” If ≥3 EXPERTS rated the probability as doubtful or no, HYPO was rated as “maybe” if ≥3 EXPERTS agreed or if there was disagreement between ≥3 EXPERTS. Two HYPO screening tools, computer-aided self-interview (CASI) and paper surveys (PAPER), were compared to CHART and to EXPERT ratings. A HYPO Prediction Scale was developed to weight available evidence to determine the probability of HYPO.

**Results:** Population (N=141) was 96% African American and 61% female with mean age 53 ± 11 yr, diabetes duration 8.9 ± 8.6 (median = 6.0) yr and A1C 8.3± 2.4%. Since their last visit, severe HYPO was uncommon (7%), but HYPO was common 33% definite and 22% possible. It was most frequently nocturnal and felt to be precipitated by reduced food intake. History of HYPO, being on insulin or secretagogues and lower A1C were risk factors for HYPO (all P<0.05). CASI (85%) was more sensitive than PAPER (63%) or CHART (55%) for detecting HYPO, but with more false positives (30%, 27%, 11%, respectively). CHART HYPO question was not answered 25% of time. Subjects liked the CASI and providers liked having the pre-visit screening report. This HYPO Prediction Scale score was highly correlated with average EXPERT rating (R=0.81, P<0.0005).

**Discussion:** These results illustrate how difficult it is to determine if patients had HYPO episodes. The risk factors identified are consistent with other findings. The use of the screening tools detects more HYPO than what is reported in a routine clinic visit. Data from the HYPO Prediction scale warrants validation against continuous glucose monitoring.

**Conclusion:** Optimal glycemic management demands good screening for hypoglycemia, which occurs frequently, most often at night and with reduced food. A CASI is the most sensitive method of detection. The multi-factor HYPO Prediction Score may prove useful in the clinical setting.

Abstract #269

**MANAGEMENT OF DIABETIC POSTPRANDIAL REACTIVE HYPOGLYCEMIA WITH ACARBOSE (DPRH)**

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**Objective:** Acarbose suppresses GLP-1 and insulin responses after liquid sucrose in post-surgical alimentary PRH (APRH). GLP-1 release that is mediated by an osmotic effect of unabsorbed nutrients can vary with different nutrient characteristics. Little is known about hormonal patterns after CHO mixed meals versus liquid sucrose with acarbose (AC) in DPRH.

**Methods:** Plasma GLP-1, insulin, and glucose were quantitated after taking a CHO breakfast meal (78 g) and a liquid sucrose meal (75 g) w/ and w/o acarbose (100mg) in an 84-yr-old patient diagnosed with DPRH on a standard 6-h OGTT. The glucose, GLP-1 and insulin responses and areas under the curves during a time course of 4 hours were calculated and compared.

**Case Presentation:** (1) AC inhibited glucose peak, increased glucose nadir and prevented late glucose fall after both types of meals. (2) Like in APRH, AC suppressed stimulated GLP-1 (34 at 1 h without AC vs 16 pm at 1 h with AC) and insulin release(1894 without AC vs 801pm with AC at 1 h) after a sucrose drink that improved glycemic profile (3) AC produced a higher GLP1 peak (61 at 2 h with AC vs 34 pm at 1 h without AC) and a sustained course of GLP-1 response after a CHO mixed meal (4) There were no overall differences in insulin peaks (3343 at 1 h without AC vs 3557 pm at 3 h with AC) or integrated insulin responses (349,333 vs 328,730 pmXmin) after a CHO mixed meal.

**Discussion:** We showed therapeutic benefits of acarbose irrespective of different changes in insulin and GLP-1
responses after various nutrients differing in rapidity of absorption, loading size, nutritional constituents, and gastric emptying. Limitations of AC are taking CHO-rich with high GI foods and weight loss with potential increased insulin sensitivity for a long-term use.

**Conclusion**: Alpha-glucosidase inhibitors is a successful treatment modality for DPRH that is not associated with exaggerated GLP-1 secretion and is pathophysiologically distinct from APRH.

**Abstract #270**

**DIABETIC KETOACIDOSIS COMPlicated BY ARTERIAL THROMBOSIS OF RIGHT LOWER EXTREMITY**

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**Objective**: To report a case of diabetic ketoacidosis (DKA) complicated by a rare complication of right lower extremity arterial thrombosis.

**Case Presentation**: A 17 year old Caucasian female with past medical history of poorly controlled type 1 diabetes mellitus (T1DM) for 12 years presented with two days history of abdominal discomfort associated with worsening nausea and vomiting. Patient endorsed medications being glargine 44 units nightly, aspart 8 units with meals, and intermittent use of oral contraceptives in the last year. Initial examination reveals a young female with Kussmaul’s respirations, dry mucous membranes, and sinus tachycardia. Laboratory findings are significant for WBC 25.2 k/ul, sodium 147 mmol/l, potassium 6.3 mmol/l, chloride 108 mmol/l, bicarbonate 3 mmol/l, glucose 598 mg/dl, hemoglobin Alc 13.2%, ABG (pH 7.06, PaCO2 11 mmHg, PO2 144 mmHg), lipase >4000 u/l, and urinalysis positive ketone bodies. EKG showed sinus tachycardia. Patient was aggressively hydrated with normal saline infusion and treated with intravenous insulin in the emergency department. Two hours into the treatment the patient complained of right lower extremity pain. Re-examination revealed pallor, coldness on palpation, and absence of pedal and dorsal pulses with no evidence of wound or ecchymotic lesion identified. CT angiography showed a filling defect at the level of the tibioperoneal trunk with runoff vessels not well opacified raising possibility of a thrombus. Patient was urgently taken for right transpopliteal angiogram, compartment fasciotomy, pharmacologic thrombolysis with alteplase, and right posterior tibial balloon angioplasty and thrombectomy. Echocardiogram showed no heart abnormalities and hypercoagulable workup was initiated.

**Discussion**: DKA is a state of severe insulin deficiency with a mortality rate as high as 5%. This systemic inflammatory response has been found to promote a prothrombotic state while activating the vascular endothelium. Oxidative damage with glycosylation produced in T1DM also causes abnormalities in coagulation factors such as decreased activity in protein C and S accompanied by increased levels of factors VII, VIII, XI, von willebrand and prothrombin. In addition the metabolic insult during DKA causes abnormalities of platelet activation, blood volume, blood flow and vascular reactivity. The patient’s intermittent use of oral contraceptives is also a risk factor that might add to a prothrombotic state.

**Conclusion**: Many cases have been reported of venous thrombosis complicating DKA. However acute arterial thrombosis has been rarely seen as a complication of DKA. Clinicians should be aware of this uncommon complication of DKA that necessitates prompt detection and intervention.

**Abstract #271**

**HIGH RATES OF INSULIN SYRINGE SELF-DOSING ERRORS IN THE ELDERLY DESPITE NORMAL VISION AND DEXTERTY**

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**Objective**: Frequent self-dosing errors with insulin syringe use are thought to occur in elderly patients because of more prevalent visual dysfunction and manual dexterity problems (stroke, arthritis, etc). This crossover study (NCT #01240200) assessed dosing accuracy of glargine delivery by pen versus syringe in older patients with type 2 diabetes and its association with A1c, fasting blood glucose (FBG), hypoglycemia, visual acuity and upper extremity function.

**Methods**: 56 insulin-naïve patients >60yr old with A1c >7% on oral antidiabetic drugs were assigned to 3 months each of insulin pen and insulin syringe use in randomized order. A Certified Diabetes Educator taught the patient how to use each device upon its initiation. Observed preparation of doses and injection into a pillow 5 times at baseline and again at 3 months was used to assess accuracy with each device. Dosing errors were defined as inaccurate preparation or injection by ≥10% of intended dose. Upper extremity function was assessed by the 9-Hole Peg Test (9HPT) and the Test Évaluant les Membres supérieurs des Personnes Âgées (TEMPA) and visual acuity by Snellen Test.

**Results**: 46 subjects with complete data were analyzed:
48% had no clinical comorbidities affecting upper extremities; 20% had normal function on TEMPA; 72% normal on 9HPT; 30% had 20/20 vision. A1c and FBG improved after 3 months with pens (A1c: 8.5±1.3 to 7.6±1.0%; FBG: 157±38 to 134±32mg/dl, both p<0.05) and vials (A1c: 8.7±1.1 to 7.6±0.8%; FBG: 159±47 to 126±19mg/dl, both p<0.01). Overall frequency of dosing errors was similar at baseline and 3 months with both devices, but fewer errors (90% vs 20%, p<0.01) and hypoglycemic events (1.5±2.6 vs 0.8±1.3/person, p<0.05) occurred with pens than syringes. Patients making syringe dosing errors at 3 months versus those that did not had more hypoglycemia (1.5±2.4 vs 0.4±0.5 events/person, p=0.01) and higher A1c’s (7.6±0.8 vs 6.8±0.6%, p<0.05); trend not seen with pen dosing errors. Syringe preparation errors at 3 months were observed in 86% of subjects with 20/20 vision versus 90% of the others (p=NS). Upper extremity comorbidities did not increase syringe error rates (91% vs 87%, p=NS). Performance times >2 standard deviations above mean for age, on the 9HPT and TEMPA were not associated with increased syringe dosing errors compared to those subjects with normal times (both p=NS). Abnormal times on the 9HPT were associated with pen injection errors (p<0.05) although injection errors were uncommon (6.5%).

Discussion: Dosing errors with insulin syringes are extremely common in older adults even in the absence of visual and manual dexterity problems.

Conclusion: Insulin pens mitigate the self-dosing errors and associated hypoglycemia.

Abstract #272

SIGNIFICANT REDUCTION IN HYPOGLYCEMIA WITH THE THRESHOLD SUSPEND FEATURE OF THE VEO INSULIN PUMP FROM THE CARELINK DATABASE

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Objective: The Medtronic Paradigm® Veo pump provides a threshold suspend feature can stop insulin delivery for up to 2 h when a sensor glucose (SG) threshold is met. The threshold suspend feature cannot be used when SG data are unavailable, and can be turned ON or OFF when SG data are available.

Methods: The CareLink Personal database was interrogated to provide routine usage data from 7810 people outside the US (where this feature has been available since 2009) from 1/2010 to 11/2011 totaling 398,902 patient-days. SG data from days when the threshold suspend feature was on at any time (‘ON’) were used to determine typical settings. SG data from ON vs. OFF days were compared to determine the glycemic effects of the feature.

Results: The threshold suspend feature was ON during 73.6% (293,592) of the patient-days. Alerts were most commonly set in the 70-80 mg/dL range (mean, 77.58 mg/dL) and suspends were most commonly set in the 50-60 mg/dL range (mean, 59.94 mg/dL). Threshold suspend ON days were associated with significantly less hypoglycemia than threshold suspend OFF days as measured by AUC<70 mg/dL (0.60 vs 0.99 mg/dL x min, p<0.001), time spent <70 mg/dL (5.3% vs 7.4%, p<0.001), and duration of excursions to <70 mg/dL (37.9 vs 46.5 min, p<0.001). Threshold suspend ON days were associated with statistically significantly less time spent >240 mg/dL than threshold suspend OFF days (11.23% vs 11.30%, p=0.001). Of the 270,042 threshold suspend events recorded, 44% lasted for <5 min and 11% lasted for 2 h. Among nocturnal pump suspension events (those starting between 10:00PM and 8:00AM), 22.8% lasted for 2 h. The mean SG value at the onset of 2-h threshold suspend events was 61.79±14.01 mg/dL, rose to 130.26±60.3 mg/dL at 2 h (when insulin delivery was automatically resumed), and was 158.67±71.3 mg/dL at 4 h. Among these 2-h events, the median time between a threshold suspend event and a user-pump interaction was 2.07 min.

Discussion: Automatic suspension of insulin delivery, including nocturnal suspensions lasting the full 2 hours, appears to be able to mitigate hypoglycemia. The use of this automatic feature is the first step towards the artificial pancreas.

Conclusion: Based on our data-mining analysis, a feature that automatically suspends insulin delivery can mitigate hypoglycemia, particularly at night when the patient does not respond, suggesting that clinical outcomes in type 1 diabetes are improved.
diabetes may be improved by this technology.

Abstract #273

LOW HYPERTENSION AND HYPERCHOLESTEROLEMIA AWARENESS, TREATMENT AND CONTROL IN ASIAN INDIAN SUBJECTS WITH TYPE 2 DIABETES: A POPULATION BASED STUDY

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Objective: Hypertension and hypercholesterolemia are risk factors for cardiovascular disease in type 2 diabetes. To determine prevalence, awareness, treatment and control of hypertension and hypercholesterolemia in population based diabetic subjects we performed an epidemiological study.

Methods: Study was performed at eleven urban locations in different regions of India using simple cluster sampling. Subjects were evaluated for demographic, biophysical and biochemical risk factors using uniform protocol. We recruited 6198 subjects and in 5359 (86.4%) (men 54.8%, women 45.2%) details of diabetes (known or fasting glucose >126 mg/dl), hypertension (known or BP >140/>90 mm Hg) and hypercholesterolemia (cholesterol >200 mg/dl) were available. Among known diabetics, details of awareness, treatment, and control of hypertension (BP >140/>90 or >130/>80 mm Hg) and hypercholesterolemia (total >200 mg/dl or LDL >100 mg/dl) were obtained. Inter-group comparison was performed using X2 test.

Results: Age-adjusted prevalence of diabetes was in 973 (18.1%), hypertension in 2044 (38.1%) and hypercholesterolemia in 1459 (27.2%). Among diabetics, 705 (72.4%) were aware of diabetes while 268 (27.5%) undiagnosed. Among known-diabetic vs. undiagnosed vs. non-diabetic subjects age-adjusted prevalence of hypertension was 589 (83.5%) vs. 238 (88.8%) vs. 1217 (27.3%) and hypercholesterolemia 272 (38.6%) vs. 102 (38.0%) vs. 1085 (24.4%). In known diabetics vs. non-diabetics, hypertension awareness (79.9 vs. 43.2%), treatment (48.7 vs. 31.3%) and control (BP >140/>90) (40.7 vs. 20.6%) was better but control to target (>130/>80 mm Hg) lower (16.3 vs. 20.6%) (p<0.01). Hypercholesterolemia awareness (61.0 vs. 12.0%), treatment (19.1 vs. 5.0%) and control (cholesterol <200 mg/dl, 45.9 vs. 6.8%; LDL <100 mg/dl, 66.5 vs. 8.6) were better, but also low, in known diabetics (p<0.01). Discussion: This is the first population based from India that highlights low awareness, treatment and control of important cardiovascular risk factors.

Conclusion: There is high prevalence of hypertension and hypercholesterolemia in type 2 diabetes Asian Indians. Low status of hypertension and hypercholesterolemia awareness, treatment and control is observed.

Abstract #274

EVALUATION ON THE ACCURACY OF FIVE GLUCOMETERS AVAILABLE IN SRI LANKA

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Objective: The aim of this study was to compare the accuracy of five glucometers available in Sri Lanka with a reference laboratory method among diabetes patients

Methods: We evaluated the performance of Six different point-of-care testing devices, One touch Ultra 2, Freestyle Optium xceed, Mega Check, Ez smart, Major 2 and Sure step. The results were compared with those of the laboratory reference method (Glucose oxidase method). Glucose measurements were performed by an experienced technician under standardized conditions in the hospital laboratory, using venous blood samples.

Results: Fifty-two subjects completed the study. 94% had diabetes and 69% were female. Patients’ mean BMI was 26 (S.D +/- 5; range 15-36). Mean venous blood glucose in glucose oxidase method was 195 mg/dl (SD +/- 32 mg/dl; range 72-436 mg/dl). Deviation range of One touch Ultra 2, Optium xceed, Mega Check, Ez smart and Sure step readings from the venous blood glucose value were 0-96, 1-96, 1-77, 3-137, and 1-88 in mg/dl respectively. Glucometer precision failed the standard criteria (error margin of ±20%) of the International Organization for Standardization (ISO) and the Food and Drug Administration (FDA) in 14 (27%), 10 (19%), 11 (21%), 23 (44%) and 12 (24%) of cases, respectively. However, Glucometer readings outside the acceptable error margin of ±5% set by the American Diabetes Association (ADA) were in 44 (85%), 40 (77%), 38 (73%), 51 (98%) and 37 (71%) of cases, respectively.

Discussion: Glucose results from five point-of-care testing devices were inaccurate compared to the laboratory
glucose oxidase method as per the ISO, FDA and ADA standards. The Ez smart was significantly associated with less accuracy and less precise compared to the other meter systems. Among diabetic patients, inaccurate glucose readings of all glucometers were most frequently falsely elevated, resulting in misinterpretation of high glucose values that can lead to subsequent inappropriate insulin administration.

**Conclusion:** Most point of care glucometers seem inaccurate and some machines are significantly associated with less accuracy and less precise.

**Abstract #275**

**GLUTAMIC ACID DECARBOXYLASE AUTOANTIBODY AMONG TYPE TWO DIABETES MELLITUS PATIENTS IN ZARIA, NIGERIA**

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**Objective:** The objective was to determine the prevalence and the characteristics of Nigerian T2DM patients with anti-GAD autoantibody positivity.

**Methods:** Two hundred newly diagnosed type two diabetes (T2DM) patients were recruited from the diabetes clinic of the Ahmadu Bello University Teaching Hospital, Zaria with their consent. T2DM was diagnosed using the American Diabetes Association criteria. Parameters studied included age, sex, age at diagnosis, duration of diabetes, treatment type, body mass index (BMI), waist circumference (WC), fasting blood glucose (FBG), lipid profile. Average values of indices studied are expressed as mean (SD), comparison of group means was by student’s t-test.

**Results:** The mean age of the T2DM subjects was 53.2 (8-9) years [range 34-75] comprising 94 males and 106 females. A total of 29 subjects were glutamic acid deacetylase antibody positive with a prevalence of 14.5%. The age at diagnosis in the GAD autoantibody positive group 42.5 (9.8) years was significantly lower than in the GAD autoantibody negative group 49.6 (8.1) years p<0.05. The mean BMI 22.9 (5.4) kg/m2 and mean WC 87.7 (11.3) cm of those who were GAD positive were significantly lower than those with GAD negative 27.2 (4.8) kg/m and 93.5 (10) cm respectively p<0.05. Comparing the blood sugar values and glycated hemoglobin of the two groups, the mean FBG 11.7 (2.6) mmol/L and glycated hemoglobin 8.3 (1.4)% of those who were GAD positive were significantly higher than the group negative for GAD antibody 5.7 (1.5) mmol/L and 7.0 (2.1)% respectively.

**Discussion:** The rate of β cell decline among patients with type one diabetes varies with some manifesting early in life, while others present late as in latent autoimmune diabetes in adults (LADA). The islet cell autoantibody (GAD) is present in >75% of newly diagnosed type one diabetes and 5-10% of newly diagnosed type 2 diabetes (T2DM).

**Conclusion:** The prevalence of GAD autoantibody positivity in our T2DM patients was 14.5%. This finding was associated with earlier age of onset, lower BMI and WC and poorer diabetes control. Therefore, early screening for GAD antibody positivity in our T2DM patients will identify those with LADA. Appropriate management will reduce the devastating complications we have from poor diabetes control.

**Abstract #276**

**EVALUATING SUDOSCAN AS A NEW DIAGNOSTIC TOOL FOR DIABETIC NEUROPATHY AND AUTONOMIC DYSFUNCTION**

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**Objective:** Sudomotor dysfunction is an early detectable abnormality in diabetic small fiber neuropathy. Sweat glands are innervated by small unmyelinated C-fibers. Degeneration of these fibers may be the first finding in prediabetes and diabetes. The aim of this study was to evaluate Sudoscan as a tool for assessing neuropathy in patients with Diabetes Mellitus (DM), and to examine the efficacy in detecting diabetic neuropathy (DN), in comparison with other standardized tests for DN.

**Methods:** Sudoscan measures electrochemical skin conductance (ESC) of the hands and feet through reverse iontophoresis. Sudomotor function was evaluated in 78 DM patients with and without DN defined by the Toronto Convention and 210 healthy controls. Neuropathy impairment scores (NIS-LL) were calculated. Quantitative autonomic function testing (QAF) and Quantitative sensory testing (QST) were performed. Symptomatic pain was recorded using a visual analog scale (11 Point Scale). Analysis of variance was used to compare mean differences between the groups, with post hoc analysis. Correlations were determined using Spearman’s rho rank tests. Receiver-operator characteristic (ROC) curves were calculated to evaluate efficiency of Sudoscan in detecting DN compared with traditional modalities. Results are
**Results:** Diabetic patients with DN had significantly worse ESCs than patients without DN (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 DN had significantly worse ESC of their feet than patients with non-painful DN (52.8±3.6 vs 68±6.6, p<0.05). Patients with abnormal hands and feet ESC readings had significantly worse NIS-LL scores (7±0.8 vs 2.8±0.6 p<0.0001 for feet, and 5.7±0.7 vs 2.6±0.8 p<0.005 for hands). ESCs correlated significantly with clinical (NIS-LL), somatic (QST) and autonomic (QAFT) measures of neuropathy, and with pain scores. ROC curve analysis, used to evaluate sensitivity of Sudoscan in detecting DN showed AUC of 0.8563 for feet and 0.8775 for hands ESC (p<0.0001) with sensitivity of 78% and specificity of 92% for feet. NIS-LL Total Score showed an AUC of 0.8429 with sensitivity of 76% and specificity of 86%. Test-retest reliability in 112 healthy controls before and after VO2max test was excellent for the feet (rho=0.8, p<0.0001).

**Discussion:** ESC is decreased in patients with DN. Sudoscan results correlated significantly with clinical neuropathy scores, pain scores and measures of somatic and autonomic dysfunction.

**Conclusion:** Sudoscan is a promising, sensible tool to detect DN. This is a very simple, non-invasive test easily performed in the clinical setting and can be done in 5 minutes.

**Abstract #277**

**KNOWLEDGE, ATTITUDES AND DECISION MAKING IN HOSPITAL GLYCEMIC MANAGEMENT: IS FACULTY UP TO SPEED?**

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**Objective:** Identify barriers in knowledge, attitudes and decision making in the management of hospital hyperglycemia among faculty.

**Methods:** We surveyed 69 clinical faculty members in an academic hospital.

**Results:** Failure to recognize glycemic targets for critically ill, non-critically ill and postoperative patients, to adequately select subcutaneous (SQ) or intravenous (IV) insulin, to properly transition patients from IV to SQ insulin, and frequent use of sliding scale insulin was prevalent. Most providers recognized that inadequate control is associated with poor outcomes and acknowledged the importance of good control. Faculty perception of existing barriers showed that not knowing when and how to start and how to adjust insulin, fear of causing hypoglycemia, and preferring to defer management to other services was common. Faculty indicated that trainees are responsible for most glycemic management decisions and acknowledged that not adequately addressing glucose management during inpatient rounds constituted a barrier to care. Many providers were not familiar with existing hospital’s order resources and hypoglycemia protocols.

**Discussion:** The clinical and economic impact of hospital hyperglycemia is recognized and professional societies advocate for systematic practice changes. Administrative support is needed to create multidisciplinary steering committees to evaluate safety and efficacy of existing processes; provide policies, protocols, and order sets; standardize communication for patients’ transfer; and provide continuing education programs. Knowledge and confidence deficits are common among resident, nurses, and midlevel providers and some institutions have conducted educational programs to address this matter. However, it is unclear where knowledge and attitudes of faculty stand. A quality initiative project consisting of an educational mentored program on glycemic management for hospitalist was created by the Society of Hospital Medicine to guide through web-based resources representing a step forward to address this important aspect of the care of hospitalized patients. The American Association of Medical Colleges advocates for alignment of education and quality initiatives in academic medical centers. Faculty play a crucial role in the clinical decision making process and care delivered by trainees; therefore, faculty knowledge and attitudes may impact their own clinical performance and the education of physicians in training.

**Conclusion:** Deficits in the management of hospital hyperglycemia among faculty are prevalent. To enhance the impact of educational programs for faculty we need to tailor interventions to address areas of knowledge, decision making, and attitudinal barriers.
Abstract #278

CANAGLIFLOZIN (CANA), A SODIUM GLUCOSE CO-TRANSPORTER 2 (SGLT2) INHIBITOR, IMPROVES INDICES OF BETA-CELL FUNCTION ($\beta$CF) IN PATIENTS WITH TYPE 2 DIABETES MELLITUS (T2DM) ON METFORMIN (MET) PLUS SULFONYLUREA (SU)

David Polidori, PhD$^1$, Frank Verceyssse$^2$, Eleuterio Ferrannini$^3$


Objective: Progressive loss of $\beta$CF is thought to underlie the pathophysiology of T2DM. CANA, an inhibitor of SGLT2, is in development for the treatment of T2DM. In hyperglycemic, partially pancreatectomized rats, $\beta$CF can be restored when normoglycemia is achieved with SGLT2 inhibitor treatment. In a Phase 3 study, 26 weeks of CANA monotherapy treatment improved glycemic control and indices of $\beta$CF in patients with T2DM inadequately controlled with diet and exercise. To further assess the effects of CANA on $\beta$CF, indices of $\beta$CF were evaluated in a Phase 3 study of patients with T2DM inadequately controlled with MET + SU.

Methods: This 26-week, randomized, double-blind, placebo (PBO)-controlled study evaluated CANA 100 and 300 mg compared with PBO as add-on therapy to MET + SU in patients with T2DM (N = 469; mean baseline characteristics: age, 57 years; A1C, 8.1%; BMI, 33.0 kg/m²; duration of T2DM, 9.6 years). A subset of patients (n = 168) were given a meal tolerance test at baseline and Week 26 and plasma glucose (G) and serum C-peptide (C) were measured at 7 time points over 3 hours. $\beta$CF was assessed using the AUC$_{C/AUC_G}$ ratio and a model-based method relating the insulin secretion rate (ISR; obtained by deconvolution of C) to concomitant G using linear regression. $\beta$-cell glucose sensitivity as the slope of ISR vs G relationship and ISR at 9 mM G were calculated. All changes were reported as PBO-subtracted least squares (LS) mean changes using an ANCOVA model.

Results: At Week 26, CANA 100 and 300 mg significantly reduced A1C from baseline compared with PBO (ΔA1C, -0.71% and -0.92%, respectively; P < 0.001) and were generally well tolerated. The ISR vs G relationship was unchanged with PBO and was shifted upwards (indicating increased ISR at each PG concentration) with both CANA doses. Mean values of all calculated indices of $\beta$CF increased with both CANA doses versus PBO, although some of the changes did not reach statistical significance.

Mean AUC$_{C/AUC_G}$ increased by ~20% from baseline values of 123-132 pmol/mM (increases of 27.1 (95% CI: -0.2; 54.4; P = 0.051) and 27.4 (-0.7; 55.6; P = 0.056) for CANA 100 and 300 mg). Mean ISR at 9 mM G increased by ~50-60% from baseline values of 114-117 pmol/min/m² (increases of 54.6 (7.7; 101.5; P = 0.02) and 69.2 (19.7; 118.9; P = 0.007) for CANA 100 and 300 mg). Mean $\beta$-cell glucose sensitivity increased by ~20% from baseline values of 31-34 pmol•min$^{-1}$•m$^{-2}$•mM$^{-1}$ (increases of 7.6 (-2.6; 17.9; P = 0.14) and 6.7 (-4.1; 17.5; P = 0.22) for CANA 100 and 300 mg).

Conclusion: In T2DM patients (mean T2DM duration of 9.6 years) on background MET + SU, CANA 100 and 300 mg improved glycemic control and measures of $\beta$CF compared with PBO after 26 weeks of treatment.
Patients were included in the meta-analysis if they were receiving an IDeg or IGlar dose of >0.45 U/kg at end-of-trial (upper quartile).

**Results:** Approximately 25% (235/950) of patients received an end-of-trial basal insulin dose >0.45 U/kg (IDeg: 23.1% [147/635]; IGlar: 27.9% [88/315]) and were included in the meta-analysis. Mean end-of-trial basal insulin dose was similar for IDeg (0.63 U/kg) and IGlar (0.65 U/kg). Patients achieved similar mean end-of-trial HbA1c values with IDeg and IGlar (7.41% vs 7.55%; treatment difference (TD) IDeg-IGlar: -0.08 %–points [-0.29; 0.12]; NS); mean end-of-trial fasting PG levels were also comparable (133 vs 136 mg/dL; TD: -8.7 mg/dL [-27.8; 10.5]; NS). Rates of overall confirmed hypoglycemia (PG <56 mg/dL or severe) were similar for IDeg and IGlar in the full trial period (rate ratio (RR): 1.01 [0.72; 1.42], NS) and the maintenance period (RR: 0.91 [0.62; 1.33], NS). However, IDeg was associated with significantly lower rates of nocturnal confirmed hypoglycemia (confirmed episodes with onset between 12:01AM and 5:59AM): by 36% in the full trial period (RR: 0.64 [0.42; 0.99], p=0.046) and by 44% in the maintenance period (RR: 0.56 [0.33; 0.95], p=0.033).

**Discussion:** Consistent with the conclusions for the overall meta-analysis population, patients receiving high doses of IDeg obtain similar overall glycemic control as those receiving IGlar but with a significantly lower rate of nocturnal confirmed hypoglycemia during the entire treatment period as well as the maintenance period.

**Conclusion:** Patients with T1D receiving high doses of once-daily insulin degludec (>0.45 U/kg) experienced significantly lower rates of nocturnal confirmed hypoglycemia than patients receiving similar high doses of insulin glargine.

**Abstract #280**

**TESTOSTERONE REPLACEMENT INCREASES INSULIN SENSITIVITY IN HYPOGONADAL MEN WITH TYPE 2 DIABETES**

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**Objective:** One third of men with type 2 diabetes(T2D) have hypogonadotropic hypogonadism(HH). Testosterone(T) concentrations are inversely related to BMI. We conducted a randomized placebo controlled trial to evaluate the effect of T replacement on insulin resistance in T2D men with HH.

Methods: 50 men with T2D were recruited into the study. HH was defined as free T concentrations <5 ng/dl with normal or low LH and FSH. 26 men had HH(mean total T 247±82ng/dl; free T 4.2±1.1ng/dl) and 24 men had normal total and free T concentrations(means 527±205 and 7.3±2.0ng/dl). Insulin sensitivity was calculated from the glucose infusion rate(GIR) during the last 30 min of a 4 hour hyperinsulinenic-euglycemic clamp(80mU/m2/ min) and expressed as mg/kg body weight/min. Lean mass and fat mass were measured by DEXA. Men with HH were randomized to receive intramuscular injections of T(250 mg) or placebo(1ml saline) every 2 weeks for 6 months(n=13 in each group). Clamps and DEXA were repeated at 6 months.

**Results:** Men with HH had similar age (54±8 vs. 53±10years, p=0.56) but higher BMI (40±9 vs. 34±7kg/m2, p=0.02) than eugonadal men. Men with HH had higher fat mass(451±15 vs. 341±15kg, p=0.02) but similar lean mass(731±21 vs. 66±9kg, p=0.12) as compared to eugonadal men. Mean GIR was lower in men with HH as compared to eugonadal men(4.1±2.4 vs. 6.9±3.6 mg/kg/min, p=0.003) even after adjustment for fat mass, lean mass and age(4.6±2.7 vs. 6.4±2.7 mg/kg/min, p=0.05). Total and free T concentrations increased after 6 months of T therapy(273±96 vs 561±249 ng/dl, p=0.01; 4.2±1.1 vs. 11.8±7.1 ng/dl, p=0.007; blood sample drawn 1 week after the final T injection) but did not change in placebo group(271±40 vs 349±215 ng/dl, p=0.23; 4.0±0.8 vs. 4.8±2.1 ng/dl, p=0.3). There was no change in SHBG concentrations in either group(30±15 vs. 27±10nmol/l, p=0.17 in T group; 35±14 vs. 34±19nmol/l, p=0.67 in placebo group). There was no change in weight(123±23 vs 122±24kg, p=0.37) or fat mass(37±16 vs 36±14kg, p=0.09) but lean mass(71±10 vs 72±10kg,p=0.03) increased slightly but significantly after 6 months of T therapy. There was no change in weight(111±38 vs 112±38kg, p=0.85), fat mass(37±16 vs 36±14kg, p=0.19) or lean mass(67±14 vs 67±13kg, p=0.57) in placebo group. GIR increased by 30% after 6 months (4.1±2.0 vs 5.3±2.3 mg/kg/min, p=0.005) of T therapy but did not change in placebo group(3.4±1.5 vs 3.5±1.9 mg/kg/min, p=0.88). Change in GIR did not relate to increase in free T(r=-0.16, p=0.68) or to change in lean mass(r=-0.13, p=0.73) in T group.

**Conclusion:** Our data show for the first time that men with T2D and HH are more insulin resistant than those with normal T, and insulin resistance is reversed following T replacement.
HYPOGLYCEMIA

Abstract #300

REDUCED RISK OF CONFIRMED HYPOGLYCEMIA (PLASMA GLUCOSE <41 MG/DL) WITH INSULIN DEGLUDEC VS INSULIN GLARGINE IN PATIENTS WITH TYPE 2 DIABETES: A META-ANALYSIS OF FIVE RANDOMIZED TRIALS

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Objective: Insulin degludec (IDeg) is a new basal insulin with an ultra-long and stable glucose-lowering effect with low day-to-day and hour-to-hour within-patient variability. A previous, prospective patient-level meta-analysis of phase 3a trials showed IDeg to be associated with a significant 17% lower rate of overall confirmed hypoglycemia and significant 32% lower rate of nocturnal confirmed hypoglycemia vs insulin glargine (IGlar) in patients with type 2 diabetes (T2D). In that analysis, hypoglycemia was defined as episodes confirmed with a plasma glucose (PG) value <56 mg/dL (<3.1 mmol/L) and severe episodes (requiring assistance). To investigate these findings further, we performed a post-hoc meta-analysis to compare hypoglycemia rates for IDeg and IGlar using an alternative definition of hypoglycemia with a lower PG threshold.

Methods: This patient-level meta-analysis included all five phase 3a, randomized, treat-to-target trials in which once-daily IDeg (n=2,262) and IGlar (n=1,110) have been compared in patients with T2D. All trials were open-label and were 26 or 52 weeks in duration. Confirmed hypoglycemia comprised severe episodes (requiring assistance) and episodes confirmed by a PG value of <41 mg/dL (2.3 mmol/L); nocturnal confirmed hypoglycemia included confirmed episodes with an onset between 12:01AM and 5:59AM.

Results: There was a significant 33% lower rate of overall confirmed hypoglycemia for IDeg vs IGlar for the full meta-analysis population (rate ratio (RR) IDeg/IGlar: 0.67 [0.56; 0.82], p<0.0001) and a significant 45% lower rate in a subset of patients (IDeg: n=1,290; IGlar: n=632) who were insulin-naive prior to trial entry (RR: 0.55 [0.39; 0.76], p<0.001). IDeg was also associated with a 27% lower rate of nocturnal confirmed hypoglycemia compared with IGlar in the full population (RR: 0.73 [0.53; 1.01], p=0.06). It was not possible to perform an equivalent analysis for insulin-naive patients because an insufficient number of nocturnal hypoglycemic episodes were recorded in this group.

Discussion: Using a more stringent PG threshold to define hypoglycemia (<41 rather than <56 mg/dL), this post-hoc analysis confirms the original, pre-planned meta-analysis findings: IDeg was associated with lower rates of overall and nocturnal confirmed hypoglycemia compared with IGlar.

Conclusion: Lower rates of overall and nocturnal confirmed hypoglycemia were observed for insulin degludec compared with insulin glargine in patients with type 2 diabetes regardless of whether a PG concentration of <56 mg/dL or <41 mg/dL is used as the criterion for hypoglycemia.

Abstract #301

COMPARISON OF PREMIXED AND BASAL BOLUS INSULIN ON THE RISK OF HYPOGLYCEMIA

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Objective: Objective: To compare the rates of hypoglycemia with premixed and basal bolus insulin regimens in patients with Type 2 diabetes hospitalized at Greenville Health System.

Methods: A randomized, prospective, open label study designed to compare the rates of hypoglycemia of adult patients with Type 2 diabetes on premixed insulin. Subjects were randomized to either continue premixed or change to basal bolus insulin. Patients in the comparison group were converted from their initial premixed dose according to the formula: 85% of total daily dose divided 55% glargine at bedtime and 45% lispro evenly divided between 3 meals. Future insulin adjustments were made by the primary hospital physician based on routine glucose monitoring. Any episodes of hypoglycemia were treated according to protocol.

Results: A total of 100 patients, 50 men and 50 women, were enrolled and randomized in this study. The mean age of the cohort was 60 years. The mean fasting glucose was 167 mg/dL, the mean hospital stay glucose was 167 mg/dL. A total of 54 subjects, 29 males and 25 females, were randomized to the premixed insulin subgroup. The mean age of this group was 61 years, the mean fasting glucose was 162 mg/dL, the mean hospital stay glucose was 171 mg/dL, and the mean number of days in the study was 7. Twenty one of 54 (38.9%) subjects experienced at least one episode of hypoglycemia. The rate of hypoglycemia was 0.24 hypoglycemic episodes per hospital day. Future insulin adjustments were made by the primary hospital physician based on routine glucose monitoring. Any episodes of hypoglycemia were treated according to protocol.

Discussion: Using a more stringent PG threshold to define hypoglycemia (<41 rather than <56 mg/dL), this post-hoc analysis confirms the original, pre-planned meta-analysis findings: IDeg was associated with lower rates of overall and nocturnal confirmed hypoglycemia compared with IGlar.

Conclusion: Lower rates of overall and nocturnal confirmed hypoglycemia were observed for insulin degludec compared with insulin glargine in patients with type 2 diabetes regardless of whether a PG concentration of <56 mg/dL or <41 mg/dL is used as the criterion for hypoglycemia.
Discussion: Hypoglycemia is a safety concern in the treatment of hospitalized patients with Type 2 diabetes. Premixed and basal bolus are the two insulin regimens used primarily in the inpatient setting. The baseline demographics between the groups were comparable. The rate of hypoglycemia was lower in the basal bolus group compared with the premixed group. A lower percentage of patients experienced episodes of hypoglycemia in the basal bolus group compared with the premixed group. Conclusion: The basal bolus insulin regimen had a lower rate of hypoglycemia and a lower percentage of patients with inpatient hypoglycemia compared with premixed insulin. In the inpatient setting, basal bolus insulin is a safer alternative with regard to hypoglycemia.

Abstract #302

RECURRENT REVERSIBLE SEVERE HYPERTRANSAMINASEMIA IN ANOREXIA NERVOSA WITH SEVERE HYPOGLYCEMIA

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Objective: Anorexia nervosa (AN) is an eating disorder characterized by a distorted self image and an overwhelming obsession with a thin body habitus. Protein energy malnutrition in these patients proves caustic to organ systems. Complications include myocardial damage, arrhythmias, amenorrhea, bone loss, thyroid abnormalities, severe hypoglycemia, transaminitis, gastroparesis, dyselectrolemia, and pancytopenia.

Case Presentation: 27 year old male was admitted for sweating, tremulousness and light-headedness. Blood glucose levels were 19mg/dl. Vital signs were stable. Weight was 37.3 kg with a BMI of 14.07. Labs showed AST 352, ALT 167 with total bilirubin of 1.1, INR 1.3, creatinine of 0.4, calcium 5.8mg/dl, phosphorus 2.2mg/dl, Magnesium 1.5mg/dl. Blood counts were normal initially. Patients LFTs increased to an AST of 4096 and ALT of 2600. INR increased to 2 with a drop in platelets to 68000. With improvement in nutritional status with the help of TPN and increased oral intake, the lab abnormalities returned to normal. Patient had multiple episodes of the same with transaminase levels in 2000’s following exacerbation of AN episodes with complete resolution with an improved nutritional status.

Discussion: Marked elevation of liver enzymes in AN is considered a poor prognostic indicator and a marker of multi-organ failure. Hepatic hypoxia has been noted with a decrease in portal pressure because of decreased cardiac output from cardiac muscle atrophy, arrhythmias secondary to hypokalemia and hypocalcemia and refeeding syndrome resulting in heart failure. This in combination with chronic hepatic glycogen depletion may lead to cytolysis of liver cells. Autophagic cell death with autophagosomes and liver cell glycogen depletion is seen. The permeability of the hepatocyte plasma membrane is altered allowing for a leak of transaminases, even in the absence of actual hepatocyte necrosis. Plasma concentration of homocysteine, glycine and glutamine are higher in anorexics suggesting a decreased utilization for glutathione synthesis. Thus, the ability to detoxify metabolites and reactive oxygen species is impaired. Protein energy malnutrition is complicated by hepatic steatosis because of the increased production of triglycerides from impaired mitochondrial function followed by decreased beta oxidation of fatty acids and reduced synthesis of lipoproteins which play a role in exporting triglycerides from the liver, in turn resulting in lipid accumulation.

Abstract #303

USE OF CONTINUOUS GLUCOSE MONITORING REDUCES INCIDENCE OF HYPOGLYCEMIA AND IMPROVE METABOLIC STATUS (HBA1C) AND QUALITY OF LIFE (QOL) IN HYPOGLYCEMIA PRONE TYPE 1 DIABETIC PATIENTS

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Objective: Present study was aimed to assess effectiveness of continuous glucose monitoring (CGM) on glycemic control, QOL and incidence of frequent hypoglycemic event in type 1 diabetic patient on insulin pump therapy (CSII).

Methods: This crossover design retrospective study involves twenty patients of type 1 diabetes who are prone to hypoglycemia with mean duration of diabetes 19.3±8.7 years and CSII duration 4.7±3.2 years, patient were included if at least three hypo events (Blood glucose level <70 mg/dL) noted in last 14 day prior to baseline visit. Patients were divided in two groups, patients in group 1 (n=10) was advised for CGM and patients in group 2 (n=10) was advised for SMBG for 24-week, after 24-weeks patients on CGM shifted on SMBG and patients on SMBG were shifted on CGM for next 24-weeks. The level of HbA1c and frequency of hypoglycemic events were evaluated at 3 months and at 6 months after SMBG or CGM. The QOL was evaluated according to the Diabetes Quality of Life (DQOL) questionnaire, were assessed at baseline then after at 3 and 6 month follow up.
**Results:** Results of present study were shown significant reduction in incidence of hypoglycemia and improvement in HbA1c level in CGM group. One patient from group 1 and two patients from group 2 withdrew from study during the first period. A significant reduction in HbA1c level was noted at 3 and at 6 months after CGM compared to baseline and HbA1c level was increased while patients on CGM was shifted on SMBG. Moreover, incidences of hypoglycemic events were found less in CGM group compared to SMBG group. Few patients in CGM group did not achieve desired glycemic control even their QOL was improved.

**Conclusion:** In conclusion, the study supports the hypothesis and revealed that the use of CGM can significantly improve glycemic control, QOL and decreases incidence of hypoglycemic events in hypoglycemia prone type 1 diabetic patients who are on insulin pump therapy.

**Abstract #304**

**A RARE CASE OF ADULT-ONSET NESIDIOBLASTOSIS PRESENTING WITH PERIPHERAL NEUROPATHY AND ASYMPTOMATIC HYPOGLYCEMIA**

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**Objective:** Nesidioblastosis, or non-insulinoma pancreatogenous hypoglycemia syndrome, is a rare cause of hypoglycemia in adults. Hypoglycemia-induced peripheral neuropathy is also rare. We present a case of adult-onset nesidioblastosis presenting as peripheral neuropathy with no hypoglycemic symptoms.

**Case Presentation:** A 51 year old male with no significant past medical history was admitted with a one month history of progressive bilateral lower extremity weakness. Electromyography showed severe distal motor and sensory axonal polyneuropathy. Work up for neuropathy was negative. With suspicion of Guillain-Barre syndrome, he was managed with iv immunoglobulin with no improvement. He was also noted to have fasting hypoglycemia in the range of 40-50 mg/dl without symptoms. Work-up on three separate occasions revealed, inappropriately elevated insulin, proinsulin and c-peptide levels during hypoglycemic episodes (glucose levels of 30-50 mg/dl). Imaging studies including CT, MRI, endoscopic ultrasound and Indium-111-labelled octreotide scan did not show any pancreatic lesion. Selective intra-arterial calcium stimulation with hepatic venous sampling of insulin showed some increments in all of the three arteries with a predominance in the gastro-duodenal and superior mesenteric arteries. While this may indicate insulinoma in the pancreatic head, the less than robust response was suggestive of nesidioblastosis. The patient underwent laparotomy and no lesion was found on intra-operative ultrasound or direct palpation of the pancreas. A pylorus-preserving modified Whipple’s procedure with removal of the proximal two-thirds of pancreas was done. Pathology showed diffuse islet hypertrophy and hyperplasia consistent with nesidioblastosis. Postoperatively, the patient had complete resolution of hypoglycemia and significant improvement in the neuropathy.

**Discussion:** Nesidioblastosis is a cause of endogenous hyperinsulaminic hypoglycemia characterized by diffuse beta-cell hypertrophy and hyperplasia in the absence of a pancreatic tumor. Most reports in adults are following bariatric surgery. Less than 40 cases have been published in the absence of bariatric surgery. Even though cases of peripheral neuropathy associated with other causes of hypoglycemia have been reported, to our knowledge, this is the first reported case in nesidioblastosis. Improvement of our patent’s weakness supports the causal nature of hypoglycemia in the pathogenesis of peripheral neuropathy. The asymptomatic hypoglycemia in our patient has also not been reported before.

**Conclusion:** We report the first case of adult-onset nesidioblastosis presenting with peripheral neuropathy. The presentation also included asymptomatic fasting hypoglycemia.

**Abstract #305**

**UNUSUAL CAUSE OF HYPOGLYCEMIA IN A DIABETIC PATIENT - SALICYLATE TOXICITY**

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**Objective:** Hypoglycemia is a common morbidity seen in diabetic patients and is usually a complication of diabetic medications. We present a case of hypoglycemia in a diabetic patient due to salicylate toxicity.

**Case Presentation:** A 59 year old man was brought to our emergency room from home with generalized seizures and hypoglycemia with a blood glucose level of 35 mg/dl.
dl. Patient has type 2 diabetes and was on insulin. He was not on any other diabetic medications and never had hypoglycemia before. Serum creatinine was normal. Hypoglycemia was attributed to insulin use. Insulin dose was decreased and patient was discharged home. Next day, he was mildly confused and disoriented. Suddenly, he became diaphoretic, tachypneic, agitated and blood glucose was 38 mg/dl which was corrected to 168 mg/dl with intravenous dextrose. But, symptoms persisted for more than two hours and arterial blood gas was done which showed primary metabolic acidosis and primary respiratory alkalosis. Patient’s last dose of insulin was more than twenty four hours back. We went back to patient’s room to get more information and found several unmarked white pills at bedside, for which patient admitted to taking a handful of aspirin tablets a few hours earlier. Also, he has been taking at least 20 to 30 aspirin tablets daily for the last one month for peripheral neuropathy. Salicylate level was found to be 78 mg/dl (usual therapeutic range: 0-30 mg/dl). Since patient had neurological symptoms, emergent hemodialysis was done which resulted in complete clinical recovery. No new hypoglycemic episodes were seen after restarting the initial insulin regimen.

**Discussion:** Salicylates are ubiquitous agents which are not an uncommon cause of accidental poisoning. Hypoglycemia occurs usually due to increased glycolysis and impaired gluconeogenesis. Increased cellular metabolic activity due to uncoupling of oxidative phosphorylation can occur resulting in intracellular hypoglycemia. This can cause neuroglycopenia even with normal blood glucose levels. In our patient, persistent neuroglycopenic symptoms was seen even after correction of low blood glucose level. Persistent change in mental status is one of the absolute indications for hemodialysis. Mixed acid-base disorder is classical for salicylate toxicity and should raise the suspicion for toxin ingestion. **Conclusion:** Salicylate toxicity should be considered in the differential diagnosis for unexplained hypoglycemia. Neuroglycopenia with normal blood glucose levels can occur.

**Abstract #306**

**HYPERINSULINEMIC HYPOGLYCEMIA IN POST GASTRIC BYPASS ADULTS**

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**Objective:** Persistent Hypoglycemia is an important complication after Roux-en-Y gastric bypass (GB) surgery. Nesidioblastosis causing hyperinsulinemic hypoglycemia is seen in adults post gastric bypass that is being described increasingly in recent literature.

**Case Presentation:** A 49 year old Caucasian lady with past medical history significant for HTN, gastric bypass surgery 2 years ago with a 100 pounds weight loss presents with tonic-clonic seizures and profound hypoglycemia of 30 mg/dl. Patient was found to be seizing by her daughter. She received 1ampule of D50 enroute and her Blood sugar improved to 127 mg/dl. Besides confusion and sleepiness patient was largely asymptomatic. Her physical examination was normal and a electroencephalogram failed to demonstrate any abnormality. Laboratory findings on two different occasions revealed low venous fasting plasma glucose concentrations (46.8mg/dl and 30mg/dl) with high insulin (15.5mU/L and 55.3mU/L) and C-peptide (0.762nmol/L and 0.53nmol/L) levels. A 72-hour fasting test had to be stopped after 18 hours because of a glucose level of 32mg/dl. Anti-insulin antibodies were negative. An abdominal computed tomography (CT) and MRI did not reveal any lesions. No specific lesion could be confirmed by endoscopic ultrasonography of the pancreas also, making the diagnosis of nesidioblastosis most likely. A calcium-stimulated test of the pancreas was not done in this case and patient was started empirically on diazoxide and her blood sugars have been well maintained since then.

**Discussion:** Nesidioblastosis in adults is a rare but potentially dangerous complication of gastric bypass surgery. It has been postulated that increased levels of a glucagon-like peptide 1 after surgery, may contribute to the hypertrophy of pancreatic beta cells in these patients. Diagnosis is based on laboratory work up ruling out other common causes. Once hyperinsulinemic hypoglycemia is established radiological localization studies, such as CT scan, endoscopic ultrasound, and selective arterial calcium stimulation test (SACST) with hepatic venous sampling, can be performed to distinguish between a focal abnormality (insulinoma) and a diffuse process (nesidioblastosis). Treatment with medical therapy includes Octreotide, Diazoxide, and Nifedipine that decrease insulin secretion. If the patient continued to
have symptomatic hypoglycemia subtotal 80% distal pancreatectomy is the treatment of choice.

**Conclusion:** Adult-onset nesidioblastosis is an important cause of hypoglycemia and should be considered in patients with previous history of gastric bypass surgery to prevent serious complications from uncontrolled hypoglycemia.

**Abstract #307**

**POST BARIATRIC SURGERY HYPOGLYCEMIA - A DESCRIPTIVE ANALYSIS**

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**Objective:** The purpose of this study is to determine the incidence of hypoglycemia after bariatric surgery at a large bariatric surgery program in a community hospital and also the frequency with which such hypoglycemia required endocrine referral and medical therapy.

**Methods:** A retrospective chart review was undertaken of all patients who had bariatric surgery and hypoglycemia at Gundersen Lutheran Medical center over a 10 year period, from 9/2001 to 9/2011. All patients who developed symptoms of hypoglycemia after bariatric surgery were included in the study; however patients who had other known causes of hypoglycemia (such as alcohol dependence, adrenal insufficiency, type 1 diabetes or type 2 diabetes on medical therapy) were excluded.

**Results:** Of the 1092 total patients defined as having had bariatric surgery from 09/2001 through 09/2011, 407 patients (37%) had a diagnosis of hypoglycemia or of symptoms that might be related to hypoglycemia. Ultimately 394 patients (36%) were sent for Endocrinology consultation, of which 75 patients (6.9% of the total) were referred for symptomatic and documented hypoglycemia. Only 6 patients met the full criteria for the post-bariatric hypoglycemia (0.55% of the total). All 6 were current or past smokers. A total of 29 patients (2.7% of the total) required counseling on dietary modification, including the ingestion of frequent small meals with high protein content and avoidance of large carbohydrate loads. Out of the 29 patients, diet therapy failed in 4 patients (14%) and drug therapy was thus required in only 4 patients (0.37% of the total). Drugs that were used included prednisone, acarbose and extended-release nifedipine.

**Discussion:** Post-bariatric hypoglycemia was first described in 2005 by J Service. Criteria included demonstration of an inappropriately high insulin level during an episode of hypoglycemia in a bariatric surgery patient in the absence of evidence of an insulinoma or other causes of hypoglycemia, such as insulin or sulfonylurea use. The incidence and appropriate management of this condition has been unknown. The originally recommended management was pancreatectomy, but more recently medical management has been used. In this study, we found a low incidence of the condition in our large bariatric program. All cases were successfully managed with diet and occasionally medical therapy.

**Conclusion:** Post-bariatric hypoglycemia is a rare but serious complication of bariatric surgery. In our study the incidence was 0.55% of all bariatric surgery cases. The condition was successfully managed with diet and/or medical therapy in all cases, without the need for surgery. Only 4 patients (0.37% of all bariatric cases) required pharmacologic treatment.

**Abstract #308**

**HYPERINSULINEMIC HYPOGLYCEMIA SECONDARY TO NESIDIOBLASTOSIS**

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**Objective:** Nesidioblastosis, a rare cause of hypoglycemia in adults, is defined as hyperinsulinemic hypoglycemia due to hyperplasia of pancreatic cells lines. It is associated with persistent hyperinsulinemic hypoglycemia of infancy and gastric bypass in adults. This is a puzzling case of severe hypoglycemia secondary to nesidioblastosis in a patient with no history of gastric bypass.

**Case Presentation:** A 72 yo WM with a PMH of cholelithiasis, cholangitis s/p ERCP, and rheumatoid arthritis, on chronic prednisone presented to an outside hospital after waking up around 2:00 am sweating and shaking violently. His wife, who takes glipizide, byetta and metformin, checked his blood glucose (BG) level. It was 14. EMS was called and gave two amps of D50 while in transit to the hospital. At the hospital his BG on BMP was 34. Insulin and c-peptide were elevated. He was started on D10W IV fluids and transferred to the ICU. Vitals were stable and physical exam was unrevealing. Despite continuous D10W for IV fluids, he became hypoglycemic. He was started on D 25% IV fluids. On admission, he had a HbA1c of 5.1, Cr 1.2, TSH of 0.26 and Free T4 1.46. The patient’s BG was monitored with hourly finger sticks. A finger stick was done at 16:30 when the D25W was stopped for 5 minutes. BG dropped to 29. On BMP, BG was 38, with a C-peptide 22.6, insulin level 98, proinsulin level 17, and his beta hydroxybutyrate < 0.2. A sulfonylurea and meglitinide screen was negative.
CT ABD showed a pancreatic cyst. MRI ABD showed no pancreatic neoplasm. EUS showed a unilocular cyst in the body of the pancreas. FNA showed mucin and no neuroendocrine tumor. Arterial Ca stimulation revealed diffuse elevation in insulin secretion in all venous territories of the pancreas, consistent with nesidioblastosis. **Discussion:** Hyperinsulinemic hypoglycemia can be due to endogenous hyperinsulism, non islet cell tumors, or drugs. Treatment of nesidioblastosis depends on the clinical presentation of the patient and results of localization tests. If it is located in a specific region of the pancreas, a resection of the pathologic area can be done. In his case, with diffuse elevation in his insulin levels in the pancreas, a total pancreatectomy was suggested. Treatment with medications such as diazoxide or calcium channel blockers in patients that are not good operative candidates is possible. **Conclusion:** The tumor board endorsed total pancreatectomy vs a pancreatectomy with islet transplant. The patient refused surgery. He was euglycemic at discharge and at 4 week check up in the clinic. He reported an episode of hypoglycemia into the 50s. The patient did well on frequent small meals per day with Megace for his appetite.

**Abstract #309**

**LEVOFLOXACIN INDUCED METABOLIC COMA**

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**Case Presentation:** Fluoroquinolones are a commonly used class of antibiotics and are generally well tolerated. Except for Gatifloxacin (withdrawn from the market), no significant glycemic disturbances have been reported. We present a rare case of a 65 y/o lady with Type 2 DM on glipizide therapy, hypothyroidism and recent history of pneumonia. She was found comatose by the EMS with fingerstick glucose of 15 mg %. She was resuscitated with glucagon and 50% dextrose and denied any prior hypoglycemic episodes. Self monitored blood glucose values were mostly b/w 120- 150 mg%. She denied overdosing on oral hypoglycemic agent or surreptitious self injection of insulin. This was corroborated by reconciliation of her medication supplies and pill counting. After initial recovery, recurrent hypoglycemic episodes occurred over the next two days with no clear explanation. On the third day, she recovered completely, however an extensive workup was initiated for recurrent hypoglycemia. HbA1c was 6.8 mg% (4.4-6.4 mg %), insulin 51.3 uU/ml(2.6-24.9 uU/ ml), IGF-1, 301ng/ml ( 27-223 ng/ml) and C peptide 9.3 ng/ml( 0.8-3.5 ng/ml). All levels were elevated but in the setting of fluctuating glucose values after glucagon administration, these values were deemed as non diagnostic. Cortisol level was 20.7 ug/dl ( 5-23 ug/ dl) , TSH 7.490 uU/ml (0.27-4.20 uU/ml), free T4, 1.54 ng/ml (0.90-1.70 ng/ml) and Total T4, 5.30 ug/dl (4.6-12 ug/dl). She was also evaluated for hyperinsulinemic states and hypoglycemic syndromes with a 72-hour fast. Her blood glucose values remained consistently above 120 mg% during this period. Endoscopic ultrasound did not reveal any mass like pathology in pancreas. Repeat medical reconciliation revealed that she took her last dose of oral levofloxacin for therapy of pneumonia on the same day she developed severe hypoglycemia. In the absence of any other plausible explanation, we concluded that our patient experienced a rare but life threatening adverse effect to levofloxacin. **Discussion:** Patients with Type 2 DM and on sulphonylureas are at risk of fluoroquinolone-induced hypoglycemia. Proposed mechanism includes stimulation of insulin secretion from pancreatic B-cells by direct action at pore forming KIR 6.2 subunits of potassium ATP channels. This effect may not be clinically significant in all patients because of physiologic mechanisms that regulate blood glucose levels. Our patient probably had low baseline glycogen stores due to poor intake. This was further compounded by the fact that she was taking both glipizide and levofloxacin. **Conclusion:** The clinicians should remain vigilant when prescribing fluoroquinolones, especially for patients who are prone to dysglycemic events.

**Abstract #310**

**RECURRENCE OF FASTING EVOKED EN-ROUTE HYPOGLYCEMIA IN DIABETES (FEEHD) IN A PATIENT WITH DIABETES DESPITE PRIOR EDUCATION FOLLOWING A PRIOR FEEHD INCIDENT: A CALL TO INCREASE CLINICIANS’ AWARENESS ABOUT THIS OVERLOOKED PROBLEM**

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**Michigan State University**

**Objective:** We recently reported on a newly recognized form of hypoglycemia we referred to as FEEHD (Fasting-evoked en-route hypoglycemia in diabetes). In a case series report, we described a patient with type 2 diabetes (T2DM) who developed severe asymptomatic hypoglycemia caused by taking insulin while he was
failing for lipid testing. He was then properly educated about FEEHD. Nevertheless, he recently has another hypoglycemic incident. We describe how he developed the recurrent hypoglycemia.

Methods: A case presentation.

Case Presentation: A 70 year old man with T2DM for over 30 years takes NPH Insulin (20 units) and Regular insulin (10 units) in the morning, in addition to metformin 1 gm twice daily. 2 years prior, he had a FEEHD incident (glucose of 31 mg/dl) due to taking insulin (both Levemir and Regular Insulin) while he was fasting for the purpose of lipid testing. He was instructed at the time to never fast again for lab testing, or to call for instructions should fasting for medical reasons be unavoidable. We have been monitoring his lipids with non-fasting testing. However, recently a fasting lipid test was ordered by the patient’s family doctor. The patient tried to explain that he should not fast for lipid tests, but the patient was instructed, nevertheless, to proceed with the fasting test. While the patient had been instructed that he should not take insulin while fasting, he took his full dose of NPH (20 units) and Regular Insulin (10 units) and proceeded to the laboratory facility. His glucose was reported later as 65 mg/dl. The patient felt little hungry but had no other symptoms. From prior experiences, he always kept a snack in the car while going for fasting lab tests, so following the blood draw, he left the lab and rushed to his car and took his breakfast immediately.

Discussion: Diabetes education programs lack guidelines to prepare patients fasting for lab tests. Searching the literature revealed a fatal case of FEEHD published in 2004. Since 2010, we presented and published multiple studies and cases describing FEEHD, an overlooked safety problem in diabetes management. For the first time, and since 2012, the American Diabetes Association began to include a brief mention about this issue in its annual practice guidelines in the section about hypoglycemia. However, this critical educational piece is universally lacking in clinical settings. This case illustrates this assertion: Despite the patient’s explanation to his family doctor, he was advised to proceed with the fasting lab tests.

Conclusion: Clinicians should properly instruct their patients on adjustment of anti-diabetic medications, when fasting for lab tests, to avoid hypoglycemia.

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Abstract #311

RESISTANT HYPOGLYCEMIA IN GASTRIC LYMPHOMA WITH DISTAL PANCREATECTOMY IN SETTING OF RECURRENT SUBCUTANEOUS OCTREOTIDE TREATMENT

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Case Presentation: A 64-year-old woman with hypertension and type 2 diabetes mellitus (A1C 5.6%) diagnosed with gastric lymphoma and one month post partial gastrectomy, distal pancreatectomy and splenectomy, presents with resistant hypoglycemia since surgery, requiring D10 IVF for support. Octreotide acetate (250 mcg TID) treatment had been initiated two days postoperatively for pancreatic leak and fistula prevention. Treatment with low dose insulin led to refractory hypoglycemia (as low as 5 mg/dL) even while receiving tube feeding. The hypoglycemia was in context of long-standing diabetes requiring 65 units Lantus daily at home, critical illness and post-op stress. Differential diagnoses include exogenous insulin, octreotide treatment, adrenal insufficiency, thyroid disease, kidney injury, pancreoprivic DM due to pancreatectomy, and sepsis. Patient had no kidney injury (creatinine 1.0 mg/dL), no adrenal insufficiency (ACTH stimulation test: basal cortisol 15.6 mcg/dL, post 28 mcg/dL), no thyroid dysfunction (TSH 0.590), no exogenous insulin, and no clinical or laboratory signs of sepsis. C-peptide (0.2 ng/ml) showed no endogenous insulin production. On chart review, hypoglycemia corresponded temporally to octreotide treatment. Discontinuing octreotide improved hypoglycemia within hours and resolved it by 24 hours, with baseline insulin resistance apparent.

Discussion: Octreotide is a synthetic peptide analog of somatostatin that binds to G protein-coupled somatostatin-2 receptors in pancreatic beta-cells, decreasing calcium influx and inhibiting insulin secretion. It has been used for supplemental treatment of insulinomas and sulfonlurea-induced hypoglycemia, where it markedly inhibits insulin secretion and decreases hypoglycemic events. However, in context of recurrent use without sulfonlurea toxicity or other insulin-secreting pathology, octreotide’s role in inhibiting a broad range of hormones, including growth hormone and glucagon (but not cortisol, epinephrine, IGF-1 or IGFBP-3), impairs the ability to mount a counter-regulatory response, resulting in severe hypoglycemia with any hypoglycemic stimulus, even low dose insulin. Somatostatin analogues impair hepatic glucose output and also delay intestinal absorption of carbohydrates. Some reports indicate that continuous low-dose IV octreotide
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may have less hypoglycemic side effects than intermittent subcutaneous injections. This may be a treatment consideration if octreotide is needed and hypoglycemia is severe.

Conclusion: Octreotide, a somatostatin analog helpful for treating hypoglycemia of insulinomas or sulfonylurea toxicity, can otherwise cause hypoglycemia by blocking counter regulatory hormones needed to maintain normoglycemia.

Abstract #312

PSEUDOHYPOGLYCEMIA - INEFFECTICACY OF FINGER-STICK GLUCOSE MEASUREMENT IN AUTOIMMUNE MICROVASCULAR DISEASES

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Case Presentation: A 56 year old African-American woman with a past medical history of Systemic Lupus Erythematous (SLE), Raynauds Syndrome, and Sjogren’s syndrome, was admitted for treatment of a neck abscess after recent surgical correction of Zenker’s diverticulum. Unable to eat, she was placed on Total Parenteral Nutrition (TPN) support. During her stay, she was intermittently found to have finger-stick glucose measurements as low as <35 mg/dl, and symptoms of dizziness, blurry vision, and overall weakness. Her symptoms were vague, and happened while on TPN, as well as while being fasted (no oral or intravenous (IV) feeding for more than 8 hours). Even with really low finger-stick glucose, the patient maintained normal mental status, and had only vague symptoms of weakness and blurry vision. However, IV glucose administration seemed to relieve the symptoms during some of the episodes. The “hypoglycemic” episodes with low finger-stick glucose and symptoms were not correlated with low venous blood glucose drawn concurrently. Workups for autoimmune hypoglycemia, insulinoma, alcoholism, adrenal insufficiency, or surreptitious use of sulfonylureas were all negative. It was noted that during episodes of the above mentioned symptoms, the patient’s hands were very cold, and it was difficult to express blood for finger-stick glucose measurements. An ear lobe stick, done when the finger-stick glucose was “really really low”, revealed a glucose level of 101 mg/dl, proving pseudohypoglycemia in this patient.

Discussion: Pseudohypoglycemia has been reported in the literature in the setting of autoimmune diseases, especially those that affect the micro-vasculature (e.g. SLE, Raynaud’s syndrome, etc). In such cases, measurements of low finger-stick glucose have been attributed to low flow, increased glucose transit time, and hence, increased extraction by tissues. Therefore, finger-stick glucose measurements can be inaccurate and must be correlated to clinical symptoms and blood glucose levels. In our case, there was a clear discrepancy between the level of “hypoglycemia” and the clinical picture.

Conclusion: If there is a discrepancy between the finger-stick glucose measurement and the clinical picture, pseudohypoglycemia can be an occult culprit and can be detected by using other sites (e.g. ear lobe) to measure glucose.
LIPID/CARDIOVASCULAR DISORDERS/HYPERTENSION

Abstract #400

IMPACT OF LIPID DISORDERS AND OTHER VASCULAR DISEASES IN MORTALITY AMONG SAUDI PATIENTS WITH HEART FAILURE

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Objective: To assess the impact of dyslipidemia and other lipid disorders in patients with congestive heart failure.

Methods: This retrospective, single center study was done at King Abdulaziz Medical City, Riyadh, Saudi Arabia from 2002-2008. 392 of the 500 cases seen were included. Charts were reviewed and information on medical history, medications and lipid status were documented.

Results: Having a low HDL-cholesterol level was the most common lipid disorder with 82.9%, followed by hypertriglyceridemia (35.2%), atherogenic dyslipidemia (27.8%) and hypercholesterolemia (9.2%). Diabetes mellitus is the single most significant predictor for mortality (p = 0.001). Among the lipid disorders, only low-levels of HDL-cholesterol contributed to significant mortality risk [OR 1.29 (Confidence Interval 1.04-1.59)] (p-value < 0.01) adjusted for age, gender and statin use.

Discussion: The main findings is that the prevalence of lipid disorders remains high particularly low-HDL cholesterol levels despite majority of the subjects taking lipid-lowering agents and that DMT2 is the significant independent predictor of mortality among Saudi patients with congestive heart failure. The results of the present study have clinical implications. That emphasis should be given in elevating HDL-cholesterol levels among subjects with congestive heart failure, without compromising current management on LDL-lowering drugs. Current management should not be limited to conventional statin use and should promote other treatments that would elevate HDL-cholesterol levels.

Conclusion: The results of the present suggest that emphasis should be given in elevating HDL-cholesterol levels among subjects with congestive heart failure, without compromising current management on LDL-lowering drugs. Current management should not be limited to conventional statin use and should promote other treatments that would elevate HDL-cholesterol levels.

Abstract #401

HYPERTENSION IN IKORODU: A COMMUNITY SURVEY

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Objective: The aim of this pioneer study in a rural community, Maya, in Ikorodu a suburb of Lagos is to determine the prevalence of hypertension in a rural area.

Methods: The blood pressure of 54 Maya dwellers (mayaites) were taken in a day after obtaining consent through their opinion leader. The exercise lasted for 3 hours with each of the participants taking turns, the mercurial sphygmomanometer was used to measure the blood pressure at heart level. None of the participant took alcohol nor smoked at least 24 hours before measurement of blood pressure and no medication was taken at least 4 hours to the exercise.

Results: A total of 54 participants were recruited with age range 25 to 72 years. Of these 28(51.85%) participants were male while 26 (48.15%) participants were female. 33 participants were hypertensive representing a prevalence of hypertension of 61.1% among these rural dwellers. Of these hypertensives 16(48.49%) are male and 17(51.51%) are female. Hence the male hypertensive prevalence was 29.6% while the female hypertensive prevalence was 31.5%. The literature that put the prevalence of hypertension in a rural area.

Discussion: The literature that put the prevalence of hypertension in rural communities in Nigeria as 5-7% needs to be reviewed as this appears to be obsolete based on this study. The exercise lasted for 3 hours with each of the participants taking turns, the mercurial sphygmomanometer was used to measure the blood pressure at heart level. None of the participant took alcohol nor smoked at least 24 hours before measurement of blood pressure and no medication was taken at least 4 hours to the exercise.
Conclusion: Since hypertension cannot be eradicated, then concerted effort should be put in place by our government towards primary prevention. Banning the use of tobacco will be an efficacious national health policy towards primary prevention of hypertension.

Abstract #402

MULTIFACTORIAL DYSLIPIDEMIA RESULTING IN DIABETES IN A PATIENT WITH HIV INFECTION

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Objective: To present the journey of a patient who developed severe dyslipidaemia which eventually led to diabetes due to multifactorial causes during the course of his HIV infection and treatment.

Methods: A narrative description of a patient who developed an adverse metabolic environment due to HIV infection and its treatment leading to hyperlipidemia and diabetes.

Case Presentation: A 40 year Zimbabwean man was diagnosed with HIV infection in 2008 with symptoms of weight loss, pruritus and renal impairment. His CD4 count was 30 (5%) with a creatinine of 180 µmol/L and nephrotic range proteinuria and biopsy showed tubulo-interstitial nephritis. He was commenced on HAART (Combivir and Kaletra) with serial monitoring of metabolic parameters. He was normoglycemic at presentation but his lipid profile was deranged with cholesterol (TC) of 13.9 mmol/L and triglyceride (TG) of 7.5 mmol/L. Over the next three years his lipid profile deteriorated further and he was tried on different preparations of statins (due to intolerance) and ezetemibe. A switch of his Kaletra was made to Efavirenz to make his anti retroviral (ARV) treatment more lipid friendly which had minimal effect. He represented in 2012 with overt osmotic symptoms (Glucose 34 mmol/L, HbA1c-91 mmol/mol) and gross dyslipidaemia (TC-31.7 mmol/L, TG-53.8 mmol/L). An experienced ophthalmologist graded his fundus findings as proliferative retinopathy (PR). This study was conducted in SRM Medical College situated about 40km from Chennai, Tamilnadu, India.

Results: Among the 25 patients belonging to the study group, 21 patients had NPDR and 4 patients had PDR. Patients with DR had significantly elevated levels of Lp(a) and plasma glucose levels. 3 patients of the control group and 10 patients of the study group were on lipid lowering medications.

Discussion: Abnormalities in lipid metabolism in HIV infected patients occur due to the interplay between host factors, systemic inflammatory response associated with persistent viremia and the metabolic effects of anti-retroviral (ARV) agents used as a part of HAART regimes. The pattern of dyslipidaemia is variable although hypertriglyceridaemia is often more common. Studies have linked hypertriglyceridaemia and insulin resistance but whether it is a “cause” or “consequence” is not known. The combined effect of HIV infection, ARV treatment and nephrotic syndrome in our patient had led to severe dyslipidaemia which in turn had led to altered insulin sensitivity and resistance leading to frank diabetes.

Conclusion: This case illustrates that an abnormal metabolic milieu created by the effect of HIV virus and HAART treatment can lead to severe hyperlipidemia which can be a forerunner for dysglycemia.
Abstract #404

A STUDY ON THE PATTERN OF LIPID PROFILE AND APOLIPOPROTEINS IN PATIENTS WITH DIABETIC RETINOPATHY (DR) IN RURAL POPULATION IN SOUTH INDIA

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Objective: To know if the measurements of apolipoprotein AI (apo AI) and apolipoprotein B (apo B) may be more directly relevant to the biophysiological changes associated with DR than the traditional lipids.

Methods: The study subjects consisted of 30 type 2 diabetic patients with DR and 20 type 2 diabetic patients without DR. Diabetic retinopathy was determined by an ophthalmologist using fundoscopic examination. Serum levels of lipids and lipoproteins were measured by standard enzymatic methods. This study was carried out in SRM Medical College situated about 40km from Chennai, south India.

Results: The mean level of apo AI was decreased in the DR group when compared with the control group, but the difference was not statistically significant. Similar results were obtained for HDL cholesterol. There was no significant difference between apo B levels in both the groups.

Discussion: Dyslipidemia is associated with initiation and progression of diabetic retinopathy). Higher apo B levels which may reflect higher lipoprotein related toxins are destructive to arterial and retinal vascular cells. In the present study we have analysed the levels of apolipoprotein AI and B in patients who have developed diabetic retinopathy. Apo AI has anti-inflammatory and antioxidant effects and is involved in intra-retinal lipid transport. A decrease in apo AI levels has been observed in the diabetic retinopathy group, although no significant difference was observed between the apo AI levels of the two groups. Apo B levels were not statistically significant between the two groups. These findings could be due to variations in the severity of diabetic retinopathy among the participants, moreover the control group comprised of patients with type 2 diabetes. The major limitation of this study was the small size of the study groups. There was widespread use of statins in both the study and control groups.

Conclusion: In conclusion in this study we did not find any relationship between serum apolipoprotein levels and diabetic retinopathy in type 2 diabetic patients.

Abstract #405

HYPERTRIGLYCERIDEMIC PANCREATITIS TREATED WITH PLASMAPHERESIS

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Case Presentation: A 37 year-old man with type 2 diabetes and hyperlipidemia, presented with abdominal pain and vomiting about 8 hours after a fatty meal. The symptoms consisted of severe (9/10), sharp, burning and constant, mid-epigastric pain, radiating to the upper abdomen and associated with nausea and yellow vomitus devoid of blood and coffee grounds. He did not adhere to prescribed medications or diet, denied drug use, recent travel and alcohol use. Family history was not significant. Pertinent exam findings were obesity, BMI of 33kg/m2 and epigastric tenderness without rebound. The rest of the exam was normal. Significant laboratory findings included grossly lipemic blood, glucose of 349mg/dL without acidosis, WBC count of 12.5K with neutrophil predominance, lipase of 1,780Units/L and triglyceride (TG) level of 6,220mg/dL. CT scan of the abdomen revealed peri-pancreatic inflammation consistent with pancreatitis and no hepatobiliary disease. Initial treatment with intravenous normal saline, metoclopramide, pantoprazole, morphine and ondansetron improved subjective pain to 5/10. The patient was admitted to the...
medical service, made NPO, and started on subcutaneous insulin. In the next 12 hours he became lethargic, developed bandemia, increased anion gap metabolic acidosis and elevated creatinine. He was transferred to the MICU and continuous insulin infusion with goal glucose of 150-200mg/dL, aggressive fluid resuscitation with normal saline at 200cc/hr, and electrolyte supplementation were initiated. Despite correction of glucose and electrolytes, symptoms and very severe hypertriglyceridemia persisted. On day 2, plasmapheresis was initiated and TGs decreased from 2,920 to 1,136mg/dL. After the second session on day 3, they fell to 510mg/dL. The patient was transferred out of the MICU on day 4 and continued on basal and prandial insulin, simvastatin, gemfibrozil and omega-3-acids. He was discharged home on day 7 and remains symptom free to date.

Discussion: Acute pancreatitis is a medical emergency requiring prompt diagnosis and treatment with fluid resuscitation, analgesia, bowel rest and removal of inciting agents. Most common causes are gall stones, alcohol and hypertriglyceridemia. TGs ≥ 1,000mg/dL increase the risk of pancreatitis and associated complications. Hypertiglyceridemic pancreatitis requires urgent therapy, such as insulin and heparin infusions, to rapidly lower TG levels. If deterioration occurs despite the aforementioned measures, plasmapheresis should be initiated.

Conclusion: In addition to insulin infusion, plasmapheresis should be considered in the early management of hypertiglyceremic pancreatitis to achieve rapid and effective lowering of triglyceride levels.

Abstract #406

ENDOTHELIAL DYSFUNCTION AND INFLAMMATION MARKERS OF DIABETIC PATIENTS FOLLOWED IN PRIMARY AND TERTIARY CARE IN ABU DHABI, UNITED ARAB EMIRATES

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Objective: Comparing the cardiovascular risk profile including endothelial dysfunction and inflammation markers in diabetic patients followed in primary and tertiary care.

Methods: We studied Adult Emirati diabetic patients attending two primary care clinics and the diabetes center at a tertiary hospital in Abu Dhabi, United Arab Emirates. Levels of hs-CRP, IL-6, IL-1ra, NT-ProBNP, sICAM, and sVCAM were measured. Logarithmic transformation was done if the distribution was skewed.

Results: Diabetic patients followed in tertiary care were older (54.2±10.2 vs. 51.9±11.9 years, P=0.09), had longer duration of diabetes (11.7±7.1 vs. 6.3±7.0 years; P<0.001) and were more likely to be males (47.8 vs. 23.7%; P<0.001), to be on statins (78.4% vs. 67.2%; P=0.03) and to have micro- (25.5 vs. 13.6%; P=0.01) and macrovascular (33.1 vs. 22.0%; P=0.06) diabetic complications compared to those followed in primary care. They also had significantly higher NT-ProBNP and IL-1ra levels.

Discussion: Obesity, smoking, dyslipidemia, hypertension and ageing increase the risk of endothelial dysfunction, atherosclerosis and therefore the overall cardiovascular risk profile. The hs-CRP levels were lower in the tertiary care center.

Conclusion: Diabetic patients followed in tertiary care have more advanced disease compared to those followed in primary care. However, they have better lipid profile and blood pressure, and lower hs-CRP levels which suggest more aggressive cardiovascular risk reduction particularly with statin therapy.
Abstract #407

ERUPTIVE XANTHOMAS DUE TO SEVERE HYPERTRIGLYCERIDEMIA IN A PATIENT WITH UNCONTROLLED DIABETES MELLITUS

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Objective: Severe hypertriglyceridemia (HTG) is a term given to triglyceride levels above 1000 mg/dL. We present a case of severe HTG complicated by insulin resistance and uncontrolled type 2 diabetes mellitus.

Case Presentation: A 50 year old man without any medical problems presented complaining of generalized weakness, abdominal pain, nausea and vomiting. He did not seek any medical care for several years and denied smoking or alcohol use. Family history was negative for diabetes, lipid or cardiovascular disorders. Vital signs were stable and physical examination revealed eruptive xanthomas, involving mainly the extensor aspects of both knees, and other scattered elsewhere (Picture). Plasma glucose was 877 mg/dL, and glycated hemoglobin A1c was 15.4 %. He was found to be in diabetic ketoacidosis which resolved after treatment with intravenous fluids and insulin infusion. He was found to have acute pancreatitis with lipase of 1846 U/L and amylase of 453 U/L. Workup for a possible etiology for pancreatitis revealed elevated triglycerides (TG) of 1958 mg/dL. Thyroid and liver function tests were normal. Creatinine was 2.22 mg/dL. Ultrasound of the abdomen showed fatty infiltration of the liver without gall stones, but the pancreas could not be visualized. Pancreatitis resolved with bowel rest and intravenous fluids, and his glucose reading improved on insulin therapy. Considering his renal function, fibrates were not given and Niacin was started for his HTG. TG levels decreased to 733 mg/dL. The patient was discharged home on subcutaneous insulin and Niacin with a plan to institute fibrates after recovery of renal function.

Discussion: HTG can be primary due to familial lipid disorders or secondary from drugs, uncontrolled diabetes, hypothyroidism, alcohol use, high fat diet or pregnancy. Our patient had no known family history of lipid disorders, therefore we hypothesize uncontrolled diabetes has either caused or exacerbated his HTG. Diabetes causes HTG by increasing hepatic secretion of very low density lipoprotein and decreasing lipoprotein lipase levels. Treatment of HTG includes oral fibrates, omega 3 fatty acids, niacin and limiting alcohol and dietary fats. Severe HTG sometimes necessitates treatment with insulin even in euglycemic patients. In our case, impaired renal function precluded the use of fibrates; however insulin along with niacin may have helped lower the TG levels.

Conclusion: Poorly controlled DM can exacerbate primary HTG or can be one of the principal secondary causes of HTG. Severe HTG poses significant risk for acute pancreatitis, and may result in other manifestations including eruptive xanthomas, an example of which is depicted in this case presentation.
METABOLIC BONE DISEASE

Abstract #500

PREVALENCE OF MULTIPLE ENDOCRINE NEOPLASIA TYPE 1 SYNDROME IN PRIMARY HYPERPARATHYROIDISM

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Objective: To assess the prevalence of multiple endocrine neoplasia type 1 (MEN 1) in patients with symptomatic primary hyperparathyroidism (PHPT).

Methods: A retrospective analysis of 75 consecutive patients with symptomatic PHPT from January 1994 to July 2012 was done, who underwent parathyroid surgery at our centre. Five patients had MEN 1 syndrome. Among them 1 was familial MEN 1. The patients with MEN 1 were analyzed based on clinical presentation, biochemical and hormonal profile, imaging modalities and treatment outcome.

Results: Mean age of the study patients was 28.6 ± 12.9 years (male: female= 4: 1). Mean age of the rest all patients was 43.5 ± 11.5 yrs. Four were symptomatic at presentation and 1 was diagnosed on family screening. Mean duration of symptoms was 23.8 ± 12.1 months. Bone pains and painful proximal myopathy were the commonest presentation (4/4), followed by pathological fractures in 1 case. Distal renal tubular acidosis was diagnosed in 1 case, which normalized after surgery. The most common presenting manifestation was PHPT in 4 patients (80%), followed by hyperprolactinemia due to pituitary tumor in 1 patient (20%). PHPT was a universal feature (100%) in all MEN 1 syndrome followed by pituitary tumors in 3 cases (60%) and enteropancreatic neuroendocrine tumors in 2 cases (40%), with both being insulinoma. Among the pituitary tumors, prolactinoma and nonfunctioning pituitary adenoma were present in 2 each cases demonstrating equal prevalence. All PHPT patients underwent parathyroidectomy and the ones with MEN 1 had mean parathyroid gland weight was 1235.6 ± 684.5 mg, which was larger than the rest (Mean parathyroid gland weight was 835.4 ± 178.5 mg, p=0.04). Three PHPT patients with MEN 1 syndrome had double adenoma and two patients had multiglandular parathyroid involvement.

Discussion: PHPT Patients with MEN 1 tend to be younger with multifocal involvement and larger glands. Eighty % of MEN cases had PHPT as initial manifestation followed by hyperprolactinemia in 20% cases. Our series demonstrated higher incidence of symptomatic PHPT, higher prevalence of pituitary tumors (80%) and insulinoma (40%). Additionally prevalence of pituitary involvement (80%) outscores the prevalence of enteropancreatic neuroendocrine tumors (40%). These deviations from classic involvement depicted in literature could be due to small sample size of the study population.

Conclusion: All young patients with double adenoma or multiglandular parathyroid involvement should be screened for MEN1 syndrome irrespective of the symptoms. To avoid the recurrent surgical procedure, high index of suspicion is needed for diagnosis.

Abstract #501

BONE HEALTH IN TYPE 1 DIABETES PATIENTS WITH CELIAC DISEASE

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Objective: Type 1 diabetes mellitus (T1DM) is associated with various autoimmune conditions including celiac disease. Both these conditions are independently and variably associated with risk of osteoporosis. The current study intended to study bone health parameters and factors affecting it in patients with T1DM with serological evidence of celiac disease (CD).

Methods: A cross sectional study including 100 type 1 diabetes patients following up in our hospital was screened for CD by IgA tissue transglutaminase (TTG) levels. Twelve patients (12%) patients tested positive. Twenty age and sex matched T1DM (IgA TTG negative) patients served as controls. After history and physical examination, biochemical parameters including serum levels of ionized calcium, inorganic phosphorus, alkaline phosphatase, parathyroid hormone and 25 hydroxy vitamin D were measured. Bone mineral density (BMD) were measured at total body (TB), lumbar spine (LS) and left femoral neck (FN) using dual energy x ray absorptiometry (Lunar DRX DPO). Similarly DXA scan was done for measurement of total body bone mineral content (TBBMC), bone area (TBBA) and body composition. All the parameters were expressed as mean ± standard deviation. Data were analyzed using online graphpad quickcalc software and P<0.05 was considered statistically significant.

Results: TBBMD (0.77±0.04 vs 0.81±0.05 gm/cm2) and TBBMC (801±143 vs 982±196) were lower in type 1 diabetic subjects with IgA TTG positivity (p< 0.05). Similarly the total body Z score (-1.3±0.8 vs -1.0±0.9) were lower in type 1 diabetic subjects with IgA TTG positivity (p<0.05). However, TBBA (1038±149 vs 1134 ± 156 cm2) and TBBA for age Z score (-0.9±0.9 vs -0.8±0.9) did not significantly differ between
the 2 groups. 

**Discussion**: Celiac autoimmunity is associated with reduced bone mineralization in T1DM patients. Celiac disease should be considered as a possible secondary cause of osteopenia in type 1 diabetic patients found to have a reduced BMD.

**Conclusion**: Important impact of early identification of CD in T1DM could be to prevent this important complication.

**Abstract #502**

**BONE HEALTH IN CHILDREN WITH GROWTH HORMONE DEFICIENCY**

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**Objective**: The current study intended to assess the impact of growth hormone deficiency (GHD) on bone health after using various size corrections.

**Methods**: Thirty prepubescent children with GHD (Male: Female= 20:10, mean age- 9.4 ± 3.5 years) were included in the study. Data on anthropometry and total body bone mineral content (TBBMC), bone area (TBBA) and lean body mass (TBLBM) by dual energy X ray absorptiometry were collected. Anthropometric Z scores and bone parameter Z scores were computed using ethnic normative reference database.

**Results**: Mean height for age Z score (HAZ) was -5.1 ± 1.7. Mean TBBMC for age Z score was -9.2 ± 6.3 and mean TBBA for age Z score was -7.1 ± 4.3. All the study children had ‘short bones’ with HAZ < -2. Twenty four (80%) children had ‘narrow bones’ (TBBA for height Z score < -2). Twenty one (70%) children had ‘light bones’ (TBBMC for TBBA Z score < -2). Mean TBBMC for age Z scores were significantly lower than the mean HAZ (p< 0.05), indicating lower BMC after adjusting for height. Mean TBBMC for TBLBM Z score was - 3.3 ± 4.2, indicating bone mineral deficit even after adjusting for TBLBM. There was no significant gender difference in any of the parameters.

**Discussion**: GHD in children causes low bone mineral density (BMD). Height and muscle force drive bone mineralization. International society of clinical densitometry has made it obligatory to applying size corrections. Analysis of different bone health parameters lead to the demonstration that Indian children with GHD have ‘short bones’ (100% cases), ‘narrow bones’ (80% cases) and ‘light bones’ (70% cases).

**Conclusion**: Indian prepubertal GHD children had low bone mass even after applying size corrections implying need for corrective measures for their bone health.

**Abstract #503**

**VITAMIN D RECEPTOR POLYMORPHISMS AND BONE MASS INDICES IN POST MENARCHEAL INDIAN ADOLESCENT GIRLS**

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**Objective**: The aim of the present study was to assess the association between vitamin D receptor (VDR) gene polymorphism and bone mass indices in Indian adolescent girls.

**Methods**: The current study was a cross sectional one including 100 post menarcheal girls aged 15-18 years. Serum levels of ionized calcium, inorganic phosphorus, alkaline phosphatase, parathyroid hormone and 25 hydroxy vitamin D were measured. Bone mineral content (BMC), Bone area (BA) and bone mineral density (BMD) were measured at total body (TB), lumbar spine (LS) and left femoral neck (FN) using dual energy x ray absorptiometry (Lunar DRX DPO). Polymorphisms of VDR gene at the Fok1 and Bsm 1 loci were detected using SYBR Green quantitative polymerase chain reaction.

**Results**: Vitamin D deficiency (serum 25-OH D3 < 30 ng/ ml) was observed in 43% patients. The overall prevalence of genotype for Bsm1 in this study was 33.3% Bb, 29.2% bb and 37.5% BB. For Fok1 genotype, the prevalence was 44.2 % Ff, 7.5% ff and 48.3% FF. There were no significant differences in the blood parameters when classified according to Bsm1 and Fok1 genotypes. Subjects with BB genotype have significantly higher mean TBBMC (1012±178 grams), TBBA (1264 ± 186 cm²), TBBMD (0.89±0.06 gram/cm²) and LSBMD (0.81±0.04 gram/cm²) than Bb and bb (p<0.05). They showed tendency for association with LSBMC and LSBA (p<0.1). Bsm 1 genotype did not show an association with FN bone indices whereas Fok1 genotype did not show an association with TB, LS or FN bone indices.

**Discussion**: Vitamin D is important for bone health. Vitamin D deficiency is common among children and adolescents in India, in spite of abundant sunshine. With respect to the Bsm1 genotype, the Bb and bb subgroups were more prevalent (62.5%) than BB (37.5%) and were associated with worse bone health parameters. Whereas with respect to the Fok1 polymorphism, FF genotype was most common (48.3%). But there was no difference in the bone health parameters among different subgroups.

**Conclusion**: The present study demonstrates VDR gene polymorphism; defined by Bsm 1 genotype has
an influence on total body and lumbar spine bone mass indices in post menarcheal Indian girls.

Abstract #505

BILATERAL FEMORAL NECK FRACTURE DUE TO TRANSIENT OSTEOPOROSIS OF PREGNANCY (TOP)

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Objective: To report an unusual entity of transient osteoporosis of pregnancy (TOP) complicated by bilateral femoral neck fracture.

Methods: Clinical review, labs to R/O most known causes of osteoporosis & imaging studies.

Case Presentation: Pt. was a 26 Yr. old lady w/ unremarkable past medical Hx & had been on no medications. Specifically, she had never been exposed to corticosteroids, antiseizureRx, heparin, alcohol or smoking. Prior to pregnancy menses was normal. During late pregnancy she developed B/L femoral neck fracture. Elsewhere, she underwent rt. hip hemiarthroplasty & was referred to us. Physical exam was unremarkable except for limitation at both hip joints. Normal findings included CBC, renal profile, serum Ca++ (2.25 mmol/L), phosphate (1.05 mmol/L), magnesium (0.75 mmol/L), albumin (41 g/L), total serum protein (77 g/L), bilirubin (3 µmol/L), HB A1c (5.5%), ALT (8 U/L), AST (13 U/L), ALKPhos (72 U/L), Vitamin 25 OH D3 (55 nmol/L), PTH (16 ng/L), AM cortisol (417 nmol/L), ACTH (15 ng/L), E2 (595 pmol/L), FSH (12.2 IU/L), LH (78.0 IU/L). She had subclinical hypothyroidism: FT4 (10.3 pmol/L) and TSH (12.9 mU/L) abnormal antithyroid abys. Celiac serology was negative. Imaging Studies: X-rays & CT hips: intact rt. total hip prosthesis. Left hip: fractured femoral neck w/ findings of avascular necrosis, & subluxation of femoral head w/ femoral neck & greater trochanter articulating w/ superior aspect of acetabulum & diffuse osteopenia. Because her menses were resumed & she stopped breast feeding & was maintained on calcium & vitamin D, additional pharmaco Rx were avoided. FU BMD is planned in 6 mos.

Discussion: TOP was first described by Curtiss in 1959. Typically it occurs among young women late in pregnancy. The hip is commonly involved, usually unilaterally. Pts. Present w/ atraumatic groin sudden severe pain. Radiographs may be normal initially; however osteopenia involving femoral head & neck eventually become evident. MRI reveals low signal intensity of bone marrow on T1 weighted images , & high signal on T2 weighted images suggesting bone marrow edema. These changes are reported to regress after a finite duration. Alternative Rx include use of teripartide w/ an aim to improve fixation of prosthesis. Most agents, other than estrogen, remain unproven in this setting. In pts. who remain amenorrheic consideration can be given to hormonal therapy( estrogen and progesterone) or teripartide or denosumab could be valid considerations.

Conclusion: TOP is an idiopathic self-limiting condition. Dx is made by exclusion of known causes of osteoporosis. Spontaneous resolution of symptoms is usual within months. Pathological fractures are most dreaded complications.

Abstract #506

CHIN-ON-CHEST DEFORMITY: A DISABLING AND PREVENTABLE COMPLICATION OF OSTEOPOROSIS

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Case Presentation: A 69 year-old man presented to Endocrinology clinic for management of osteoporosis. His past medical history was significant for tobacco and alcohol dependence, and cardiovascular disease. He had been wheelchair bound (10 years), and disabled secondary to advanced spinal osteoporosis, complicated by prior vertebral compression and pelvic fractures. His physical examination disclosed severe cervical kyphosis resulting in a chin-on-chest deformity. There were no findings of increased neck flexor tone, neck extensor weakness, or cervical myelopathy. His weight at the time of evaluation was 102 kilograms with a height of 178.5 centimeters (body mass index = 32). BMD of the right femoral neck showed a T-score of -2.6, consistent with osteoporosis. Laboratory evaluation showed a 25-hydroxyvitamin D level of 41 ng/mL (goal greater than 30), serum calcium of 9.5 mg/dL (normal: 8.9-10.1), phosphorus of 4 mg/dL (normal: 2.5-4.5), and alkaline phosphatase of 99 U/L (normal: 45-115). Thyroid stimulating hormone and serum protein electrophoresis studies were normal. Orthopedic surgical referral was recommended, and he underwent corrective cervical spine fusion. Osteoporosis management with vitamin D and calcium supplementation, with the addition of daily Teriparatide injections was recommended.

Discussion: Etiologies of the dropped-head syndrome may be easily distinguished on the basis of the clinical examination demonstrating floppy (e.g. neck extensor myopathy), forced (e.g. cervical dystonia), or fixed neck images.
deformities (e.g. cervical spine deformity, as in our case). Chin-on-chest deformity as a result of excessive cervical kyphosis secondary to osteoporotic compression fractures is considered rare in modern times.

**Conclusion:** Our patient had multiple preventable risk factors for osteoporotic fractures, including tobacco and alcohol dependence. Our case demonstrates the disabling functional consequences of inadequately treated osteoporosis, and highlights the critical importance of preventative management.

Abstract #507

**PRIMARY HYPERPARATHYROIDISM IN PATIENTS WITH UROLITHIASIS: PREVALENCE AND PREDICTORS**

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**Objective:** To know the prevalence of primary hyperparathyroidism (PHPT) in patients presenting with urolithiasis and assess for predictors of PHPT in urolithiasis.

**Methods:** This cross sectional study was conducted between July 2005 to July 2012 in department of endocrinology and urology at our hospital. In this study a total of 165 consecutive patients with urolithiasis with radioopaque stones were evaluated for clinical and biochemical profile. Stones retrieved were analyzed for type of stone using infrared spectroscopy.

**Results:** Out of these 165 patients, 123 were males, 42 females, with a mean age of 34.5±12.1 yrs. Eleven patients (7%) had histopathologically proven PHPT. Mean age of these patients was 45.6 ± 12.4 years with male: female ratio of 4: 7. Prevalence of bone pains, backache, fracture, weakness, fatigability, joint pain, and myopathy were more common in PHPT group. Three (35%) patients in PHPT and 3 (2%) in non PHPT group had nephrocalcinosis (p<0.0001). Simultaneous renal and ureteric stones were significantly more common in PHPT patients (p<0.0001). Calcific pancreatitis was found in 2 (18.1%) patients with PHPT as compared to 1 (0.6%) in non PHPT group (P value - 0.001). Mean percent increase in TBBMC was significantly higher in group B (from 841±174 gm to 1018±226 gm, 22.3%) compared to group A (from 793±138 gm to 935±185 gm, 17.6%, P= 0.02). Improvement in TBBMC-for-age Z score was higher in the group B (from −1.1±0.9 to −0.9±0.9, 22%) vs group A (from −1.1±0.7 to −1.1±0.8,

**Discussion:** The prevalence of PHPT in our patient with urolithiasis is 7%. Urolithiasis is more common in males but prevalence of PHPT is more common in females with urolithiasis. Urolithiasis patients with PTPH are older with additional symptomatology. Serum calcium, alkaline phosphate, parathyroid hormone levels were predictors of PHPT. Nephrocalcinosis, concomitant ureteric and renal stones and calcific pancreatitis were predictors of PHPT in urolithiasis patients.

**Conclusion:** PHPT should be considered as an etiologic factor in urolithiasis.

Abstract #508

**BONE MASS ACCRUAL FOLLOWING SUPPLEMENTATION OF VITAMIN D ALONE VERSUS VITAMIN D + CALCIUM IN UNDERPRIVILEGED INDIAN PREMENARCHEAL GIRLS.**

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**Objective:** To determine effectiveness of supplementing vitamin D alone vs vitamin D + calcium on bone mass accrual in underprivileged Indian premenarcheal girls.

**Methods:** A double blind, matched pair, cluster randomization study was carried out in 200 premenarcheal girls (8-12 years) from 3 public schools. The participants were randomized into 2 clusters and were allocated to receive either vitamin D (Group A): 30000 IU oral cholecalciferol every 3 months or vitamin D + Calcium (Group B): 500 mg/ day calcium and vitamin D 30000 IU oral cholecalciferol every 3 months. The supplementation trial was done for the duration of 1 year. Anthropometry, biochemical parameters, total body bone area (TBBA), mineral content (TBBMC) and bone mineral density (TBBMD) by dual energy X ray absorptiometry were assessed at baseline and at the end of 1 year.

**Results:** At baseline vitamin D deficiency was observed in 84 (42%) girls. Post supplementation TBBMC, TBBMD and TBBA were significantly increased in both the groups in comparison to baseline. But the corresponding Z scores showed significant improvement only in group B. Mean percent increase in TBBMC was significantly higher in group B (from 841±174 gm to 1018±226 gm, 22.3%) compared to group A (from 793±138 gm to 935±185 gm, 17.6%, P= 0.02). Improvement in TBBMC-for-age Z score was higher in the group B (from −1.1±0.9 to −0.9±0.9, 22%) vs group A (from −1.1±0.7 to −1.1±0.8,
13.6%, p=0.03). Similarly increments in TBBMD was significantly higher in group B (from 0.78±0.05 gm/cm² to 0.82±0.06 gm/cm², 5.5%) vs group A (from 0.77±0.05 gm/cm² to 0.80±0.05 gm/cm², 3.3%, p=0.03). However increase in TBBA was not significantly different between the 2 groups (14.4% in group B vs 13.8% in group A, p>0.1). No significant difference in mean percent increase in TBBMC were observed across vitamin D categories (<20, 20-30, >30 ng/ml) in both the groups. The increase in height was similar in the two supplemented groups (7.3 ± 1.5 cm in group A vs 7.4 ± 1.4 cm in group B).

Discussion: Low adult bone mass is linked to osteoporosis and fractures and is dependent on the extent of childhood and adolescent bone mineralization. Though all 3 indices of bone health improved significantly following both vitamin D alone and calcium along vitamin D supplementation, the standard deviation scores showed significant improvement following the combined supplementation.

Conclusion: Calcium along with vitamin D supplementation was more effective in improving bone mass accrual in underprivileged premenarcheal girls than vitamin D alone.

Abstract #509

EFFECT OF VITAMIN D REPLACEMENT ON HEMOGLOBIN CONCENTRATION IN SUBJECTS WITH IRON DEFICIENCY ANEMIA AND CONCURRENT VITAMIN D DEFICIENCY: A RANDOMIZED SINGLE BLIND PLACEBO CONTROLLED TRIAL

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PGIMER

Objective: To study the effect of vitamin D replacement on hemoglobin concentration in subjects with concurrent deficiencies of vitamin D and iron is not known.

Methods: In an investigator-initiated, randomized, single blinded, placebo controlled, 12 weeks interventional trial; 30 subjects with iron deficiency anaemia (serum ferritin < 15 µg/dl) were randomized to intervention arm (cholecalciferol 0.6 million unit IM once) or placebo. In all subjects, iron deficiency was corrected with parental iron. Other causes of anaemia were excluded with appropriate investigation. The primary end point was rise in hemoglobin concentration.

Results: Baseline parameters of age, body mass index, hemogram, levels of serum ferritin, 25(OH) D and PTH were similar in both the arms. Twelve weeks after vitamin D replacement, there was significant increase in 25 (OH) D levels (57.7±20.5 vs 14.1±6.2 ng/ml, p<0.0001) and decrease in PTH levels (32.4±16.4 vs 52.9±18.4 pg/ml, p=0.003) in subjects in the intervention arm compared to the placebo arm. However, the increments in serum ferritin and hemoglobin concentration in the intervention and placebo arm did not differ.

Discussion: Vitamin D receptor has been found on bone marrow progenitor cells. Previous studies on patients with varying stage of CKD have demonstrated linear correlation between 25(OH) D levels and hemoglobin concentration and few interventional studies showed that supplementation of ergocalciferol in CKD patients reduces the erythropoietin requirement significantly. However, these were mainly cross-sectional studies and carried out in patients with CKD where PTH levels are high and 1,25(OH) D2 levels are low. Therefore, it is difficult to demonstrate the effect of vitamin D on hemoglobin concentration in patients with CKD. Contrary to previous studies, our study did not find any benefit from vitamin D replacement over Iron in these subjects. There are few plausible reasons for the negative findings of our study. One possibility is that vitamin D has a negligible effect on erythropoiesis in subjects with normal renal function. Second, PTH levels in our study are not as high as seen in patients with CKD. Marrow fibrosis has been reported in cases of primary and secondary hyperparathyroidism with very high levels of PTH. Third, calcitriol (1,25(OH)2 D) may be the major regulator of erythropoiesis rather than 25(OH)D which may be normal in subjects with vitamin D deficiency.

Conclusion: Vitamin D replacement in subjects with iron deficiency anemia after iron correction does not improve hemoglobin concentration further.

Abstract #510

ATYPICAL FEMORAL FRACTURES: RADIOGRAPHIC AND HISTOMORPHOMETRIC FEATURES IN 17 PATIENTS

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Objective: This study describes characteristics and histomorphometric and radiographic features of atypical femoral fractures (AFF) as seen in 17 cases referred for evaluation.

Methods: All patients referred for evaluation of AFF were reviewed. Patients meeting the ASBMR criteria for AFF were evaluated and tetracycline labelled bone biopsies were completed. Radiographs were reviewed by a musculoskeletal radiologist.
**Case Presentation:** All fracture lines were transverse or short oblique with thickened cortices. We report 17 cases of AFF in patients on long term bisphosphonate (BP) therapy. 13 of 17 fractures occurred without a fall or direct trauma to the femur with 4 cases occurring after a fall from standing height. All patients were female; average age was 65 years (range 23-80 years). 4 of 17 cases were of Chinese descent, 4 were East Indian, with 9 being Caucasian. Average BP durations of use was 9.8 years (range 6-15 years). 9 of 17 patients were on alendronate, 2 patients were on risedronate, 5 patients on a combination and 1 patient on a combination of pamidronate and alendronate. Prodromal thigh or groin pain was seen in 12 of 17 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 1 patient on prednisone for asthma. 1 patient had a diagnosis of osteogenesis imperfecta type IV with a history of multiple fragility fractures and had 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. All patients with radiographic features of AFF had been on a bisphosphonate for > 6 years. 7 of 17 patients had bilateral femoral fractures.

**Discussion:** A large number of patients with radiographic features of an AFF had evidence of mineralization abnormalities on tetracycline labelled bone biopsy. These women had normal or mildly reduced serum vitamin D levels. Decreased bone formation was seen in 3 patients. A number of these women were of Asian descent (8 of 17). 13 of 17 AFFs occurred in the absence of a fall. Prodromal thigh or groin pain was commonly seen. PPI were used in 6 of the 17 patients.

**Conclusion:** Histomorphometric features seen on bone biopsy in women sustaining an AFF in association with long term bisphosphonate use included mineralization abnormalities and decreased bone formation. Improved understanding of the pathophysiology leading to these fractures may be gained with further histomorphometric data in larger numbers of patients. A significant number of women were of Asian descent and further evaluation of all AFF with identification of predisposing key clinical risk factors is needed.

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**Abstract #511**

**XGEVA® (DENOSUMAB) INDUCED SEVERE HYPOCALCEMIA IN A METASTATIC CASTRATE RESISTANT PROSTATE CANCER (CRPC) PATIENT**

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**Case Presentation:** A previously healthy 78 y/o Caucasian male diagnosed with prostate cancer four years ago with initial T3N0M0 and Gleason score of 9, s/p definitive external beam radiation presented to our practice for consultation for persistent hypocalcemia. Patient developed becalutamide & leuprolide resistance with diffuse lumbar spine metastases one year after initial diagnosis. Due to metastases, patient received denosumab 120mg SC every four weeks for two cycles five months prior. Before starting denosumab, patient had baseline serum calcium of 8.6 mg/dL (8.6-10.3 mg/dL), albumin of 3.4 g/dL (3.6-5.1 g/dL), and ALP 299 U/L (40-115 U/L). No baseline magnesium and phosphorous levels were obtained. Two weeks after his first denosumab administration, his calcium declined to 6.4 mg/dL and albumin of 3.5 g/dL. After second administration of denosumab four weeks later, repeat calcium was 5.9 mg/dL and albumin of 3.6 g/dL. No baseline magnesium and phosphorous levels were obtained. Two weeks after his first denosumab administration, his calcium declined to 6.4 mg/dL with an albumin of 3.5 g/dL. After second administration of denosumab four weeks later, repeat calcium was 5.9 mg/dL and albumin of 3.6 g/dL. Patient’s ALP remained unchanged. Due to hypocalcemia, denosumab was stopped and patient was started on oral calcium carbonate 1200mg PO four times daily and calcium gluconate 2g IV twice a week by his oncologist. When we evaluated patient, despite above therapy for five months, his calcium was consistently between 6.5-6.8 mg/dL with an appropriately elevated PTH of 505.2 pg/mL (10-65 pg/mL). His physical exam was positive for Chovostek and Trousseau sign and inability to perform the “get up and go” test due to weakness rising from chair. We started calcitriol 0.25mcg PO daily and recommended stopping IV calcium. After one month, his calcium improved to 7.7 mg/dL (8-10.6mg/dL) with improved strength.

**Discussion:** Newer therapies for metastatic prostate cancer such as Xgeva® can cause significant hypocalcemia. Despite aggressive intravenous and oral replacement therapies, hypocalcemia are often refractory and until the pharmacological effects decline with each subsequent half life (t½=28 days) will it gradually return to normal level. Xgeva® is FDA approved for solid tumor associated...
bone metastases and prevention of skeletal-related events associated with solid tumor. Its dosage and frequency of administration are different than its biological identical, Prolia® (denosumab), which is indicated for osteoporosis only. Due to its higher dose intensity and longer half-life, Xgeva® carries a higher risk of causing severe hypocalcemia.

**Conclusion:** To avoid potential severe hypocalcemia with Xgeva®, clinician should correct any underlying hypocalcemia prior to initiation of therapy, provide supplemental calcium and vitamin D during therapy, and close serological monitoring of calcium and other electrolytes with treatment.

**Abstract #512**

AN EXAGGERATED RESPONSE TO PAMIDRONATE?

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**Objective:** We report the case of a patient with immobilization related hypercalcemia, who after treatment with Pamidronate developed hypocalcemia, requiring Calcium and Vitamin D supplementation.

**Case Presentation:** A 23 year old man, involved in a car accident, suffered multiple skull, rib, upper and lower extremity fractures, brain and lung contusions that placed him in an immobilized, non-weight bearing state for eight weeks. Six weeks into his immobilization, he developed progressive hypercalcemia peaking at 11.9mg/dl and hyperphosphatemia 4.9mg/dl requiring phosphate binders. Urine Calcium was high 613.9mg/24h, PTH and 1,25OH Vitamin D were undetectable and 25OH Vitamin D was 30.8ng/ml. Adrenal and thyroid functions, PTHrp level were normal and there were no skeletal lytic lesions, thus excluding other causes of resorptive hypercalcemia. The clinical diagnosis was immobilization hypercalcemia in the context of active bone turnover secondary to multiple healing fractures. Fluids and Furosemide did not resolve the hypercalcemia and subcutaneous calcitonin had transient effect. As heterotopic bone and ligament ossifications were seen on the skeletal survey and to prevent nephrocalcinosis and renal dysfunction, Pamidronate 60mg was administered. Over the subsequent week, Calcium level progressively dropped to 6.5mg/dl and Calcium and Ergocalciferol were administered which normalized the Calcium.

**Discussion:** Hypercalcemia of immobilization is a rare phenomenon and always a diagnosis of exclusion. Although described in patients with neuromuscular disorders and stroke, high resorption and bone turnover in fractures augment the risk of developing such hypercalcemia. Median onset is after one month of immobilization and the maximum effect at four months. It is accompanied by hyperphosphataemia, hypercalciuria and can be complicated by nephrolithiasis and renal failure. The first line in treatment is mobilization, volume repletion and loop diuretics, and if unsatisfactory results, antosteoclastic agents are the next step. After literature review, we concluded that bisphosphonates do not delay fracture healing and can be safely given to patients with immobilization hypercalcemia and fractures. Since bisphosphonates are antiresorptive agents, it is logical to use them in states of high resorption. In our patient, Pamidronate induced a “hungry bone syndrome”. When used in such a setting, close Calcium level monitoring is imperative, along with Calcium and Vitamin D administration if hypocalcemia ensues.

**Conclusion:** Given the high incidence of vitamin D deficiency, in patients with immobilization hypercalcemia, bisphosphonates may need to be used with vitamin D supplementation especially if levels are low or marginal.

**Abstract #513**

MILK ALKALI SYNDROME

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**Case Presentation:** A 60 y/o Pakistani female was found to have hypercalcemia. She reported a h/o T2DM, hypothyroidism, anxiety and renal stones which she passed spontaneously 3 years ago. She denied symptoms of hypercalcemia. However her serum calcium levels were noted to be above the upper end of reference range, but consistently below 11. She was noted to have alkalosis and low intact parathyroid levels despite a normal renal function. A 24 hr urine stone profile revealed a high normal calcium and low citrate level.Upon further history, it was noted that she avidly chewed betel nut up to 15 times a day along with lime paste and tobacco paste. She was physically and psychologically addicted to this. She was also taking calcium supplemnetations. On physical exam, she was noted to have dark pigmentation of her tongue from chronic use of lime paste and retention of betel nut in her mouth. Milk alkali syndrome was highly suspected to be the cause of her hypercalcemia. Patient was encouraged to decrease the frequency of betel nut chewing and discontinue the calcium supplements, along with fluid hydration. Her calcium levels eventually decreased to the reference range after 3 months of discontinuation.
**Discussion:** Milk Alkali Syndrome (MAS) was first described in the beginning of the 20th century when the sippy diet (milk and absorbable alkali) was introduced for the treatment of peptic ulcer disease. MAS is characterized by the triad of hypercalcemia, metabolic alkalosis and renal failure. Although hypercalcemia resolves quickly, the renal impairment is slow to respond. With the development of H2 blockers and proton pump inhibitors, the incidence of MAS secondary to treatment of ulcers has decreased. But now the more common link is excess calcium intake for osteoporosis prevention. There are several case reports of milk alkali syndrome with betel nut chewing in Southeast Asia. It is also shown that MAS from betel nut chewing can cause urinary stones. It is not well recognized in the Western world.

**Conclusion:** Betel nut chewing is common in Southeast Asia and is used in combination with other ingredients. The nut of the betel palm is called ‘Areca catechu,’ and is rolled in Piper betel vine leaf along with lime paste to mask the bitter taste of the nut. The calcium paste is produced by grinding oyster shells and is known to have considerable amount of calcium hydroxide. The calcium is absorbed in the ionized form in the lower intestine and depends on dietary phosphates to be precipitated and hence is non-absorbable. An excess in calcium and ionization by the fermentation due to a high carbohydrate diet, can ultimately lead to excessive absorption and hypercalcemia.

**Abstract #514**

**HYPERCALCEMIA ASSOCIATED WITH ELEVATED PTHR P IN A PATIENT WITH A CHRONIC SACRAL ULCER**

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**Case Presentation:** We describe a 45-year-old paraplegic African American man, paralyzed below T6 due to a gunshot wound in 1989, whose course has been complicated by chronic sacral ulcers, with biopsy confirmed osteomyelitis. Prior to admission, he moved independently in a wheelchair and could transfer from bed to chair in the nursing home. He presented with a history of weakness, fatigue, anorexia, dehydration, and 14 kilograms weight loss over approximately 2 months. He had no known history of fractures or nephrolithiasis, and denied use of thiazide diuretics, lithium, herbal supplements, or vitamins. He also had no past history of hypercalcemia. Physical examination demonstrated a 16 cm x 27.5 cm unstageable lower back ulcer with ulceration extending to the left thigh. The ulcer had a yellow fibrous exudate in its center. There were bilateral rock hard, tender 4 cm inguinal nodes. The patient was admitted after serum albumin-corrected calcium concentration in the Emergency Department was found to be 16.6 mg/dL (nl: 8.7-10.2). Further evaluation was remarkable for an ionized calcium: 1.71 mM/L (nl: 1.12-1.32); phosphorus: 3.0 mg/dL (nl: 2.5-4.3); blood urea nitrogen: 21 mg/dL (nl: 7-20); creatinine: 0.8 mg/dL (nl: 0.5-1.1). Intact PTH: undetectable; 25-hydroxyvitamin D: 18 ng/mL (nl: 30-80); 1,25-dihydroxyvitamin D: 11 pg/mL (nl: 15-75); alkaline phosphatase activity: 130 U/L (nl: 33-96). PTHrP was 40 pg/mL (nl: 14-27). CT of the pelvis showed the posterior decubitus ulceration; bony destruction of the medial aspect of the left ilium and ischial bones, left posterolateral aspect of the vertebral body of L5, and bilateral femoral heads; and lytic lesions in the bilateral iliac bones and lower lumbar spine. CT of the chest showed no evidence of nodal or pulmonary parenchymal metastatic disease. A sacral skin biopsy and right inguinal lymph node biopsy were performed. Pathology revealed invasive moderately differentiated squamous cell carcinoma.

**Discussion:** Dr. Jean-Nicolas Marjolin first described aggressive epidermoid tumors arising from areas of chronic injury such as chronic ulcers and burn wounds in 1828. Hypercalcemia due to Marjolin’s ulcer is a rare complication and the etiology of the hypercalcemia has not been well defined. While past case reports have proposed humoral hypercalcemia of malignancy as a possible mechanism, to our knowledge, this is one of the first reports to document an elevated PTHrP as the likely etiology.

**Conclusion:** Acute hypercalcemia in the setting of a large, chronic ulcer should raise suspicion for an underlying Marjolin’s ulcer and a PTHrP-mediated mechanism.

**Abstract #515**

**PROLONGED HYPOPHOSPHATEMIA ASSOCIATED WITH BISPHOSPHONATE THERAPY**

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**Objective:** Hypophosphatemia (serum phosphorus concentration <2.5 mg/dl) is commonly seen in hospitalized patients for a variety of reasons including sepsis, trauma, and alcohol-related disorders but is less commonly seen in outpatients. There are a limited number of drugs that can cause hypophosphatemia including diuretics, acyclovir
and bisphosphonates. However, bisphosphonate-induced hypophosphatemia is almost always short-lived and thought to be related to transient hypocalcemia with compensatory elevation of PTH causing phosphaturia. Herein, we report a patient with previously undescribed prolonged hypophosphatemia following zoledronic acid infusion.

**Case Presentation:** 68 yr old male with a history of steroid-induced osteoporosis, hypertension, diabetes mellitus type 2, and elevated free kappa light chains presented to the Endocrinology Clinic for evaluation of hypophosphatemia and fatigue that appeared following an infusion of zoledronic acid 5 mg on 12 August 2011 and which has persisted for 1 year. He did not drink alcohol or take phosphate-binding antacids. His medications were simvastatin, esomeprazole, modafinil, levethyroxine, cyanocobalamin, telmisartan, ferrous sulfate, metformin, and aspirin. Base line (before zoledronic acid infusion) serum phosphate was 3.1mg/dl (normal 2.5-4.5 mg/dl). After the infusion it dropped to 2.1 and stayed long for a year in a range of 2.1 to 2.3mg/dl. Base line PTH before infusion was 70 pg/ml (normal 30-100). PTH dropped to 44 after the infusion and stayed low in 40s. Tubular reabsorption of phosphate (TRP) was dropped to 32 % (normal is > 80%) after the infusion. A 24-hour urine phosphate was normal at 922 mg (normal 400-1300 mg) but the fractional excretion of phosphate was elevated at 30% (normal 5-20%) suggesting a phosphate wasting disorder. However, he has no evidence of overt hyperparathyroidism, Fanconi syndrome, or other condition that would cause this. Pt was started on phosphate treatment. Labs showed within a month there is improvement in serum phosphate levels. Increased the Phosphate level to 2.8 in one month. TRP increased to 47% from 32%.

**Discussion:** This is the first description of a prolonged adverse effect of a zoledronic acid infusion. The mechanism for this effect is unknown but may be due to either zoledronic acid’s direct effect on tubular reabsorption of phosphate or its causing a mild secondary hyperparathyroidism (PTH at baseline was 29 and was subsequently 40-50) due to a hypocalemia which is masked by his kappa light chain disease.

**Conclusion:** Prolonged Hypophosphatemia is one of the rare adverse effects of bisphosphonate infusions.

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**Abstract #516**

**DOES RECOGNITION OF VITAMIN D DEFICIENCY AFFECT THE INDICATION FOR SURGICAL TREATMENT IN ASYMPTOMATIC PRIMARY HYPERPARATHYROIDISM?**

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**Objective:** Current guidelines for the management of asymptomatic primary hyperparathyroidism (A-pHPT) recommend that levels of 25-hydroxyvitamin D should be assessed in all patients suspected of having pHPT, and vitamin D deficiency (VDD) should be cautiously corrected at the time it is detected. However, it is unknown whether vitamin D deficiency (VDD) affects the probability to meet surgical criteria currently proposed for A-pHPT patients. Aim of this study was to evaluate whether VDD recognition affects the probability to meet surgical criteria in A-pHPT patients.

**Methods:** 80 consecutive A-pHPT patients with age ≥ 50 years were studied (mean ± S.D. : age = 66.5±8.9 years; male / female = 10 / 70; PTH = 179.8±134.7 ng/l, serum calcium = 10.8 ± 0.7 mg/dl; ionized calcium =1.39±0.10 mmol/l, 25OHD = 30.0 ± 21.3 ng/ml). VDD was defined as 25-hydroxyvitamin D levels < than 20 ng/ml. "The Third International Workshop on the Management of Asymptomatic Primary Hyperparathyroidism" criteria for parathyroid surgery in A-pHPT were considered: 1- Serum calcium (> upper limit of normal) >1.0 mg/dl; 2- Creatinine clearance (calculated) reduced to <60 ml/min; 3- T-score < -2.5 at any site.

**Results:** VDD was present in 32 patients (40%). A-pHPT patients with VDD showed higher levels of PTH (240.8 ± 155.0 vs 139.1 ± 102.0 ng/l; p=0.0007), total (11.0 ± 0.7 vs 10.7 ± 0.66 mg/dl; p=0.04) and ionized calcium (1.42 ± 0.1 vs 1.37 ± 0.08 mmol/l; p=0.013) and lower levels of forearm T score (-3.00 ± 1.5 vs -2.15 ± 1.4, p=0.019) compared with A-pHPT patients without VDD. No significant difference in fulfillment of any surgical criteria was present between A-pHPT patients with VDD and without VDD (criterion of primary hyperparathyroidism = 25% vs 14.6%, p =0.2586; eGFR criterion = 19.4% vs 21.7%, p=1.000; T-score criterion = 78.1 % vs 64.6 %, p = 0.2226; respectively).

**Discussion:** VDD is frequently detected in A-pHPT and affects biochemical and densitometric features of these patients, but the recognition of VDD in A-pHPT patients does not affect the probability to meet surgical criteria.
Conclusion: The results of this study make questionable the routinely assessment of vitamin D status in all pHPT patients, as recommended by current guidelines for clinical management of A-pHPT.

Abstract #517

PROLONGED SEVERE HYPOCALCEMIA WITH DENOSUMAB

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Objective: To describe a case of prolonged severe hypocalcemia after a single subcutaneous injection of denosumab.

Methods: We describe the clinical course of the patient and our experience with hypocalcemia following denosumab and zoledronic acid at our institute.

Case Presentation: A 65 year old man with a history of stage IV glioblastoma and stage IV poorly differentiated adenocarcinoma (likely prostate cancer) with lytic lesions to the lumbar spine was seen five days after he received his first injection of denosumab 120mg subcutaneously for treatment of bone metastases. He complained of fatigue, confusion, blurry vision and leg pain. He denied numbness, tingling or cramps. He was on no other medications which would cause hypocalcemia. He took no supplemental calcium or vitamin D prior, but did start oral calcium/vitamin D supplement 3 days after receiving the denosumab injection. Physical examination was unremarkable. He had a corrected serum calcium (cCa) of 5.8mg/dl (8.4-10.2). Other labs were: phosphorus 2.3mg/dl (2.4-5), magnesium 2.5mg/dl (1.8-2.5), PTH 424ng/ml (12-90), alkaline phosphatase 1378 units/L (39-117), albumin 3.8mg/dl (3.4-5), Vitamin D 25 OH 17ng/ml (30-100) and creatinine 0.6mg/dl. EKG showed prolonged QTc interval at 492ms. A day prior to receiving denosumab he had a cCa of 8.6mg/dl and normal cCa in the past. He required large doses of intravenous and oral calcium, vitamin D and calcitriol over the next six days to maintain a cCa in the (7.5-7.7)mg/dL range. Over the following two months his cCa gradually improved to (8-8.5)mg/dl.

Discussion: Hypocalcemia has been described with both zoledronic acid and denosumab in clinical trials and case reports. A case report from Spain describes a 79 year old female who had severe hypocalcemia (4.6mg/dL) after denosumab which lasted for 6 days. The mechanism by which denosumab causes hypocalcemia may be stimulation of osteoblastic activity. We looked at 6932 patients at our institution who were given either denosumab (175) or Zoledronic acid infusions (6757) over a 6 year period. There were a total of 106 cases of hypocalcemia (cCa <8.0mg/dl up to 6 months after receiving denosumab or zoledronic acid), all in patients who had received zoledronic acid infusions. There were no reports of hypocalcemia in patients who received denosumab at our institution during this time period.

Conclusion: This is a case of prolonged, severe hypocalcemia. Physicians should be vigilant of the possibility of hypocalcemia even in patients who are normocalcemic, especially in patients at high risk of developing hypocalcemia, such as those with severe renal impairment. All patients should be supplemented with calcium and vitamin D unless hypercalcemia is present.

Abstract #518

HYERCALCEMIA CRISIS INDUCED BY INCIDENTAL HCTZ CHALLENGE IN A 75-YEAR-OLD WOMAN WITH NORMOCALCEMIC HYPERPARATHYROIDISM

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Case Presentation: Primary hyperparathyroidism (PHPT) is one of the most common causes of hypercalcemia in adult patients. The presentation of PHPT has been changing over the years. When it was initially identified 80 year ago, it was symptomatic with kidney stones, bone disease and marked hypercalcemia. More recently the presentation is more likely asymptomatic with mild hypercalcemia. Increasing number of patients with persistent normocalcemia are found to have elevated PTH levels due to the widespread use of testing for the evaluation of osteoporosis or fractures. The latest form of PHPT, termed, normocalcemic primary hyperparathyroidism (NPH), may represent an early phase of PHPT, or be a distinct phenotype of PHPT. The epidemiology and pathophysiology of NPH remains unclear. Therefore, there are no current guidelines regarding the management of this entity. We report a patient who had persistent normal calcium levels ranging from 9.6 to 10.2 mg/dl (normal range 8.4-10.3 mg/dl), normal VitD levels ranging from 30 to37 ng/ml (normal range 30-60 ng/ml) and osteoporosis. She had history of VitD deficiency in 2007 and takes Calcium-VitD2 supplements 1200mg-1000 units daily. She developed severe hypercalcemia (14.5 mg/dl) and required hospitalization and intravenous hydration soon after starting thiazide diuretics 25mg daily for hypertension management. PTH was 77 pg/ml (15-65 pg/ml) on admission and remained elevated afterward. There was no discernible secondary cause for hyperparathyroidism (renal failure, VitD deficiency,
familial hypocalciuric hypercalcemia or medications such as lithium, etc. Her calcium levels remained mildly elevated around 11 mg/dl even after the thiazide diuretic was discontinued. Subsequent parathyroid scan revealed a parathyroid adenoma.

Discussion: It is not uncommon that thiazide diuretics precipitate hypercalcemia in patients with underlying PHPT. The underlying mechanisms that thiazides induce hypercalcemia in patients with PHPT are reviewed here. It is important to clarify the diagnosis of NPH in any patient with normal calcium levels and an elevated PTH, particularly in those who have end organ involvement such as osteoporosis, as it may change the management.

Conclusion: Since the majority of patients with NPH are asymptomatic and remain normocalcemia for many years, a challenge test with thiazide diuretics may provide a shortcut to expose the underlying PHPT. Close monitoring is warranted in these patients during the test.

Abstract #519

20 FRACTURES IN 67 YEAR OLD FEMALE PATIENT: TUMOR INDUCED OSTEOMALACIA.

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Case Presentation: 67 year old Caucasian female who presented to our clinic with a history of 20 fractures over 10 years period. Her fractures included: bilateral metatarsal fractures, several tibial fractures, bilateral subtrochanteric femur fractures and numerous ribs fractures. Those fractures have never healed quickly nor completely despite inserting rods whenever was indicated. As a result she became wheelchair bound. She has been seen by multiple physicians in few centers, however no diagnosis was reached. Patient was also under the care of rheumatologist who treated her with bisphosphonates with no improvement. However with 2 years use of teriparatide there has been some improvement in the number of fractures developed and healed. Her medications at that time also included methadone, pregabalin and meloxicam for chronic pain syndrome. She presented with huge lab record that showed hypophosphatemia but no further work up was done in that regards. X-rays of her fractures showed significant osteopenia. In addition she had negative genetic testing for osteogenesis imperfecta. Our work up revealed hypophosphatemia, hyperphosphaturia, low 1, 25 dihydroxyvitamin D, normal 25-hydroxyvitamin D, normal serum PTH and elevated FGF-23. She had malignancy workup done including PET/CT scan which failed to localize a tumor. Based on our workup she was diagnosed with tumor induced osteomalacia and started on Neutra-Phos and calcitriol, both were titrated to normalize her serum phosphorus level. Her symptoms improved significantly and for last 2 years she did not develop any fractures, she is off pain medications and fully functional to the extent that she painted a room in her house.

Discussion: Tumor induced osteomalacia (TIO) is a rare entity which could be missed even by experienced physician. Patients usually present with history of chronic bone pain, fractures and proximal motor weakness. Hypophosphatemia occurring because of excessive renal phosphate excretion is usually secondary to various types of mesenchymal tumors. These tumors are historically known to be benign, small and difficult to detect. Fibroblast growth factor 23 (FGF-23) is the most reliable marker for detection of these tumors. FGF23 activity at the kidney reduces the expression of the sodium-phosphate cotransporter resulting in impairment of the phosphate reabsorption.

Conclusion: A step-wise approach utilizing functional imaging followed by anatomical imaging and selective venous sampling may be successful in some patients. For tumors that cannot be localized treatment with active forms of Vitamin D and phosphorus is usually successful like in our patient in whom till now we were not able to localize the tumor.

Abstract #520

THE MYSTERY OF HIGH CALCIUM-NORMOHORMONAL PRIMARY HYPERPARATHYROIDISM

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Case Presentation: Normocalcemic hyperparathyroidism is well recognized in primary hyperparathyroidism, however not much is known about patients with hypercalcemia but normal parathyroid hormone (PTH). We present the case of a 66-year-old female with a history of hypercalcemia for 15 years with calcium as high as 15-16mg/dl and PTH ranging between 20-30pg/ml(N12-65). 25-hydroxy-vitD was normal at 39ng/ml and 1,25-dihydroxy-vitD was mildly elevated at 87pg/ml(N15-75). Phosphorus was normal at 3.1mg/dl. She has no history of nephrolithiasis, fractures, weight loss, palpitations or excessive sweating. There was no history suggestive of a granulomatous disorder. She was not on any medications which could cause hypercalcemia.
A thorough investigation to find any non-PTH mediated cause of hypercalcemia had been negative over the years. A Sestamibi scan done in 2002 had shown possible right inferior increased activity after which she underwent right partial parathyroidectomy for primary hyperparathyroidism. Even after surgery her calcium levels stayed elevated with low normal PTH. A repeat sestamibi scan done last year showed increased focus in the left inferior parathyroid gland and then she was referred to us. After reviewing her records we decided to perform prednisone suppression test for the possibility on an underlying granulomatous disease. After 7 days on prednisone 10 mg tid, calcium was still high at 12.7 mg/dl, PTH 29 pg/ml and elevated 24hr urinary calcium level of 483.6 mg (N100-300 mg/24h). This seemed consistent with hyperparathyroidism despite the low normal PTH. She was again referred for a surgical treatment of primary hyperparathyroidism and underwent a left upper parathyroid gland removal which was enlarged and hypercellular on biopsy. The calcium has normalized to 9.9 mg/dl and PTH dropped to 8 pg/ml.

Discussion: Primary hyperparathyroidism is suspected with hypercalcemia and inappropriately high PTH. Hypercalcemia with suppressed or low-normal PTH value usually suggests a PTH independent hypercalcemia like granulomatous disorders, malignancy-associated hypercalcemia, drug induced or familial hypocalciuric hypercalcemia. A recent large study however showed that lower PTH set points as low as 5 pg/mL may exist in some patients with otherwise typical primary hyperparathyroid features. This entity has been called as normohormonal primary hyperparathyroidism. Awareness of the unusual phenotype may facilitate earlier diagnosis and surgery.

Conclusion: Normohormonal primary hyperparathyroidism is a recently described entity which should be considered in the differential of hypercalcemia with normal PTH after other secondary causes have been ruled out.

Abstract #521

HUNGRY OSTEOBLASTS IN MALIGNANCY

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Objective: Hypocalcemia is commonly seen in patients with metastatic cancer. Usually the total calcium is low with normal ionized calcium because of hypoalbuminemia. True hypocalcemia with low ionized calcium is not common.

Case Presentation: A 79 yr old Caucasian male with history of prostate cancer for 20 yrs was admitted to the hospital with suprapubic cellulitis at his cystostomy catheter insertion site. He had developed urinary retention secondary to a urethral stricture. He had previously been treated with prostatectomy, radiation and a GnRH analogue. He was in remission until a month prior to admission when his PSA was found to be elevated. Radiological investigation revealed osteoblastic metastases to spine and pelvis. Plasma calcium levels were normal (8.7 mg/dl) before the metastases were diagnosed. He denied any history of diarrhea. His oral intake of calcium was adequate. As his PSA increased (267 ng/ml), there was a decline in both total and ionized calcium levels. During hospitalization, calcium levels dropped to 6.4 and 3.2 mg/dl (corrected and ionized respectively). Clinical sings of hypocalcemia like Chvostek, Trousseau and tetany were absent. EKG was normal. CT scans revealed diffuse osteoblastic and sclerotic lesions in spine and pelvis. Bone scan showed diffuse uptake throughout whole body. Plasma concentrations of creatinine, BUN and magnesium were normal while 25 hydroxy vitamin D (25 ng/ml) was low and 1,25 di-hydroxy vitamin D (175 pg/ml) was elevated. PTH was elevated at 257 pg/ml. He was started on Calcium carbonate 1250 mg thrice daily, Vitamin D 50000 Units twice weekly and calcitriol 0.25 mcg daily. Despite this, calcium levels remained low, and he was given IV Calcium gluconate 1-2 gm daily. As his calcium levels increased, PTH decreased to 67 pg/ml. He was discharged from the hospital once his cellulitis resolved and corrected calcium increased to 8.5 mg/dl.

Discussion: Though most cases of hypocalcemia in malignancy are due to low albumin, malnutrition, poor oral calcium intake, renal failure, and severely low vitamin D, our patient had no evidence of the above conditions. The lack of other causes of hypocalcemia and emergence of hypocalcemia concomitantly with the increase in PSA due to osteoblastic metastases suggests that it was related to metastases. Pathophysiology is thought to be due to significantly increased calcium uptake by osteoblastic metastases leading to secondary hyperparathyroidism. The treatment is calcium replacement and aggressive treatment of malignancy.

Conclusion: The above case highlights a rare and interesting cause of hypocalcemia in patients with prostate cancer with osteoblastic metastases. This has been reported rarely in literature.
Abstract #522

**DXA-MEASURED CORTICAL BONE MINERAL DENSITY REFLECTS PARATHYROID HORMONE LEVELS IN CHRONIC DIALYSIS PATIENTS**

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**Objective:** The role of dual X-ray absorptiometry (DXA) in predicting fractures in chronic kidney disease (CKD) patients is controversial, partially because it fails to capture bone quality. However, by measuring bone quantity, DXA reflects many bone-related parameters strongly affected by dialysis. Our objective was to correlate T and Z scores for bone mineral density (BMD), measured by DXA, with various clinical and laboratory parameters in dialysis patients.

**Methods:** Serum parathyroid hormone (PTH) and 25-hydroxyvitamin D (25OHD) were measured in fifteen dialysis patients (6 males, 9 females [4 premenopausal], mean age 48±15 years, 6 peritoneal and 9 hemodialysis). Femoral neck and 1/3 radius T and Z scores were measured by DXA. Clinical parameters like sex, age, BMI and dialysis years were also collected. All patients were naïve to antosteoporotic treatments except vitamin D.

**Results:** In the univariate regression analysis only PTH serum levels significantly correlated with femoral neck (r=0.74 for T score and r=0.82 for Z score) and 1/3 radius (r=0.76 for T score and r=0.82 for Z score) BMD in hemodialysis patients. In the whole group both PTH and number of dialysis years significantly correlated with femoral neck (r=0.50 and 0.5 respectively) and 1/3 radius (r=0.68 and 0.5 respectively) T scores and femoral neck (r=0.66 and 0.71 respectively) and 1/3 radius (r=0.77 and 0.52 respectively) Z scores. In the stepwise multivariate regression analysis only PTH was retained in models with T and Z scores as dependent variables and sex, age, BMI, years on dialysis, PTH and 25OHD as independent variables in both hemodialysis patients and in the whole group.

**Discussion:** In CKD patients on dialysis serum PTH significantly correlated with BMD measured by DXA, particularly in the cortical bone of radius. Lack of correlation between BMD and BMI or 25OHD suggest that these factors are made insignificant by the high PTH levels. Also, dialysis years are highly related with PTH levels so in multivariate models these two parameters cannot act as independent predictors.

Abstract #523

**THE VITAMIN D LEVELS AND DXA ANALYSIS IN 377 POSTMENOPAUSAL WOMEN WITH OR WITHOUT DIABETES MELLITUS**

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**Objective:** The bone health is strongly influenced by the vitamin D status, the Body Mass Index (BMI), or by the glycemia control. The influence is reflected in the Bone Mineral Density (BMD) changes or fragility fractures (FF). We analyze the vitamin D status, DXA, as well as BMI in a group of women with or without diabetes mellitus (DM).

**Methods:** This is cross-sectional study conducted between 2010 and 2012 in C.I.Parhon National Institute of Endocrinology, Bucharest, Romania. We included only the postmenopausal patients (p) were not previously treated with anti-osteoporotic drugs. Central DXA (GE Lunar) was performed, as well as serum 25-OH vitamin D (25-OH D). The FF were confirmed by X-Ray. Linear regression (SPSS 20), and student test was used.

**Results:** 377p were enrolled: 44p with DM (DM+) and age-matched, non-diabetic 344p represented the control group (DM-). The mean age was: 58.43±7.88 yr in DM+ vs. 56±8.44 yr in DM-. The mean BMI was: 32.04±6.13 vs. 28.45±5.88kg/m2 (p=0.001). The mean 25-OH D was: 12.14 ± 6.3 (DM+) vs. 14.01 ±7.37 (DM-) (p=0.14). The mean lumbar BMD was: 0.66±1.5g/cm2 in DM+ vs. 1.11±1.31g/cm2 in DM- (p=0.04). The % of women with osteoporosis/osteopenia was: in DM+ 9.09%/43.18% vs. in DM- 16.21%/43.54%. The % of FF was 11.36% in DM+ vs. 14.11% in DM-. No correlation between 25-OH D and BMD was found (r=0.01, p=0.59 in DM+; r=0.01, p=0.14 in DM-). The % of women with diabetes mellitus was: in DM+ 12.14% vs. 9.09% in DM- (p=0.28 in DM+, but SS in DM-: r2=0.06, p=0.0001.

**Discussion:** The patients with diabetes did not present a significant difference in the serum levels of 25-OH vitamin D when compared to the patients without diabetes, but both
mean values were in the areas of vitamin D deficiency. However, the women with diabetes had a statistically significant higher BMI (absolute difference 3.59 kg/m2), and lower lumbar BMD than those without diabetes. A statistically non-significant reduction in the number of fractures (absolute reduction 2.75%, proportional reduction 19.49%) was observed.

**Conclusion:** The postmenopausal antiosteoporotics free women have an overall vitamin D deficiency. The diabetic patients did not differed by 25-OH D levels but they have a SS higher BMI and SS lower BMD, but a lower non-SS percent of FF compare to non-diabetics.

**Abstract #524**

**CALCIUM AND VITAMIN D INTAKE IN WOMEN WITH LOW BONE MASS REFERRED TO AN ENDOCRINE CLINIC FOR BONE HEALTH EVALUATION**

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**Objective:** To assess baseline calcium and vitamin D intake in women with low bone mineral density (BMD) referred to our Endocrine Clinic for bone health evaluation.

**Methods:** 400 consecutive charts of patients referred to our Endocrine Clinic for bone health evaluation were reviewed. Female patients with T scores of less than -1 at a minimum of one site were included in the study. A total of 176 patients were included. The demographics and data regarding risk factors were obtained. We also recorded the baseline calcium intake (dietary and supplements) and vitamin D intake (as supplements).

**Results:** The mean age was 63.9 years. Approximately 90.9% of patients were menopausal. The median BMD T score at the femoral neck was -2.2 (95% CI - 2.38 to -2.10) and the mean T score at the lumbar spine was -2.3(95% CI -2.47 to -2.01). The median daily intake of calcium (diet and supplements) at the time of referral was 1000 mg (mean 883 mg) (interquartile range 137 to 1325). Dietary calcium (>300 mg/day) was taken by only 34%. Approximately 71% of the women were taking calcium supplements. Total calcium intake surprisingly decreased with increasing age (spearman correlation= -0.18, p <0.02). The median daily vitamin D intake was 400 IU (mean 692) (interquartile range 0 to 800). Approximately 74% of the women reported taking vitamin D supplements and only 29% had a Vitamin D intake at or above 800 IU (95% CI, 22%-36%). There were no significant differences in the calcium or vitamin D intakes between subjects with T scores below -2.5 and those with T scores above -2.5.

**Discussion:** The National Osteoporosis Foundation recommends that adults older than age 50 years consume 1200 mg of calcium and 800-1000 IU of vitamin D daily. Most of the women in our study had intakes that were significantly less. The decrease in calcium intake with increasing age could be because of non-compliance from the need for multiple medications due to increasing co-morbidities. In addition, lack of knowledge regarding the importance of these supplements could be an important factor too.

**Conclusion:** Most of the women referred to our osteoporosis clinic had calcium and vitamin D intakes that were significantly less than the RDA. Endocrinologists and primary care providers need to ensure all their patients are taking the recommended daily allowances of calcium and vitamin D. Given the available evidence regarding cardiovascular risks, it may be prudent to advise that patients achieve as much of the RDA as possible through dietary sources of calcium.

**Abstract #525**

**THE BONE TURNOVER MARKERS AND 25-OH VITAMIN D: A STUDY IN 299 PATIENTS**

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**Objective:** The serum 25-OH vitamin D (25-OH D) is the best tool to assess the vitamin D metabolism. The bone turnover markers (BTM) abnormalities are registered in vitamin D deficiency. A direct relationship between these is still a matter of debate. We correlate to BTM and 25-OH D according to different stages of vitamin D deficiency.

**Methods:** We enrolled 299 postmenopausal women (p) in a cross-sectional study. The secondary amenorrhea was registered for at least one year. The exclusion criteria were previous therapy with anti-resorptive therapy for osteoporosis. The patients were evaluated by anamnesis, biochemical tests as serum 25-OH vitamin D, and the BTM: serum Osteocalcin (OC) and Alkaline Phosphatase (AP) as bone formation markers, and serum CrossLaps (CL) as bone resorption marker. Linear regression (SPSS20) was used for statistical analysis.

**Results:** The patients were grouped based on 25-OH D
levels: group 1 (25-OH D between 1 and 10ng/mL) 100p (av. 25-OH D: 6.67±2.15ng/mL), group 2 (25-OH D between 11 and 20ng/mL) 143p (av. 25-OH D: 14.55±2.67ng/mL), group 3 (25-OH D between 21 and 30 ng/mL) 32p (av. 25-OH D: 23.78±2.63ng/mL), group 4 (25-OH D between 31 and 40ng/mL) 12p (av. 25-OH D: 32.63±2.89ng/mL). The total av. 25-OH D level was 13.81±7.29ng/mL. The mean age was for all was 56.72±8.67 yr, and for group 1/2/3/4 was: 57.18±8.78/56.65±8.22/55.66±7.43/56.93±9.56ng/mL. Positive statistically significant (SS) correlation was found between AP and CL in groups 1 to 3, r²=0.45/0.415/0.608 (p<0.0001), and positive but not SS in group 4: r²=0.16, p=0.3. Strong positive SS correlation was between OC and CL in each group (r²=0.66/0.584/0.661/0.93), and between OC and AP and patients with 25-OH D < 20ng/mL. No correlation was found between AP and 25-OH D in either group (r²=0) but this observation was SS (p=0.001) only in group 1 and 2. No correlation (non SS) was found between CL and 25-OH D, except for group 4 were some positive correlation was found (r²=0.4, p=0.1). No correlation was found between OC and 25-OH D but SS results were only in group 1.

Discussion: The group 4 had less patients, also the mean age was similar for each group. As expected, the BTM were correlated in almost all levels of 25-OH D, suggestion that despite the lack of adequate levels of main bone action vitamin and bone formation and resorption are connected. A direct correlation between BTM and 25-OH D was not observed.

Conclusion: The BTM reflect the bone metabolism that is modified in different stages of vitamin D deficiency but the univariate analysis between each BTM and the level of 25-OH D did not show a statistically significant correlation.

Abstract #526

BONE MINERAL DENSITY AND FRACTURES IN URBAN AFRICAN AMERICANS WITH DIABETES

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Objective: This study was done to determine if urban African Americans (AA) with diabetes have a high bone mineral density (BMD) and a high rate of fractures.

Methods: In this retrospective study, 18 months of data were reviewed from 1017 medical records of AA patients whose BMD was measured using Dual-energy X-ray absorptiometry (DXA) scan at the lumbar spine (L1-L4), femoral neck and middle third of the forearm, along with T scores and Z scores, which are used to determine osteopenia and osteoporosis. Our exclusion criteria included patients who had: cancer or history of cancer, ethnicity other than AA, age <40 or >85 years, history of treatment with bisphosphonates/nuclear factor-xB ligand inhibitors/hormone replacement therapy/aromatase inhibitors, bilateral oophorectomy before the age of 35 years, history of hyperthyroidism or hyperparathyroidism, hypogonadism, malabsorption and sickle cell disease. A total of 230 patients were excluded. The remaining 787 patients were grouped based on the presence or absence of diabetes. Fracture history was obtained from patient questionnaire.

Results: 787 AA patients fulfilled our inclusion criteria; 179 had diabetes (22.7%) and 608 did not have diabetes (77.3%). In the diabetes group, the prevalence rate for osteoporosis was 25.7%, osteopenia was 34.1% and 40.2% had a normal BMD. Comparing patients with and without diabetes, the mean BMD at lumbar spine was 1.051 g/cm2 and 1.009g/cm2 (p=0.009), femoral neck was 0.834 g/cm2 and 0.786g/cm2 (p=0.000) and forearm was 0.683 g/cm2 and 0.664g/cm2 (p=0.021), respectively. In the diabetes group, mean BMD at all three sites was higher even after adjusting for factors such as previous fracture, history of parent with hip fracture, steroid use, alcohol use, and smoking. The rate of fractures was comparable between the two groups (21.1% in non-diabetes group vs.15.6% in diabetes group) (p=0.111).

Discussion: Osteoporosis is the most important metabolic bone disease in patients with diabetes mellitus. The mechanisms underlying low bone strength are not fully understood but could include altered biomechanical quality, impaired peak bone mass and complications of diabetes, such as nephropathy. Several studies have suggested that patients with diabetes have an increased fracture risk despite a higher BMD. Patients with diabetes represent a diagnostic and prognostic dilemma since the value of BMD measurement in predicting osteoporotic fractures is limited.

Conclusion: African American patients with diabetes have higher BMD than controls. The presence of diabetes does not appear to carry an increased fracture risk in our patient population.
Abstract #527

MANAGEMENT OF SECONDARY HYPERPARATHYROIDISM WITH CINACALCET IN X-LINKED HYPOPHOSPHATEMIC OSTEOMALACIA ASSOCIATED WITH RENAL FAILURE

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Methods: Renal functions, Urine phosphorus (P) excretion, Serum parathyroid hormone (PTH) and FGE 23 levels were assessed.

Case Presentation: A 32-yrs old lady with X-linked hypophosphatemic osteomalacia (XHL) presented to our clinic with a history of chronic renal failure (Laboratory values: serum creatinine (Scr) 170 umol/L; RR:45-96), low serum phosphorus (P) (0.57 mmol/L; RR:0.8-1.45), increased urinary P excretion (35.3 mmol/D), elevated serum PTH 140 ng/L (RR: 10-65). Patient had previously parathyroidectomy (PTHX) with half-gland implantation in the forearm. Patient was treated in the past with oral phosphate supplements 500mg TID and calcitriol 1 ug/d for several yrs. Despite this treatment serum P remained low (0.57-0.75), with normal 1, 25 (OH)2, and serum Ca levels and GFR remained at 49 ml/min/1.73m2. Progressive increase in serum PTH levels (2345 ng/L), declining urine P excretion (20.8 mmol/24 hrs), and diminishing GFR occurred during the next 3 years. Serum alkaline phosphatase had increased from 36 to 160 U/L (RR: 50-120). Serum FGF 23 remained markedly elevated (6130 RU/ml, RR :< = 180). Parathyroid scan performed at this time showed a focal uptake at the transplanted site only. US confirmed bilateral atrophic kidneys. Plain X-rays of the femoral neck revealed looser zone and bone density confirmed osteoporosis. Patient was treated with cinacalcet and with this treatment serum PTH level declined. Renal transplant is planned.

Discussion: Diagnosis of of XLH is based on hypophosphatemia, decreased tubular reabsorption for P, slow growth and osteomalacia. Both males & females are affected. This disorder is caused by mutation in PHEX on X chromosome expressed mainly in bone and teeth. Hyperparathyroidism occurs frequently as a treatment complication. Complexed Ca++ with phosphorus results in intermittent hypocalcemia which stimulates PTH secretion. Despite abnormal FGF-23 levels and elevated levels of serum PTH phosphaturia declined in our patient in response to nephron loss.

Conclusion: Hyperparathyroidism occurs commonly as a treatment complication necessitating parathyroidectomy and or cinacalcet treatment. In our patient who developed renal failure there was progressive resistance to the phosphaturic actions of FGF-23 & PTH resulting in hyperphosphatemia.

Abstract #528

CLINICAL CLUES TO DIAGNOSIS OF PARATHYROID CANCER: A CASE PRESENTATION

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Objective: To highlight the importance of increased clinical suspicion of parathyroid carcinoma (PC) in patients presenting with hyperparathyroidism (HPT).

Case Presentation: 59 year old man with history of hypertension and diabetes presented with a 2 week history of anorexia and constipation and 7 months of unintentional 80lbs weight loss. He denied nausea, vomiting, abdominal or bone pain. Family history was not significant. His exam was only remarkable for cachexia. Labs revealed a potassium of 3.1 (3.5-5mEq/L), HCO3 of 28 (22-26mEq/L), creatinine of 3.5 (0.6-1.4mg/dL), BUN of 35 (8-20mg/dL), calcium of 15.7 (8.5-10.5mg/dL), phosphorus of 2.4 (2.5-4.5mg/dL) and albumin of 4.2 (3.8-5.2g/dL). There were no prior labs for comparison. PTH level was 810 (6-65pg/ml) and 25 OH Vit D was <4 (30-100ng/ml). 24 hour urine calcium excretion was 73 (50-150mg/24hrs) but sample collection was inadequate. CT chest/abdomen, kidney ultrasound and DEXA scan were normal. Ultrasound of the neck was ordered but not done. Parathyroid scan revealed retention of radiopharmaceutical in the inferior aspect of the left gland. He underwent surgery with level VI lymph node dissection. Histological examination showed a 2.3x1.9x0.4 cm mass that weighed about 1g with vascular as well as capsular invasion and irregular fibrous bands dividing it into several compartments, consistent with parathyroid carcinoma. There was no evidence of regional spread.

Discussion: Parathyroid carcinoma is rare occurring in 0.1-5% of patients with HPT. Certain clues on history and exam can raise a red flag. Benign HPT is commoner in females, while the incidence of PC is similar in both sexes. Most PC cases present in the 5th decade and symptoms of hypercalcemia are more profound and can commonly present with hypercalcemic crisis. About 45% of patients present with a palpable neck mass (average size 2.9cm). The serum calcium level is usually >14mg/dl, PTH level 5-20 and alkaline phosphatase 5-10 times the upper limit of normal. Complications like impaired glomerular filtration rate, bone disease and nephrolithiasis
are also more frequent (86 vs. 25%, 91 vs. 55% and 56 vs. 15% respectively). Adenomas are soft, round and reddish brown easily separated, while carcinomas are firm with dense grayish capsule adherent to and invading surrounding tissue. Metastatic disease is found commonly in cervical lymph nodes and lungs.

**Conclusion:** PC is a rare endocrine malignancy which can mimic benign HPT. A high index of suspicion based on the features highlighted above will lead to a more appropriate and complete surgical therapy.

**Abstract #529**

**THE ROLE OF TERIPARATIDE IN THE MANAGEMENT OF BISPHOSPHONATE-ASSOCIATED ATYPICAL FRACTURE**

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**Objective:** The optimal management of patients who suffer subtrochanteric or femoral shaft fractures after prolonged bisphosphonate use remains unclear. We present a 58 year-old woman treated with teriparatide (recombinant human PTH1-34) after delayed healing of a bisphosphonate-associated atypical fracture (BAAF).

**Case Presentation:** A 58 year-old woman was walking upstairs when she heard a “snap” and felt her right leg give out. X-rays revealed a right mid-shaft femur fracture. She reported a prodrome of right thigh pain for the prior month. The fracture was surgically repaired, but she was referred to endocrinology 3 months later due to concern for slow fracture healing. She had been taking alendronate since age 47 when DEXA showed T-score L1-L4 of -2.4. She experienced menopause at age 50. Follow-up DEXA at ages 50, 52, 55 and 57 showed T-scores L1-L4 of -2.1, -2.1, -2.4, and -2.5, respectively. Total hip score was T -1.1 initially and T-1.3 nine years later. Alendronate was stopped at the time of her surgery. The patient was taking calcium 600 mg bid and vitamin D 1000 IU daily. Levels of TSH, 25-hydroxy vitamin D, intact PTH, and calcium were all within normal limits. Urinary N-telopeptides were 41 nmol BCE/mmol Cr (nl range 4-64). Teriparatide was discussed with the patient and the surgeon but the surgeon opted to use a bone stimulator device. By the 10th post-operative month, however, incomplete fracture healing was still noted, and teriparatide 20 mcg sq daily was started. After six weeks, x-rays showed significantly enhanced fracture healing with sclerosis and callus formation.

**Discussion:** Because of the relatively recent clinical recognition of BAAF, the ideal management strategy is unknown. Withdrawal of bisphosphonate is generally recommended, as are assessment of dietary calcium intake and vitamin D status, with supplementation if necessary. The use of teriparatide, an anabolic bone agent, for the treatment of BAAF has been reported in a few case series and reports. Teriparatide promotes osteoblast proliferation and activity, and in these anecdotal reports appears to improve fracture healing in patients with BAAF. In our patient, the rapid radiologic improvement with teriparatide following a prolonged period of delayed healing supports the hypothesis that teriparatide accelerates bone repair in BAAF.

**Conclusion:** In the absence of randomized clinical trial evidence, the optimal management of BAAF will remain uncertain. Our case provides further support for a role for teriparatide in these patients. Teriparatide should be considered in the therapy of patients with BAAF, particularly when fracture healing is delayed.

**Abstract #530**

**SEVERE HYPERCALCEMIA FROM SARCOIDOSIS: CASE PRESENTATION, LITERATURE REVIEW, UNDERSCORING THE UTILITY OF STEROIDS AS A DIAGNOSTIC TEST**

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**Objective:** Recent literature has emphasized severe hypercalcemia as the presenting manifestation of undiagnosed sarcoidosis. We describe a case of severe hypercalcemia with elevated 1,25- dihydroxyvitamin D (1,25-OH D) that posed a diagnostic dilemma. We describe the management challenges of such a medical emergency.

**Case Presentation:** A 36 year old man was hospitalized for severe dehydration and altered mental status, and was found to have a serum calcium of 14.1 mg/dl. He had no prior personal or family history of calcium, bone, parathyroid or renal disorders or nephrolithiasis. He denied use of lithium or thiazide diuretics. Physical exam revealed no lymphadenopathy. Thyroid and liver function tests were normal. Creatinine was 3.0 mg/dl. Plasma 25-OH-D, ACE level, vitamin A level, Parathyroid hormone related peptide (PTHrP) were normal. PTH was suppressed at <2.5 pg/ml while 1,25-OH-D was elevated at 155 pg/ml (18-64). Serum protein electrophoresis was normal. Chest X-ray was negative. Calcium levels showed no significant improvement with aggressive saline infusion and loop diuretics. Considering the elevated 1,25 OH D, sarcoidosis was the top diagnostic
possibility, in spite of a normal ACE level. CT could not be obtained due to his acute kidney injury (AKI). Hence, and due to persistent severe hypercalcemia and in the absence of other diagnostic modalities we opted to give a trial of steroids as a diagnostic/therapeutic trial. Calcium levels normalized, from 11.9 to 9.8 mg/dL within 8 hours after one dose of prednisone 20 mg orally. Calcium remained normal on continued steroid therapy. He was discharged with a plan to obtain CT of the chest and pursue further workup (to rule out lymphoma) after recovery of renal function.

Discussion: In patients with suppressed PTH and PTHrP and elevated 1,25-OH D, the diagnosis is usually narrowed down to granulomatous disease (mainly sarcoidosis), fungal infections, tuberculosis (TB), and lymphoma. However, our patient’s AKI precluded further diagnostic imaging studies. A remarkable response to steroids suggests that his hypercalcemia is 1α hydroxylase mediated; thereby suggesting that steroids can be an important tool in the diagnostic workup of hypercalcemia. However, care must be exercised to exclude infectious processes (mainly TB) before an empirical trial of steroids. Similarly, lymphoma cannot be excluded based on response to steroids, because lymphomas may partially respond to steroids.

Conclusion: Steroids may play a role in diagnosing the cause of hypercalcemia, especially in cases where advanced imaging cannot be performed due to comorbid conditions and in cases of severe hypercalcemia where timely management is crucial.
Abstract #600

IMPROVEMENTS IN BLOOD PRESSURE (BP) AND LIPID PARAMETERS ASSOCIATED WITH DIFFERING DEGREES OF WEIGHT LOSS (WL) IN OBESE SUBJECTS TREATED WITH PHENTERMINE AND TOPIRAMATE EXTENDED-RELEASE (PHEN/TPM ER) OVER 2 YEARS

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Objective: Obesity is associated with significantly increased morbidity related to cardiovascular disease (CVD). WL of ≥5% increases the odds of improvements in CVD risk factors, and odds are further improved with greater WL. PHEN/TPM ER has previously demonstrated significant WL in the 56-week CONQUER study and 52-week SEQUEL extension study of obese and overweight subjects with ≥2 weight-related comorbidities. This post hoc analysis evaluated CVD risk factors by magnitude of WL at time points spanning 108 weeks.

Methods: CONQUER completers at selected sites were eligible to enroll in SEQUEL and remain on their original randomized blinded treatment. Primary outcomes were percent WL and percentage of subjects achieving ≥5% WL between weeks 0 and 108. In this post hoc analysis, lipid parameters and BP were assessed in subjects achieving <5%, 5% to <10%, 10% to <15%, and ≥15% WL.

Results: At baseline, mean weight was 101.7 kg; 51.1% had hypertension, and 34.5% had hypertriglyceridemia. At week 108, for placebo (PBO; n=227), PHEN 7.5mg/TPM ER 46mg (7.5/46; n=153), and PHEN 15mg/TPM ER 92mg (15/92; n=295), least-squares (LS) mean absolute difference in lipid parameters vs PBO, all comparisons). Significantly more PHEN/TPM ER-treated subjects achieved ≥5%, ≥10%, or ≥15% WL vs PBO (P<.0001, all comparisons). Significant improvements in CVD risk factors were seen in all WL categories, and the magnitude increased with greater WL: LS mean change from baseline for those achieving WL of <5%, 5% to <10%, 10% to <15%, and ≥15%, respectively, for systolic BP (mmHg) were -1.6, -4.0, -6.1, and -8.7 (P<.05 vs <5% WL, all comparisons), and for diastolic BP (mmHg) were -2.0, -3.6, -3.6, and -5.9 (P<.0001 vs <5% WL for WL ≥15%); LS mean percent change in lipid parameters for each WL category, respectively, were: HDL-C, 1.9, 7.8, 10.7, and 24.3 (P<.001 vs <5% WL, all comparisons); non-HDL-C, -7.1, -7.7, -9.3, and -13.1 (P=.0016 vs <5% WL for WL ≥15%); triglycerides, 4.6, -8.7, -17.1, and -28.9 (P<.0002 vs <5% WL, all comparisons). When comparing those in the same WL category, no differences across treatment groups in magnitude of improvement were observed. Common adverse events were constipation, paraesthesia, sinusitis, and dry mouth.

Discussion: PHEN/TPM ER led to significant WL in obese and overweight subjects in the SEQUEL trial. Significant improvements in systolic BP, HDL-C, and triglycerides were seen in those achieving as little as 5% to <10% WL, which increased with the degree of WL.

Conclusion: Sustained WL over 108 weeks had positive effects on subjects’ CVD risk factors of hypertension and dyslipidemia.

Abstract #601

BODY MASS INDEX, WAIST CIRCUMFERENCE, WAIST HIP RATIO AS PREDICTORS OF OBESITY AND ABDOMINAL OBESITY IN IKORODU: A COMMUNITY SURVEY

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Objective: The aim of this pioneer study in a rural community, Maya, in Ikorodu a suburb of Lagos is to determine the prevalence of obesity and central obesity in a rural area.

Methods: The weight, height, waist circumference and hip circumference of 52 participants living in Ikorodu a suburb of Lagos was taken using standard measurement protocol. The United States National Institute of Health (NIH) protocol for the measurement of waist circumference for the Multi-Ethnic Study of Atherosclerosis (MESA) study, the WHO STEPS protocol recommendation and the NHANES (United States National Health and Nutrition Examination Survey) III protocol were followed in taking the measurement using a stretch resistant tape. The United State criteria for waist circumference cut offs associated with increased risk was used that is >102 cm in men and >88 cm in women, since in Africa no ethnic specific cut offs is determined yet.

Results: A total of 52 participants were recruited with age range of 25 to 72 years. 30(57.69%)were male while 22(42.31%)were females. 19(36.54%)participants were overweight, 18(34.62%)participants were obese. By using the waist hip ratio, 36(69.23%)participants had central obesity. In contrast by using waist circumference only 12(23.08%)had.

Discussion: This study is the pioneer study of obesity and central obesity in Ikorodu. The prevalence of obesity in Ikorodu is 34.62%. The prevalence of male obesity and female obesity are 21.15% and 13.46% respectively. The prevalence of male obesity in Ikorodu is 34.62%. The prevalence of male obesity is 21.15% and 13.46% respectively.
central obesity in Ikorodu using the waist circumference is 12(23.08%). The prevalence of male central obesity and female central obesity using same waist circumference is 1.92% and 21.15%. The prevalence of central obesity in Ikorodu using the waist hip ratio is 69.23%, the prevalence of male central obesity and female central obesity using same measurement is 28.85% and 40.39%. The prevalence of underweight in Ikorodu is 1.92%.

Conclusion: The prevalence of obesity in Ikorodu is 34.62%. Increased physical activity like sporting activity will help to reduce the incidence since 36.54% of the population is presently overweight.

Abstract #602

25-HYDROXY VITAMIN D STORAGE AND OBESITY: A CLINICAL CONUNDRUM

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Objective: 25-hydroxy vitamin D is a fat-soluble vitamin stored in body fat when present in large quantities. 25 (OH) D levels are presumed to be higher in obesity since a larger fat storage component is available. Moreover, obese individuals have a larger body surface area and would be expected to produce more vitamin D3 from sun exposure. However, studies have persistently showed that obesity is associated with low vitamin D levels. 25(OH)D levels are significantly lower in obese patients compared with non-obese patients across all ethnicities and age groups. For the same body weight and fat mass, some racial groups, appear to be more prone to be vitamin D deficient. Body mass index (BMI) has been shown to be inversely related to circulating levels of 25(OH). A BMI of > 30 kg/m2 is considered as a high risk group for vitamin D deficiency by the Endocrine society guidelines.

Methods: We conducted a review of the available studies of vitamin D in obesity and summarized the current evidence to date.

Results: There is no study linking 25(OH) D deficiency in the obese individuals to diminished sun exposure from decreased outdoor activity and sedentary lifestyle. Wortsman et al demonstrated that obese persons have decreased bioavailability of vitamin D due to the sequestration of vitamin D in adipose tissue. Bell et al suggest that vitamin D metabolism in obese persons is altered, with increased production of 1,25-dihydroxyvitamin D exerting negative feedback control on the hepatic synthesis of 25(OH)D. It has also been reported that the metabolic clearance of vitamin D may increase in obesity, possibly with enhanced uptake by adipose tissue. Wamberg et al suggested that obesity is characterized by a decreased expression of the 25-hydroxylase (CYP2J2) and the 1α-hydroxylase (CYP27B1) in subcutaneous adipose tissue. There is also some experimental data suggesting that vitamin D deficiency promotes lipogenesis and modulates adipogenesis through vitamin D receptor dependent inhibition of critical molecular components involved in differentiation and maturation of adipocytes.

Discussion: Due to the worldwide epidemic of obesity, screening and supplementation of vitamin D deficiency in obese individuals is a major public health concern. While the etiology of vitamin D deficiency in obese individuals remains to be determined, it is plausible that these patients may require higher than usual replacement doses.

Conclusion: Further studies are needed to determine whether the guidelines for the diagnosis and therapy of vitamin D deficiency in obesity should be adjusted.

Abstract #603

A NEW CARDIOMETABOLIC DISEASE RISK STAGING SYSTEM TO GUIDE TREATMENT FOR OBESITY USING A COMPLICATIONS-CENTRIC APPROACH - VALIDATION USING CARDIA AND NHANES DATA

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Objective: The recent approval of new weight loss medications has enabled a medical model approach to obesity therapy. This model requires the staging of obesity complications in order to rationally guide selection of treatment modality and intensity for optimal patient outcomes. This particularly applies to cardiometabolic disease and attendant risk of T2DM and cardiovascular disease. To date, the emphasis has been a BMI-centric approach (i.e., NHLBI Guidelines), even though a major portion of cardiometabolic disease risk exists independent of general adiposity, and weight loss can be used as a tool to effectively diminish T2DM and CVD risk regardless of baseline BMI. This study is to validate a cardiometabolic disease risk staging system for obesity.

Methods: We validated this staging system using two large national cohorts, the CARDIA Study for risk of T2DM, and the NHANES III-linked mortality file for all-cause and CVD mortality with Cox regression models. For all BMI ≥27, Stage 0 represents metabolically healthy; Stage 1 has 1 or 2 Metabolic Syndrome Risk factors (other than IFG); Stage 2 has IFG or IGT or Metabolic Syndrome (without IFG); Stage 3 has at least 2 of 3: IFG, IGT, and/or Metabolic Syndrome; Stage 4 has T2DM and/or CVD.

Results: In overweight or obese subjects, during a 10-
year follow-up, there were 167 new cases of diabetes in the CARDIA study. Cumulative diabetes incidence was 8.9% overall, and the risk levels for Stage 0 to 3, were 2.3%, 6.5%, 15.0% and 40.4%, and multivariable adjusted hazard ratios increased exponentially (p for trend <0.001). Compared with metabolically healthy subjects, adjusted risk for diabetes increased from Stage 1 (HR 2.72, 95% CI 1.30-5.69) to Stage 2 (HR 7.23, CI 3.41-15.3) to Stage 3 (HR 20.4, CI 9.43-44.0). In NHANES III, over a median follow up of 173 months, there were 662 mortality cases and 274 cases of CVD-related deaths. The mortality rates increased (p <0.001 for trends) over Stages 0 to 4 with values of 3.2, 6.9, 10.2, 17.4 and 28.0 per 1000 person years for all-cause mortality and 1.0, 2.1, 3.6, 4.9 and 14.3 for CVD mortality, respectively. The multivariable adjusted hazard ratios for both all-cause and CVD mortality markedly increased with each higher risk stage. BMI minimally affected risks for T2DM and all-cause/ CVD mortality using this staging system.

Discussion: This staging system using readily available clinical data provides a strong predictor of diabetes, CVD mortality, and all-cause mortality independent of BMI. Conclusion: This risk staging system can be used to rationally guide treatment for obesity according to a complications-centric model designed to optimize benefit/risk ratio, outcomes, and social costs of the disease.

Abstract #604

THE CORRELATION BETWEEN WAIST CIRCUMFERENCE AND LIVER FUNCTION TESTS AMONG PATIENTS WITH PRE-DIABETES AND PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Objective: To determine the association between waist circumference and abnormal liver function tests among patients with pre-diabetes and type 2 diabetes mellitus attending the National Center of Diabetes, Endocrinology, and Genetics (NCDEG), Amman, Jordan.

Methods: A total of 1068 patients (719 with T2DM and 349 with pre-diabetics) above the age of 18 years attending the NCDEG during the period between 1st November 2011 to 1st March 2012 were included. All socio-demographic, clinical and laboratory data were collected from the patients files at the time of presentation to the diabetes clinic in the NCDEG, including age, gender, waist circumference body mass index, smoking status, educational level, hypertension, dyslipidemia, glycosylated hemoglobin HBA1C and liver function tests (ALT, AST, GGT and ALP).

Results: The prevalence of elevated waist circumference was (74%) in diabetics patients while it was (71.9%) in pre-diabetics. Overall, the prevalence of having one or more elevated liver enzymes was 32% among diabetic patients whereas was 25.2% in pre-diabetics. The prevalence of elevated of any liver enzyme was significantly higher in diabetics and pre-diabetics with elevated waist circumference than with normal waist circumference. For each once centimeter increment in waist circumference, there was (3-5%) increased in liver enzymes in diabetic patients (OR: 1.04 CI: 1.08) and (5-15%) in pre-diabetic (OR: 1.1 CI: 1.21).

Discussion: Our study showed that for each one-centimeter increase in waist circumference, the odds of elevated liver enzymes increased by 3% to 5% in diabetics and by 5% to 15% in pre-diabetics, after adjustment for age, gender, smoking status, marital status, metformin, education, hypertension and dyslipidemia.

Conclusion: Waist circumference is an indirect measure of visceral obesity. Our study showed that there is a significant association between elevated liver enzymes and increase waist circumference in the diabetic and pre-diabetic patients.

Abstract #605

INTER RELATIONSHIP BETWEEN INDICES OF NUTRITURE AMONG INHABITANTS OF CALABAR, SOUTH EAST NIGERIA

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Objective: To determine the inter relationship between the indices of nutriture among the inhabitants of Calabar, South East Nigeria.

Methods: A sample comprising 1134 subjects (645 males and 489 females) representative of the entire population of Calabar metropolis aged 15-79 was studied. A multistage sampling method was applied to select the subjects for the study using the table of random numbers, out of which eligible individuals aged between 15 years and 79 years from 200 households selected were recruited. Indices of nutriture were expressed as mean (95% Confidence Interval). The comparison of means between groups was done using independent student t test and the strength of association between quantitative variables by using the
Pearson’s correlation coefficient. The level of significance was taken as P < 0.05.

**Results:** The mean (95% CI) Body Mass Index (BMI) for males and females were 27.0kg/m² (95% CI 26.5-27.2) and 28.5kg/m² (95% CI 28.0-29.0) respectively. The mean (95% CI) Waist Circumference (WC) for males was 91.0cm (95% CI 90.2-91.8) and for females was 89.8cm (95% CI 88.8-90.8). The mean (95% CI) Waist Hip Ratio (WHR) for males was 0.90 (95% CI 0.88-0.89) while that for females was 0.85 (95% CI 0.87-0.89). The relationship between the indices of nutriture was strongest between WC and BMI (r = +0.70 P <0.01), followed by WHR and BMI (r = +0.65 P <0.01) then WC and WHR (r =+0.49 P <0.01).

**Discussion:** Body Mass Index (BMI), Waist Circumference (WC) and Waist Hip Ratio (WHR) are indices of nutriture. Increasing evidence suggests that abdominal adiposity has a direct influence on health and that visceral fat correlates with health risks to a greater extent than does adipose tissue in other regions of the body. BMI has been shown to contribute to the prediction of non-abdominal, abdominal, subcutaneous and visceral fat. Compared to body mass index, waist circumference is more closely linked to cardiovascular disease risk. WHR is used to assess regional adiposity and is good predictor of intra-abdominal adiposity. It is therefore a practical index of regional adipose tissue distribution and has been widely used to investigate the relationship between regional adipose tissue distribution and metabolic profile.

**Conclusion:** The findings showed that there was strong positive linear relationship between all indices of nutriture.

**Abstract #606**

**CARDIAC DIASTOLIC DYSFUNCTION AND REGIONAL BODY FAT DISTRIBUTION IN INSULIN RESISTANT PERIPUBERTAL OBESE MALES**

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**Objective:** To evaluate presence of diastolic dysfunction in obese peripubertal males in age group of 8-18 years. To correlate diastolic dysfunction with insulin resistance & insulin levels. To evaluate association of diastolic dysfunction with omental fat & epicardial fat as an index of cardiac adiposity.

**Methods:** This cross-sectional study includes 23 obese males & 24 age matched healthy controls in age group of 8-18 years. Height, weight, BMI, WHR was recorded & detail history taken. Investigations performed: Fasting blood sugar, fasting serum insulin levels, fasting lipid profile, abdominal CT scan to measure omental fat thickness & 2-D Echo to assess left ventricular diastolic function (using Canadian Consensus Guidelines) & epicardial fat thickness.

**Results:** 47.82% of cases had metabolic syndrome. Increased Isovolumetric relaxation time (IVRT) >100 msec seen in 14/23-60% cases. E/A ratio of 0.75 seen in 2/23-8.7% [Peak early diastolic filling (E) velocity, peak late diastolic filling velocity (A)] of cases. Left ventricular mass (LVM) >125gm seen in 5/23 cases (21.74%). All parameters of left ventricular diastolic function were normal in controls. Significant difference in LVM (p=0.00099), LVPW (p=0.0018), IVS (p=0.007), E/A ratio (p=0.043) & Epicardial fat (p=0.0000) seen in cases as compared to controls. Correlation of visceral fat mass with HOMA-IR, fasting serum insulin levels & left ventricular diastolic parameters in cases were HOMA vs omental fat (p-value=0.0008), Insulin vs omental fat (p-value=0.0015), E/A vs omental fat (p-value=0.015), LVM vs omental fat (p-value=0.005), IVRT vs omental fat (p-value=0.005), HOMA vs epicardial fat (p=0.0000), Insulin vs epicardial fat (p=0.0000), E/A vs epicardial fat (p=0.09), LVM vs epicardial fat (p=0.006), IVRT vs epicardial fat (p=0.011). These correlations were statistically insignificant in controls.

**Discussion:** Increased IVRT is observed in obese children as compared to lean controls in other studies with a similar finding in our study. Myocardial fatty infiltration (reflected in epicardial fat mass) may affect cardiac structure & function, leading to development of severe diastolic dysfunction. Visceral fat depot beyond a certain critical level becomes pathologic in its functioning is evident from the fact that positive correlations were observed between visceral & epicardial fat with diastolic left ventricular parameters in cases but not in controls.

**Conclusion:** Diastolic derangements & Left ventricular hypertrophy start early in childhood obesity. Positive correlation between left ventricular diastolic dysfunction & HOMA-IR & fasting insulin levels is seen. Epicardial fat mass and visceral fat deposition show positive correlation with diastolic dysfunction.
Abstract #607

DURABILITY OF TYPE 2 DIABETES REMISSION AFTER ADJUSTABLE GASTRIC BANDING

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Objective: Recent data demonstrates that approximately one-third of patients may have recurrence of type 2 diabetes (T2D) within five years after gastric bypass. Weight regain, duration and severity of disease may influence recurrence or worsening of disease. This study reports the changes in T2D 2 and 3.5 years after laparoscopic adjustable gastric banding (LAGB), and the factors which predict remission.

Methods: This is an interim analysis of subjects participating in the LAP-BAND AP® Experience (APEX) trial, an ongoing 5-year, prospective, multi-center, open-label, observational study. This analysis describes subjects who reported T2D requiring daily medical therapy at baseline and who have completed both their 2 and 3.5-yr post-operative visit. “Remission” is defined as elimination of hypoglycemic medication and “improvement” as reduction in hypoglycemic medication.

Results: There were 116/521 (22.3%) subjects with T2D at baseline, of which 57/116 (49.1%) had evaluable data at both 2 and 3.5-ys. At 2 yrs remission and improvement of T2D was achieved by 45.6% (n=26) and 49.1% (n=25) of this population respectively, with 5.3% (n=3) experiencing no change. At 3.5 yrs, these values remained relatively unchanged, with 49.1% (n=28), 43.9% (n=25) and 7% (n=4) experiencing remission, improvement and no change respectively. Changes from 2 to 3.5 years included 4 patients from improvement to remission, 2 from remission to improvement, and 1 from improvement to no change. Weight remained relatively unchanged in these patients; however, one patient with initial remission at 2-yr regained 29% of weight that had been lost, resulting in a recurrence of T2D. Duration of T2D was 4.4, 6.0 and 8.9 years in the remission, improvement and no change groups, respectively. Percent weight loss was not statistically different between groups, with 21.8%, 15.8% and 24% in the remission, improvement and no change groups respectively. Logistic regression analysis shows that younger age, shorter T2D duration, and higher percent weight loss predict remission. Females were 20% more likely to have remission by year 3.5. Revisions or explants occurred in 6% and 4.3% respectively of the total T2D population.

Discussion: These data in LAGB patients support published literature, mainly observed with gastric bypass, that duration of T2D and amount of weight lost (or regained) significantly affect likelihood of remission of T2D, as well as the durability of that remission.

Conclusion: Early T2D intervention with LAGB should be considered as a relatively durable approach to T2D management in appropriate patients.

Abstract #608

IMPROVEMENTS IN WEIGHT AND GLYCEMIA IN OBESE AND OVERWEIGHT SUBJECTS RECEIVING PHENTERMINE AND TOPIRAMATE EXTENDED-RELEASE WHEN STRATIFIED BY BASELINE HBA1C

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Objective: This post-hoc analysis of a 56-week, Phase 2, double-blind study of obese and overweight subjects with type 2 diabetes mellitus (T2DM) assessed the effects of PHEN/TPM ER on weight loss (WL) and glycemia when stratified by baseline HbA1c (7%-8% or >8%). T2DM was actively managed to the ADA standard of care (goal HbA1c<7.0%) throughout the study, including changes in dose and/or number of antidiabetic medications, simulating real-world conditions.

Methods: Obese and overweight subjects (BMI ≥27 and ≤45 kg/m²) with a diagnosis of T2DM controlled with diet and/or oral medications were randomized to placebo (PBO; morning and afternoon; n=105) or PHEN 15 mg (morning) and TPM 100 mg (afternoon; n=105) for 28 weeks. Completers continuing for an additional 28 weeks remained on PBO (n=55) or active treatment with once-daily PHEN 15 mg/TPM ER 92 mg (15/92; n=75). All subjects were counseled on lifestyle modifications.

Results: At baseline, 78 (60%) subjects had a history of T2DM for ≥5 years, 79 (61%) were receiving ≥2 antidiabetic medications, 50 (38%) had an HbA1c level of 7%-8% (PBO, n=21; 15/92, n=29), and 80 (62%) had an HbA1c >8% (PBO, n=34; 15/92, n=46). At week 56, least-squares (LS) mean percent WL for PBO and 15/92 was -4.0% and -12.4% in the HbA1c 7%-8% group and -2.0% and -7.5% in the HbA1c >8% group, respectively (P<.001 vs PBO, all comparisons). LS mean change in HbA1c for PBO and 15/92 was -0.3% and -0.8% in the HbA1c 7%-8% group (P<.05 vs PBO) and -1.8% and -2.0% in the HbA1c >8% group, respectively (not significant vs PBO). LS mean decrease in fasting glucose was numerically greater but not significant in 15/92-treated subjects vs PBO, regardless of baseline HbA1c. Importantly, in subjects receiving 15/92, reductions in HbA1c coincided with a net decrease in antidiabetic-medication use vs a net increase in those receiving PBO (P=.0131 vs PBO). Common
adverse events were constipation, hypoglycemia, and paraesthesia.  

**Discussion:** PHEN/TPM ER induced significant WL vs PBO in obese and overweight actively managed subjects with relatively advanced T2DM. PHEN/TPM ER treatment was associated with improvements in glycemia in addition to decreased use (number/dose) of antidiabetic medications vs increased use with PBO. Absolute decrements in HbA1c were greater in subjects with higher baseline values across treatment groups.  

**Conclusion:** These data suggest that PHEN/TPM ER may be part of an effective overall regimen for WL leading to an improvement in glycemic control in obese and overweight subjects with T2DM, including those with refractory or chronic disease.

**Abstract #609**

**BODY MASS INDEX (BMI), DEXA AND CLINICAL OUTCOMES: IS THERE A NEED FOR A BMI MODIFIER TO BETTER PREDICT CLINICAL OUTCOMES ACROSS RACIAL GROUPS?**

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**Objective:** Racial differences are being increasingly recognized within calculated indices utilized for health assessment. Muscle mass and bone mass are commonly reported to be higher in African Americans compared to their non-African American counterparts. Therefore calculated indices, which are dependent on these factors, may require modification for improved accuracy. The now validated and widely utilized “correction factor” for estimated glomerular filtration rate (eGFR) in African Americans, represents one example.

**Methods:** Given the increasing recognition of BMI as a predictor of cardio-metabolic outcomes we explored the relationship between BMI and both % body fat and total lean body mass (as assessed by DEXA) for 2,557 blacks and 6,570 non-Hispanic whites enrolled in the NHANES 1999-2004.

**Results:** The estimated correction factor for % body fat for a given BMI for Blacks was 1.082 and for total lean body mass (excluding bone mineral content [g]) was 1.016. The % body fat x total lean body mass correction ratio was 1.099. Thus, a BMI of 25 for the white population is proposed to be equivalent to a BMI of 27.48 in the African-American population when equilibration for % body fat & total lean body mass, the two most metabolically active elements of the BMI calculation, is accounted for. Using cox proportional regression models, the odds of death {Hazard Ratio [HR] (95% confidence interval)} in blacks compared to non-Hispanic whites was 1.65 (1.4-2.0) controlling for age and gender; 1.73 (1.4-2.1) controlling for age, gender and BMI; and fell to 1.70 (1.4-2.1) when controlling for age, gender and “adjusted BMI”.

When socioeconomic status and clinical factors such as hypertension, high cholesterol, diabetes, smoking, federal poverty level, insurance, and education were added to the model, the odds of death in blacks showed a trend toward increased risk but was no longer statistically significant.  

**Discussion:** Prospective studies should consider exploring correction factors across multiple racial/ethnic groups when comparing risk and cardio-metabolic outcomes based on BMI across these diverse groups, in an effort to make more informed public health recommendations at a community level.

**Abstract #610**

**RETROSPECTIVE STUDY EXAMINING THE EFFECTIVENESS OF BARIATRIC SURGERY IN PATIENTS WITH DIABETES IN SAN ANTONIO, TEXAS**

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Diabetes & Glandular Disease Clinic

**Objective:** Our objective is to examine the outcome of bariatric procedures in patients with DM in South Texas. Glycemic control, weight loss and medication use were analyzed. The findings between lap band (LB) and gastric bypass (GB) were compared.

**Methods:** This is a retrospective analysis of patients with diabetes post bariatric surgery. Glycemic control, BMI, and medication use were compared over time points. The data gathered was processed in accordance with federal standards concerning patient confidentiality. 86 patients (40 LB, 46 GB) met the inclusion criteria.

**Results:** Prior to LB the mean age was 55.5 year, 75% female, 47% Hispanic, average BMI 43.5, average HA1c 7.5%, 65% took oral anti-diabetics, 50% used an average of 103 IU of insulin a day. Prior to GB the mean age was 53.6 year, 78% female, 37% Hispanic, average BMI 43.5, average HA1c was 8.0%, 60% took oral anti-diabetics, 72% used an average of 128 IU of insulin a day. For LB patients linear regression showed significant decrease for BMI (p=0.0021), no further significant difference was seen by the 3rd year (ANOV A p=0.0882). For LB it was no linear regression correlation for HA1c. It was a progressive statistically significant decrease of oral medications use with LB at 0.5, 1, 2 and 3 years (ANOVA p<0.05). Insulin use was significant less than baseline until the second year (ANOVA p<0.05). For GB patients linear regression showed significant
decrease in BMI, A1c, use of insulin and oral anti-diabetics. This trend continued by the end of the third year (p<0.0001). A significant greater decline of BMI was seen in GB patient compared to LB patients at 0.5, 1, 2 and 3 years post procedure (ANOVA p<0.001). HA1c was significantly lower at the 3rd year for GB patients (ANOVA p=0.0045). Although it was a numeric trend, GB was not significantly superior to LB in the discontinuation of oral anti-diabetics or insulin.

Discussion: South Texas is a hub for obesity and diabetes. Our findings concur with existing literature reporting that bariatric surgeries are effective in improving glucose control and the effects are lasting up to three years.

Conclusion: In a large private endocrine practice in South Texas bariatric surgeries were effective in lowering BMI and improving glucose control. The effects lasted up to three years. Oral anti-diabetics discontinuation and decrease insulin use were statistical significant in both groups compared to baseline however neither was superior to the other. GB resulted in a greater weight loss, which continued over three years, than LB which stabilized its loss at 180 days. By the third year post procedure, GB patients had lower HA1c than LB patients.
OTHER

Abstract #700

METACHRONOUS CAROTID BODY TUMOR (CBT) AND ABDOMINAL FUNCTIONAL PARAGANGLIOMA (PGL) ASSOCIATED WITH A NOVEL GENETIC MUTATION AND POSING THERAPEUTIC CHALLENGES

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Objective: Hypervascular functional retroperitoneal PGL can be meaningfully managed using multimodality Rx regime. Metyrosine does not interfere w/ avid uptake of radiolabelled MIBG & effectively controls BP during MIBG Rx & tumor embolization. Molecular genetic studies continue to unfold novel mutation.

Methods: A 31 yrs. old male presented w/ 10 cm rt. abdominal mass & BP 180/124, urine normetanephrine (16 umol/D: RR: 0-3.43), nl. metnephrine (0.38 umol/D). Imaging studies: CT & MRI chest/ abdomen/pelvis, Whole body FDG-PET-CT scan showed 10.7 cm rt. retroperitoneal hypervascular mass, avid FDG uptake encasing rt. renal artery. MIBG scan was strongly positive. He had previously undergone resection of 5 cm rt. CBT w/ vascular invasion, wedge resection of hilar lymph node consistent w/ PGL . Both tissues were positive for chromogranin, synaoptophysin, & S-100. CBT had ki-67 index of 4 %. Genetic studies: for SDHB/C/D & RET oncogene: heterozygote variant in exon 4 of SDHB gene (C409A>G; p.lys137 Glu: p.K 137E) as the only abnormality.

Case Presentation: HTN. was controlled using phenoxybenzamine (PNZ) & metoprol . To render hypervascular abdominal tumor resectable embolization was done. Post procedure pt. developed hypertensive encelopathy (BP 200/124) & was resuscitated using IV regitine & nitroprusside. Several days later this was followed by administration of I131 MIBG under cover of metyrosine(4 G/day) & PNZ. Postablation scan was again strongly positive documenting combination of these 2 drugs did not interfere w/ MIBG uptake. This was followed by a second & uneventful embolization procedure under cover of metyrosine & PNZ w/ reduction in tumor hyper vascularity. A 3rd embolization followed by tumor resection is planned.

Discussion: We report a case of sporadic metachronous nonfunctional CBT & functional abdominal PGL ass’td w/ novel heterozygous variant detected in SDHB gene. Software prediction programs (SIFT, polyphen-2, mutation Tasters) indicate that this missense is likely to impact protein function. Lys residue in codon 137 is a highly conserved AA, conserved all the way to yeast. Taken together, this suggests that p.K137E variant is potentially pathogenic.

Conclusion: Hypervascular functional PGL can be meaningfully managed using a multimodality therapeutic regime consisting of combination of targeted antihypertensive drugs, repeated tumor embolization, radiolabelled MIBG, & surgery. There is scanty literature information regarding the impact of metyrosine on MIBG uptake. Metyrosine did not interfere with avid uptake of radiolabelled MIBG & effectively controlled BP during MIBG Rx and embolization. Molecular genetic studies should be undertaken to advance knowledge for PGLs.

Abstract #701

LANGERHANS' CELL HISTIOCYTOSIS (LCH) IN AN ADULT SAUDI MALE

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Objective: LHC occurs rarely & mostly among whites. We report a case of multisystem LCH in adult Saudi male w/ distinctly unusual features.

Methods: High resolution CT chest (HRCTC), MRI brain, skeletal survey, FDG-PET & bone scans, hormonal analysis, bone marrow(BM) skin lesion Bx & thyroid nodule FNA.

Case Presentation: A 18-yrs male presented w/ lt-pneumothorax & was resuscitated. O/E: Pt. dehydrated, had polyuria/polydipsia, hypogonadism, & inguinal skin lesion. Labs: hypopituitarism w/central diabetes insipidus(CDI): serum testosterone <0.10 nmol/L, LH/FSH each 0.1 IU/L, FT4 8.3 pmol/L (RR: 12-22), TSH 0.96 (RR: 0.27-4.2),normal synacthen test. 24-hr fluid intake/urine output 5-6 L. Serum Na+ 144 mmol/L, Plasma/urine osmolality 293/41 mOsm/kg respectively. Following DDAVP Rx fluid intake/ output improved to 1.5 L/D, plasma/urine osmolalities improved to 276/728 & serum Na+ decreased to 137.

Imaging Studies: HRCTC:multicystic lesions, w/ fibronodular infiltrates, mediastinal & hilar lymphadenopathy. MRI Brain: Enhancing suprasellar 16 mm lesion involving pituitary stalk, loss of posterior pituitary bright signal, a
small hypotrophy pituitary gland. PET: diffuse FDG activity seen in both lungs, intense focal FDG uptake in suprasellar region, parotids, lt. submandibular salivary gland, lt. thyroid, & Rt. inguinal region. LFTs, BM Bx, skeletal survey & bone scan were WNL. Skin & thyroid Bx: infiltration by LH cells stained +ve for CD 1a, langerin, & S-100 protein. Hormonal Rx started W/ improvement. ChemoRx started.

**Discussion:** LCH is a rare disorder w/ wide spectrum of clinical manifestations characterized by monoclonal proliferation & infiltration of organs by abnormal histiocytes .The clinical manifestations are heterogeneous ranging from indolent disease limited to a single organ to disseminated multisystem disease. Osteolytic bone lesions are seen most frequently (77% cases). Extraosseous lesions seen in descending order of frequency are: skin(40%), lymph nodes (20%), liver & spleen (16% each), lungs (10%) & CNS (6%). About 35 % pts. develop endocrinopathy w/ high frequency of central DI. Our pt. had “risk organs” involved, absence of bone lesions but had uncommon findings of salivary glands & thyroid lesion. LH cells are abnormal histiocytes that express CD-207 & CD-1a antigens, S-100 protein & Birbeck intracytoplasmic rod-shaped organelles on EM. These are hallmarks of disease.

**Conclusion:** For a pt. presenting w/ spontaneous pneumothorax & polyuria/polydipsia, a serious consideration should be given to LCH & a thorough evaluation should be undertaken to define the “risk organs” & extent of disease. Appropriate hormonal & therapy directed to primary disease are necessary.

**Abstract #702**

**ASSESSMENT OF SMALL FIBER NEUROPATHY THROUGH A QUICK, SIMPLE AND NON INVASIVE METHOD IN A DIABETES OUTPATIENT CONSULT CLINIC**

**Jean-Henri Calvet**, **Julien Dupin**, **Peter Schwarz**

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**Objective:** Sudomotor dysfunction is one of the earliest neurophysiologic abnormalities to manifest in distal small fiber neuropathy. SUDOSCAN was developed to provide a non invasive, quick, simple and quantitative measurement of sweat function. This observational study aimed to assess the feasibility and usefulness of sweat function assessment in a diabetes outpatient consult clinic.

**Methods:** The study was conducted on patients from a diabetes outpatient clinic in Germany with type 1 and type 2 diabetes. Renal function was assessed in a subgroup of patients through the measurement of Modification of Diet in Renal Disease (MDRD). Sweat function was evaluated by measuring the electrochemical conductance (ESC) of the hands and feet. Patients were required to place their palms and soles - where sweat gland density is the highest - on two large stainless-steel electrodes on which a small current (<4V, direct current, DC) is applied, and then to stand still for 2 minutes. ESC, expressed in microSiemens (µS), is the ratio between current generated and the constant DC stimulus applied on the electrodes. A risk score based on demographic data and ESC was calculated. The method’s reproducibility between two devices and a 1-year follow-up of ESC according to insulin administration were also assessed.

**Results:** 52 patients with type 1 diabetes and 115 patients with type 2 diabetes (69 receiving insulin) were involved in this observational study. Hand and foot ESC were lower in patients with type 2 diabetes when compared to patients with type 1 diabetes. The hand and foot ESC of the 20 subjects who presented with nephropathy (MDRD < 60 ml/mn/1.73 m2) were lower than those of the 104 patients without nephropathy (63±18 vs 72±15 p=0.07 and 73±16 vs 82±11 p=0.009 respectively). During the 1-year follow-up, a slight decrease in hand and foot ESC was observed in patients with type 2 diabetes not receiving insulin, while an increase was observed in patients receiving insulin (-3.8±9.7 vs 1.0±9.7 µS, p =0.02 for the hands and -2.2±7.5 vs 4.1±8.8 µS, p<0.001 for the feet). Coefficient of correlation between measurements performed with the two different devices was 0.85 for hands and 0.93 for feet, p<0.001. No subject experienced discomfort during the tests.

**Discussion:** This is the first comparison for sweat dysfunction between type 1 and type 2 diabetes. The observation that ESC improves with insulin treatment must be confirmed in a clinical study performed on a larger population.

**Conclusion:** This preliminary study shows that assessment of small C fiber neuropathy through a quick, non invasive and quantitative measurement of sweat function can be performed in standard diabetes outpatient practice.

**Abstract #703**

**ENDOCRINE MANIFESTATIONS OF CELIAC DISEASE**

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LLRM Medical College

**Objective:** To study the initial presentation of disease in patients diagnosed to have celiac disease from an endocrine department. To study the prevalence of other endocrinopathies in patients diagnosed to have celiac
disease. To study the clinical profile of celiac disease with extra gastrointestinal presentation.

Methods: Patients who were diagnosed to have celiac disease in the endocrinology department, LLRM Medical College, India, from Jan 2011 to Sept 2012 were studied (Total 68 patients). Presenting complaint was defined as the complaint for which the patient sought endocrinology services. Clinical and laboratory profiling was done and patients screened for other endocrinopathies.

Results: Short stature was the commonest presentation (25%) and 10% patients had delayed puberty as the presenting complaint. 21% of patients had both short stature and delayed puberty as the main presentation. Other presenting complaints included hypothyroidism with increase dose requirement (10%), rickets (6%), Type 1 DM with recurrent hypoglycaemia (7%), osteomalacia (3%). 18% of patients were diagnosed during screening for celiac disease in Type 1 DM patients. The clinical profile of celiac disease (after complete evaluation) is as - 59% patients had short stature, 31% had delayed puberty, carpopedal spasm in 6%, History of GI symptoms elicited included abdominal pain or bloating sensation in 85%, chronic diarrhoea in 68%, and sticky stools in 40% patients. 15% patients had no GI symptoms. Presence of other endocrine dysfunctions included short stature in 59%, delayed puberty in 31% low calcium in 22%, elevated alkaline phosphatase in 68%, hypothyroidism in 28%, subclinical hypothyroidism in 18%, Anti TPO antibody positivity in 53%, type 1 DM in 25% patients. 7% patients had Xrays suggestive of osteomalacia or rickets.

Discussion: Celiac disease has atypical, extra gastrointestinal presentations many of which endocrine, making it mandatory for the endocrinologist to recognise and diagnose the disease. Celiac disease is associated with other endocrine conditions like Type 1 DM, thyroid disorders, adrenal insufficiency, and infertility. The coexistence of these diseases could be explained by molecular mimicry by which gliadin or tissue transglutaminase activates T cells that are cross-reactive with various self-antigens.

Conclusion: Celiac disease is an endocrine disrupter as well as the great masquerader, with varied endocrine presentations. Some patients who have celiac disease may not have any GI symptoms. Significant incidence of celiac disease in hypothyroidism and Type 1 DM, makes screening for it important in these diseases.

Abstract #704

BISPHOSPHONATE-REFRACTORY HYPERCALCEMIA OF MALIGNANCY TREATED WITH DENOSUMAB

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Objective: To present two cases of bisphosphonate-refractory hypercalcemia of malignancy treated successfully with Denosumab.

Case Presentation: A 54 year old male with stage 4 squamous cell lung carcinoma presented with nausea, constipation, and polyuria. The admission corrected serum calcium was 15.2 mg/dL, creatinine 1.3 mg/dL, PTH 2.8 pg/mL and PTHrP 37 pg/mL. After four days of aggressive hydration, 5 doses of calcitonin and 4 mg of IV zoledronic acid his calcium was 11.7 mg/dL and increased back to 13.5 mg/dL five days later. He received Denosumab (60 mg SC) and within two days, his calcium was 10.8 mg/dL and declined to normal levels the following day. He was discharged home with hospice care.

A 63 year old male with stage 4 laryngeal cancer, presented with confusion and recurrent hypercalcemia with corrected serum calcium of 13.8 mg/dL, PTH 5 pg/ml and PTHrP 74 pg/mL two weeks after treatment with 60 mg of IV pamidronate during a hospitalization for hypercalcemia. After aggressive hydration, 6 doses of calcitonin, pamidronate 90 mg IV, and zoledronic acid 4 mg IV serum calcium ranged between 11.3-13.8 mg/dL. Following Denosumab (60 mg SC), his calcium levels declined to 10.8 mg/dL within three days.

Discussion: Malignancy associated hypercalcemia (MAH) is the most common cause of hypercalcemia in hospitalized patients and portends a poor prognosis, with a median survival of less than 6 months. IV bisphosphonates are the cornerstone of pharmacologic treatment of MAH. In a pooled analysis, success rates have varied from 69% with pamidronate and up to 88% with zoledronic acid, but ~ 22% being refractory to bisphosphonate therapy. In such patients, Denosumab, a fully humanized monoclonal antibody against RANKL, may be useful for the management of hypercalcemia. Denosumab blocks RANKL-RANK interaction and inhibits osteoclast formation and function leading to potent inhibition of bone resorption. Dose adjustment for renal impairment is not required as it is not renally cleared. Hypocalcemia can occur after Denosumab administration especially in patients with renal impairment and has to be monitored.

Conclusion: Denosumab is a novel agent currently FDA
approved for treatment of postmenopausal osteoporosis and for prevention of skeletal-related events in patients with solid tumors. Our experience indicates that Denosumab is an effective therapeutic agent for treatment of bisphosphonate-refractory hypercalcemia of malignancy. Large prospective randomized studies are needed to determine the efficacy of Denosumab for the treatment of malignancy-associated hypercalcemia.

Abstract #705

HYPOGLYCEMIA UNMASKING RARE DISEASE ENTITY

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SUNY Downstate

Objective: To document a case of hypoglycemia in a 24-year-old female patient with special consideration to alarming clinical signs that can point to rare disease diagnosis.

Methods: We present the diagnostic approach of a female patient with hypoglycemia.

Case Presentation: A 24-year-old female of Caribbean descent, presented with a syncopal episode due to hypoglycemia. Physical exam was unremarkable except for central obesity and multiple pedunculated skin lesions in the abdomen and back. Past medical history was positive for a macroadenoma secreting prolactin and the patient has been off bromocriptine for one month. Secondary adrenal insufficiency was suspected and morning cortisol level was remarkably low. The patient was placed on steroid replacement and dextrose drip, but she still became severely hypoglycemic. Insulin level and C-peptide was inappropriately normal for the low glucose level. Corrected calcium level was also found to be elevated. Multiple Endocrine Neoplasia syndrome type 1 (MEN 1) was suspected and indeed the patient was diagnosed with hyperparathyroidism and insulinoma that was treated surgically. Post pancreatectomy, ACTH stimulation test was performed that showed normal response.

Discussion: MEN 1 syndrome is a pleiomorphic tumor disease and can be associated with non-hormonal tumors like collagenomas, which can become pedunculated. It is of great importance for clinicians to suspect and screen patients with multiple collagenomas for MEN syndrome. According to studies, angiofibromas and collagenomas either single or multiple have sensitivity of 50-65% and 92-100% specificity in diagnosing MEN 1.

Conclusion: Recurrent hypoglycemia in patients with insulinomas blunt the counterregulatory hormone response and neuroglycopenic symptoms, which can return to normal after surgical treatment. During spontaneous hypoglycemia a seemingly low plasma cortisol is not sufficient evidence of adrenocortical insufficiency. Multiple collagenomas should raise suspicion for MEN 1 syndrome.

Abstract #706

THERAPEUTIC REINDUCTION OF HYPNATREMIA FOR PREVENTION OF CENTRAL PONTINE MYELINOLYSIS FOLLOWING OVERCORRECTION OF SERUM SODIUM.

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Objective: Osmotic demyelination syndrome (ODS) has been described following rapid correction of chronic hyponatremia. Ideal rate of correction has been recommended at 10-12 meq/24 hrs. We present a case of symptomatic severe hyponatremia with iatrogenic dangerously rapid correction warranting reinduction of controlled hyponatremia to prevent neurological catastrophe.

Case Presentation: 68-year-old female was transferred to our ICU facility after she was found unconscious. She was found to have severe hyponatremia with a serum Sodium level of 103 and treated with 100 cc of 3% saline and 3 liters of normal saline which brought her sodium to 109 within 2 hours of presentation. Seven hours after presentation, lab work showed a serum sodium level of 117. Urine output was noted to be averaging at 300 cc/hour with an osmolarity of 156. In light of such rapid correction and the ability to excrete water load, namely >2 meq/hour of sodium correction it was decided to start her on D5 ½ normal saline to keep up with her output and prevent rapid correction of serum sodium levels. Labwork done about 19 hours after initial presentation showed a continued rise in sodium levels up to 129. She was then switched to D5W. On day 3 of hospitalization, 43 hours following initial presentation, Serum Sodium levels were noted to be at 123. A correction by 20 meq (from 103 at presentation to 123 now) was thought to be appropriate for this 43 hour period, and the rate of D5W was decreased to ensure a correction of 0.5 to 1 meq/hour. On day 4 of hospitalization, 67 hours following initial presentation Serum Sodium levels had improved to 129 with stable urine output. She was then put on fluid restriction of 1.2 liters. Serum Sodium levels were intentionally relowered for therapeutic purpose of preventing central pontine myelinolysis with success. Improvement in mental status was seen with serum sodium levels in normal range, and no evidence of ODS was found on MRI.

Discussion: Our patient’s acute symptomatic severe
hyponatremia was thought to be multifactorial, primarily precipitated by polydipsia, in the presence of baseline chronic mild hyponatremia. Rapid over correction was likely from overzealous use of hypertonic intravenous fluids in the presence of normal renal function. Inadvertent overcorrection of sodium level could happen if the diluting capacity of the nephrons was to return following transient compromise, as may happen in primary polydipsia, where nausea might impair this mechanism.

Abstract #707

SUDOMOTOR FUNCTION ASSESSMENT AS A SCREENING TOOL FOR MICROVASCULAR COMPLICATIONS IN TYPE 2 DIABETES

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1. Impeto Medical, 2. Apollo

Objective: Sweat glands are innervated by small C-fibers, and sudomotor dysfunction is one of the earliest abnormalities to manifest in distal small fiber neuropathy. SUDOSCAN was developed to provide a non invasive, quick, simple and quantitative measurement of sweat function. The aim of this study was to evaluate this new method as a screening tool for microvascular complications in patients with type 2 diabetes.

Methods: 309 patients with type 2 diabetes from Apollo Center (Hyderabad, India) were evaluated for microvascular complications, including peripheral neuropathy using a biothesiometer, nephropathy through measurement of creatinine clearance and calculation of Modification of Diet in Renal Disease, and retinopathy through fundus of the eye examination. Small C-fiber status was assessed through sudomotor function by measurement of hand and foot Electrochemical Sweat Conductance (ESC) and calculation of a risk score using SUDOSCAN. Patients were required to place their palms and soles - where sweat gland density is the highest - on two large stainless-steel electrodes on which a small current (<4V, direct current, DC) was applied, and then to stand still for 2 minutes. ESC, expressed in microSiemens (µS), is the ratio between current generated and the constant DC stimulus applied on the electrodes. A risk score based on demographic data and ESC was calculated. Results were immediately available.

Results: Hand and foot ESC were lower in patients with at least one microvascular complication as compared to patients without: 49 ± 20 vs 62 ± 17 µS, p <0.001 and 59 ± 21 vs 69 ± 15 µS, p<0.001, respectively. Area Under the Curve (AUC) of the Receiver Operating Characteristics (ROC) curve for detection of at least one microvascular complication was 0.76 for SUDOSCAN risk score, with a sensitivity of 82% and a specificity of 61%.

Discussion: Decrease in ESC observed in patients with peripheral neuropathy are in accordance with previous studies but it is the first study to assess screening performance of SUDOSCAN for microvascular complications.

Conclusion: Assessment of small C-fiber status based on measurement of sweat function by SUDOSCAN could be used for the screening of microvascular complications and may aid in adhering to currently unfulfilled follow-up recommendation guidelines for patients with type 2 diabetes.

Abstract #708

DEFINING “GIANT PARATHYROID ADENOMA” WITH A CONSECUTIVE SERIES OF 1,074 PARATHYROIDECTOMIES AND LITERATURE REVIEW

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Objective: On rare occasions parathyroid adenomas causing hyperparathyroidism are found to be extremely large, however there is no consensus definition for the term “giant parathyroid adenoma”. We aimed to objectively define this term by comparing size data from a large series of parathyroidectomies with what has previously been reported in the literature. We also present one of the largest parathyroids ever removed in the United States.

Methods: We retrospectively reviewed the charts of 1,074 consecutive patients having undergone parathyroidectomy at our institution. Our literature review included a MEDLINE and PubMed search with the terms “parathyroid adenoma” AND “giant” OR “huge” OR “large” OR “big” or “massive”.

Results: Of the 1,074 parathyroidectomies, there were 870 (81%) single adenomas, 115 (11%) double adenomas, and 89 (8%) cases of multigland hyperplasia. In the single adenoma group the average serum calcium was 11.2 mg/dL and PTH was 138pg/mL, and the median weight of the glands was 630 mg (range: 40 to 70,600 grams). The largest 5% and 1% of single adenomas weighed ≥ 3.2 and ≥ 9.2 grams respectively, and the smallest 5% and 1% weighed ≤ 150 mg and ≤ 102 mg respectively. The largest parathyroid removed at our institution weighed 70.6 gm and was found in a 71-year-old man with a palpable neck
mass, and elevated serum calcium (14.5 mg/dL) and parathyroid hormone (654 pg/mL). CT revealed a 3.7 x 5.6 x 9.5 cm tumor in the left neck extending into the mediastinum, with corresponding uptake on a sestamibi scan. The abnormal parathyroid gland was removed through a cervical incision, and was not fibrotic or adherent to surrounding structures. Intraoperative parathyroid hormone values returned to normal after excision. Pathology showed an 8.5 x 5.5 x 2.5 cm hypercellular, cystic parathyroid adenoma. Literature review revealed 20 case reports and 4 retrospective reviews published between 1976 and 2011. The glands ranged in weight from 12.7 gm to 135 gm. There was one suspected parathyroid carcinoma (5%), and four glands with cystic components (20%).

Discussion: Parathyroid adenoma weights are not normally distributed, thus using percentiles is an appropriate method for defining their distribution. We propose that the term “giant parathyroid adenoma” be reserved for the top 1% of cases, which in our series is greater than 9 grams.

Conclusion: By better defining the term “giant parathyroid adenoma” we hope to make it easier to research this rare phenomenon in the future. We also report here one of the largest parathyroid tumors ever removed in the United States.

Abstract #709

MULTIPLE ENDOCRINE NEOPLASIA TYPE 1: 30 YEARS OF SURGICAL MANAGEMENT OF PHPT IN PEDIATRIC PATIENTS AT A TERTIARY CARE CENTER

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Objective: We describe the clinical course and management of Primary Hyperparathyroidism (PHPT) in the pediatric population, focusing on the use of genetic testing (GT) for Multiple Endocrine Neoplasia Type 1 (MEN1) and its influence on operative strategy. PHPT will be the initial disease manifestation for 90% of MEN1 patients, with an age of onset decades earlier than in sporadic PHPT. Optimal operative timing remains undefined in the pediatric population.

Methods: A research database at a tertiary care center was queried for patients referred for evaluation of PHPT at 18 years of age or younger. Clinical data was collected on 54 patients from 1981-2012. 36 patients had surgery for PHPT. Differences between groups were evaluated using Pearson’s χ2 or Fisher’s exact test, where appropriate.

Results: 36 patients had parathyroidectomy (n=20 at our institution; n=16 off-site) with median age of 15 at initial presentation, and 18 at surgery. Nephrolithiasis was the most common presenting symptom (54.5%), whereas 21% were “asymptomatic.” GT for MEN1 occurred in 28 (77%) with 18 (64%) positive results. GT was not pursued in 8 patients with clinical diagnosis or positive family history. Patients with clinical MEN1 or positive GT were more likely to have >3 gland resection (64%, P<0.0001) and thymectomy (57%, P=0.008). However, pre-operative GT was done in 14 (70%) patients at our institution, compared to only 2 (12.5%) in the off-site group (P<0.0001). At our institution negative GT changed the operation for 7 patients to minimally-invasive surgery. Recurrence ensued in 5 (25%) patients at our institution and 11 (69%) off-site (P=0.017); and was less likely in those with pre-operative GT than without (2 vs. 9, P=0.001). Permanent hypocalcaemia occurred in 5 (14%) patients, none had pre-operative GT (P=0.034); all were associated with >1 operations (P=0.008). There were no other documented complications. Median follow-up after initial surgery was 4.3 years.

Discussion: Our findings suggest that pre-operative GT in pediatric patients with PHPT helps the surgeon determine the extent of initial operation. It was also associated with lower rates of recurrence and permanent hypocalcaemia. Additionally, GT helps identify patients who need continued MEN1 screening.

Conclusion: Pre-operative genetic testing is a helpful tool for operative planning in PHPT. Three-or-more-gland parathyroidectomy with cervical thymectomy is the operation of choice for MEN1 patients. Referral to a high-volume center with genetic testing and experienced clinicians should be considered in young patients with PHPT.

Abstract #710

VITAMIN A TOXICITY: A RARE CAUSE OF HYPERCALCEMIA

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Objective: To report a case of vitamin A induced hypercalcemia and to emphasize importance of pharmacovigilance when taking a medical history.

Case Presentation: The increasing use of dietary supplements and over-the-counter medicines, ‘natural’ or otherwise, may pose significant health risks. The association of vitamin A toxicity and hypercalcemia is rare but recognized. We describe a case of a 35 year old woman with severe hypercalcemia who was taking vitamin A, 250,000
A 35 year old woman presented with a 1 week history of myalgia, chills, and generalized malaise. No history of recent weight loss, fevers, or night sweats. Home medications included Lexapro, vitamin A 3000 IU daily, vitamin D 3000 IU daily, zinc and iron supplements prescribed by a Naturopath. Reported recent travel to Connecticut and Costa Rica where she spent some time in the sun but wore sunscreen daily. Her physical exam was normal. Labs demonstrated a calcium 14.4, phosphorus 3.2, and Magnesium 1.2. She had acute renal insufficiency with GFR of 42. Hypercalcemia was treated with vigorous hydration (IVF). Further diagnostic evaluation of the hypercalcemia revealed Intact PTH less than 2.5, am cortisol 16.4, TSH 1.3, 25 hydroxy vitamin D 34 and 1, 25 dihydroxy vitamin D 16. ACE level was slightly elevated at 74. Serum and urine protein electrophoresis were normal. Microbiologic and rheumatologic evaluations were unremarkable. Vitamin A Retinyl Palmitate level was measured and was elevated to 1.4 (normal range 0.0-0.1). Examination of the patient’s supplement bottle revealed she was not taking 3000 IU but instead 250,000 IU of vitamin A, daily for 6 months. Calcium level normalized with IVF and renal function returned to normal. The patient was counseled about the risks and potential complications of high doses of vitamin A as well as dietary supplements.

**Discussion**: Excessive amounts of vitamin A in the absence of any other comorbidities was able to induce severe hypercalcemia in this patient. The patient was taking a dose of vitamin A 50 times greater than the recommended daily dose of 5000 IU. Ingestion of large amounts of vitamin A may inhibit osteoblast activity and stimulate osteoclast formation leading to accelerated bone resorption resulting in hypercalcemia.

**Conclusion**: Excessive amounts of vitamin A in the absence of any other comorbidities can induce severe hypercalcemia. Given the increased use of alternative medicines and supplements, more such cases may occur, which highlights the importance of a detailed medication history.

**Abstract #711**

**GERMLINE MEN1 MUTATION WITH FEATURES OF MEN1 AND MEN2**

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**Objective**: Multiple endocrine neoplasia (MEN) type 1 (MEN-1) is an autosomal dominant (AD) disorder with endocrine tumors in 2 or 3 of its main tissues (parathyroid, anterior pituitary, and enteropancreatic neuroendocrine cells) resulting from germline inactivation of the MEN1 tumor suppressor gene. MEN-2 refers to 3 variants of an AD disorder with medullary thyroid cancer, each due to germline activating missense mutation of the RET protooncogene. Variant features include pheochromocytoma, hyperparathyroidism (HPT), thickened corneal nerves, and neurofibromas.

**Case Presentation**: The index case of this family initially presented with primary HPT. She next developed cushingoid features and underwent bilateral adrenalectomy, which revealed left cortical adenoma and right medullary pheochromocytoma. A pancreatic neuroendocrine tumor was found at surgery requiring distal pancreatectomy. Her Cushing’s syndrome resolved postoperatively. She then developed Zollinger-Ellison syndrome (ZES), treated by total gastrectomy. She also underwent transsphenoidal resection of a prolactinoma. Physical features included cutaneous lipomas and thickened corneal nerves (slit-lamp examination). Genetic testing revealed a germline 1132delG frameshift mutation in MEN1, but no mutation in RET exons 10 through 16. Prior to her death she showed a bronchial carcinoid, and liver metastases consistent with metastatic gastrinoma. The patient’s daughter and son tested positive for the 1132delG mutation in MEN1. MEN-1 features in the daughter included HPT, prolactinoma, ZES, bronchial carcinoid and cutaneous lipoma. In addition she presented with a 4 x 2.4 x 2.4 cm left inguinal mass found to be neurofibroma.

**Discussion**: We report here mixed MEN-1 and MEN-2 manifestations in two generations, the first such report to our knowledge. Both mother and daughter carry germline MEN1 mutation, yet manifest MEN-2 like features, including pheochromocytoma and thickened corneal nerves (mother) and a large neurofibroma (daughter). Pheochromocytoma has also been a rare (<1%) feature of MEN1. RET mutational testing was negative in the index case. Possible explanations include a previously unrecognized phenotype-genotype association with the
1132delG frameshift mutation in MEN1, the presence of an occult RET mutation in both mother and daughter outside the tested exons, or the presence in both of a mutation or polymorphism in one or more additional gene(s) that might promote MEN-2-related expressions such as in genes for cyclin-dependent kinase inhibitors.

**Conclusion:** Germline MEN1 mutation can rarely be associated with classic expressions of both MEN-1 and MEN-2 together, and that persist in two generations.

**Abstract #712**

**FALLS AND VITAMIN D SUPPLEMENTATION AT A COMMUNITY HOSPITAL: HOW FAR ARE WE FROM CURRENT RECOMMENDATIONS?**

*Janna Prater, Joumana Chaiban, Giesele Greene*

**SVCMC**

**Objective:** To improve rates of supplementation with Vit D among patients who are at increased risk of falls.

**Results:** Falls are a common serious cause of morbidity and mortality in older adults. They occur in up to 30-40% of community-dwelling adults and up to 50% of institutionalized older adults. It has been demonstrated in institutionalized elderly that patients who fall have lower serum vitamin D concentrations than those who don’t. Data suggests that the muscles and the nervous system are target organs of vitamin D and that vitamin D supplementation (800 IU/day) alone or in combination with calcium (500-1200 mg/day) allows a marked reduction in the number of falls in the same individual and in the number of fallers, with a reduction of up to 50%. As part of a quality improvement project, we conducted a retrospective cohort study looking at patients hospitalized at our institution in 2009 and 2010. We specifically identified patients admitted with falls and those who fell during their hospital stay. Their vitamin D levels were collected and subsequent vitamin D supplementation was evaluated. Data of 97 patients who met the criteria were reviewed. 73 out of 97 patients (70.5%) were 65 years or older. Only 10 patients (10.3%) had their vitamin D levels checked during the same admission or had a prior result within 1 year. 6 of them had their levels checked subsequently after the admission (within a year). Surprisingly only 24 (25%) out of the 97 patients were started on different forms of Vitamin D supplementation upon discharge (either multivitamins containing vitamin D or Oscal D or Vitamin D 400, 800,1000 Units daily or 50000 Units weekly), most of those were older than 65 (21 out of 24).

**Discussion:** It is known that vitamin D supplementation is an effective and inexpensive strategy for reducing falls and subsequent morbidity in older adults and it should be incorporated into the clinical practice of providers caring for them, especially those at risk for falling. Improving rates of vitamin D level evaluation and subsequent appropriate supplementation in elderly patients at risk for falls are essential, moreover with the new Medicare regulation stating that in-hospital falls is a publically reportable event and its complications are non-reimbursable.

**Conclusion:** In an effort to increase awareness and with the institution of the electronic medical records, a plausible and important tool to our institution would be to incorporate an automatic reminder regarding the association of vitamin D status and falls along with suggestion of vitamin D treatment in that specific population.

**Abstract #713**

**THE CRYSTALLINE PARATHYROID: A CASE REPORT**

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**Objective:** Cholesterol crystals have been described in various cysts of the neck (thyroglossal duct, branchial cleft, and thymic cysts), however crystals in the parathyroid gland have only been described once previously in the literature. We report, to our knowledge, the second known case of crystals within a parathyroid cyst.

**Methods:** We performed a literature review with a focus on cholesterol crystal formation and parathyroid hemorrhage. We identified patients admitted with falls and those who fell during their hospital stay. Their vitamin D levels were collected and subsequent vitamin D supplementation was evaluated. Data of 97 patients who met the criteria were reviewed. 73 out of 97 patients (70.5%) were 65 years or older. Only 10 patients (10.3%) had their vitamin D levels checked during the same admission or had a prior result within 1 year. 6 of them had their levels checked subsequently after the admission (within a year). Surprisingly only 24 (25%) out of the 97 patients were started on different forms of Vitamin D supplementation upon discharge (either multivitamins containing vitamin D or Oscal D or Vitamin D 400, 800,1000 Units daily or 50000 Units weekly), most of those were older than 65 (21 out of 24).

**Discussion:** It is known that vitamin D supplementation...
granuloma formation. Also seen were parenchymal fibrous bands with partial capsular penetration. There were no abnormal mitotic figures, vascular invasion, or invasion of surrounding structures.

Discussion: Cholesterol crystals are commonly found in the gallbladder, or as a breakdown product after hemorrhage in atheromatous plaques. It is highly unusual for them to form in the parathyroid gland. In the only other reported case of parathyroid crystals, microscopic cholesterol crystals were found among fibrotic tissue with hemosiderin deposition suggesting that a previous hemorrhage had occurred. However, after reviewing 36 additional cases of parathyroid “apoplexy” and/or hemorrhage we found no other described crystal formation in the parathyroid gland. In our case the finding of fibrous bands raised the suspicion for parathyroid carcinoma, however this could also be the result of an inflammatory response after hemorrhage into the gland.

Conclusion: Cholesterol crystal formation in a parathyroid gland is extremely rare. When it does occur it is likely related to a previous hemorrhage within the parathyroid gland. It is important to recognize this phenomenon so as not to confuse these benign adenomas with parathyroid cancer, or with other cysts in the neck that often contain such crystals.

Abstract #714

HYPERCALCEMIA DUE TO PTH RELATED PEPTIDE PRODUCING TUMOR

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Case Presentation: A 63 yo Caucasian woman presented for elective ventral hernia repair and was noted to have a serum calcium level of 12.7mg/dL (8.6-10.0). She was discharged home in good condition and returned to the hospital 1 month later with complaints of abdominal pain, nausea, and vomiting with a calcium level of 13.1. Her past medical history was significant for rheumatoid arthritis, treated methotrexate and entanercept, and a dermoid cyst on her ovary. Initial workup included: PTH <3 pg/mL, 1,25(OH)2 vitamin D 40.8 pg/mL, 25-OH vitamin D 5.9 ng/mL, TSH 1.3 mIU/mL, and UPEP/SPEP which were normal. Quantiferon TB gold assay and histoplasmosis urine antigen were also normal. A PTHrP value did return elevated at 7.2 pmol/L (<2). She was up to date on her mammogram and colonoscopy screening and did not have any complaints worrisome for malignancy. Physical exam did not reveal obvious malignancy. A chest CT was performed in search of a lung malignancy which revealed bilateral pulmonary emboli, but no evidence of malignancy was seen. Incidentally found was a small renal mass. PET/CT imaging was performed searching for a malignancy and revealed increased uptake in uterus and endometrium. Subsequent bedside endometrial biopsy was negative for malignancy. Transvaginal ultrasound only showed uterine fibroids. Because renal cell carcinoma has been known to produce PTHrp more commonly than other tumors a CT guided biopsy of the renal mass was performed which did not show evidence of malignancy. Over the next month the patient developed a small amount of vaginal bleeding. She underwent vaginal hysterectomy without oophorectomy and was found to have a high grade undifferentiated endometrial sarcoma with monomorphic features involving the myometrium without involvement of the serosa with lymphovascular invasion. Post operatively her serum calcium decreased from 12.0mg/dL to 9.4mg/dL within 24 hours and the PTHrP decreased to <0.74 pmol/L.

Discussion: Few cases have been described of gynecologic malignant neoplasms producing PTHrP outside of the ovary. Because of the rarity of endometrial sarcoma as a cause of PTHrP production the diagnosis was met with some challenges. Her initial workup revealed that her hypercalcemia was not mediated by PTH and she did not have a history fitting for milk alkali syndrome. Ultimately a PTHrP value did return high placing malignancy high on the differential, but due to the patient’s initial lack of symptoms related to her malignancy the diagnosis was delayed.

Conclusion: Endometrial sarcoma is a rare cause of PTHrP mediated hypercalcemia and should be considered as part of the differential diagnosis in patients with hypercalcemia.

Abstract #715

ELEVATED PTH: TRUE OR FALSE POSITIVE?

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Objective: Intact parathyroid hormone (PTH) assay with Siemens kit on Centaur using EDTA plasma is a “sandwich” technique targeting 2 distant sites on the ligand. A capture antibody and signal antibody target different epitopes. PTH is quantified by measuring the signal antibody generated reaction.

Case Presentation: A 55 year old female presented for evaluation of hyperparathyroidism. She had hypercalcemia one year prior. A parathyroid scan showed increased
activity at the right lower thyroid pole consistent with adenoma. She subsequently had a parathyroidectomy. A post-operative serum PTH was 20.4 pg/mL and calcium was 9.3 mg/dL. Five months later she had an elevated plasma PTH of 223 pg/mL with a repeat of 553 pg/mL. She remained normocalcemic and asymptomatic. A repeat parathyroid scan did not show a recurrent or residual parathyroid adenoma. We requested patient have PTH performed at another laboratory. Serum based PTH using Siemens kit on Centaur was 75 pg/mL and repeat was 73 pg/mL. It was concluded that the initial PTH results were falsely positive secondary to assay interference by a patient EDTA-affected antibody.

Discussion: The possibility of antibody interference should be considered when the test result does not correlate with the clinical picture and negative imaging results. The prevalence of interfering antibodies in blood samples varies among reported studies. The possibility of an anti-animal antibody interference should prompt testing with murine antibody-based sandwich assay, incubation with heterophile antibody blocking tubes, and/or a goat antibody-based PTH testing system.

Conclusion: This case highlights the importance of careful interpretation of laboratory results in conjunction with the clinical picture and using confirmatory testing with discordant results.

Abstract #716

A CASE OF HYPOKALEMIC HYPERTENSION...
PRIMUM NON NOCERE

Shamsuddin Shaik, Ajay Abichandani, Robert Gayner, Mohammad Arastu

St. Luke’s Hospital

Objective: We present an uncommon case of surreptitious diuretic usage mimicking Gitelman syndrome.

Case Presentation: A 31 year old Caucasian female who works as a pharmacy technician with fatigue, polyuria, polydipsia, intermittent leg cramps and tingling in her feet. She reports that she was diagnosed with hypertension two months before admission and was started on metoprolol succinate. This was discontinued several weeks later and she was started on spironolactone as her potassium was noted to be decreased. Her serum potassium had been persistently low for a month prior to admission and was receiving potassium supplementation. Interestingly her serum potassium was noted to be low (2.8 mmol/L) ten years ago but had normal values until one month prior to admission. On admission, the patient was noted to be normotensive with the following lab values: serum sodium 130 mmol/L(136-145); potassium 2.2 mmol/L(3.5-5.3); bicarbonate 35mmol/L(23-33); BUN 42 mg/dL(5-25); creatinine 1.4 mg/dL(0.6-1.3); uric acid 10.4 mg/dL(2.7-6.8); calcium 10.6 mg/dL(8.3-10.1); renin 92.56 ng/ml/hr(1-4) and aldosterone 74.9ng/dL(0.0-30.0). Twenty four hour urine potassium and calcium were 58 mmol (25-150) and 84mg (42-353) respectively. Serum magnesium was normal. Serum metanephrines, cortisol, TSH and PTH were normal. The patient denied self-induced vomiting and licorice consumption. She persistently denied surreptitious diuretic usage. Renal arteriogram and MRI abdomen ruled out renal artery stenosis and renin secreting tumor respectively. Her potassium normalized with supplementation and she remained normotensive without antihypertensive medications. Urine analysis performed by high performance liquid chromatography showed hydrochlorothiazide 14mcg/ml and furosemide 5.4mcg/ml. Spironolactone was discontinued and was discharged without any potassium supplementation.

Discussion: The diagnosis of surreptitious diuretic usage is largely one of exclusion, made in someone who presents with unexplained hypokalemia and metabolic alkalosis with a normal or low blood pressure. This condition mimics Gitelman syndrome except that urine diuretic screen will be positive. High urine chloride variability suggests the possibility of diuretic usage whereas urine chloride persistently greater than 25 meq/L suggests Gitelman syndrome. The diagnosis is usually made with a careful history, physical examination, measurement of the urine chloride concentration, and a urine diuretic screen.

Conclusion: In patients who present with unexplained hypokalemia, metabolic alkalosis, and an index of suspicion for surreptitious diuretic use should undergo a urine diuretic screen to provide the most cost-effective care.

Abstract #717

HYPERCALCEMIA AS A CLUE FOR RARE PRESENTATION OF RARE EXTRAPULMONARY SARCOIDOSIS

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Case Presentation: Isolated extrapulmonary sarcoidosis is often difficult to make a diagnosis. Here, we tease out the triad of abdominal sarcoidosis, liver-spleen-bone marrow involved, as a diagnosis by carefully investigating of hypercalceemia. A 30-year-old African-American male with past medical history of hypertension, presented with a three month history of progressive difficulty swallowing for solid food with nausea and vomiting. He also described
non-radiating chest and stomach pain associated with solid-food ingestion. Twenty-six-pound unintentional weight loss, fatigue and weakness were observed in the past 6 months. On exam, hepatosplenomegaly was noted, but otherwise unremarkable. Initial laboratory findings showed hemoglobin of 8.0 g/dL, serum creatinine (Cr) of 3.86 mg/dL, corrected serum calcium level of 12.7 mg/dL, serum phosphorus was 3.5 mg/dL, serum alkaline phosphatase of 199 U/L, low 25-hydroxyvitamin D and intact PTH, but high level of 1,25-dihydroxyvitamin D. Chest X ray was unremarkable and CT of abdomen/pelvis confirmed hepatosplenomegaly. Esophagogastroduodenoscopy revealed no ulceration or mass with negative biopsy result of distal esophagus. Bone survey was negative for any lytic lesion and serum protein electrophoresis revealed polyclonal elevation of IgG. Hence, we worked up for extrapulmonary sarcoidosis which high serum Angiotensin Converting Enzyme (ACE) was found, 110 U/L. The triad of abdominal sarcoidosis was provisionally diagnosed. Bone marrow aspiration and biopsy nicely revealed 70% of the cellular bone marrow was replaced with non-necrotizing granulomatous inflammation. His odynodyshphagia, hypercalcemia and acute kidney injury dramatically improved with vigorous intravenous fluid, diuretic, prednisone and hydroxychloroquine. Further work-up of other organs involvement was unremarkable. He was discharged home in a stable condition.

Discussion: Odynodyshphagia is an extremely rare presentation of sarcoidosis. Its clinical manifestations often masquerade many diseases like multiple myeloma. In this case, we successfully worked up the finding of hypercalcemia which leads to the pathology of increased 1-alpha hydroxylase activity from granulomatous tissues. Carefully taking the history, physical examination combined with solid background of hypercalcemia approach should allow physician to prevent further organs damage and improve quality of life of sarcoidosis patient

Conclusion: Hypercalcemia can be used as a clue to diagnosis of various diseases especially when they atypically present. We demonstrated a case of abdominal sarcoidosis which rarely presents with odynodyshphagia/dysphagia, but successfully diagnosed by the finding of hypercalcemia.

Abstract #718
PARAGANGLIOMAS OF THE URINARY BLADDER: A REVIEW OF CASES TREATED AT THE NATIONAL CANCER INSTITUTE

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NIH NCI

Objective: Bladder paragangliomas (BP, also called bladder pheochromocytomas) account for only 0.06% of bladder tumors. They can occur sporadically but are often associated with familial cancer syndromes such as von Hippel-Lindau (VHL) and succinate dehydrogenase B (SDHB, or familial paraganglioma type 4). We further characterize the clinical manifestations in sporadic and familial patients.

Methods: A retrospective review was performed of all cases of BP treated by the Urologic Oncology Branch at the National Institutes of Health (NIH) Clinical Center from 1989 - 2012. We reviewed the demographics, radiologic, pathologic, and laboratory data, and clinical outcomes of patients with BP.

Case Presentation: Eight patients were diagnosed with BP during the study period with a mean follow-up of 27 months following resection. Five of the cases (62.5%) were associated with genetic syndromes (three had VHL and two had SDHB mutations). Mean age of diagnosis was 21.6 years old (range 6-42 years) for all patients, and was only slightly lower for the hereditary vs the sporadic cases (20.6 vs 23.3 years). Six of the eight patients had at least two symptoms of the triad of headache, diaphoresis, and palpitations at the time of diagnosis; one patient had all three. Four patients had micturition-related symptoms. The bladder was the primary site of paraganglioma in five patients. Pre-operative lab work demonstrated that 24-plasma normetanephrine (pNMN), urine norepinephrine (uNEN), and urine normetanephrine (uNMN) had the highest sensitivity (80%, 80%, and 75%, respectively). Plasma norepinephrine and chromogranin A were both 67% sensitive. In the two SDHB patients, pNMN, pNEN, and uNMN were elevated to between nine and thirteen times the upper limit of normal, levels not seen in the other patients. The sensitivities of MRI, CT and MIBG were 100% and 83%, and 75%, respectively. Plasma norepinephrine and chromogranin A were both 67% sensitive. In the two SDHB patients, pNMN, pNEN, and uNMN were elevated to between nine and thirteen times the upper limit of normal, levels not seen in the other patients. The sensitivities of MRI, CT and MIBG were 100% and 83%, and 75%, respectively. Familial BP tended to be smaller than sporadic cases at presentation (4 cubic centimeters (cc) vs. 33 cc mean tumor volume). BP detected in pediatric patients (<18 years old) were generally small (9.8cc vs 17.7cc for patients >18 years old).

Discussion: Familial and sporadic BP present with similar signs and symptoms. Familial BP and cases occurring in
pediatric patients tend to present with smaller tumors. Urine and plasma norepinephrine and normetanephrine tend to be elevated to a greater degree in SDHB compared to VHL or sporadic cases.

**Conclusion:** BP are rare tumors, but are more common in the setting of hereditary syndromes. Micturition-related hypertensive symptoms may be important clues for diagnosis, which can be confirmed by catecholamine testing and MRI/CT imaging. The tumors are amenable to surgical resection.

**Abstract #719**

**CALORIE INTAKE AND HOSPITAL MORTALITY IN PATIENTS WITH REDUCED SERUM ALBUMIN CONCENTRATION**

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**Objective:** Endocrinologists are frequently asked for nutritional consults for inpatients with a history of weight loss and low serum albumin. Prior studies have shown a relationship between hypoalbuminemia and higher mortality rates but none have reported that providing calories improves survival. The objectives were: To evaluate the relationship between admission serum albumin and mortality, length of stay, and readmission rates, and to prospectively test if caloric intake improves hospital outcome.

**Methods:** Prospective observational study using data on hospital survival, length of stay, and readmission rates. Caloric intake was determined in 380 patients with an albumin <1.5 g/dl to test the hypothesis that caloric intake >50% influenced hospital survival. 11,441 admissions with a serum albumin with 3.4% had initial serum albumin values <1.5 g/dl admitted to hospital with a serum albumin. Daily caloric intakes and severity of injury scores were determined for the 380 patients with the severely reduced serum albumin (<1.5 g/dl).

**Results:** Admission was less than 3.0 g/dl in 54% of the patients. Mortality increased in patients with a reduced albumin (8.8% vs 2.3%, p<0.05). Hypoalbuminemic patients also had a significant increase in length of stay (11.8 vs. 7.8 days, p<0.05). Serum albumin was exponentially related to mortality (mortality = 32/albumin2 ;p<0.01).

The 380 patients with albumin <1.5 g/dL had the greatest mortality rate (18%), which is about 7-times that of patients with normal levels. These hypoalbuminemic patients also had an average hospital stay of 14.7 days, twice that of patients with normal values. These patients also had more than twice the 30-day readmission rate (63.9% vs 19%). In the 380 patients under 1.5 g/dl caloric intake averaged

50% of the recommended intake (range 0-110%).

**Discussion:** Patients who received equal to or less than 35% had a 51% hospital mortality. Those with an intake between 25-50% had a 33% hospital mortality. Patient with a serum albumin < 1.5 gm/dl and a caloric intake greater than a 50% of predicted had only a 4.0% hospital mortality. The severity of injury were similar in these groups (data not shown).

**Conclusion:** A single measurement of serum albumin identifies patients who are at increased risk of death in hospital. If caloric intake was more than 50% of the dietary needs in patients with a serum albumin < 1.5 gm/dl, then hospital mortality was reduced 12-fold (p<0.05). A prospective randomized trial is needed to confirm these data.

**Abstract #720**

**ULTRASOUND ELASTOGRAPHY IS A SENSITIVE IMAGING CHARACTERISTIC OF PARATHYROID ADENOMAS BUT NOT SPECIFIC ENOUGH TO CONCLUDE ACCURATE LOCALIZATION**

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**Objective:** To review the usefulness in clinical practice of ultrasound Elastography in patients with primary hyperparathyroidism as a pre-operative localization tool.

**Methods:** Retrospective review of the ultrasound Elastography imaging characteristics of 7 patients/cases with biopsy proven parathyroid adenomas in comparison to 7 control cases with biopsied reactive lymph nodes and thyroid nodules.

**Results:** There is no statistical difference between the ultrasound Elastography characteristics of parathyroid adenomas vs. reactive lymph nodes and cystic thyroid nodules. Parathyroid adenomas however are generally stiff lesions compared to most solid thyroid nodules. Sensitivity 85.71 %, Specificity 12.5%, Positive Predictive Value 46%, Negative Predictive Vlaue 50%.

**Discussion:** Pre-operative localization of parathyroid adenomas is important if minimally invasive surgery is to be performed, ultrasound is the most cost effective tool in this context, however with a reported 30% co-existence of thyroid nodules in the patient population with parathyroid adenomas definitive localization becomes problematic, our thought was that since parathyroid adenomas are note due be stiff lesion son ultrasound Elastography a comparison with similar lesions would help clarify the sensitivity and specificity of this technique. The results in this community based practice show high sensitivity but
limited specificity which doesn’t preclude the need for a fine needle aspiration biopsy to confirm localization.

**Conclusion:** Ultrasound Elastography has high sensitivity but limited specificity which doesn’t preclude the need for a fine needle aspiration biopsy to confirm localization.

**Abstract #721**

**A RARE CASE OF HYPERCALCEMIA DUE TO PRIMARY HYPERPARATHYROIDISM AND HUMORAL HYPERCALCEMIA OF MALIGNANCY**

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**Case Presentation:** A 65-year-old African American male was brought in by family because of decreased activity, weight loss and increasing forgetfulness for a month. Three months ago, he was diagnosed with Stage II lung adeno-squamous carcinoma. PET scan immediately prior to pneumonectomy demonstrated no evidence of metastatic disease. He underwent left pneumonectomy but denied adjuvant chemotherapy. Examination: Patient was not oriented and had poor attention span. His blood pressure was 100/88 mmHg and heart rate was regular at 72 beats/min. He had dry mucous membranes and poor skin turgor. He had no air movement on the left side of his chest, which was dull to percussion (post- pneumonectomy). Labs: Initial metabolic profile showed calcium of 12.8mg/dL (8.5 - 10.2); Albumin 3.7g/dL (3.4 - 5.2); Ionized calcium 1.68mmol/L (1.17-1.32); phosphorus 3.2mg/dL (2.2 - 4.5); PTH was high normal at 69.4pg/mL (16.5 - 70.0); 25-hydroxy vitamin D was 17.8ng/mL (30.0 - 100.0); and 1,25-OH vitamin D was 61pg/ml (10-75). Prior lab work from two years ago showed a total calcium from 10.2-11mg/dl along with PTH of 106pg/mL. Other lab results including creatinine, thyroid and serum electrophoresis were normal. Diagnosis and Management: Work up was initiated by doing a parathyroid scan; showing a focal area of activity correlating to the inferior aspect of the left gland suspicious for parathyroid adenoma. Ultrasound of thyroid also showed a hypodense 1 cm extrathyroidal lesion correlating with the suspected parathyroid adenoma. Concurrently, hypercalcemia of malignancy was also identified due to recent diagnosis of adeno-squamous cell lung carcinoma. PTH-related protein (PTH-rp) came back 2.6pmol/L (<2.0). At the time of diagnosis of lung cancer it was undetectable (<0.74). A repeat PET scan showed widespread metastatic disease. We concluded that the severe hypercalcemia was related to both primary hyperparathyroidism as well as PTH-rp being secreted from the metastatic lung cancer. Ideally, samples from metastatic disease tissue positive for PTH-rp would have been desirable, but unfortunately were not available. The patient was treated with fluids, calcitonin and pamidronate with lowering of his total calcium to 11.2mg/dl. He was deemed unstable for any intervention and was made hospice care. He died a month later.

**Discussion:** This patient represents a rare occurrence of hypercalcemia due to primary hyperparathyroidism and humoral hypercalcemia from metastatic carcinoma of the lung, mediated by PTH-rp.

**Conclusion:** This case suggests that patients with hypercalcemia and non-endocrine malignant tumors should be evaluated for the possibility of both parathyroid and non-parathyroid mediated causes of hypercalcemia.

**Abstract #723**

**THE UGLY FACE OF VITAMIN D - PRECIPITATING HYPERCALCEMIA IN A CAUCASIAN MALE WITH CUTANEOUS SARCOIDOSIS**

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**Objective:** Granulomatous inflammation in sarcoidosis leads to increased production of 1, 25-di-hydroxyvitamin D (1,25 D) with consequent hypercalciuria and hypercalcemia. Vitamin D supplementation is a ubiquitous practice in primary care clinics. We describe the case of a patient with cutaneous sarcoidosis who presented with symptomatic hypercalcemia after being started on vitamin D supplementation.

**Case Presentation:** A 75 year old Caucasian male presented with acute onset of confusion and a fall. His history was significant for diffuse erythematous skin rash treated intermittently with topical steroids for two years. Biopsy of the skin rash in the past had revealed dermal granulomas consistent with sarcoidosis. Review of history was notable for general debility and symptoms of peripheral neuropathy in the previous 12 months. His serum calcium was 9.9 mg/dl (8.5-10.5 mg/dl) with GFR>60 ml/min, four months prior to admission. He was started on Vitamin D3 1000 IU two weeks prior to admission. On clinical exam he was disoriented, dehydrated and had diffuse erythematous annular plaques over his trunks and extremities. Laboratory findings were notable for hypercalcemia with corrected calcium of 12.2 mg/dl and acute kidney injury with a serum creatinine of 1.67 mg/dl and BUN of 17 mg/dl. Further work up during the hospital
course revealed: PTH <4 pg/ml (10-60), 25-hydroxy vitamin D level (Vit D) of 16.0 ng/ml, 1,25 D level of 66.0 pg/ml (15-60), 24-hour urine calcium 789.8 mg (100-300), PTHrP 0.5 pmol/L (<2.0). Serum angiotensin converting enzyme was mildly elevated at 79 U/L (<49 U/L). A body CT was unrevealing. MRI of the brain and CSF analysis were not consistent with neurosarcoidosis. Patient was treated with hydration and oral prednisone and his mental status recovered dramatically and biochemical abnormalities reverted close to his baseline. Follow up labs 4 weeks after discharge showed: serum calcium 8.6 mg/dl, Vit D 19.6 ng/ml, 1,25 D 9.5 pg/ml and PTH 27 pg/ml.

**Discussion:** Hypercalcemia in sarcoidosis is due to unregulated extra-renal calcitriol synthesis. In sarcoidosis the high level of IFN-γ stimulates the activity of 1alpha-hydroxylase and blocks 24-hydroxylase and overrides the normal feedback inhibition by calcitriol. Vitamin D therapy should be considered only if 1, 25 D levels are low and there is no evidence of hypercalciuria (>300 mg/24 h) or hypercalcemia. Serum and urine calcium as well as renal function should be carefully monitored in patients needing supplementation.

**Conclusion:** Vitamin D supplementation can precipitate hypercalcemia in patients with sarcoidosis. Active metabolites of vitamin D and renal function should be assessed before vitamin D supplementation.

**Abstract #724**

**TO TREAT OR NOT TO TREAT? CAN PRO-CALCITONIN DIFFERENTIATE BETWEEN BACTERIAL COLONIZATION AND BACTERIAL INFECTION?**

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**Objective:** To show that Pro calcitonin (PCT) levels in patients chronically colonized with bacterial pathogens, who have no evidence of active infection, will be <0.5 ng/ml.

**Methods:** A test of concept analysis was done on the patients with chronically placed foley catheter and or tracheostomy. The inclusion criteria required were a sputum culture and or a urine culture positive with a potential pathogen but no clinical evidence of active infection based upon absence of Systemic Inflammatory Response Syndrome criteria, and must have been off antibiotics for at least 72 hours. The exclusion criteria were presence of acute pancreatitis, major surgery or trauma within 2 weeks, hemodynamically unstable, significant burns, immunocompromised patients, and patients who chose only comfort measures for their care. These patients were then followed for 2 weeks to ascertain if clinical infection developed.

**Results:** Six patients qualified as the colonized not infected cohort. Median PCT level was 0.075 ng/ml with a range of 0.05ng/ml to 0.28 ng/ml. Follow up for a mean of 6 days per patient indicated no development of acute infection.

**Discussion:** 1) PCT is the precursor for the hormone calcitonin and has a metabolic role in calcium homeostasis. Active bacterial infections have been associated with increased pro-calcitonin levels > 0.5ng/ml (due to the release of inflammatory cytokines Interleukin1 Beta and Tumor Necrosis Factor alpha in response to the bacterial lipopolysaccharide, stimulating pro-calcitonin’s release from the adipocytes). 2) The diagnostic accuracy of PCT markers was found to be higher than that of other inflammatory biomarkers for suspected bacterial infections.3) We believe performing a PCT test in patients with possible bacterial colonization but no evidence of active bacterial infection would spare the unnecessary expenditure of inappropriate antibiotic use. For example the estimated cost for a five-day course of antibiotics if meropenem, linezolid and gentamycin were used would be $1150 (in just antibiotic costs, excluding the administration costs) , and if zosyn, vancomycin and gentamycin were used, it would cost $540. PCT test cost’s $150 for a send out test and if it were performed in house it would cost around $25. 4) To our knowledge this is the only research estimating the pro calcitonin levels in patients with bacterial colonization.

**Conclusion:** Our test of concept data in this limited sample, suggests that PCT could potentially help differentiate colonization from infection, and might be helpful to physicians in interpretation of culture results. The administration of PCT test may also spare the health care institution unnecessary expenditure from in appropriate antibiotic use.
Abstract #725

AN OUNCE OF PREVENTION: THE IMPORTANCE OF CALCIUM AND VITAMIN D SUPPLEMENTATION PRIOR TO USING DENOSUMAB

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Objective: We present an uncommon case of severe hypocalcemia after two doses of denosumab injection.

Case Presentation: 82 year old male who has prostate cancer with osseous metastasis was admitted with epigastric pain, nausea and constipation. He received two doses of 120mg SC denosumab, one dose of IM leuprolide acetate 22.5mg and was taking oral bicalutamide 50mg daily. His blood tests were as follows: calcium 5.7mg/dL (8.3-10.1); ionized calcium 0.76 mmol/L (1.12-1.32); albumin 2.6g/dL (3.5-5.0); parathyroid hormone (PTH) 1053.9pg/ml (14-72); phosphorus 0.6mg/dl (2.3-4.1); 25-hydroxy vitamin D 10.8ng/ml (30-100); magnesium 2.0mg/dL (1.6-2.6); creatinine 0.89mg/dL (0.6-1.3) and alkaline phosphatase (ALP) 380 U/L (50-136). Serum calcium, albumin and ALP prior to starting denosumab were 8.4 mg/dL (8.3-10.1), 2.9 g/dL (3.5-5.0) and 541 U/L (50-136) respectively. There was no prior 25-hydroxy vitamin D level. On physical examination he had mild epigastric tenderness but no paresthesia or tetany. He was treated with multiple ampules of IV calcium gluconate, calcium chloride and IV calcitriol and was started on weekly ergocalciferol (vitamin D2) 50000 units along with daily cholecalciferol (vitamin D3) 2000 units and calcium-vitamin D3. He was also supplemented with daily sodium potassium phosphate. After three weeks, the serum calcium was 7.4mg/dL (8.3-10.1), ionized calcium 1.02mmol/L (1.12-1.32), phosphorus 1.3mg/dL (2.3-4.1) and PTH 617.9pg/ml (14-72). Calcitriol was given to counteract the secondary hyperparathyroidism. He was discharged home on daily calcitriol, calcium-vitamin D3, cholecalciferol and sodium potassium phosphate.

Discussion: Denosumab is a monoclonal antibody against receptor activator of nuclear factor kappa-B ligand (RANKL) that reduces osteoclastogenesis causing net influx of calcium into the bone resulting in low serum calcium. Hypocalcemia leads to secondary hyperparathyroidism causing phosphaturia resulting in hypophosphatemia. Most do not become hypocalcemic because of compensatory increase in PTH secretion, which may be blocked in vitamin D deficiency. The profound hypocalcemia could be due to concomitant vitamin D deficiency which resulted in an inability to up regulate gastrointestinal absorption of calcium. The guidelines suggest supplementation with calcium and vitamin D daily prior to initiation of denosumab, unless contraindicated. Most patients should receive a total of 1g of calcium (diet plus supplement) and 800 to 1200 IU of vitamin D daily.

Conclusion: We present a case of severe hypocalcemia that is temporally related to denosumab injection which could have been probably avoided with regular supplementation of calcium and vitamin D prior to initiation of denosumab therapy.

Abstract #726

OUTCOME OF PARATHYROID SURGERY: EXPERIENCE IN AN ENDOCRINE HOSPITAL

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Objective: To evaluate the outcome of Parathyroidectomy patients in a Endocrine Hospital of Bangladesh. Experience from a large Endocrine Hospital.

Methods: All the patients after Parathyroidectomy were followed up to one year. Indication of all Parathyroidectomy were Primary hyperparathyroidism due to either single adenoma or hyperplasia. All the patient has three and half gland removed with hyperplasia. With single adenoma only the single gland is removed. No PTH was done per operatively but within 24 hours post operatively.

Case Presentation: Total 33 patients were followed up todate one year post Parathyroidectomy. Only 7 patients had minimally invasive surgery. Rest (26) had conventional surgery. Twenty one have single adenoma, 3 had more than one, and 9 had hyperplasia. Preop S Cal 11.7 - 16.7 mg/dl . PTH 78-278 p/l. Post operatively 27 subjects had normal PTH but all (33) had normal S calcium. twenty four hours S Cal was normal in follow up for one year. Bone Mineral Density improved by 6-15 percent of cases. 15 had BMD less than -2.5. Only one patient has Recurrent Laryngeal Nerve injury and one had mild change of voice.

Discussion: Surgery is quite safe now a days. Though S Calcium becomes normal, PTH may not be normal in All cases after Parathyroidectomy. Quality of life is better, BMD improves significantly.

Conclusion: All subjects improves clinically . PTH may not be normal even when S Calcium is normal after Parathyroidectomy. All other parameters improves significantly. Larger RCT is necessary to determine the ideal selection of surgical procedure and extend of Resection of Parathyroid glands.
Abstract #727

METASTASECTOMY OF NEUROENDOCRINE TUMORS IN PATIENTS WITH MEN 1

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**Objective:** Patients with MEN 1 are affected by primary hyperparathyroidism (1HPT), pituitary lesions, and neuroendocrine tumors (NE) of the duodenum and pancreas. Survival in these patients is often limited by the spread of their NE tumors which most often recur within the pancreas and duodenum or metastasize to the liver. Patients with MEN 1 are thought to have improved survival compared to individuals with analogous lesions. We sought to establish the role of metastasectomy of NE tumors in patients with MEN 1 which has not been defined.

**Methods:** A review all patients with MEN 1 undergoing surgery for NE tumors from 1994-2010 at a single tertiary care center was performed. We examined tumor function, extent of spread, completeness of resection and survival.

**Results:** We identified 33 patients with MEN 1 who underwent resection of their primary tumor and either synchronous or metachronous metastasectomy. Median age was 46 years (range 20-63). There were 31 patients who had a pancreatic resection including distal pancreatectomy (24), whipple procedure (2), total pancreatectomy (1), partial (3) distal pancreatectomy with enucleation of the head of the pancreas (1) and ethanol ablation of an NE tumor. Duodenotomy with enucleation was performed in 15 patients. Synchronous metastases were identified in 23 patients with hepatic metastases resected in 43% of patients and lymph node metastases in 57% of patients. 91% of patients achieved an R0 resection. There were 13 patients who underwent surgery for metachronous disease at a median time of 60 months after initial surgery (6 liver resections, 2 liver transplants, 1 subcarinal mass, 1 small bowel resection, 2 LN). Age, islet cell function, R0 resections, extent of metastases and extent of resection were not predictive of survival (p>0.05). Median follow up was 6.1 years with an over survival of 88%. Overall metastases rate 82% with 23/27 patients presenting with hepatic disease.

**Discussion:** Patients with MEN 1 benefit from resection of metastatic NE disease. It is difficult to identify predictive factors in this subset of patients due to favorable outcomes as well as a low mortality rate.

**Conclusion:** Despite a high rate of recurrence and metastatic disease, survival is favorable compared to previously published rates for patients without MEN1.

Abstract #728

NEW FACE OF VITAMIN D DEFICIENCY

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**Objective:** Hypocalcemia after parathyroidectomy can be secondary to hungry bone syndrome (HBS) and hypoparathyroidism. Hypocalcemia associated with Vitamin D deficiency is rarely severe and symptomatic. We present an extremely rare case of post-parathyroidectomy severe symptomatic hypocalcemia secondary to vitamin D deficiency.

**Case Presentation:** We present a 24 years old female with history of lactose intolerance who had recent parathyroidectomy due to parathyroid adenoma. Four days after surgery, she developed symptomatic hypocalcemia and was started on calcitriol and calcium and doses were gradually increased. She had severe vitamin D deficiency with levels 4.7 ng/ml preoperatively which improved to 14 ng/ml with vitamin D2 and calcitriol therapy. Despite calcitriol and calcium replacement, she continued to have symptomatic hypocalcemia requiring IV calcium. Interestingly her magnesium, alkaline phosphatase and phosphorus remained normal ruling out HBS. The parathyroid gland had at least partially recovered based on follow up iPTH assessment. This showed recovery of remaining parathyroid glands ruling out hypoparathyroidism. Patient was diagnosed with vitamin D deficiency and was placed on ergocalciferol, calcitriol and calcium with resolution of symptomatic hypocalcemia.

**Discussion:** Hypocalcemia is frequently encountered in post-parathyroidectomy patients. Usual culprits are HBS and hypoparathyroidism. While risk factors for HBS include age >60, high alkaline phosphatase and large size of adenoma, our patient is young with small parathyroid adenoma and normal magnesium, phosphorus and alkaline phosphatase ruling out HBS. Also parathyroid resumed normal function post operatively ruling out hypoparathyroidism.

**Conclusion:** Though Vitamin D deficiency is common it is rarely seen to cause severe symptomatic hypocalcemia. Our case demonstrates that although extremely rare, vitamin D deficiency can present as severe symptomatic hypocalcemia after parathyroidectomy. PubMed literature review showed only two other similar cases reported. Increased awareness of this rare presentation is essential for timely diagnosis and treatment.
PROFOUND HYponATREMIA (HN) RELATED TO CHRONIC ALCOHOLISM AND POOR NUTRITION STATUS: A CASE REPORT

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Case Presentation: Patients with alcoholism frequently develop HN. However, it is rare when they present with profoundly low sodium (Na). We report a case of severe HN in a patient with chronic alcohol consumption and malnutrition. A 43-year-old man was brought to an ER after he was found down for an unknown duration. At the ER, mentation was decreased and vital signs were normal. He had decreased skin turgor and dry mouth. Lab: Na 102 mmol/L, serum osmolality 231 mOsm/kg, urine osmolality 489 mmOsm/kg, urine Na < 10 mmol/L and FeNa 0.17%. Thyroid function and cortisol were normal. He denied using diuretics. His alcohol intake is “more than 6 cans of beer” daily for several years. He received normal saline (NS) at 125 ml/hr in the ER and his Na increased to 107 mmol/L in 4 hours. Due to the rapid rate of correction, the IV fluid was stopped. The Na continued to increase slowly to 116 in the next 24 hours with oral fluids. Then, IV fluid was restarted at 75 ml/hr and his Na increased and stabilized around 120 mmol/L. NS was stopped and fluid intake was restricted, but his Na levels stayed at 120 mmol/L for 3 days. At this point, his intake of food improved to 100%. Over the next 4 days, his Na increased to 129 mmol/L with no other interventions.

Discussion: The patient had severe HN of multi-factorial etiology. Initially, he had an acute HN on chronic HN. Low urine Na and FeNa implicated hypovolemia as the etiology of acute HN. Alcohol suppressed ADH secretion which caused diuresis leading to dehydration while the patient was unresponsive and had no fluid intake. After alcohol was cleared, ADH levels rose. His Na increased gradually with slow hydration and stayed stable at 120 mmol/L for 3-4 days. Thus he had chronic HN with a reset osmostat. High carbohydrate, low protein diet seen with chronic excess beer intake markedly reduces water excretory capacity and suppresses endogenous protein breakdown. This results in a reduction of daily solute excretion and reduces maximum urine output which leads to chronic HN. With improved appetite, the Na level rose above the plateau of 120 mmol/L due to the improvement of his nutrition status.

Conclusion: Chronic beer drinkers frequently present with chronic HN due to protein malnutrition. However, as illustrated in this case all other causes of HN must be considered especially in the patient who has acute and profoundly low Na, to avoid mistreatment.
PITUITARY STALK LESIONS: THE MAYO CLINIC EXPERIENCE

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Objective: Pituitary stalk lesions have various etiologies, often not clinically apparent. Pathologic samples from these lesions are rarely obtained, due to the critical location and function of the hypophyseal stalk. Objectives: (1) To characterize the etiologic spectrum of pituitary stalk lesions seen at Mayo Clinic, Rochester, over 20 years. (2) To determine if specific MRI characteristics could provide the clinician some guidance with regard to the etiology of infundibular lesions.

Methods: Retrospective review of cases with pituitary stalk lesions seen at Mayo Clinic, Rochester between 1987 and 2006 was conducted. Demographics, clinical presentation, imaging, laboratory, operative, and pathology reports were reviewed and reported using descriptive statistics.

Results: Of the 152 pituitary stalk lesions included, 49 (32%) were neoplastic, 30 (20%) inflammatory, 13 (9%) congenital anomalies and 60 (39%) of unclear etiology. Forty-two (28%) of the 152 patients were diagnosed with diabetes insipidus and 49 (32%) patients had at least one anterior pituitary hormonal deficit. Secondary hypogonadism was the most common endocrine deficiency. Eleven of 13 congenital lesions were round in appearance and 5 of 7 neurosarcoidosis cases confirmed by pathology had a uniformly thickened pituitary stalk on MRI. There was no statistically significant correlation between hypopituitarism and the pattern of enhancement or size of the lesion.

Discussion: In this largest series of pituitary stalk lesions reported to date, we have characterized the lesions with regard to etiologic spectrum and radiological appearance. In addition to its retrospective nature, there are several limitations of our study. A referral center bias may have impacted the types of cases included. However, the referral center bias might be counterbalanced by the fairly large number of lesions diagnosed incidentally. Another limitation of our study is the lack of tissue-confirmed diagnoses. The diagnosis was frequently based on clinical findings and serial imaging. Therefore, it is prudent for the clinician to follow a stepwise process to diagnose and manage patients with pituitary stalk lesions. For the most challenging cases, an individualized approach, guided by clinical expertise, remains the best strategy.

Conclusion: Findings on MRI remain key in guiding the diagnosis of pituitary stalk lesions, particularly when used in conjunction with other clinical clues. There are no good imaging predictors for hypopituitarism, making clinical evaluation of all patients with pituitary stalk lesions crucial.

Abstract #801

YOUNG PATIENT WITH SUPRASELLAR MASS FOUND TO HAVE A GERMINOMA WITH INVOLVEMENT OF THE PINEAL GLAND

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Case Presentation: Our patient is a 21-year-old African American male who presented to the ER with complaints of headaches and visual changes. He denied any past medical or surgical history; family history was unremarkable. Physical exam only revealed bitemporal hemianopsia. Due to the patient’s symptoms and exam, CT of the head was ordered. It revealed a 1.5 cm cystic suprasellar mass as well as a calcified pineal cyst. Differential diagnosis included craniopharyngioma, Rathke cleft cyst and pituitary adenoma. Endocrine evaluation revealed an elevated prolactin (138 ng/mL), normal free and total testosterone (137.5 pg/mL and 635 ng/dL) but low ACTH (<5 pg/mL), cortisol (0.3 mcg/dL), FSH (<0.1 mlU/mL), LH (<0.1 mlU/mL), TSH (4.28 mlU/mL) and FT4 (0.3 ng/dL). Thyroid and steroid replacement were started after a failed cosyntropin stimulation test. MRI further characterized a 1.6 x 1.8 cm heterogeneously enhancing suprasellar mass abutting the optic chiasm, and a 1.2 cm pineal region mass. Transphenoidal biopsy and pathology confirmed the presence of a germinoma. Post biopsy, our patient developed diabetes insipidus and DDAVP was added. Continued work-up included normal findings on CT of chest, abdomen and pelvis, as well as testicular ultrasound. The patient was eventually found to have an elevated CSF and serum HCG but normal CSF and serum AFP. He was eventually stable and discharged with neurosurgical, endocrine and radiation oncology follow-up. He is scheduled to undergo chemotherapy and radiotherapy soon.

Discussion: Germinomas constitute between 0.4 - 3.4% of patients with primary CNS tumors. Although rare, germinomas should be considered in the differential diagnosis of younger patients, especially males, who are found to have suprasellar masses. The presence of a relatively homogeneous, well-circumscribed, extra-axial, enhancing pineal region mass in
a young male is also very characteristic of a germinoma. CSF and serum HCG elevation as well as transphenoidal biopsy can confirm the diagnosis. AFP is less likely to be elevated. Full endocrine workup should be pursued as these patients can frequently have panhypopituitarism. Prompt diagnosis is imperative as these tumors respond well to chemotherapy and radiotherapy.

**Conclusion**: Germinomas should be considered in the differential diagnosis of younger patients presenting with suprasellar masses, specifically in the presence of an enhancing pineal region mass.

**Abstract #802**

**WHAT HAPPENS WHEN A MEDICINE WORKS TOO WELL? TENSION PNEUMOCEPHALUS AFTER CARBERGOLINE TREATMENT FOR A MASSIVE PROLACTINOMA**

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**Objective**: Dopamine-agonist therapy has become the first line treatment for prolactinomas. In large macroprolactinomas with skull base erosion this success can lead to cerebrospinal fluid (CSF) leaks, infection, and pneumocephalus. We are reporting an extreme example of such a case which was complicated by a CSF leak producing a tension pneumocephalus with cognitive deficits.

**Case Presentation**: A 64-year-old male presented with a seizure with a massive prolactinoma eroding the anterior skull base floor. His initial serum prolactin was 4,358 ng/ml and the rest of his pituitary function was normal. Within 6 weeks cabergoline 0.5 mg twice a week decreased his prolactin level to 226ng/ml. At 20 weeks nasal drainage was self-diagnosed and treated as sinusitis with an antibiotic. Drainage continued for two weeks at which time he presented with encephalopathy and mild hyperprolactinemia. A CT scan of the brain demonstrated extensive pneumocephalus in the subarachnoid space and the intraventricular space. An MRI showed in addition to tension pneumocephalus almost complete tumor resolution with residual necrotic tissue. Cabergoline therapy was continued and the patient underwent an endonasal repair of the anterior skull base with CSF diversion. On postoperative day 12 the leak recurred after an episode of coughing. Cabergoline therapy was stopped and the second endonasal surgical repair attempt was successful with resolution of the pneumocephalus. Two months post-repair he remains off of DA therapy with residual cognitive deficits but no further CSF-leakage.

**Discussion**: This unfortunate case emphasizes the caution and concern that should be present when treating a massive prolactinoma with DA therapy. Prolactinomas have a proclivity for downward extension and surrounding erosion of the underlying bony structures. CSF leaks occur relatively frequently in massive prolactinoma cases treated with DA ~10%, with a subsequent risk of meningitis or encephalitis. As shown in our case, tension pneumocephalus is also a risk, which can lead to encephalopathy and a decline in cognitive function. Tension pneumocephalus develops when a dural defect is present and the surrounding tumor acts as a one-way valve. Early surgical repair of the anterior skull base is recommended in cases with a CSF leak in order to prevent the development of pneumocephalus. Consideration should be made to stop DA therapy in order to increase the chances of a successful surgical repair. An endonasal route combined with CSF diversion through a ventriculostomy is the preferred surgical route and was successful in our patient.

**Conclusion**: This emphasizes the caution that should be employed when prescribing a therapy that sometimes works too well.

**Abstract #803**

**PROLACTINOMA, ACROMEGALY AND PREGNANCY: IS IT POSSIBLE?**

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**Case Presentation**: Thirty-two years old female G1P1A0 seen at our clinic nine years ago complaining of persistent, continuous menstrual irregularities due to an elevated prolactin value. MRI done revealed a pituitary microadenoma. However she refused treatment. Patient lost to follow up, seen again at our clinic four years afterwards complaining of recurrent episode of headache. Repeated MRI showed a macroadenoma with further prolactin elevations. Bromocriptine was started but unfortunately she was unable to tolerate it due to severe gastrointestinal side effects. Early on 2011, episodes of severe headaches recurred. She was not taking any medications at this time. Another MRI was compatible with a macroadenoma grossly unchanged from the previous ones. Prolactin levels were still elevated for which Carbogeline treatment was initiated achieving a
good medical response, producing disappearance of clinical symptoms and improvement of pituitary adenoma size. Once more, patient was lost to follow up and on April 2012 she visited endo clinics at 24th weeks of gestation with history of progressive hands, feet enlargement and marked prognathism. The diagnosis of acromegaly was made, and confirmation was performed in cooperation with Dr. Harald J. Schneider from University in Munich, Germany through FIDA (Facial Image Diagnostic Aid software). Pictures from frontal and side views were taken with the patient standing in front of a white wall and pictures were sent to the investigator. After analysis, results were compatible with acromegaly. In view that patient was pregnant cabergoline was discontinued. Elevations of prolactin together with levels of IGF-1 were found more elevated than before nevertheless despite this, patient showed no visual compromise and she delivered a normal baby without any complications.

Discussion: Prolactinoma is a frequent endocrine cause of infertility in women. It usually causes infertility because of the inhibitory effect of prolactin on gonadotropin secretion for which pregnancy is a rare event. Acromegaly on the other hand is the result of increased growth hormone and its target insulin-like growth factor-1, most commonly due to a pituitary tumor. As it is also frequently accompanied by infertility, little is known about the course of this disease in pregnancy.

Conclusion: Our case represents a rare coexistence of two endocrinopathies that usually reduces fertility and pregnancy rates. Furthermore, in spite of a pituitary macroadenoma, no neurological ophthalmologic complications occurred during pregnancy and patient gave birth without complications. The clinical, endocrine and chronological sequence with the appearance of acromegaly is an unusual presentation.

Abstract #804

GIGANT MACROPROLACTINOMAS IN CHILDHOOD AND ADOLESCENCE - THERAPY COMPLIANCE AND RECIDIVES - LIFELONG FOLLOW UP

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Objective: Prolactinomas are rare in childhood and adolescence representing a half of pituitary adenomas (1% of intracranial tumors). Macroadenomas are more frequent than microadenomas. Dopamin-agonistes (DA) therapy normalize prolactin secretion and reduce tumor size ≥40% of patients with macroprolactinomas. In practice, hyperprolactinemimia recurs early in most prolactinomas followig dopamin-agonists discontinuation.

Methods: We present two cases of macroprolactinomas, a boy, 13 years old, who came to our observation after neurosurgery for symptoms of tumor expansion and a girl, 18 years old, with headache, primary amenorrhea-galactorrhea. In the first case, the diagnosis of prolactinomas was supported by ophthalmological consult: visual field: left eye=macular vision; right eye= temporal hemianopsia; fundus eye=papilar edema left eye. CT scan described a large tumor of the pituitary gland. Prolactin level >250 ng/ml (N=0.7-17). At the girl, pituitary MRI=expansive tumor (28x27x42 mm) and high prolactin level = 2346 mcg/ml (w=30-150). In the both cases the treatment was dopamine-agonists, with high level of prolactin-agonists in high doses (Bromocriptine first=25mg/day and than Cabergoline 2 mg x2/week.

Case Presentation: After one year, the prolactin level decreased in mean with 80%. After 7 years, prolactin level was normal in both cases with MRI-normal at the boy, and the recommendation to stop dopamine-agonistes treatment in the second case, with tumor residue at MRI, and the recommendation to take Cabergoline 1mg x 2/week. After 9 years, at 25 years age, the girl came to us with clinical symptoms of tumor expansion and amenorrhea. Pituitary MRI= expanding intrasellar nodular tumor (23x26x22 mm). Prolactin level was 215 μg/ml (N=30-150), the patient being under intermittent treatment with DA. The boy came to us after 12 years, at 25 years old, with high level of prolactin=1083.3 μg/ml and residual tumor at MRI: 20x13x25 mm with right cavernous sinus extension. The patient developed normal puberty. In both cases the DA (cabergoline 2mg x 2/week) was reinitiated.

Discussion: In macroprolactinomas, the first-line treatment is represented by dopamine/agonists. DA are also necessary after neurosurgery with tumor residue.

Conclusion: After the normalize of prolactin level, the signs and symptoms depend of tumor size, annually checking being necessary because, like in our cases, there are a high recurrence rates after DA withdrawal or intermittent treatment in clinical routine practice.
Abstract #805

ISOLATED ACTH DEFICIENCY IN A YOUNG NIGERIAN WOMAN

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**Objective:** To report a case of isolated ACTH deficiency; a very rare cause of adrenal insufficiency.

**Case Presentation:** We report a case of a 39 year old young woman who was referred to the endocrine unit on account of a 9 month history of progressive body weakness, easy fatigability, dizziness and a very low serum cortisol level. Comprehensive history and physical examination however failed to elucidate the etiology of the adrenal insufficiency. A repeat serum cortisol further confirmed the adrenal insufficiency, value being 148.33nmol/L (240-618) while serum ACTH was 4.4pmol/L (1.6-13.9). A synacthen stimulation test with 250µg of synthetic ACTH showed a fifteen fold rise in serum cortisol from a basal level of 15.51nmol/L to 211.03nmol/L. Serum prolactin was 9.7ng/ml (3.3-20.7), TSH- 2.87miu/L (0.37-3.50) and T4 was 12.0pmol/L (7.2-16.4). 17 β Estradiol level was 607pmol/L (350-850). Magnetic resonance imaging of the brain revealed no structural or anatomic lesion in the pituitary gland or the hypothalamus. The diagnosis of secondary adrenal insufficiency likely secondary to isolated ACTH deficiency was made and patient was placed on low dose prednisolone and continues to make sustained clinical improvement.

**Discussion:** Isolated ACTH deficiency is a very rare cause of adrenal insufficiency with few reported cases in available literature. Identified causes of isolated ACTH deficiency include idiopathic cause, lymphocytic hypophysitis, transcription factor Tpit gene mutation, pro-opiomelanocortin (POMC) processing defect and gene mutation. The diagnosis of isolated ACTH deficiency is made if the following criteria are met; 1] Demonstration of low cortisol production and low/normal ACTH 2] Stimulation of cortisol production during ACTH administration 3] Normal secretory indices of other pituitary hormones4] Normal radio-imaging. Treatment of isolated ACTH deficiency is similar to treatment of other secondary causes of adrenal insufficiency with emphasis on glucocorticoid replacement.

**Conclusion:** Adrenal insufficiency is associated with significant morbidity and mortality if not diagnosed promptly. Isolated ACTH deficiency though a rare cause should be suspected only after a comprehensive evaluation has been done to exclude more common causes of adrenal insufficiency.

Abstract #806

PREDICTIVE UTILITY OF EARLY MORNING DAY ONE (D1) CORTISOL FOR STEROID REPLACEMENT IN PATIENTS AFTER TRANSPENOIDAL SURGERY FOR PITUITARY ADENOMAS

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University Hospital Of Wales

**Objective:** To find out whether day one (D1) serum cortisol of > 400 nmol/L is a satisfactory cut-off level to safely discharge patients in the aftermath of transphenoidal surgery for pituitary adenomas.

**Methods:** This is a retrospective analysis of 46 patients who had undergone transphenoidal surgery for pituitary adenomas in a tertiary care centre between May 2011 and Jan 2012. A 9 A.M. serum cortisol was estimated on D1 after the surgery. Patients were discharged home without any steroid replacement if their D1 cortisol levels were > 400 nmol/L, otherwise were commenced on hydrocortisone (10 mg BD) as per departmental policy if cortisol levels were < 400 nmol/L. A short synacthen test (SST) and full pituitary profile was undertaken at 6 weeks post-operatively to ascertain the ability of an early morning cortisol on D1 as a predictor of adequate functioning of the HPA axis.

**Results:** 46 patients were operated for pituitary conditions, Acromegaly (AM)- 16, Non-functioning adenoma (NFA)-19, Cushing’s disease (CD)-8, others-2. 36 patients (78%) had a D1 cortisol estimated, 6 patients on day 4 or 5 and 4 patients didn’t have any cortisol estimated but was empirically sent home on steroids. 66.6 % (24/36) patients had a D1 cortisol < 400 nmol/L of which 80% (21/24) was sent home on steroid replacement. 33% (8/24) of these patients had an abnormal SST after 6 weeks and were continued on steroids. Patients (12/36) who had a D1 cortisol of < 400 nmol/L and were not on steroid replacement had a normal SST after 6 weeks. Sub categorisation shows 6/8 patients with CD, 7/15 with AM and 10/11 patients with NFA and 1/2 patients in the others section had D1 cortisol < 400 nmol/L. All 4 patients who didn’t have a D1 cortisol had normal SST at a later date.

**Discussion:** Patients with preoperative evidence of Hypothalamic Pituitary Adrenal (HPA) axis deficiency should have adequate steroid replacement during peri and post-operative period till the HPA axis is reassessed. There is no consensus guidelines for post operative steroid
replacement following pituitary surgery and the practice at present is variable in accordance with local policies. Few studies have reported about the predictive utility of D1 cortisol levels following pituitary surgery but no definite cut off levels have been suggested which can be used as a threshold for predicting satisfactory functioning of the HPA axis.

**Conclusion:** A D1 cortisol > 400 nmol/L is a reliable and accurate predictor of normal HPA function and correlates well with the stress test performed 6 weeks post-operatively.

**Abstract #807**

**MENI AND DISSEMINATED CRYPTOCOCCUS ALBIDUS INFECTION IN A PATIENT PRESENTING WITH HYPERCALCEMIA: A CASE REPORT**

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**Objective:** Multiple Endocrine Neoplasia I (MENI) is an autosomal dominant predisposition to both endocrine and non-endocrine tumors. In MENI, the parathyroid glands and the entero-pancreatic system are most commonly involved. Adenomas of the anterior pituitary are seen in 10-60% of cases. ACTH-secreting pituitary tumors causing hypercortisolemia have a number of detrimental physiologic effects including increased susceptibility to opportunistic infections. Several case reports have been described in which patients with Cushing’s syndrome have developed focal or disseminated Cryptococcus but none to date have described its occurrence in a patient with MEN type I. In this report we present a patient with Cushing’s disease in the setting of MENI who developed disseminated infection with a rare strain of Cryptococcus.

**Case Presentation:** A 49 year old previously healthy male presented with hypertension, fatigue, decreased libido and bilateral leg swelling for several months. Physical exam was significant for peripheral muscle atrophy, bibasilar rales and moderate pitting edema of the lower extremities. Renal insufficiency, hypercalcemia, and hypercortisolemia were evident on laboratory tests (see table). Further testing detected a pituitary adenoma as well as a parathyroid adenoma, thus the patient was determined to have MENI. A computed tomography (CT) scan of his chest and abdomen revealed small bilateral lung granulomas and bilateral adrenal hypertrophy. A 1mg dexamethasone suppression test resulted in nonsuppressed cortisol levels. The patient’s single parathyroid adenoma was removed and his hypercalcemia resolved. The patient was scheduled for follow-up of the pituitary lesion. Three weeks later, the patient returned with recurrent leg swelling, malaise, a right medial maleolus ulcer as well as several smaller lesions on the proximal tibia. Again, he was found to be hypercalcemic with a suppressed PTH level. With intravenous fluids and cessation of metolazone therapy the serum calcium level normalized. The leg ulcers were thought to be secondary to calciphylaxis, however a biopsy of the lesions showed encapsulated yeast. A bronchoscopy with fine needle aspiration (FNA) of the granulomatous pulmonary lesions revealed Cryptococcus albidus. The patient was successfully treated with Amphotericin and Flucytosine before eventual removal of his ACTH-secreting pituitary tumor.

**Discussion:** Pulmonary Cryptococcus infections are well-documented among persons with endogenous hypercortisolemia, however cutaneous and disseminated Cryptococcus are rare conditions.

**Conclusion:** This case of a patient with MENI illustrates the rare and widespread infections that can be manifest in patients with hypercortisolemia.

**Abstract #808**

**A RARE CASE OF CENTRAL DIABETES INSIPIDUS IN BLAST CRISIS OF CHRONIC MYELOGENOUS LEUKEMIA**

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**Objective:** Reports have shown central diabetes insipidus (CDI) associated with acute myelogenous leukemia (AML). We report a rare case of chronic myelogenous leukemia (CML) blast crisis associated with CDI.

**Case Presentation:** A 42-year-old Caucasian man with a two-year history of CML refractory to treatment with tyrosine kinase inhibitors and haploidentical stem-cell transplant presented with blast transformation. WBC count on admission was 143,100 with 30% blasts and platelet count was 39,000. Karyotype analysis showed 45,XY with inversion 3q21q26, monosomy 7, and t (9;22) in all mitotic cells. Hydroxyurea 3g PO BID was initiated for cytoreduction. Normal saline infusion was begun for intravenous hydration. Initial serum Na was 145 mEq/L (135-145 mEq/L), but it increased to 156 mEq/L on hospital day 2 with urine output of approximately 550 mL/hr. The patient reported symptoms of polydipsia and polyuria for three weeks prior to admission. Serum osmolality (Osm) was 325 mOsm/kg (285-295 mOsm/kg), urine Osm was 90 mOsm/kg, urine Na...
Diagnosis of acromegaly lead to further work up which treated for diabetes ketoacidosis (DKA). Suspected and elevated serum acetone level. Patient was diagnosed plasma glucose of 664, severe anion gap metabolic acidosis feet and hands. Initial laboratory tests revealed a random including frontal bossing, macroglossia, enlarged jaw, severely dehydrated male with acromegalic features the past 5 months. Physical exam revealed a somnolent generalized weakness and dizziness and loss of weight for medical history presented to our hospital complaining of Case Presentation

St. Joseph's Hospital

Anna Boron, MD, Laura Knecht, MD, Andrew Little, MD Shaghayegh Khayambashi, MD, Varun Mehta, MD, Anna Boron, MD, Laura Knecht, MD, Andrew Little, MD

A RARE PRESENTATION OF ACROMEGALY

Shaghayegh Khayambashi, MD, Varun Mehta, MD, Anna Boron, MD, Laura Knecht, MD, Andrew Little, MD

St. Joseph’s Hospital

Case Presentation: A 32-year-old male with no previous medical history presented to our hospital complaining of generalized weakness and dizziness and loss of weight for the past 5 months. Physical exam revealed a somnolent severely dehydrated male with acromegalic features including frontal bossing, macroglossia, enlarged jaw, feet and hands. Initial laboratory tests revealed a random plasma glucose of 664, severe anion gap metabolic acidosis and elevated serum acetone level. Patient was diagnosed and treated for diabetes ketoacidosis (DKA). Suspected diagnosis of acromegaly lead to further work up which was significant for elevated GH level of 11.9 and serum insulin-like growth factor-I (IGF-I) of 325. A subsequent magnetic resonance imaging study (MRI) revealed a 1.4 X 1.3 cm hypo-enhancing mass involving the left aspect of pituitary gland. A transphenoidal resection of pituitary tumor was performed. The tumor stained positive for prolactin and growth hormone. Patient was discharged from the hospital on subcutaneous insulin and was unfortunately lost to follow up for lack of insurance.

Discussion: Pituitary gigantism, a condition of Growth Hormone (GH) hyper-secretion, is a rare condition with an incidence of 3-4 cases per million per year. Clinical features of acromegaly or gigantism include acral overgrowth, soft-tissue swelling, arthralgia, fasting hyperglycemia, respiratory and cardiac failure to name a few.

Conclusion: Glucose intolerance is a common feature of acromegaly. Diabetes mellitus is seen in about 10-20% of patients. The mechanism by which GH induces diabetes mellitus includes increasing hepatic gluconeogenesis, glycogenolysis, inhibition of glycogen synthesis and glucose oxidation. There are only a few reports of DKA as the initial presentation of acromegaly or gigantism. A study revealed that higher GH levels, older age group and longer duration of the disease predicted the tendency of developing diabetes. In our patient, the exact duration of diabetes is unknown, however, he admitted to noticing physical changes in the past 15 years. Once the diagnosis of GH hypersecreting pituitary adenoma has been established, the first line treatment is considered to be surgical removal. Treatment of acromegaly results in an improvement in glucose intolerance with cure of diabetes in many reported cases.

Abstract #810

A CASE OF RECURRENT PITUITARY ABSCESS.

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¹. UTHSC Dept of Endocrinology and Metabolism, ². UTHSC Dept of Infectious Disease

Objective: Pituitary abscesses are uncommon. We present a case of a pituitary abscess that was initially diagnosed as a pituitary adenoma.

Case Presentation: A 34 year old female presented with headaches and progressive visual decline for two months. Physical exam was significant for bitemporal hemianopsia. Her vital signs were normal. MRI revealed a 2.7 x 2.5 x1.6 cm cystic sellar mass with irregular peripheral enhancement, elevation of the optic chiasm, and associated sphenoid sinusitis. Her preoperative investigations were consistent with central hypothyroidism, hypogonadism...
and adrenal insufficiency: free T4 0.62ng/ml (0.71-1.85), TSH 0.098mIU/ml (0.35-5.5), estradiol 13pg/ml (19-144), FSH 1.2mIU/ml (5-20), LH <0.1mIU/ml (5-22), cortisol <1.0mcg/dl (3-25) and ACTH 7pg/ml (9-52). A preoperative diagnosis of pituitary adenoma was made. Surprisingly, frank pus was evacuated during transphenoidal surgery (TSS). Post-operative recovery was uneventful and she was discharged on a 6-week course of intravenous antibiotics, which, however, she could not complete due to side effects. Five months later, she developed headaches and MRI revealed recurrence of pituitary tumor. Repeat TSS revealed pituitary abscess. Surgical pathology in both instances revealed necrotizing granulomatous inflammation consistent with pituitary abscess. Fungal, AFB, spirochete and microbiologic cultures were negative from both surgeries. Post-operatively she developed diabetes insipidus. She was discharged on intravenous antibiotics, desmopressin, hydrocortisone and levothyroxine.

Discussion: Pituitary abscess is diagnosed in about 0.3-0.6% of all pituitary surgeries. An insidious onset and non-specific symptoms makes pre-operative diagnosis difficult. Sinusitis, as noted in our patient, is a widely reported risk factor. Hormonal dysfunction is common and usually persists after TSS. Treatment approach includes TSS and decompression followed by broad spectrum antibiotics. In our patient, the abscess recurrence could have been due to persistence of initial disease. Although history of immunological disease is a predisposing factor for recurrence, investigations did not reveal immunologic disease in our patient.

Conclusion: We recommend a high index of suspicion for an abscess when MRI demonstrates a cystic pituitary fossa mass with peripheral enhancement in patients with history of sinusitis preceding diagnosis of pituitary tumor. Pituitary abscess recurrence is not infrequent; therefore, post-operative antibiotics and close follow-up are essential.

Abstract #811

EMPTY SELLA DUE TO INVOLUTION OF A PITUITARY MACROADENOMA. A CASE REPORT.

Nduche Onyeaso, Aidar Gosmanov

UTHSC Dept of Endocrinology and Metabolism

Objective: Empty sella (ES) is characterized by arachnoid herniation into the sella, resulting in compression of the pituitary against the sella, and can be associated with hypopituitarism. Primary ES occurs mainly due to congenital incomplete formation of the sellar diaphragm. Here, we report a case of secondary ES due to involution of pre-existing pituitary adenoma.

Case Presentation: A 38 year old male presented to our endocrinology clinic in January of 2011 for management of erectile dysfunction and milky discharge from breasts. He reported previous history of pituitary tumor and hyperprolactinemia diagnosed in 2005; then, he did not tolerate bromocriptine and could not afford cabergoline. In December of 2005, his prolactin level was 695 ng/mL and in June of 2006 brain MRI revealed pituitary macroadenoma measuring 11.8x6.7x11.8 mm which was unchanged a year later. He was lost to follow up in 2007. His other history was significant for morbid obesity, obstructive sleep apnea and chronic kidney disease stage 3 due to uncontrolled hypertension. Examination in our office revealed obese male (BMI 53kg/m2) with gynecomastia, demonstrable galactorrhea and no visual field defects. Endocrine testing in our clinic was as follows: prolactin 260 ng/mL (4.0-15.2), free testosterone 0.9 pg/mL (8.7-25.1), total testosterone 43 ng/dL (249-836), Cr 2.81 mg/dL (0.76-1.27) and gonadotropins were within normal limits. Growth hormone, adrenal, and thyroid axes were intact. We ordered pituitary MRI which, to our surprise, demonstrated a cystic pituitary fossa mass with peripheral enhancement in patients with history of sinusitis preceding diagnosis of pituitary tumor. Pituitary abscess recurrence is not infrequent; therefore, post-operative antibiotics and close follow-up are essential.

Discussion: Secondary ES can develop after spontaneous necrosis of a pituitary mass, surgical resection, radiotherapy, infection, trauma and treatment of a sellar mass. Only few cases, including ours, have been reported so far in which prolactinoma with or without specific therapy preceded the development of secondary ES. In our case, the involution of the gland occurred over 5-6 years without any therapy.

Conclusion: We suggest that serial MRI is an important tool to monitor the size of macroprolactinoma and pituitary morphology; if ES develops, a comprehensive assessment of pituitary hormones is warranted.
Abstract #812

PROBABLE GONADOTROPH HYPERPLASIA IN POST-SURGICAL OR EARLY MENOPAUSE

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Objective: To describe a series of five cases which may represent gonadotroph hyperplasia in women after surgical or premature menopause.

Case Presentation: Five women (ages 39 to 49 years) were referred to the Pituitary Center for hormonal and neurosurgical evaluation of suspected pituitary adenomas. Outside brain MRIs were performed due to headaches. Three had undergone bilateral oophorectomy 5-15 years previous, while another had a unilateral oophorectomy at 35y and was now symptomatic for vasomotor symptoms at 49y. One had an elevated FSH at 37y and presumed premature menopause 6 years prior to referral. Four of the women had FSH and LH levels above the upper post-menopausal limit (FSH >125 mIU/ml, LH>55 mIU/ml), three while on estrogen. Consistent pituitary findings were homogenous contrast enhancement without a discrete lesion, increased height (8.5-10 mm) with a convex superior border nearing the chiasm. Anterior pituitary hormone evaluation was normal in all cases. Alpha-subunit was elevated at 2.3 mg/mL (<1.8 mg/mL) in one patient who had FSH/LH levels of 145.8/93.8. There were no other clinical manifestations to suggest an infiltrative process, including diabetes insipidus. In one case, initiation of estrogen/progesterone therapy resulted in a drop in the FSH from >170 to 59. No patient was sent for an invasive procedure so there is no pathologic correlation.

Discussion: Hyperplasia of pituitary thyrotrophs and lactotrophs, driven by TRH with hypothyroidism, and corticotrophs and somatotrophs, driven by ectopic tumoral expression of CRH and GHRH respectively, is well described. Gonadotroph hyperplasia has been reported with end-organ failure in youth, such as with Klinefelter’s and Turner’s syndromes. From autopsy series, gonadotroph hyperplasia is not found in post-menopausal women. However, a recent case of post-menopausal tumefactive gonadotroph cell hyperplasia was proven on pathology after transsphenoidal biopsy. We believe that the combination of the imaging findings and the extreme elevation of gonadotropins could suggest gonadotroph hyperplasia in our cases.

Conclusion: Gonadotroph hyperplasia may be under recognized in women who have had early surgical or premature menopause. Misdiagnosis could lead to unnecessary invasive interventions. Some findings suggestive of gonadotroph hyperplasia rather than a pituitary adenoma are MRI images showing superior pituitary convexity, homogenous enhancement of pituitary without a focal lesion, and marked elevation of FSH and/or LH. Initiation of HRT may lower the FSH/LH levels, but whether this can lead to a reduction in pituitary dimensions remains to be elucidated.

Abstract #813

A CASE OF PITUITARY ADENOMA PRESENTING AS ATRIAL FIBRILLATION

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Emory School of Medicine

Objective: We describe a rare case of TSH-secreting pituitary adenoma and a review of literature.

Case Presentation: A 46 year old man presented with paroxysmal atrial fibrillation and hand tremor for one year. Other clinical problems were fatigue, constipation and new onset hypertension. He had repeated measurements of TSH between 3.7-4.5 mIU/L (normal 0.5-4.78). Exam showed a fine resting tremor, without features of acromegaly or goiter. Laboratory data revealed elevated free T4 of 2.8 ng/dL (normal 0.7-1.8), free T3 of 11.9 pg/mL (normal 2.4-4.2) and inappropriately normal TSH of 3.57mIU/mL. The glycoprotein hormone alpha-subunit (α-GSU) to TSH molar ratio was 3.6. Insulin-like growth factor-1, growth hormone, prolactin, and electrolytes were normal. There was no evidence for TSH heterophile antibodies. Free T4 by equilibrium dialysis was normal. MRI of the pituitary gland showed a 1x1 cm hypodense pituitary lesion. He received octreotide 50 mcg s.q. 3 times/day and TSH decreased to 0.17 mcIU/ml one week later, along with normalized free T4 and free T3. TSH subsequently normalized to 0.83 mIU/L; his tremors and palpitations resolved. A month later, he underwent trans-sphenoidal surgery and octreotide was stopped. On postoperative day 1, TSH was 0.23 mIU/L and remained slightly lower than normal for 2 months postoperatively along with normal free T4 and undetectable α-GSU.
Immunohistochemistry for TSH was strongly positive in the adenoma, along with scattered cells positive for GH and prolactin.

**Discussion**: The incidence of TSHoma is less than 1 case per million and most reported tumors were invasive macroadenomas. The main differential diagnosis is the syndrome of resistance to thyroid hormones that usually associates a normal α-GSU/TSH molar ratio. Our patient presented with multiple episodes of atrial fibrillation, which are not usually encountered in TSHomas. Also, he showed a rapid response to a small dose of subcutaneous octreotide, where it usually requires 2 months long-acting somatostatin analogs treatment to normalize the thyroid hormone levels. The tumor stained for TSH, GH and prolactin, which rarely occurs in TSHomas and suggests a potential mechanism of tumorigenesis via increased expression of Pit-1 transcription factor.

**Conclusion**: Thyroid hormone levels should be measured in patients with clinical suspicion of hyperthyroidism despite normal TSH, in order to rule out TSHoma. Although this type of pituitary tumor is rare, early detection may improve their outcome.

**Abstract #814**

**ACROMEGALY PRESENTING AS REFRACTORY DIABETIC KETOACIDOSIS AND POTENTIAL ROLE OF CONTINUOUS VENO-VENOUS HEMOFILTRATION IN SUCCESSFUL TREATMENT**

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1. Mayo Clinic, 2. allegheny general hospital

**Case Presentation**: A 54-year-old Caucasian male with obstructive sleep apnea, diabetes (diagnosed 1 day prior to admission), presented with significant lethargy. Physical exam showed large build, coarse facial features, big nose, lips, brow, hands and feet, a fruity odor and signs of dehydration. Labs showed glucose of 281mg /dl, bicarbonate <5, pH 6.96, positive ketones, anion gap >26 and osmolar gap 32. He was treated in the intensive care unit with IV fluids and insulin drip, which was gradually increased to 57 units/hr, due to minimal improvement in pH and bicarbonate. The patient required mechanical ventilation due to respiratory failure. As he developed acute renal failure in the context of renal hypoperfusion, continuous veno-venous hemofiltration (CVVH) with i.v. bicarbonate was instituted. After only 3 days of therapy, the growth hormone (GH) level dropped circa 4-fold and insulin growth factor 1 (IGF-1) level dropped 9-fold. After resolution of the septic shock, he was successfully extubated. An MRI showed 2.0 x 1.4 x 1.3 cm pituitary adenoma. The patient has been currently scheduled for trans-sphenoidal pituitary surgery.

**Discussion**: Our case is unique in the sense that our patient was a normotensive male, with no family history of diabetes, whose acromegaly presented with DKA, which was refractory to insulin therapy. Notwithstanding, ketoacidosis is very rare in this endocrinopathy. GH and IGF-1 excess induces insulin resistance in the liver, adipose tissue and muscle. This leads to increased endogenous production of glucose and decreased muscle uptake of glucose with rise in blood glucose levels. In cases such as ours, where patient instability precludes both imaging diagnosis and surgical approach, initial therapy with a somatostatin analog was the only feasible intervention. Octreotide inhibits GH secretion by binding to specific receptors for somatostatin being its analogue. Given the marked decrease in GH and IGF-1 seen in our patient in such a short period of time, we postulate a hypothetical role of CVVH in removal of plasma GH and IGF-1. This may be similar to the clearance of other medium size molecules such as brain natriuretic peptide and procalcitonin. If this is confirmed in future studies, CVVH may have therapeutic implications for the above category of patients.

**Conclusion**: Diabetic ketoacidosis (DKA) is exquisitely rare as presentation of acromegaly. We herein present a unique case report that highlights the importance of early recognition and management of acromegaly presenting as refractory DKA. Our case also suggests the need for further research on the role of continuous veno-venous hemofiltration (CVVH) in reduction of growth hormone (GH) excess in acromegaly.

**Abstract #815**

**LYMPHOCYTIC HYPOPHYSITIS PRESENTING AS PANHYPOPITUITARISM AFTER TREATMENT WITH IPILIMUMAB**

Mark Oertel, MD. PGY3
University of Kansas Medical Center

**Objective**: The objective is to describe a case report of lymphocytic hypophysitis presenting as headache and blurred vision with endocrine labs demonstrating panhypopituitarism after a patient’s third dose of ipilimumab.

**Case Presentation**: 54 year old female presented to her primary physician for swelling in her right groin. Eventual workup proved metastatic melanoma after sentinel node biopsy was performed. She chose to enroll in a clinic trail for treatment with ipilimumab infusions every 3 weeks. She tolerated the first two treatments without difficulty.
The day after her third infusion she began to have severe frontal headaches, blurred vision, fatigue, pruritus, and nausea. Serial endocrine labs demonstrated progressive adrenal insufficiency and hypothyroidism as compared to labs at initiation of treatment. Further studies with MRI of her brain demonstrated enlargement and enhancement throughout the pituitary gland and infundibulum suggestive of lymphocytic hypophysitis. She was started on dexamethasone every morning and night as well as levothyroxine therapy. Subsequent MRI of her brain showed decreasing size and enhancement of the pituitary gland and infundibulum. Per treatment protocol, further ipilimumab treatments were suspended and her symptoms abated with hormonal replacement therapy.

**Discussion:** Ipilimumab is a recombinant human IgG1 immunoglobulin monoclonal antibody which binds cytotoxic T-lymphocyte associated antigen 4 allowing enhanced T-cell activation and proliferation. It is indicated for treatment of metastatic or unresectable melanoma. As it is an immune stimulating agent it has been known to induce various immune-mediated adverse effects including pericarditis, nephritis, dermatitis, and most commonly colitis. There have been few documented cases of hypophysitis in patients treated Ipilimumab according to product labeling and literature review. Management of immune-mediated adverse effects may include discontinuation of ipilimumab and initiation of corticosteroids.

**Conclusion:** Hypophysitis is a rare complication of treatment with ipilimumab for metastatic melanoma. In phase III trials 1.8% had severe hypopituitarism with another 2.3% having moderate symptoms requiring hormonal replacement. This provides another case report of a growingly recognized adverse effect from treatment. Prompt treatment with dexamethasone along with targeted hormonal replacement is imperative. Often cessation of treatment is required when severe auto-immune adverse effects occur from ipilimumab. Oncologist and Endocrinologist alike must be diligent in monitoring patients receiving ipilimumab with frequent laboratory testing and imaging when symptoms arise.

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**Abstract #816**

**LYMPHOCYTIC HYPOPHYSITIS - A RARE CAUSE OF A PITUITARY MASS**

Swarna Rai, MD, Sindhura Reddy, MD

John H Stroger Jr Hospital of Cook County

**Objective:** To recognize lymphocytic hypophysitis (LH) as a cause of pituitary mass

**Case Presentation:** 25 year old woman with no significant past medical history presented with frontal headaches for the past 3 months. She had a child 15 months before presentation and her pregnancy was complicated by gestational diabetes. Physical examination was unremarkable including visual field and neurological examination. Her MRI showed a pituitary mass, non-homogeneous, 1.9 x 1.4 x 1.7 cm in size with minimal mass effect on the chiasma with no increase signal in the optic tracts. Endocrine evaluation revealed pan hypopituitarism without diabetes insipidus. She was started on prednisone and levothyroxine. A transphenoidal resection was done. Intra-operatively the tumor was found to be “very fibrous” and only small amounts could be removed “piecemeal”. Frozen section revealed pituitary adenoma. Post-operative MRI showed 70% persistence of the mass. A repeat surgery was scheduled. However, the pathology report showed lymphocytic hypophysitis with a dense infiltrate of mostly T-lymphocytes with fibrosis. A diagnosis of lymphocytic adenohypophysitis (LAH) was made and the patient was started on glucocorticoids.

**Discussion:** LH is a rare disease but the most common among the autoimmune hypophysitis (AH). The incidence is <1%. It is morphologically classified into LH, lymphocytic inbundibulo-neurohypophysitis (LINH) and lymphocytic pan hypophysitis (LPH). LAH is more common in women who present at a younger age and usually during pregnancy or postpartum. Headache is the most common presenting symptom. Other symptoms include visual abnormalities such as visual field defects and decreased acuity. Hormonal evaluation shows partial or complete deficit of the anterior pituitary hormones, producing the classic signs and symptoms of hypoadrenalism, hypothyroidism, and hypogonadism, diabetes insipidus and hyperprolactinemia. The defining pathological feature of LH is the infiltration of the pituitary gland with lymphocytes. Fibrosis is also common. Diagnosis of LH is made histologically. Clinical features and measurement of pituitary autoantibodies are not very sensitive or specific. The imaging modality of choice is a MRI, which shows a homogenous enhancement of the pituitary gland, but this feature is not specific for LH. The treatment of choice is glucocorticoids since they can...
reduce the size of the pituitary gland. Azathioprine and methotrexate can be used in resistant cases. Surgery and radiotherapy are recommended for persistent symptoms. **Conclusion**: LH is a rare cause of pituitary mass and should be in the differential especially in pregnant and post partum women as they usually respond to medical management.

**Abstract #817**

**NON HEMORRHAGIC PITUITARY APOPLEXY PRECIPITATED BY AN AIRFLIGHT**

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**Case Presentation**: 63 y/o male with a past history of hypertension and obesity presented with severe frontal headache that started while he was in a transatlantic flight. He described the headache as sharp, non-radiating, worsened by light and noise with no alleviating factors. It was the worst headache of his life. He had associated nausea, vomiting and blurring of vision and diplopia. His only medication was valsartan and his blood pressure was well controlled. Physical examination revealed ptosis of right eye and diplopia on left upper gaze. Extraocular movements of the right eye were restricted especially adduction, upward and downward gaze. The right pupil was dilated with sluggish reaction. Visual fields were normal by confrontation. The remaining exam was normal. MRI-brain showed lobular, heterogeneous enhancement sellar and suprasellar mass with displacement of the optic chiasm and bilateral cavernous sinus encroachment consistent with a pituitary macroadenoma with a central necrotic area. The size of the tumor along with visual symptoms and compression of the optic chiasm was an indication for surgery. He was started on stress dose steroids prior to the transsphenoidal surgery for the suspected apoplexy. Pathology confirmed the adenoma with focal infarct and necrosis. He has low cortisol level and inadequate response to ACTH after surgery. His symptoms improved but he continues to be on hydrocortisone postsurgery.

**Discussion**: Pituitary apoplexy is an endocrine emergency which can occur due to infarction or hemorrhage of pituitary gland. The incidence of apoplexy in pituitary adenomas is between 1% and 26% and can often be the first presentation of the underlying pituitary tumor in over 80% of patients. The exact cause of pituitary apoplexy still remains elusive but pregnancy and anticoagulation are known precipitating causes. This is an unusual cause which has been reported in only one other case report in the past when a patient rapidly ascended to a higher altitude from sea level. Hypoxia and low atmospheric pressure may cause cerebral vasodilatation and increased cerebral blood flow, predisposing to pituitary injury. This case highlights keeping high altitude in the list of possible precipitating causes for apoplexy especially in large pituitary lesions.

**Conclusion**: Rapid ascent to high altitudes could be an independent predisposing factor for pituitary apoplexy in patients with underlying pituitary adenoma.

**Abstract #818**

**ATYPICAL PROLACTINOMAS: A CASE SERIES HIGHLIGHTING UNIQUE HISTOPATHOLOGY AND MAGNETIC RESONANCE IMAGING FEATURES**

Aashish Shah, MD, Robert Smallridge, MD, Gunjan Gandhi, MD

Mayo Clinic

**Case Presentation**: We review 3 cases of atypical prolactinomas recently seen at our institution to highlight a variety of unique features and characteristics that underscore criteria being used to classify pituitary adenomas as atypical. The included patients were a 16 year old male, 32 year old male and 54 year old female. All patients presented with headache and vision changes. Magnetic resonance imaging performed pre-, intra- and postoperatively, revealed that all patients had macroadenomas. Tumor size ranged from 23 to 62mm (mean: 38mm). In addition, all of the prolactinomas demonstrated invasion of surrounding optic chiasm and at least one cavernous sinus. Two of the three cases demonstrated both supra- and infrasellar extension. In particular, one of the cases had two areas of hemorrhage within the atypical prolactinoma, concerning for apoplexy, thus initially leading to emergent neurosurgery. All three tumors overproduced prolactin. The 16 year old patient had prolactin of 824 ng/mL and the 32 year old patient had prolactin measured to be 4,388 ng/mL. Interestingly, the 54 year old patient, who had the largest tumor size, had the lowest prolactin after serial dilutions (58 ng/mL). All of the patients underwent resection of pituitary adenoma using a transsphenoidal approach. The 16 year old patient was the only case in this series medically managed with cabergoline initially. He was on this therapy for one year, before having neurosurgery. All tumor specimens were submitted to a single neuropathology laboratory in Mayo Clinic Florida for analysis. Immunohistochemical studies diagnosed all three tumors as atypical prolactinomas.

MIB-1 labeling index ranged from 5 to 15% (mean: 10.3%). Two of the three cases showed excessive p53...
immunoreactivity. All exhibited high mitotic rates.

**Discussion**: The WHO pathological classification of pituitary adenomas designates an atypical variant as having MIB-1 proliferative index greater than 3%, excessive p53 immunoreactivity and increased mitotic activity. Based on previous estimates, atypical pituitary adenomas are present in 15% of resected pituitary adenomas and typically tend to be aggressive and invasive macroadenomas. There is also a higher rate of recurrence.

**Conclusion**: Characteristics noted in our series of patients are similar to those in other larger case series studies. These findings present unique challenges when assessing surgical outcomes, monitoring for recurrence and surveying for metastasis. Future larger, longitudinal and prospective studies observing trends in patients with atypical pituitary adenomas should be done to provide insight into management options for these individuals that are efficacious, yet cost-effective.

**Abstract #819**

**PRIMARY RENAL CARCINOID: A RARE CASE REPORT**

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Howard University Hospital

**Objective**: To present a rare case of primary renal carcinoid tumor

**Case Presentation**: A 45 year old man from Trinidad and Tobago with a history of hypertension presented with complaint of leg swelling, palpitations, dyspnea on exertion, abdominal pain, diarrhea, history of heart valve problem and flushing during eating. He denied chest pain, paroxysmal nocturnal dyspnea, orthopnea. He was seen by cardiology and a cardiac catheterization was done which showed a left renal mass. Subsequently he had CT of abdomen and pelvis with IV contrast which confirmed the left renal mass measuring approximately 7.5cm X 6.5cm X 6.5cm. A preliminary diagnosis of renal cell carcinoma was entertained and patient was referred for surgery. He underwent radical left nephrectomy and periaortic lymph node dissection. Pathology revealed primary renal neuroendocrine tumor. The tumor was graded as low grade evidenced by low KI67 immuno staining strongly positive for synaptophysin and for chromogranin with 4 of 6 lymph nodes positive. A post-operative 24 hour urine 5-HIAA was abnormal (28.8 mg/24 hr., normal ≤6.0 mg/24 hour).

**Discussion**: Primary renal carcinoid tumors are extremely rare with only 56 cases reported. Carcinoid tumors occur most frequently in the gastrointestinal system with the appendix being the most common site. The pathogenesis is uncertain because neuroendocrine cells are not found in normal renal parenchyma. It is hypothesized that the tumors are derived from misplaced neural crest tissue in the hilar aspect of the kidney during embryogenesis. Another theory suggests they arise from neuroendocrine cells associated with intestinal metaplasia of the pyelocalyceal urothelium that occurs as a sequel of chronic inflammation. Renal carcinoids are solid but 49% have cystic components with necrosis as was seen in our patient. The median age is 49 years with no sex predilection. The frequency is higher in patients with abnormal kidneys.

**Conclusion**: The prognosis for primary renal cancer is relatively optimistic. The presence of metastasis at time of diagnosis seems to be an integral prognosticator of survival. Whenever a renal carcinoid tumor is found, the search for an unknown primary in indicated. Somatostatin receptor scintigraphy is an integral diagnostic and staging tool. For differentiation of malignancy, immune staining for p53 is useful.

**Abstract #820**

**A CASE OF ACUTE HYPOPHYSITIS AND SECONDARY PANHYPOPITUITARISM IN A PATIENT ON IMMUNE MODULATING DRUG EPILIMAMAB FOR RECURRENT MELANOMA**

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**Case Presentation**: A 72 year old Asian gentleman was diagnosed with melanoma of the left 2nd toe in 2011 and underwent amputation of the same. In 2012, the melanoma re-occurred at the amputation site and has metastasized to the ipsilateral lymph node. Patient enrolled into a clinical trial and received 3 cycles of epilmamab therapy. At the start of the therapy (baseline) his labs were: Na: 134, TSH 0.91, testosterone 221, cortisol: 12, free T4: 1.6: After the third cycle, (6 weeks later) patient developed diplopia and came to the ER. Patient was found to have a serum sodium of 124 (low). His other endocrine labs were: ACTH <1.1,FSH: 3.7, LH 0.3,TSH:0.2, Free T4:0.7, Cotisol 0.7, prolactin 0.9. MRI Imaging showed enlarged pituitary with suprasellar extension. Patient was given 10 mg iv of dexamethasone in the ER and was started on oral dexamethasone. Patients diplopia improved. Patient continues to be on dexamethasone 6 mg po every day, levothyroxine 75 mcg p
qday and testosterone replacement (2 months). Patient now has developed Cushingoid features and hyperglycemia. We have been trying to taper dexamethasone, however any dose less than 6 mg po q day leads to recurrence of diplopia. Outpatient follow-up along with repeat Pituitary MRI is awaited.

**Discussion:** Ipilimumab is a human monoclonal antibody directed against the cytotoxic T-lymphocyte antigen-4 receptor. Blocking cytotoxic T-lymphocyte antigen-4 signaling has been shown to enhance T-cell activation and to amplify T-cell-mediated immunity. It has shown to markedly improve the survival rate in patients with melanoma. It has been reported [Chris Fellner, P T. 2012 September; 37(9): 503-511, 530] that moderate endocrinopathies (grade 2) occured in 12 patients (2.3%), including hypothyroidism, adrenal insufficiency, and hypopituitarism. Here, we report a case of pituitary hypopysitis in a patient with metastatic melanoma - which eventually required replacement of glucocorticoid, levothyroxine and testosterone.

**Conclusion:** We report a rare case of possible ipilimumab-induced hypophysitis and that it is important to be aware of this association. The hypophysitis responds rapidly to glucocorticoid therapy and subsequent normal hormone replacement therapy. Endocrinologists need to be aware of relatively new immune modulating agents used in cancer treatment, that can cause pituitary inflammation secondary to an auto-immune reaction. Hypophysitis in acute situations mediated by drug therapy could be life threatening if unrecognized.

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**Abstract #821**

**BISPHENOL-A ACUTE EXPOSURE FROM LEACHATES OF ELECTRONIC GADGETS DOES NOT INDUCE OXIDATIVE STRESS IN RAT’S BRAIN.**

*Neeraj Kumar, PhD¹, Vinod Sharma²*

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**Objective:** To investigate the effects of BPA on oxidative damage in terms of activity level of antioxidant enzymes in different regions of the rat’s brain.

**Methods:** The ever increasing uses of electronic gadgets are becoming a widespread source of Bisphenol-A accumulation. As studies have been reported that low level BPA accumulation may produce neurological effects but still limited studies have re-examined for its adverse effects in terms of acute exposure from electronic devices. In this study, BPA migration was estimated through physio-chemical parameters and leachate (equivalent to 4mg/kg body weight) was used for animal dosing. Three groups of Albino Wister rats (190+20grm) were used for control, sham, and treated. The antioxidant enzymes including superoxide dismutase (Mn-SOD), catalase (CAT), glutathione peroxidase (GPx) and reduced glutathione level (GSH) were measured in different brain regions i.e. corpus striatum, frontal cortex, thalamus and midbrain.

**Results:** No significant changes were observed in most of the brain regions yet the level of GPx activity in corpus striatum (29.65±0.98 nmole/min/mg protein) and level of GSH activity in frontal cortex (2.33±0.12 µmole/g protein) was found to decrease significantly (p<0.05) when compared to controls.

**Discussion:** No significant effects were observed for the oxidative damage in sham group compared to control group. This tends that the specific designed exposure cage i.e.CCPE cage did not produce any additional stress in sham group.

**Conclusion:** Study suggested that acute exposure (4mg/kg body weight per day up to 28 days) of BPA does not induce significant oxidative damage in the rat’s brain. Furthermore, study might re-examine before affirm the final remark for subscribers and regulatory bodies at similar doses.

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**Abstract #822**

**CHRONIC PITUITARY DISEASE AFTER TRAUMATIC BRAIN INJURY: IMPLICATIONS OF INCREASED RECOGNITION**

*Harold Pretorius, M.D., Ph.D., Luis Pagani, M.D., Dennis Menke, A.A., Nichole Richards, B.S., CNMT, Elizabeth Budke, CNMT, Henry Hartsock*

Blue Ash Nuclear Medicine

**Objective:** Review our experience evaluating traumatic brain injury (TBI) patients for pituitary disease and related comorbidities.

**Methods:** Outpatients with TBI had pituitary evaluations including serum hormone levels, brain MRI and a cerebral flow reserve index (FRi) from basal and perfusion-stimulated brain SPECT. Oxidative stress was monitored with fractionated urine porphyrins (LabCorps) and cognition by Test Your Memory (TYM). TBI patients were compared to similar age patients with renal hyperfiltration (RH) and diabetes (DM) who did not have TBI but had similar cognitive deficits.

**Case Presentation:** Among 212 patients age 50.6±13.9 years, 49.1% male, 50.4% female, 0.5% transgender, 98.1% civilian, 1.9% military, followed with neurological complaints for 2.0±1.9 years, 42.0% (89/212) had pituitary abnormalities which involved a single axis
Abstract #823

FACTORS AFFECTING REPORTED RESPONSE RATES TO SOMATOSTATIN ANALOG THERAPY IN ACROMEGALY CLINICAL TRIALS

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Objective: Somatostatin receptor ligands (SRLs) are a mainstay of medical therapy for patients with acromegaly. Serum insulin-like growth factor-1 (IGF-1) and growth hormone (GH) are routinely monitored to assess treatment response; however, reported response rates among published trials are highly variable, as are the criteria for response. Response rates reported in more recent SRL clinical trials have been lower than in earlier investigations. However, despite divergent study designs, early SRL trial experiences have established expected response rates for subsequent trials. The objective of this analysis is to clarify sources of variations in reported response among clinical trials of acromegaly patients treated with SRLs and to determine specific trial design factors that influence reported response rates.

Methods: A systematic literature review was performed as part of an ongoing meta-analysis designed to explore these matters in detail. A PubMed search was performed for English-language clinical trials in acromegaly patients published from 2003-2012 (N=192) studying SRL (octreotide or lanreotide) medical monotherapy. Response rate variations were then compared among trials according to the following variables:
- Single vs. composite biochemical endpoint (e.g., GH < 2.5 µg/L and IGF-1 normalization)
- Single- vs. multi-center
- Prospective vs. retrospective design
- Trial duration
- Number of patients
- Pre-selection for SRL response

Results: This systematic literature analysis indicates that a number of trial design factors influence reported response rates. Lower response rates were generally reported in trials that were prospective, multi-center, studied > 20 patients, used a composite rather than single biochemical endpoint (particularly when GH < 2.5 µg/L), excluded previously treated patients (particularly patients with previous response to SRL therapy), or had treatment duration < 1 year. Interestingly, these factors tended to be more common in more recent trials.

Discussion: This apparent trend toward more rigorous trial design parameters in more recent trials may drive a trend to lower overall reported response rates over time. The years during which a trial was performed may have significant implications on trial methodology and, therefore, on reported response rate.

Conclusion: Our analysis indicates multiple methodological changes in these studies over time, and that key factors in design have a direct effect on reported response rates. Several factors in the current analysis require rigorous meta-analysis to better understand and quantify the effect of each variable on reported outcomes.
Abstract #824

IDIOPATHIC Cavernous Sinus Inflammation; The Tolosa-Hunt Syndrome with Sellar Extension Presenting with Hypopituitarism

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Objective: We report a case of Tolosa Hunt Syndrome causing anterior pituitary hypofunction & its successful management.

Case Presentation: A 61 y/o F presented with palpitations. She also gave a 3y h/o headache, diplopia & h/o stroke. On exam she had R 6th & 7th cranial nerve palsy & L hemiparesis. TSH 0.52mIU/L(0.4-4.5) FT4 0.7ng/dl(0.8-1.8) RAIU of thyroid 2%. With TTFs suggestive of secondary hypothyroidism pituitary panel was checked. 8am ACTH 13 pg/ml(6-50), cortisol 2.6mcg/dl, FSH 2.3 mIU/L(23-116.3) LH 0.3 mIU/ml(10-54.7) Prolactin 17ng/ml(2-20) IGF-1 71 ng/ml(41-279), GH 0.2 ng/ml. She failed an ACTH stimulation test. Pituitary MRI showed extensive abnormality at the skull base centered in the sella turcica with mild enlargement of the gland at 12mm, heterogeneous enhancement & extensive infiltrating tissue in both cavernous sinuses & adjacent dural surfaces & ICA encasement. Subsequently ESR 75mm/hr(0-20) CRP 27.3(1-5) ANA 80(≥80). Autoantibody Panel + for SSA. Negative dsDNA, SSB, SM RNP, CentromereB scleroderma70, JO-1, Histone. Lyme AB<0.91(0.0-0.9) RPR 1.4ng/ml(0.8-1.8) SPEP UPEP ml, Urine immunofixation neg. Serum IGG 1344mg/dl IGG subclasses nl. CSF mild elevated protein, CSF ACE nl, cytology neg, CT torso neg. PET showed minimal FDG uptake associated with skull base abnormality. Endoscopic transphenoidal sellar biopsy showed dura with chronic inflammatory cell infiltrate of CD3 Tcells, CD138+ lymphocytes, plasma cells extending into the adenohypophysis. The patient was treated with prednisone & azathioforest. Upon treatment headaches resolved immediately, diplopia, ESR & CRP normalized in a few weeks, the cavernous & sellar lesion significantly improved on MRI 2 months later. Immunosuppressive therapy is gradually being tapered.

Discussion: The patient ran an extremely indolent course & was diagnosed during work up of failed hypothalamic pituitary axis. She had no persistent diabetes insipidus & preserved posterior pituitary function, unlike the few reported cases of Tolosa Hunt presenting with panhypopituitarism & diabetes insipidus(1,2,3). Laboratory work up was significant for elevated ESR & CRP which normalized on treatment, mild elevated CSF protein & +ANA. These are usually nl in Tolosa Hunt(4) but have been rarely reported to be abnormal(5).

Conclusion: This is a rare presentation of Tolosa Hunt Syndrome extending to the sella turcica & interfering with adenohypophysial function. Extension of granulomatous inflammation into the cavernous sinus, to the pituitary portal system, the pituitary & hypothalamus itself causes pituitary failure. As Tolosa Hunt has a relapsing course, we are monitoring for recurrence with consideration of radiation therapy for treatment failure or recurrence.

Abstract #825

CHRONIC MARIJUANA USE AS A POTENTIAL CAUSE OF HYPOPITUITARISM

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Objective: Hypopituitarism is most often caused by a mass lesion and less commonly by inflammatory, infiltrative, or vascular disease. Tetrahydrocannabinol (THC), the psychoactive ingredient of marijuana, has ability to alter various neural transmitters in the hypothalamus or neural transmitters in the CNS which affect the hypothalamus. We report a case of hypopituitarism seemingly secondary to chronic marijuana use.

Case Presentation: A 37-year-old male presented to the Emergency Department with symptoms of dyspnea on exertion, increasing fatigue, and loss of libido. The patient reported daily use of marijuana for 15 years. There was no history of radiation exposure or head trauma. On physical exam, significant findings of bibasilar rales, gynecomastia, and bilateral atrophied testis were noted. Considering the possibility of hemochromatosis, iron studies and echocardiography were completed, which were normal. Hormonal evaluation revealed low LH (0.2 mIU/mL), FSH (0.8 mIU/mL) and testosterone (2 ng/dL) along with high prolactin (53.3 ng/mL). Further endocrine chemistry revealed ACTH of 6 pg/dL, and cortisol at 0 and 60 minutes following administration of cosyntropin of 6.4 ug/dL, and 9.3 ug/dL respectively. Additional lab studies revealed low total T3 (30 ng/dL), high T3 resin reuptake (49%), low total T4 (3.94 ug/dL), normal free T4 (0.97 ng/dL) and low TSH (0.22 ulU/mL). In addition, growth hormone was within normal limits (5.0 ng/mL) and IGF-1 was low (75 ng/ml; Z-score of -1.3). MRI of head showed a protuberant pituitary gland that was slightly larger than expected size, but there was no identified mass...
lesion. The patient was started on cortisone 25 mg in the morning and 12.5 mg at bedtime and levothyroxine 25 mcg daily. Subsequent to this his fatigue and edema improved dramatically.

Discussion: THC impairs GnRH release resulting in lowered LH and FSH, which is responsible for reduced testosterone production by the Leydig cells of the testis. Several studies have also shown impaired cortisol response to stress resulting from cannabis exposure. Similarly, animal models have shown that endogenous cannabinoids suppress multiple hypothalamic-pituitary pathways, including growth hormone, and thyroid hormone. Given these findings, we postulate that chronic cannabis use, by modulating the hypothalamic-pituitary axis, is a potential cause of hypopituitarism.

Conclusion: Given the climate of increasing legalization of cannabis in the United States, the relationship between chronic marijuana use and its potential effects on the endocrine system warrants further study.

Abstract #826

CORRELATION OF CLINICAL SMELL TEST AND MAGNETIC RESONANCE IMAGING OF OLFAC TORY SYSTEM IN IDIOPATHIC HYPOGONADOTROPIC HYPOGONADISM

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Objective: 1. To measure olfactory bulbs and sulci using dedicated magnetic resonance imaging (MRI) sequences in idiopathic isolated hypogonadotropic hypogonadism (IHH) patients with a well detailed phenotype characterization, 2. To correlate MRI findings with a clinical smell test.

Methods: MRI was performed in 20 patients (all male, aged between 11 and 45 years, mean age of 26) with IHH and olfactory dysfunction was assessed using the Smell Identification Test (UPSIT), a qualitative supratreshold olfaction test obtained from the University of Pennsylvania. Coronal spin echo T2-weighted and volumetric T1-weighted gradient echo sequences were acquired in a 1.5T system. ImageJ software was used to obtain olfactory bulb volumes and olfactory sulcus depths and lengths. Data were analyzed with SPSS 15.0 and the Kappa index was used to evaluate the agreement between the UPSIT and MRI.

Results: The UPSIT revealed normosmia, hyposmia and anosmia in 10 (50%), 4 (20%) and 6 (30%) patients respectively. Fourteen patients (70%) had olfactory abnormalities in the MRI. Commonest abnormality was olfactory bulb. One patient had unilateral olfactory bulb with normal sense of smell. There was moderate agreement between the MRI quantitative evaluation and the UPSIT (overall Kappa =0.55).

Discussion: Olfactory bulb and sulcus aplasia were the most common findings in IHH patients (70%). We objectively demonstrated agreement between MRI findings and the smell test, especially the presence of bulb aplasia and anosmia, confirming the high specificity of MRI findings.

Conclusion: Therefore, our findings help ascertain MRI accuracy in the diagnosis of IHH, differentiating patients with hypogonadotropic hypogonadism with an apparently normal or difficult to evaluate sense of smell.

Abstract #827

TUBEROUS SCLEROSIS: AN UNCOMMON CAUSE OF HYPERPROLACTINEMIA

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Objective: To report a case of tuberous sclerosis presenting with hyperprolactinemia.

Methods: Clinical, laboratory and radiographic data are reported on a 26 year old female presenting with galactorrhea and menstrual irregularities.

Case Presentation: A 26 year old female with no premorbidities presented with complaints of galactorrhea for the past 10 days and menstrual irregularities over the past six months. Galactorrhea was spontaneous. Her last childbirth four years ago was uneventful. She had no head ache, vomiting, and visual impairment. She denied any history of substance abuse, drug intake hypothyroidism, chronic liver or kidney diseases, and epilepsy. She was well nourished female with mild pallor, tiny nodule on face, subungual fibroma in hands. There was spontaneous galactorrhea and mildly tender breasts without any signs of inflammation. Systemic examination was entirely normal with normal IQ. Ophthalmologic evaluation revealed white disk shaped retinal hamartoma. Routine laboratory investigations including renal and liver function tests, thyroid profile were normal. Serum prolactin was 85 ng/mL with FSH-4.66 and LH-4.21 mIU/ml. Tests for evaluation of other anterior pituitary hormones were normal. Abdominal and pelvic ultrasound revealed no abnormality. Chest X ray showed bilateral interstitial infiltrates. Echocardiogram of heart was normal.
Computed tomography (CT) scan revealed multiple intracerebral calcifications. These calcified lesions/ subependymal hamartomas are seen along the lateral surface of the lateral ventricles giving rise to characteristic candle dripping appearance. Magnetic resonance imaging (MRI) of the brain ruled out the presence of any pituitary mass. The combined clinical scenario along with the radiologic findings leads to the diagnosis of TSC with hyperprolactinemia. Patient was prescribed cabergoline 0.5 mg twice daily which resulted in amelioration of galactorrhea and regularization of menses.

Discussion: Tuberous Sclerosis (TSC) is a multi system genetic disorder which infrequently affects the endocrine system. Cushing’s disease, hypoglycemia secondary to insulinomas, precocious puberty, thyrotoxicosis, hypercalcemia secondary to parathyroid adenomas, hyperprolactinemia and acromegaly have all been reported in TSC patients. The circulating prolactin of our patient may be of pituitary origin or may possibly be secreted ectopically by a hamartoma.

Conclusion: TSC patients develop hormone secreting tumors involving the neuroendocrine system.

Abstract #828

HEADACHE AND DIABETES INSIPIDUS AS PRESENTATION OF METASTATIC RENAL CELL CARCINOMA OF THE PITUITARY GLAND

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Objective: Pituitary metastasis is an uncommon presentation of primary malignancy. It is more common to have pituitary metastasis when primary disease is already known. Our case is a discussion of recurrent metastatic renal cell carcinoma presenting as headache and then polyuria.

Case Presentation: A 59 year old male with history of renal cell carcinoma presented 7 months later with headaches associated with polyuria, weight loss, fatigue and erectile dysfunction. MRI brain showed enhancement of the infundibulum of the pituitary gland and 2.5 cm x 2 cm frontal lobe lesion with vasogenic edema with midline shift. Due to midline shift, the patient underwent right craniotomy and right frontal tumor resection. Shortly postoperatively, the patient developed hypoalectremia with a serum sodium of 150 meq/l. Laboratory studies also revealed serum osmolality 318 mOsm/kg, urine osmolality 199 mOsm/kg, and urine specific gravity of 1.006 suggesting diabetes insipidus. Prolactin was normal at 14.1 ng/ml. ACTH and cortisol were not checked as the patient was receiving glucocorticoids. Lutenizing hormone was 1.2 IU/l, testosterone <3 ng/dl, TSH 0.02 microIU/ml and free T4 was 2.15 ng/ml, and a degree of hypopituitarism was suspected. He was treated with dexamethasone for vasogenic edema, desmopressin for diabetes insipidus and later, testosterone replacement therapy for hypogonadism. Urine studies after desmopressin showed appropriate urine concentrating ability. Pathology showed adenocarcinoma consistent with renal cell carcinoma, and the patient underwent chemotherapy with pazopanib for metastatic renal cell carcinoma and whole brain irradiation for brain metastasis.

Discussion: Pituitary metastasis occurs in 3.5% of metastatic disease. The vascular supply allows direct communication with the systemic circulation via the internal carotid arteries. Metastatic spread more commonly is to the posterior pituitary gland. Some neoplasms are occult and of unknown origin. These primarily present as diabetes insipidus, like in our patient. It is rare to have pituitary failure. On imaging, metastatic disease may be difficult to distinguish from an adenoma. In our case, the patient also had other brain lesions. In one small case series, the following disturbances occurred in pituitary metastasis in renal cell carcinoma: bitemporal hemianopia, lethargy, headaches, and two had diabetes insipidus. Panhypopituitarism was present in three patients.

Conclusion: Our patient who had headache and was later discovered to have diabetes insipidus, already was known to have renal cell carcinoma. Patients in whom metastatic pituitary disease is expected should be monitored for the development of diabetes insipidus perioperatively.

Abstract #829

PITUITARY APOPLEXY - A DIAGNOSTIC CHALLENGE

Akilandanayaki Angamuthu, Vijay Babu Balakrishnan

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Case Presentation: A 69-year-old male came to emergency room with acute onset severe headache which woke him up from sleep. Patient did not have diplopia, nausea, vomiting, vision loss, photophobia, fever, neck pain, or any other focal neurological deficit. He had diet controlled hypertension and type 2 diabetes. Admitting blood pressure was 150/90 mmhg. Initial Physical examination was unremarkable. Non-contrast CT scan of head did not showed any hemorrhage. Patient was admitted for observation and his headache improved. In the next 12 hours, patient complained of diplopia and was found to have isolated right oculomotor nerve palsy with right sided ptosis, mydriasis and an inferolaterally
deviated eye. No decreased visual acuity, field defects or other focal neurological deficits seen. A CT angiogram was done to rule out cavernous sinus thrombosis and was negative. A working diagnosis of isolated third nerve palsy associated with diabetes was made. Next day, Patient became hemodynamically unstable with blood pressure of 70/40 mmhg. Spot serum cortisol was 1.6 mg/dl. Intravenous hydrocortisone was started and blood pressure stabilized. Review of the reconstructed images of CT angiogram showed a possible enlarged sella which was not appreciated before and on the admitting CT scan. MRI brain was done which showed a 2.2 cm pituitary macroadenoma with hemorrhagic components. Transphenoidal surgical removal was done and pathology showed complete hemorrhagic necrosis. Clinical recovery with significant improvement of ocular symptoms was seen.

**Discussion**: Pituitary apoplexy is rare, seen in 0.5-10% cases of pituitary adenoma. Previous diagnosis of pituitary adenoma was not seen in 80% of cases. The diagnostic challenge is due to the rarity, difficult clinical suspicion and poor sensitivity of CT scans for pituitary lesions which are often used to evaluate these patients. MRI has a sensitivity of over 90% to detect pituitary apoplexy. Acute onset headache, decreased visual acuity, visual field defects and decreased level of consciousness are the common presenting features. Lateral expansion of the bleeding leading to compression of the cavernous sinus can result in cranial nerve palsies. Our patient had third nerve palsy which is the most commonly affected. Pituitary tumors are five times more likely to bleed than other brain tumors and are attributed to the unusual vascular supply from the portal system. The gradually enlarging pituitary tumor gets impacted at the diaphragmatic notch, compressing its vascular supply causing ischemia, necrosis and bleeding.

**Conclusion**: Pituitary apoplexy is a diagnostic challenge and needs a high index of suspicion.

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### Abstract #830

**COMBINATION THERAPY USING OCTREOTIDE LA AND PEGVISOMANT IN THE MANAGEMENT OF INVASIVE INOPERABLE PERSISTENT GROWTH HORMONE-PRODUCING PITUITARY TUMORS.**

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**Objective**: To report efficacy of combination Octreotide LA & pegvisomont in the management of invasive & inoperable persistent GH-secreting tumors.

**Methods**: Clinical exam, hormonal analysis, imaging modalities (CT/MRI pituitary, histopathology, tumoral labeling indices (Ki-67 & p53) response to Rx & FU.

**Case Presentation**: Pt A. 34-yrs. old lady underwent transphenoidal surgery (TSS) x2 & external radiation for invasive macroadenoma (Ki-67 index 3%, & excess p53 immunoreactivity 10%); despite this Rx large residual tumor persisted involving bilateral carotid/sphenoid sinus, clival body & tumor had encased internal carotid arteries. Escalating doses of OctreotideLAR (60 mg/mos.) resulted in modest decline of abnormal IGF-1 from 769 to 544 ng/ml (RR:108-247). Addition of pegvisomant 10 mg daily along w/ reduction in Octreotide LAR to 30 mg/mos resulted in further decline in IGF-1 from 769 to 544 ng/ml. There was no increase in tumor size. Pt. experienced substantial clinical improvement & no side effects of combination Rx. Pt B: 30-yr.old man had persistent GH-secreting macroadenoma following TSS x2 ( Ki-67 index 3% & negative for p53). He did not respond to octreotide. Following addition of pegvisomant 10 mg daily, IGF-1 declined from average 542 to 148 & GH increased from 4 ng/ml to 80 at 10 mos. fU & no increase occurred in tumor size. Combination medical Rx afforded significant clinical improvement w/ no side effects.

**Discussion**: GH-secreting invasive macroadenomas pose therapeutic challenge. Persistent/recurrent tumor following debulking is reported in up to 19%. Our pts. posed special Rx problems since they had persistent tumor despite repeated TSS & remained nonresponsive to radiation &/or Octreotide. Addition of pegvisomant resulted in hormonal & clinical response w/ no adverse effect on tumor size & no other side effects. Pegvisomant is an analogue of human GH that selectively binds to GH receptors, blocking binding of endogenous GH, leading to decreased serum concentrations of IGF-I & other GH-
responsive proteins. A decline in IGF-1 level results in an expected increase in GH level. Early experience w/ the use of the drug had raised concern of increase in tumor size; however subsequent experience has shown safety in this regard. A combination of Octreotide & pegvisomant provides safety in prevention of tumoral growth.

**Conclusion:** Invasive GH-secreting pituitary tumors pose therapeutic challenge. When tumor persists despite multimodality Rx consisting of repeated surgical debulking, Octreotide, and irradiation, it is reasonable to add pegvisomant. This strategy results in clinical and hormonal remission.

**Abstract #831**

**GIANT PROLACTINOMA PRESENTING AS BILATERAL HEARING LOSS**

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UMDNJ - NJMS

**Case Presentation:** Classic presentation of prolactinoma includes oligo-amenorrhea, infertility and galactorrhea in women and headache, vision loss and decreased libido in men. Unusual presentations include rhinorrhea, photophobia, Horner’s syndrome and twelfth nerve palsy. Few have reported unilateral hearing loss. We describe a case of a man who presented with bilateral hearing loss and was found to have a giant prolactinoma. A 41-year-old presented with bilateral hearing loss. Following a trial with hearing aids, he noticed blurry vision and presented to our emergency room with headaches, peripheral vision loss and impotence. He denied taking any medications. Physical exam was significant for bitemporal hemianopsia, bilateral gynecomastia and small testicles. A MRI of his head revealed a 3.0 cm x 3.0 cm x 3.3 cm lobulated mass arising from the sella turcica, extending superiorly into the suprasellar cistern, compressing the left half of the optic chiasm. Labs were significant for prolactin 3711 ng/ml, testosterone 128 ng/dl, FSH 2 mIU/ml and LH 2 mIU/ml. The patient was started on bromocriptine and intravenous dexamethasone. Over the next 3 days his prolactin level decreased to 410 ng/ml. Two months later a repeat MRI revealed a decrease in tumor size and mass effect. He reported marked improvement in his vision and headaches and mild improvement of his hearing. Prolactin was 196 ng/ml.

**Discussion:** Prolactinomas have a reported prevalence range of 10 to 50 per 100,000. Typical presentations include oligo-amenorrhea and galactorrhea in women and headaches, visual changes and impotence in men with auditory presentations being rare. Whereas bilateral hearing loss is typically associated with systemic exposures, focal processes tend to cause unilateral hearing loss. Although prolactinomas have been associated with tinnitus, vertigo and unilateral hearing loss, the hearing deficits are secondary to mass effect. Meniere’s disease, characterized by tinnitus, unilateral sensorineural hearing loss followed by vertigo, has been associated with elevated levels of prolactin. Many theories question the relationship between prolactin and hearing loss. K.C. Horner has theorized that prolactin receptors located on the lymphocyte-macrophage complexes within the endolymphatic sac are affected during stress when high levels of prolactin are released, thus affecting the immune-defense of inner ear.

**Conclusion:** Regarding our patient, six months later he noted both visual and auditory improvement, the former being more prominent. His improvement may be attributed to shrinking the tumor and lowering his prolactin. However after further questioning, we discovered that he was a former musician, which may also have contributed to his hearing loss.

**Abstract #832**

**PANHYPOPITUITARISM IN OPSOCLONUS-MYOCLOCNUS SYNDROME**

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**Objective:** We report a case of panhypopituitarism in Opsoclonus Myoclonus Syndrome (OMS). The OMS is a rare autoimmune neurological disorder which predominantly affects children and can cause lifelong neurological disability.

**Case Presentation:** 41 years old Caucasian woman with OMS, learning disability and hypothyroidism on levothyroxine presented to the ER with one week history of fatigue and lethargy. At the time of presentation, it was unclear if she has primary or secondary hypothyroidism. The medical history was significant for OMS diagnosed at age 5 months following DPT vaccination and was treated with prednisone and dilantin for 36 months. She had subnormal growth velocity and delayed puberty. She had secondary amenorrhea since age 25, four years after partial hysterectomy and unilateral oophorectomy for uterine fibroid. Her height was 134 cm and weight was 109 pounds. She had opsoclonus, myoclonus with truncal ataxia and titubation without any focal neurological deficit. The laboratory evaluation revealed TSH < 0.02 (0.34-5.60 mIU/ml), Free T4 1.23 (0.58-1.64 ng/ml) and Free T3 3.3 (2.5-3.9 pg/ml) on 112 mcg of levothyroxine daily. A random cortisol level was 1.6 ug/dl. ACTH stimulation test
showed a subnormal response with the cortisol of 8.6 ug/dl at 30 min and 11.6 ug/dl at 60 min. Baseline ACTH was 8 (6-58 pg/ml). FSH was 0.73 (3.85-8.78 mIU/ml), LH was < 0.20 (2.12-10.89 mIU/ml, Estradiol was < 20 (27-122 pg/ml), IGF-1 was 32 (118-298 ng/ml) and Prolactin was 11.75 (3-36 ng/ml). On review of previous health records, she was diagnosed with secondary hypothyroidism two years prior to the presentation. The hormonal evaluation was diagnostic of panhypopituitarism. The sellar and suprasellar region was unremarkable on MRI scan. She was started on hydrocortisone and levothyroxine was continued.

**Discussion:** OMS is a debilitating autoimmune central nervous system disorder with varied clinical expression. It causes motor and speech abnormalities, cognitive dysfunction and behavioral problems. The pathogenesis of OMS is immune mediated and a sustained active autoimmune response has been reported. Several putative autoantibodies against neurons and cerebellar cells have been reported. Corticosteroids, corticotrophin and immunomodulating therapy are the mainstay of treatment. Growth failure and delayed puberty has been reported with long term use of corticosteroids in these patients. The etiology for pituitary dysfunction is unclear.

**Conclusion:** To the best of our knowledge, no case of panhypopituitarism has been reported in patients with OMS. We hypothesize that autoimmunity is likely responsible for panhypopituitarism in our patient.

**Abstract #833**

MASSIVE ELEVATION IN SERUM CHROMOGRANIN A DUE TO PROTON PUMP INHIBITOR THERAPY

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Baystate Medical Center

**Objective:** To describe a case of significantly elevated serum Chromogranin A (CgA) which normalized rapidly after discontinuation of PPI therapy.

**Case Presentation:** A 56-year-old male with gastroesophageal reflux disease on chronic PPI therapy was referred for evaluation of elevated CgA. This was initially checked as he was found to have thickening at the pancreatic neck on endoscopic ultrasound, with a background of chronic recurrent pancreatitis of unclear etiology. Fasting CgA was noted to be very high at 4040 ng/ml (Normal 0-225 ng/ml). Gastrin was also elevated at 403 pg/ml (0-115 pg/ml) He had no symptoms or signs of carcinoid tumor or other neuroendocrine tumors. No clinical or biochemical evidence of congestive heart failure, renal insufficiency or liver cirrhosis. Other studies including 24-hour urinary 5-HIAA, plasma metanephrines, normetanephrines, CEA, CA 19-9, insulin and vasoactive intestinal peptide were normal. CT and MRI of the abdomen and pelvis were normal. Somatostatin receptor scintigraphy showed no focal lesions. Given above findings, CgA elevation was suspected to be iatrogenic related to PPI therapy. CgA level was rechecked after discontinuation of PPI therapy for 2 weeks, and was noted to be normal at 62 ng/ml. Following this, PPI therapy was reinitiated with repeat CgA level again rising to 2080 ng/ml.

**Discussion:** CgA is a sensitive but nonspecific marker for neuroendocrine tumors such as carcinoids. It can be falsely elevated in several conditions including chronic heart failure, renal failure, chronic atrophic gastritis and use of anti secretory medications. Fasting CgA levels are elevated in all PPI users, even at very low dosages and withdrawal of PPI therapy leads to normalization of CgA within 1 to 2 weeks. The rise in CgA levels may occur within 6 days of initiating therapy, and tend to increase further with prolonged use. The increase in CgA levels is thought to be due to antral G cell gastrin secretion resulting from gastric acid suppression. This in turn leads to hyperplasia of gastric enterochromaffin-like cells and release of CgA.

**Conclusion:** In most patients treated with PPI, a two to fourfold increase in CgA may be found. However, this case illustrates that CgA can rise massively in response to PPI therapy to the order of 20 fold and normalize rapidly after cessation of therapy. This also demonstrates the importance of discontinuing PPI therapy for at least 1-2 weeks before checking CgA to avoid patient anxiety and unnecessary diagnostic studies.
Abstract #834

DIABETES INSIPIDUS IN BREAST CANCER METASTATIC TO THE PITUITARY STALK: A CASE REPORT

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Objective: Metastases to the pituitary gland are rare and symptomatic in only 6-8% of cases; breast cancer in women and lung cancer in men are the commonest sites of the primary tumor; diabetes insipidus, visual field narrowing and anterior pituitary insufficiency are the most commonly reported symptoms.

Methods: Pituitary MRI and computed tomography scan; water deprivation test.

Case Presentation: B.A., 58 years old woman, diagnosed with breast adenocarcinoma (estrogen receptor- positive 30%, progesterone receptor- positive 30%, cerbB2 negative) 13 years ago, underwent partial mastectomy, chemotherapy, radiotherapy and hormonal therapy (tamoxifen) for 5 years. During evolution, bone and pulmonary metastases appeared. Twelve years later, the patient presented narrowing of visual field and diplopia. MRI revealed macronodular aspect of optic chiasm and thickening of pituitary stalk; hormonal assessment revealed gonadotroph insufficiency (FSH= 10.13 IU/L, estradiol < 20 pg/mL) and mild hyperprolactinemia (52.36 ng/mL). Chemotherapy with Paclitaxel and Bevacizumab was administered and visual field significantly improved and diplopia disappeared. However, the patient developed polyuria and polydipsia one year later. Water deprivation test confirmed central diabetes insipidus. Pituitary CT scan revealed tumoral thickening of proximal pituitary stalk (5.6/6.5/4.5 mm) and normal pituitary gland and optic chiasm. Desmopressin treatment was administered with positive clinical response. There was persistence of gonadotroph insufficiency.

Discussion: The most common sign of metastatic pituitary involvement is diabetes insipidus, because the posterior pituitary lobe is more affected than the anterior lobe; the cause is the lack of a direct arterial blood supply to the anterior lobe and a larger area of contact between the posterior lobe and the adjacent dura mater. However, in our case there is also gonadotroph deficiency.

Conclusion: Pituitary stalk and optic chiasm are unusual breast cancer metastases, occurring in patients with disseminated disease; they may respond differently to the chemotherapy.

Abstract #835

ORAL ANTIDIABETIC MANAGEMENT OF HYPERGLYCEMIA IN A PATIENT WITH CUSHING’S DISEASE TREATED WITH PASIREOTIDE: A CASE STUDY

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Objective: Pasireotide, a multireceptor-targeted somatostatin analog (SSA), has been evaluated as a pituitary-directed medical therapy for Cushing’s disease (CD), and has demonstrated urinary free cortisol (UFC) reductions in the majority of patients. The safety profile of pasireotide is similar to other SSAs, except for rate of hyperglycemia. Management of hyperglycemia in CD patients can be challenging, with varying results. Here, we present a CD patient successfully treated with pasireotide for 15 months who developed worsening hyperglycemia that was effectively managed with oral antidiabetic medications.

Case Presentation: A 57-year-old man presented with signs and symptoms of CD (UFC 231.5 µg/d; normal, <80). He was enrolled in the phase III trial (CSOM230B2305) of pasireotide and received 900 µg BID of study drug. His baseline fasting plasma glucose (FPG) and HbA1c levels were slightly elevated (107 mg/dL and 6%, respectively). Within the first month of treatment, UFC level was normalized (37.3 µg/d; normal, <80), but FPG and HbA1c increased to diabetic levels (175 mg/dL, 7.6%, respectively). Glycemic values remained elevated after 3 months’ treatment with pasireotide (and with no antidiabetic intervention), and the patient was started on metformin. One month later, FPG and HbA1c were further elevated (202 mg/dL and 8%, respectively). Metformin was discontinued and glipizide was initiated. After 1 month of the new therapy, FPG was reduced to 113 mg/dL; HbA1c remained elevated (8%). Over the next 3 months, FPG levels varied from 115-140 mg/dL, then increased to 177 mg/dL, at which point metformin was restarted. Subsequently, FPG levels settled between 125 - 129 mg/dL for the next 2 months, by which time HbA1c was reduced to 6.9%. At month 10 of the study, pasireotide was increased to 1200 µg BID. The patient withdrew from the study after 15 months to pursue surgical treatment for...
his CD. FPG levels returned to baseline levels 1.5 months after pasireotide discontinuation.

**Discussion:** Pasireotide treatment can result in clinically relevant glucose elevation. After 12 months of oral antidiabetic treatment, the patient’s FPG and HbA1c levels were significantly reduced and returned to near baseline levels. However, glycemic values were not completely normalized by the oral medication provided, potentially warranting intervention with insulin or a different class of antidiabetic drug. A DPP-4 inhibitor or GLP-1 agonist may be considered, as these agents address the underlying inhibition of insulin secretion with pasireotide.

**Conclusion:** This case illustrates that substantial reduction in pasireotide-induced hyperglycemia can potentially be achieved with oral antidiabetic agents.

**Abstract #836**

**SUSTAINED IMPROVEMENTS IN CLINICAL STATUS AND QUALITY OF LIFE IN A PATIENT WITH RECURRENT CUSHING’S DISEASE TREATED WITH PASIREOTIDE**

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**Objective:** Cushing’s disease (CD) is associated with numerous comorbid conditions (e.g., central obesity, dyslipidemia), as well as reduced functional status and health-related quality of life (HRQoL). In addition to biochemical measures of treatment success (i.e., urinary free cortisol [UFC] reduction), improvements in signs and symptoms of CD, such as body weight and waist circumference, are important clinical outcomes. Current treatment options for CD beyond pituitary surgery are few, limiting the potential for effective management. In a recent 12-month Phase III study, pasireotide demonstrated mean reductions in cortisol levels, with associated improvements in the signs and symptoms of CD. Here, we report a patient who achieved sustained normalization of UFC, and improvements in clinical symptoms and HRQoL, with pasireotide.

**Case Presentation:** A 67-year-old man presented with signs and symptoms of CD (UFC, 1791 µg/day, [ULN, 50], positive Dex-CRH, and IPSS, mild facial rubor, and dorsal and supraclavicular fat pads). He underwent transphenoidal surgery in August 2008, but had persistently elevated UFC (167µg/day [ULN, 50]), indicating surgical failure. He was enrolled in the Phase III trial one month later and randomized to pasireotide 600 µg BID (increased per protocol to 900 µg BID after month 3). At baseline, he weighed 97.8 kg (BMI, 31.2 kg/m2). He was able to care for himself, but unable to carry on normal activity or do active work (Karnofsky performance status [KPS] <71). Beck depression inventory (BDI) score was 32 and CushingQoL score was 41.7. He achieved normal UFC that was maintained during the 12-month study period. Glycemic status worsened on treatment (peak fasting plasma glucose [FPG], 183 mg/dL), and was normalized with basal insulin and glipizide. After 12 months of treatment, both body weight (86.3 kg) and BMI (27.5 kg/m2) were reduced by 11.8% compared to baseline. Waist circumference also decreased (96 cm at study end vs. peak on-treatment measurement of 109 cm [-11.9%]). He displayed minor signs and symptoms of disease (KPS >90); facial rubor and dorsal and supraclavicular fat pads were absent. Depression and HRQoL were significantly improved (BDI score, 10; CushingQoL, 66.7).

**Discussion:** This case illustrates successful long-term medical treatment of CD with pasireotide. The patient achieved sustained improvements in clinical signs and symptoms of CD and functional performance status, as well as UFC. Further, despite worsened hyperglycemia treated with daily insulin, he attained significant improvements in BDI and HRQoL.

**Conclusion:** In addition to biochemical parameters, clinical signs and symptoms are important measures of CD treatment success.

**Abstract #837**

**EXCESSIVE THIRST DURING PREGNANCY**

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**Case Presentation:** A 38 yo female, 36 w (G2 P1) of pregnancy arrived to the ED complaining of uterine contractions. Her prenatal care was uneventful. On admission, her blood pressure range was 140-150/90-103 mmHg and she had 1+ proteinuria. PE was unremarkable. Fetal heart rate had deep variable decelerations and the patient was taken for an emergent C-section. The newborn had low Apgar scores at 0 and 5 min after delivery, respectively. The patient reported polyuria and polydipsia for the 2 w prior to admission. Significant laboratory data from admission: sodium of 168 mEq/L, BUN of 12 mg/dL, creatinine of 1.29 mg/dL, LDH of 5220 U/L, AST of 634 U/L, ALT of 582 U/L, and osmolality of 333 mOsm/kg. The patient was started on magnesium sulfate for seizure prophylaxis and received 750 mL of LR solution during the C-section with 5% dextrose and 1/2 NS drip thereafter. 2-h
later her Na increased to 172 mEq/L and in the subsequent hours she became drowsy. Urine osmolality was 170 mOsm/Kg, urine Na was 57 mEq/L, and vasopressin level was 8.8 pg/mL. At this point, the patient was transferred to the ICU for closer monitoring. Urine osmolality increased to 622 mOsm/Kg with 10mcg of desmopressin intranasal. Her mental status became normal and Na level as well as her liver enzymes and creatinine decreased to normal values progressively within 96 hr.

**Discussion**: During pregnancy, placenta secretes oxytocinase to degrade oxytocin and prevent uterine contractions. This enzyme also degrades vasopressin and to compensate this, vasopressin secretion is increased. Rarely vasopressin balance is altered and GDI is triggered. GDI has been classified into 3 independent groups: pre-existing DI (exacerbated nephrogenic DI, subclinical vasopressin deficit); transient DI during pregnancy (hepatic disturbance, preeclampsia, acute fatty liver, HELLP syndrome, idiopathic); DI after delivery (Sheehan’s syndrome, permanent hypopituitarism, autoimmune hypophysitis). Our patient had preeclampsia w/ partial HELLP syndrome, any of them can cause a transient liver dysfunction that decreases the degradation of oxytocinase, causing a transient vasopressin deficit until the liver function normalizes. The treatment of choice is desmopressin until remission, same dose as for central DI. It should be noted that sometimes DI of another cause can become symptomatic during pregnancy and can then persist.

**Conclusion**: Gestational diabetes insipidus (GDI) is a rare disorder affecting 4 /100 000 pregnancies. It is important to have GDI in the differential and recognize the key signs and symptoms such as polydipsia and polyuria. Usually this syndrome manifests in the third trimester and is transient.

**Abstract #838**

**ACTH DEPENDENT ADRENAL ADENOMA**

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**Case Presentation**: A 24-year-old, unmarried female admitted in the endocrinology department of BIRDEM 2010 with the complaints of gradual weight gain, excessive facial hair, acne and generalized weakness for two years. She did not take steroid in any preparation. Examination revealed moon facies, facial plethora with acne, hirsutism (Ferriman-Gallway score more than 8), mild frontal baldness, buffalo hump with supraclavicular fat pad, BMI 30.06 kg/m2, waist circumference 91 cm, mild pitting ankle edema, paper thin skin with multiple pale purple striae over lower abdomen directed upwards laterally, breast development stage B5 with no clitoromegaly or acanthosis negricans, thin upper and lower limbs with muscle power grade 4/5. Provisional Diagnosis was Cushing’s syndrome and the differential diagnoses were Pseudo-Cushing’s syndrome, metabolic syndrome or PCOS. Investigation profile are: Hb% 8.2 gm/dl, triglyceride-223 mg/dl, IGT (8.1 mmol/L). HbA1c % 5.7%, FT4-8.17pmol/L, TSH-10.32mIU/L, antithyroid antibody were positive, normal FSH and LH, 24 hour urinary free cortisol 594 nmol/L; Midnight (11pm) salivary free cortisol 35.20 nmol/L, basal cortisol 770.23 nmol/L, Overnight 1 mg dexamethasone suppression test: basal cortisol 685.97 nmol/L, basal ACTH level 17.80 pg/ml, High dose dexamethasone suppression:basal cortisol 501.25nmol/L, USG whole abdomen enlarged left suprarenal gland (23x24 mm) with fatty change in liver, CT scan of abdomen: left adrenal mass (24x23 mm), MRI of sella and parasellar region: pituitary hyperplasia, concluding the diagnoses as a case of Cushing’s disease (ACTH dependent adrenal adenoma variety) with primary hypothyroidism. Patient did not want to have neurosurgery. On 17/4/10 bilateral adrenalectomy was performed. Histopathological study showed that Left adrenal gland was 4.5x4.0x2.5 cm in size and revealed capsulated adrenocortical adenoma brownish yellow in cut surface, composed of cells of zona fasciculata. No malignant cell was seen. Two weeks later patient was successfully discharged with oral glucocorticoid replacement therapy.

**Discussion**: Chronic ACTH excess results in hyperplasia of adrenal zonae fasciculata and reticularis which results in increased secretion of cortisol and androgens. Biochemical tests and adjunctive use of CT, MRI can often provide a diagnosis. In the face of hypercortisolism, a normal or elevated ACTH (>15 pg/ml) level is consistent with an ACTH producing tumor.

**Conclusion**: In recent years it has been shown that in some patients with pituitary-dependent Cushing’s syndrome, a unilateral adrenal nodule suggestive of a cortical adenoma can develop.
Abstract #839

EMPTY SELLA SYNDROME IN A POSTMENOPAUSAL WOMAN

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Case Presentation: Mrs. X, 50-year-old diabetic woman with normal menarche, obstetric, lactation history got admitted in BIRDEM on January 2011 with the complaints of recurrent vomiting, anorexia, loose motion, generalized weakness for 10 days with no unconsciousness or syncope. Previously she suffered from repeated electrolyte imbalance due to adrenal insufficiency. She took steroids irregularly and totally discontinued them 3 months before this episode of illness. She had menopause at 39 years of age. Examination revealed: BMI 21 kg/m², no thyromegaly, pulse 92/min, blood pressure 110/70 mm of Hg with postural hypotension. Clinical scenario suggested diagnosis for this premature menopausal woman adrenal insufficiency, diabetes mellitus. Investigation profile was as follows: Hb%-10.4gm/dl, ESR-15mm in 1st Hour. HbA1C%-10.6%, S. creatinine-0.6mg/dl, S.Chol-220, TG-122, HDL-36, LDL-160. Serum Na, K, Cl and TCO₂ in mmol/L were 109, 3.7, 76 and 26 respectively. On 11/01/11 after steroid replacement values of those were 137, 4.6, 91 and 36 respectively. Hormone study reports were as follows: Basal cortisol - 105 nmol/L [116-1065], S.ACTH -14.80 pg/ml[8.3-57.8], FSH -5.61 mIU/ml[3.2-10.0], LH - 1.29 mIU/ml, S.Prolactin -352.83 mIU/ml[66-1065], TSH -0.37 microU/ml [0.47-5.0], FT4 -8.58 pmol/L [9.14-23.18]. MRI of sella and parasellar region revealed features suggestive of empty sella. Thus clinical parameters, investigation reports suggested that this prematurely postmenopausal woman had been suffering from panhypopituitarism due to Empty sella Syndrome with diabetes mellitus and dyslipidemia.

Discussion: Empty sella occurs predominantly in obese adult women, many of whom have hypertension and diabetes. Conditions that suggest empty sella syndrome are hypertension, hypogonadism, hyperprolactinemia, adrenal insufficiency, low DHEA level, hypothyroidism, low estrogen level, hypertriglyceridemia. In our case, this middle aged women with normal BMI, was suffering from panhypopituitarism due to Empty sella Syndrome with diabetes mellitus and dyslipidemia.

Conclusion: This case gives insight that early menopause warrants proper evaluation, and during evaluation, along with other factors, panhypopituitarism should be considered as an etiology for such condition.

Abstract #840

UNUSUAL PRESENTATION OF PITUITARY APOPLEXY

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Objective: Pituitary adenoma are common, but pituitary apoplexy as a complication is less common. Cerebral infarction as a manifestation of pituitary apoplexy is very rare and there are few cases reported.

Case Presentation: A 63 year old male with past medical history of hypertension, diabetes, prostate cancer presented to emergency room complaining of sudden onset of worsening headache for 5 hours, throbbing 8 out of 10 in severity, accompanied with nausea and no visual disturbance. He is alert, but severely distressed. His neurological exam was positive for right pronator drift without any motor or sensory dysfunction. His computed tomography revealed heterogenous sellar mass measuring 2 x 2.6 cm without any intracranial bleeding. 3 hours later he became more confused, had visual disturbance, slurred speech and developed right sided hemiparesis. Repeated head CT scan did not reveal any changes from prior CT. CT showed complete occlusion of the left carotid artery, acute infraction in the left cerebral hemisphere and hyperdensity within the large pituitary mass suggestive of hemorrhage. He was given stress dose of hydrocortison 100mg and sent for emergent endoscopic transphenoidal section of mass. Histopathology revealed pituitary adenoma with hemorrhage and early necrosis. Cells were immunoreactive for fsh. He recovered well after surgery with some residual right sided weakness.

Discussion: Pituitary apoplexy presents usually with severe headache, visual disturbance and nausea. Apoplexy causing focal neurological symptoms is uncommon. The underlying mechanism for ischemia is attributed to mechanical internal carotid artery compression or vasospasm. Pituitary apoplexy increases intrasellar pressure, which can worsen ischemia and necrosis. Signs and symptoms of hormonal deficiencies should be monitored and replaced carefully. Supportive conservative management is the initial treatment for pituitary apoplexy. Decompressive surgery is recommended in most cases. However optimal time for surgery is debatable for the high mortality rate.
Conclusion: Clinicians should be meticulous when managing patients with cerebral infraction related to pituitary apoplexy.

Abstract #841
AN UNUSUAL CAUSE OF SYNCOPE IN A PATIENT WITH TYPE 2 DIABETES MELLITUS
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Objective: To discuss an unusual case of syncope in a patient with Type 2 Diabetes Mellitus
Case Presentation: A 56 year old Caucasian male with Type 2 Diabetes Mellitus (diet and lifestyle controlled), hypertension (Amlodipine, HCTZ, Lisinopril) and Type 1 Sensory Polyneuropathy, was referred to Endocrinology for Syncope. He is also known to have 3 yrs of neurogenic orthostatic hypotension (NOH), treated with nonpharmacologic therapy (fluids, salt) Over the past month, he had developed at least 30 episodes of heavy coughing followed by syncope. The patient described these episodes as 20 sec. complete loss of consciousness without warning signs, after prolonged coughing, which recoveres spontaneously. Physical examination: BMI 34.22, decreased pinprick, vibration, and position sensations in lower extremities. Laboratory showed the following: AM Cortisol 4.56 mcg/dl, ACTH 9 pg/ml (0-47), TSH 0.70 uIU/ml (0.34-4.82) , Free T4 0.78 ng/dl (0.59-1.61), HgA1C 5.6 % (4-6%), Serum Catecholamines 1114 pg/ml (242-1125) ; urine Metanephrines 98 mcg/24 hr (26-230) and 5-HIACA 4.1 mg/24 hr (0-6.0), Vitamin B12 324 pg/ml (211-911). CXR-severe COPD , EKG-NSR with prolonged QTC=486 mm, Holter-normal, EEG-normal. He was then diagnosed with stage IV COPD and bronchodilator therapy was started. The symptoms improved dramatically and syncopal episodes resolved.

Discussion:This case represents an unusual cause of syncope in a patient with Type 2 Diabetes Mellitus

Abstract #842
ADIPSIC DIABETES INSIPIDUS: CHALLENGES IN DIAGNOSIS AND MANAGEMENT - A CASE SERIES

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Objective: Patients with adipsic diabetes insipidus (DI) are prone to develop severe hypernatremia as well as thermoregulatory disturbances, venous thromboembolism, obesity and seizures. Severe dehydration in these patients can lead to higher than expected urine osmolality and thus may delay the diagnosis of DI. We describe our clinical experience in 5 patients with adipsic DI from 2009-2012 at the Cleveland Clinic.

Methods: Retrospective patient’s chart review.

Case Presentation: All patients were diagnosed with DI and absence of thirst in the setting of severe hypernatremia. All were on DDAVP and daily water replacement at the time of analysis. The primary diagnosis included neurosarcoïdosis (n=2), post pituitary surgery for macro-adenoma (n=2) and hypothalamic germinoma (n=1). Mean (±SD) age was 35±10 y and BMI was 33.6±9.2 kg/m2. Serum sodium and osmolality on initial presentation were 157±7.7 mEq/L and 327±23 mosm/kg, respectively. Three patients had urine osmolality >300mosm/kg (564, 719, 900 mosm/kg) and did not have a 24-hour urine output in the polyuric range (1.5L, 0.8L, 0.6L) on initial presentation. The diagnosis of DI was delayed in 3 patients, who did not undergo pituitary surgery for 7, 11 and 337 days, and was ultimately confirmed by the presence of hypotonic polyuria after achieving eunatremia. All patients had anterior pituitary deficiencies with adequate replacement of thyroid and glucocorticoids. All developed deep vein thrombosis and hypo/hyperthermia during their clinical course. Since the time of initial admission for hypernatremia, the average reflex-mediated hypotension-bradycardia, laryngospasm, augmentation of left ventricular outflow obstruction, impaction of a brainstem herniation, decreased cerebral blood flow, internal jugular vein valve insufficiency, and rarely seizures. No definitive treatment has been discovered other than controlling the cough and other secondary triggers.

Conclusion: This case highlights the importance of evaluating for unusual causes of syncope, which can also occur in a diabetic patient with known neurogenic orthostatic hypotension.
number of hospitalizations not only for hypernatremia but also for hyponatremia has been 5±3 episodes/year with hospital stays ranging from 5-25 days.

**Discussion:** As confirmed in 3 of our cases, adipsic DI may present with misleading urine output and osmolality findings at times of severe dehydration. These findings may be related to an increased renal concentrating capacity at high serum osmolality. Patients with adipsic DI need DDAVP and daily obligate fluid intake. Fluid requirements may rise with increasing obesity and during episodes of hyperthermia.

**Conclusion:** Patients with adipsic DI can develop higher than anticipated urine osmolality during times of severe dehydration. Dismissing the diagnosis of DI might result in recurrent hypernatremia. The co-morbidities of thermoregulatory dysfunction and obesity can alter fluid requirements. These patients should have health care and social support to aid in close monitoring of body weight and serum sodium to avoid recurrent admissions for dysnatremia.

**Abstract #843**

**NOT SO “EMPTY” SELLA**

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**Objective:** To describe a case of adrenal insufficiency as a diagnostic dilemma in a patient with Empty Sella syndrome on chronic opiates and suggest a possible natural history of pituitary cyst leading to Empty Sella.

**Case Presentation:** A 44-year-old African-American female presented to the ER with severe lightheadedness. On admission she was noted to be bradycardic, hypotensive and orthostatic. Initial work up revealed no electrolyte abnormality, a low 7 a.m cortisol level of 4.6 µg/dL and an undetectable baseline ACTH. Further evaluation with a 250 µg ACTH stimulation resulted in a cortisol of 11.3 µg/dL. Other laboratory data: TSH 1.44 µU/ml (0.27-4.2 µU/ml), total T4 8 µg/dL (4.6-12 µg/dL), prolactin 12.3 ng/ml (4.7-23.3 ng/ml), IGF1-137 ng/ml (58-318 ng/ml), GH 0.9 ng/ml (n<3.61 ng/ml), LH 14.3 mU/ml, FSH 33.6 mU/ml. Glucocorticoid replacement therapy was initiated. MRI pituitary revealed an empty sella. In 2004 and 2005, MRI pituitary done as part of investigation for secondary amenorrhea showed a 10 mm pituitary cyst. For last 7-8 years she has been on chronic opiates for back pain. In the following few months, at times when the patient did not adhere to glucocorticoid treatment she was symptomatic and also required hospitalizations for loss of consciousness. Her morning cortisol levels were noted to be persistently low (<1.5 µg/dL) at these visits.

**Discussion:** Our patient’s presentation was suggestive of adrenal crisis, but further evaluation excluded primary adrenal failure. Secondary adrenal insufficiency is an isolated central hormonal problem in this patient. The etiology may be chronic opiate therapy versus Empty Sella syndrome. In our patient, the pituitary cyst seen on the MRIs few years ago is no longer present and has been replaced by an empty sella, likely a result of the former. Medical literature review revealed one case report describing an adolescent with spontaneous rupture of a pituitary cyst leading to an empty sella. This is the probable natural history of the pituitary cyst in our patient. Review of literature suggests variable hormonal deficiencies in patients with Empty Sella syndrome. The hormonal sequelae in our patient remain unpredictable at this time.

**Conclusion:** Patients can develop Empty Sella syndrome from a pituitary cyst that may lead to hormonal deficiencies like adrenal insufficiency. Careful follow up is warranted for patients with pituitary cysts even if considered innocuous initially.

**Abstract #844**

**PROLACTINOMA IN MALES AND CHOICE OF THERAPY**

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**Objective:** The objective of this case report is to highlight late presentation of prolactinoma in males and the choice of dopaminergic agonist.

**Methods:** A case report.

**Case Presentation:** A 43-year old man presented with generalised intermittent headache for 13 years that became severe 7 years prior to presentaion. There was blurring of vision, decrease libido and secondary infertility for 7 years but no galactorrhea or gynaecomastia, no vomiting. He was initially managed for hypertension because of elevated blood pressures when headache was severe. Had MRI 6 years ago which shows a pituitary macroadenoma. Hormonal assays showed Hyperprolactinaemia. Transphenoidal Microsurgery was done with relief of symptoms but the headache relapsed 6 month after the surgery. Repeat MRI shows an enlarged pituitary tumour (2.64*2.26 Cm) and serum Prolactin >100ng/Ml (2.1-17.7) and low Testosterone 1.0 (3-16ng/ml)). He was commenced on Bromocriptine 2.5mg thrice a day which lead to nausea, vomiting, dizziness and lack of concentration. He was converted to Cabergoline 0.25mg twice a week 7 month ago.
Headache has subsided, libido has improved, Prolactin and Testosterone have return to normal levels; 13.9ng/ml and 4.0ng/ml respectively and Pituitary tumour size has decreased to 2*1.6 Cm. His wife is now pregnant.

**Discussion:** Prolactinomas in males present late due absence of commonest features of the disease such as cessation of menstrual and galactorrhea and mostly present as Macroadenomas. Dopamine inhibits prolactin, dopaminergic agonist are the mainstay in the treatment of Macroprolactinoma while surgery is the treatment of choice for microadenoma due to ease of complete resection. Dopaminergic agonist varies in their potency and side effects.

**Conclusion:** Diagnosis of Prolactinoma in Males may be delayed, however Prolactin macroadenoma respond well to medical therapy. Patients that have side effects with Bromocriptine may tolerate Cabergoline.

### Abstract #845

**PRECOCIOUS PUBERTY AND INVASIVE THYROTROPINOMA**

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**Objective:** Thyrotropinoma are a rare cause of hyperthyroidism, while in children this is even rarer. The association of precocious puberty might be related to TSH crossreactivity at gonadotroph receptor level, or to the treatment of TSH-oma itself.

**Methods:** TSH, fT4, T3, were evaluated basal, during TRH and Octreotide tests. GH was measured during OGTT and IGF1, while PRL, E2, FSH and LH as basal sampling. Pituitary tumour was evaluated by 1.5 T MRI scan.

**Case Presentation:** We present a 7 years girl admitted with severe thyrotoxicosis, diffuse goitre and a giant pituitary adenoma, which developed precocious puberty. Basal thyroid function assays confirmed severe TSH-dependent thyrotoxicosis, which was measurable only after 1:50 dilution. TSH was as high as 3450 mU/L, which was not stimulated during the 400 ug i.v. TRH test but suppressed by octreotide from 3500 to 2450 mU/L. Tumour GH co-secretion was documented basal as well as during OGTT (nadir GH=12.1 ng/mL) and by increased IGF1 of 559 ng/ml (N= 52-297 ng/ml).

**Discussion:** After three months when long acting SMSa (Octreotide LAR) were given, thyrotoxicosis was managed by metimazole, and precocious puberty by Cyproterone and Tamofoxifen. After 3 months, E2 normalised, as well as the diameter of ovarian cysts, TSH and GH improved.

**Conclusion:** Thyrotropinoma in children are very aggressive tumours, impact upon height progress and pubertal development, requiring a multiple approach.

### Abstract #846

**PRIMARY CNS B CELL LYMPHOMA AS A CAUSE OF DIABETES INSIPIDUS AND HYPOPITUITARISM**

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**Objective:** To describe a case of primary B cell lymphoma causing diabetes insipidus and hypopituitarism.

**Case Presentation:** A 54-year-old woman with no history of systemic illness seeks ophtalmologist evaluation after developing headaches and left eye blindness of two months of evolution. After initial evaluation the patient develops progressive altered mental status and is admitted to neurosurgery service. Laboratory workup reveals hypernatremia with a urine output over 3 L per day. The patient is consulted to endocrinology service for evaluation of diabetes insipidus (DI). Questioning to patient’s family reveals polydipsia, polyuria, nausea, vomiting, fatigue, increased somnolence, constipation, and amenorrhea of one year of evolution, and right sided weakness. On physical exam patient was critically ill, not following commands. Head and neck examination revealed left eye ptosis, right nasolabial flattening, dry oral mucosa, dry skin with decreased turgor and capillary refill. Laboratory workup as follows: Na: 157 mg/dL, Cl: 119 mg/dL, BUN: 17 mg/dL, Cr: 0.9mg/dL, Total T4: 3.90 ng/L, TSH: 1.087 uIU/mL, prolactin 79.6 ng/mL, cortisol 2.46 ug/dL, urine osmolarity 276. CT Scan reveals a...
suprasellar mass extending to the left thalamus with vasogenic edema on the left hemisphere causing mass effect. Initial working diagnosis due to location of mass includes a glioma vs metastatic brain lesion causing DI, secondary hypothyroidism and hypocortisolism. Patient is treated with hypotonic fluids, DDAVP, levothyroxine, cortisol acetate and Dilantin. A biopsy of the brain mass is obtained. The biopsy was consistent with a large B cell lymphoma (positive for CD79a, CD20, Bcl-6 and Ki67 in 60% of neoplastic cells). Neck, thorax, abdomen and pelvis CT scans were negative for suspicious lymphadenopathy. Patient was transferred to hematology-oncology unit for chemotherapy.

**Discussion:** DI causes include CNS surgery, trauma, tumors, or may be idiopathic in origin. The most common tumor producing DI is craniopharyngioma. Among metastatic tumors, breast and lung cancer can be common culprits. Lymphoma is considered a rare cause of diabetes insipidus, specially like in the present case a primary CNS B cell lymphoma. This case raises the concern that even though, there are more common causes of this condition, we have to keep in mind other diseases in the differential diagnosis of DI, since they warrant a different management and delaying diagnosis can limit the possibility of survival.

**Conclusion:** Even though, lymphoma is a rare cause of DI and hypopituitarism, this possibility should be kept in mind since prompt diagnosis may make the difference in terms of survival.
CLINICAL AND MOLECULAR EVALUATION OF A 47 YEAR OLD FEMALE WITH MOSAIC TURNER 45,X/46,X, PSUDIC YQ11.2 KARYOTYPE

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Objective: This report demonstrates the clinical and molecular evaluation of a treated lady with mosaic Turner syndrome. It adds to the literature focusing on genotype phenotype correlation.

Case Presentation: A woman with Turner syndrome (Mosaic 45. X/46. X,psudicYq 11.2 karyotype) was re-evaluated at the age of 47 years in an endocrine clinic. She was diagnosed at the age of 17 years presenting with primary amenorrhea in a female phenotype with short stature, cubitus valgus and low set ears. She underwent prophylactic gonadectomy at time of diagnosis and placed on replacement hormone therapy. Current analysis by fluorescence in situ hybridization (FISH) and polymerase chain reaction (PCR) showed a 64% 45X cell line and 36% 45 X/XY (psudic. Yq). At the time of her current evaluation her lab results showed an unexplainable rise in transaminases which were normalized after assuring compliance with hormonal treatment in the form of oral tibolone.

Discussion: In this report we highlight the importance of detecting Y chromosome material in a patient with TS as its presence puts the patient at an increased risk for developing gonadoblastoma and thus prophylactic gonadectomy is essential in these patients. We also demonstrate that molecular techniques using FISH and PCR are complementary to classical cytogenetic techniques in the diagnosis of these cases. Molecular studies in our patient showed the presence of a duplicated SRY gene which was sequenced, in her recent evaluation, revealing no mutations. Absence of any signs of virilisation in a mosaic 45. X/46. XY Turner syndrome patient with double SRY could be related to the presence of inactivating mutation in the SRY gene or to the loss of specific a loci critical for sex determination during the formation of the structurally abnormal chromosome, or related to the dominance of the mosaic cell line especially in the gonadal tissue.

Conclusion: The early diagnosis of mosaic Turner involving a Y chromosome cell line with timely gonadectomy and hormone replacement therapy alleviated the risk of developing gonadoblastoma in this case. The genotype phenotype correlation of this type of Turner mosaicism remains under ongoing investigation.

Abstract #901

EFFECTS OF CAFFEINE ON INSULIN RESISTANCE AND GLUCOSE METABOLISM IN WOMEN WITH POLYCYSTIC OVARY SYNDROME

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Objective: Polycystic Ovary Syndrome (PCOS) is characterized by anovulatory menstrual cycles, hyperandrogenism, and insulin resistance. Up to 45% of women with PCOS have impaired glucose tolerance or type 2 diabetes by their fourth decade. Thus, it is important to identify modifiable factors that may impact their metabolic health. Previous studies in older non-PCOS patients have shown that acute caffeine ingestion impairs insulin sensitivity. Thus, the objective of this study was to investigate whether caffeine exerts similar effects in women with PCOS by examining the effects of acute caffeine ingestion on insulin and glucose levels following a mixed-meal tolerance test (MMTT).

Methods: The study was a double-blind, placebo-controlled, cross-over study in which women with PCOS underwent a MMTT after ingestion of caffeine (250 mg) or placebo, followed by a second MMTT after ingestion of the other treatment. PCOS was defined by NIH criteria. Subjects on medications that may affect carbohydrate metabolism (including metformin and oral contraceptives) were excluded. The primary outcome was the within-subject difference in the area under the 2-hour curve (AUC2h) insulin levels between treatment with caffeine versus placebo. Secondary outcomes were within-subject differences of the following: 1-hour insulin, 1-hour glucose, 2-hour insulin, 2-hour glucose, and AUC2h glucose.

Results: Eighteen women (11 Caucasian, 6 African American, and 1 mixed Caucasian/African American) completed the study. Subjects were young (mean age 31.4 [+/- 5.9] years), obese (body mass index 38.5 [+/- 6.7] kg/m2), hirsute (Ferriman-Gallwey score 11.3 [+/- 3.3]), hyperandrogenemic (bioavailable testosterone 10.2 [+/- 3.9] ng/dl), and insulin resistant (HOMA-IR 5.3 [+/-1.8]). There was marked variability in insulin response during the MMTTs among participants. There were no significant within-subject differences in AUC2h insulin or in any of the secondary outcomes. The median (25%,75%) within-subject difference (caffeine minus placebo) in AUC2h insulin was -153 (-2736,
Abstract #902

INFLAMMATORY MARKERS IN POLYCYSTIC OVARIAN SYNDROME AND THEIR ASSOCIATION WITH CARDIOVASCULAR RISK FACTORS.

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Objective: To determine and compare inflammatory markers including adiponectin, visfatin and IL-18 in patients with polycystic ovarian syndrome (PCOS). To find out whether adiponectin and interleukin-18 (IL-18) is associated with markers of insulin resistance, hyperandrogenism and carotid intima-media wall thickness (CIMT) as a cardiovascular disease (CVD) risk factor.

Methods: This is a prospective controlled study involving 60 consecutive euglycemic patients with PCOS (Rotterdam criteria) and 50 age and body mass index (BMI) matched controls were included in the study. After detailed clinical evaluation including anthropometry, besides oral glucose tolerance test, fasting venous samples were analysed for IL-18, visfatin, adiponectin, highly sensitive C reactive protein (hs CRP) and complete lipid profile. We estimated body composition (total body fat and visceral adipocity index, VAI by dual energy xray absorptiometry), CIMT (by Doppler ultrasonography), indices of insulin sensitivity (QUICKI) and resistance (homeostasis model assessment for insulin resistance, HOMA-IR) and free androgen index (FAI). Data were analyzed using online graphpad quickcalc software and P <0.05 was considered statistically significant.

Results: PCOS patients had greater FAI (1.42 ± 0.83 vs 0.64 ± 0.4), higher HOMA-IR (2.13± 1.05 vs 1.91 ± 1.8) and lesser QUICKI (0.156 ±0.025 vs 0.163 ± 0.015) than the control groups. Patients with PCOS have significantly increased serum IL-18 and visfatin levels than that of the control group (IL 18: 213.48± 76.84 vs 170.4 ± 41.11 pg/ml, visfatin: 73.35±11.54 vs 55.56±9.27 ng/ml, p<0.05) and hsCRP (2.56± 0.64 vs 1.62 ± 0.78 mg/l, p=0.004). Similarly the PCOS group had significantly lower level of adiponectin (0.8 ± 0.6 vs 1.04 ± 0.49 ng/ml, p< 0.001). Correlation coefficients of IL-18 were as follows: with CIMT (0.355), FAI (0.328), HOMA-IR (0.345) and waist circumference (0.367), each with p <0.05. Similarly the correlation coefficients of adiponectin were with CIMT (-0.312), FAI (-0.343), HOMA-IR (-0.352) and waist circumference (-0.359), each with p <0.05.

Discussion: There is alteration of adipokines and other inflammatory markers in PCOS with increase in visfatin, IL 18 and hs CRP and reduction in of adiponectin levels. Increased IL 18 and decreased adiponectin levels correlated with insulin resistance, obesity and hyperandrogenism.

Conclusion: This altered adipokine profile is associated with increased CVD risk in PCOS patients, leading to the suggestion that one of these markers like IL 18 can serve as potential therapeutic target in future for decreasing their CV risk.

Abstract #903

MICROPURIFICATION OF PHOSPHOFRUCTOKINASE-1 AND ENZYMATIC INHIBITION BY ASCORBATE IN CANCER CELL GROWTH

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Objective: The objective of this research was to demonstrate that when rabbit muscle is at rest, ascorbate facilitates glycogen storage by inhibiting the glycolytic enzyme PFK-1.

Methods: We compared rabbit and rat muscle PFK-1 inhibitions by ascorbate and ascorbyl fatty acids and some ascorbyl fatty acid derivatives to determine how species differ. PFK-1 was purified by performing an initial suspension, heat step, ion exchange column, and ascorbic acid titrations.

Results: Inhibition analyses from rabbit and rat muscle purification of PFK-1 revealed that L-ascorbyl 2,6-dipalmitate and L-ascorbyl 6-stearate were several folds more inhibitory to PFK-1 than ascorbate. Results showed inhibition of cancer cell growth and metastasis by an ascorbyl fatty acid observed. Since cancer cells require glycolysis as an energy source, we believe that the results observed were due to an inhibition of glycolysis rather
than an decrease of reactive oxygen species (ROS), as was postulated by the authors.

Discussion: These results suggest that other ascorbyl fatty acid derivatives may inhibit also cancer cell growth and metastasis and that it is unlikely that cancer cells would produce a PFK-1 isozyme that is inhibited by ascorbate.

Conclusion: The objective was achieved because with glycolysis inhibited, glucose forms glycogen. When muscle is active, glycolytic enzymes form a complex with contractile proteins that protects them from ascorbate inhibition; glycolysis proceeds, ATP is formed, and muscle contracts. Further research will focus on the reversible and irreversible constants for the Michaelis Menten equilibrium constant, KI.

Abstract #904

WEIGHT LOSS ON SELF IMAGE AND SEXUALITY IN FEMALES WITH CYSTIC OVARIAN DISEASE

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Objective: To evaluate the effects of significant weight loss on sexuality/corporal image/hyperandrogenicity/self image in sexual circumstances.

Methods: Prospective study, on 320 young females, with ages between 20-45 (mean of 31.5±2.4 years), enrolled in the period of June 2010-June 2012, end of study June 2012. 65 cases with hyperandrogenicity secondary to PCOS.

Evaluation: anamnesis, Ferimann Gallwey scale, TVU, FSFI and BESAQ questionnaire, metabolic and hormonal assays. Intervention: low glycemic index diet, caloric intake lowered with 800 kcal/day.

Results: Observed compliance in the follow-up period: 270/320 evaluated women (84.37%), respective 54/65 of PCOS cases (83.07%). Mean weight loss from a BMI of 32.2 kg/m²sc to 26.9 kg/m²sc, respectively in PCOS group from 32.4 to 26.4 kg/m²sc. We observed improvement of sexuality, assessed by total FSFI score: from 101 cases (35 with PCOS) with FSFI < 23 versus to 48 cases (11 with PCOS) after 1 year of intervention. We observed significant statistical improvement of excitability, lubrication, orgasm, sexual satisfaction, starting month 6 of intervention. Also there was a correlation between decrease of hyperandrogenicity and weight loss (free testosterone r=0.5264 p=0.0134), respectively between hyperandrogenicity and increase of self-image, assessed by BESAQ score (0.76, p=0.043). There was also a correlation between BESAQ and FSFI total score, independent of age (0.46, p=0.078).

Discussion: It is a matter of interest that decrease in body weight increases self confidence and self image perception, and increases sexual interest, arousal, desire and satisfaction domains, despite a significant decrease in the levels of hyperandrogenicity.

Conclusion: Significant and sustained weight loss improves hyperandrogenicity, with secondary improvement of sexuality and self image, especially in sexual circumstances.

Abstract #905

TRANSLATION AND VALIDITY OF THE FEMALE SEXUAL FUNCTION INDEX FILIPINO VERSION (FSFI-FIL)

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Objective: To translate and validate the Female sexual function index Filipino version (FSFI-Fil).

Methods: This is a cross-survey validation study following a two-step protocol of translation and cross-sectional validation of FSFI-Fil among Filipino women. Translation was done by forward-backward approach, reviewed by the committee consisting of endocrinologist, gynecologist, clinical epidemiologist, bioethics expert and the authors. Questionnaires were distributed to 85 Filipino ambulatory women aged 19 years old and above with stable marital relationship, no psychiatric illness and with sexually active partner. Analysis was done using SPSS package 20.

Results: Convergent validity test found high correlation of each questionnaire on its respective domain. On the construct validity, 15 out of 19 items were retained on their original domains. In the concurrent validity, good correlation was noted among the 6 domains. Using Receptor Operative Curve (ROC) analysis, the following cut off values were derived: 48.5, 5, 10, 11, 7.5, 9.5, and 5.5 for total sexual function, desire, arousal, lubrication, orgasm, satisfaction and pain domains respectively. Test-retest reliability was high at range of r = 0.94-0.99 while Cronbach’s alpha for overall FSFI score is excellent at 0.953. Preliminary report revealed that age and educational attainment have no significant association on FSFI scores in contrast to diabetes.

Discussion: The study has a good concurrent validity. Although the factor analysis regrouped some items in other domains, majority of which, 15 out of 19 (79%) of the items were retained within the same domain. Overlapping of domains is expected because sexual response involves temporal sequencing and coordination of several phases and each domain may interact with other in complex fashion. Concurrent validity test showed highest interdomain correlation between pain and lubrication,
A 40 year old man presented with growth and reduction of breast size. He is currently on replacement therapy. The patient has remarkable improvement of subjective sexual functions, facial hair, and female pattern of hair distribution. Examination revealed few gynaecomastia that was noticed 20 years ago. It started during puberty and has not regressed since then. Nil galactorrhoea. There was associated history of reduced libido, erectile dysfunction and primary infertility. No history of testicular injury before. Childhood and puberty were reported to be normal. There was no family history of endocrine abnormalities. Examination revealed bilateral gynaecomastia, decreased body and absent facial hair, female pattern of hair distribution, atrophic testes, eunuchoidism [arm span (182cm), lower segment >upper segment]. Hormonal assay revealed hypergonadotropic hypogonadism on the basis of serum testosterone of 0.78ng/ml (normal 1.25-22). LH of 16.8miu/ml (normal 2-15), FSH of 67.6 miu/ml (normal less than 22). Testicular biopsy revealed few seminiferous tubules with thickened basement membrane. Many of the tubules exhibit complete hyalinization with associated hyperplasia of the interstitial cells of Leydig’s. On the basis of the data collected, an assessment of KS was made and the patient was placed on testosterone replacement therapy. The patient has remarkable improvement of subjective sexual functions, facial hair growth and reduction of breast size. He is currently being followed up in medical out-patient unit of Usmanu Danfodiyo University Teaching Hospital Sokoto, Nigeria.

Discussion: Klinefelter’s syndrome is a common genetic form of primary infertility, however it is rarely diagnosed in our environment because of absent cytogenetic studies. A high index of suspicion is thus required to make clinical diagnosis; more so that the patients may remain asymptomatic until they attain puberty. Klinefelter’s syndrome is by no means absent in our environment, and making cytogenetics studies available in Nigeria will improve case identification of Klinefelter’s syndrome.

Conclusion: Klinefelter’s syndrome is the most common genetic cause of human male infertility, but many cases remain undiagnosed because of substantial variation in clinical presentation, insufficient professional awareness of the syndrome itself and lack of cytogenetics analysis in our environment. Early recognition and hormonal treatment of the disorder can substantially improve quality of life and prevent serious consequences.

Abstract #907

OVARIAN HYPERSTIMULATION SYNDROME ASSOCIATED WITH TYPE 1 DIABETES DURING IN-VITRO FERTILIZATION TREATMENT

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Objective: Ovarian hyperstimulation syndrome (OHSS) is an iatrogenic complication of ovulation induction (OI) that is severe enough in 2% of patients to require hospitalization. Type 1 diabetes (T1DM) is not among the known risk factors for OHSS. We describe 2 patients with T1DM undergoing OI for in-vitro fertilization (IVF) who developed severe OHSS.

Case Presentation: CASE 1 A 25 year old woman with multiple sclerosis and well-controlled T1DM for 12 years developed severe OHSS while undergoing OI for resistant anovulation. Her first IVF cycle used leuprolide 20μg/day in the midluteal phase for ovarian suppression. OI was initiated with recombinant FSH 150 IU for 4 days followed by 75 IU for 5 days. Menotropin 75 IU was added on stimulation day 5-9. Choriogonadotropin alfa (r-hCG) 250μg was given, and estradiol peaked at 8115 pg/mL. 29 oocytes were retrieved, and all embryos were cryopreserved. She continued leuprolide 20μg as well as bromocriptine 2.5mg for 7 days. On post-retrieval day #1 she developed abdominal pain, distension and dyspnea.
Her HR was 135, Hct 52.7%, Na 134, and ultrasound (US) showed large ovaries and moderate ascites. She required therapeutic culdocentesis and paracentesis during hospitalization for OHSS. She eventually achieved pregnancy complicated by pre-eclampsia and preterm delivery. CASE 2 A 28 year old woman with hypothyroidism and well-controlled T1DM for 15 years underwent IVF for male factor infertility. Her first OI cycle was complicated by mild OHSS. Cycle #2 used leuprolide 20μg/day in the midluteal phase for ovarian suppression. OI was initiated with recombinant FSH 225 IU for 2 days followed by 150 IU for 7 days. Estradiol peaked at 3046pg/mL, r-hCG 250μg was given and 23 oocytes were subsequently retrieved. All embryos were cryopreserved. 7 days after HCG trigger she complained of orthopnea and tachycardia. US showed large ovaries and ascites. In the ER her HR was 122, Hct 49.5%, Na 132, transaminases 4 times above her baseline and repeat US showed ascites and a small right pleural effusion. During cycle #3 she had another mild episode of OHSS. She ultimately achieved pregnancy complicated by pre-eclampsia and preterm delivery of twins.

Discussion: We report two patients with T1DM and other autoimmune diseases who experienced a total of 4 episodes of OHSS during OI, of which 2 were severe. Additionally, both patients had pregnancies complicated by pre-eclampsia.

Conclusion: T1DM has not previously been reported as a risk factor for severe OHSS. These cases highlight a possible association and the need for further investigation so that patients may be informed of treatment risks.

Abstract #908

ANDROGEN INSENSITIVITY SYNDROME (AIS) AND TESTICULAR TUMOR.

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Objective: To underscore the association between androgen insensitivity syndrome (AIS) & testicular tumor. Methods: We report 2 brothers, w/ same parental linkage w/ androgen AIS consisting of female phenotype, gynecomastia, penoscrotal hypospadias, & undescended testes. Studies done: Hormonal/chromosomal analysis, US/CT/MRI abdomen/pelvis, tumor markers, & histology of resected testis.

Case Presentation: Pt. A: 25 yrs. Old, w/ absent facial & axillary hair, was referred following lt. orchidopexy. Our WU: Karyotype 46, XY, serum testosterone (T) >26 nmol/lx3(RR:9.9-27.8), DHT 497 pg/ml(RR 112-955), hi FSH(31.3)/LH (31.1), androstenedions18.9 nmol/l (RR 2.4-12.6), E2 189 pml/l(RR 28-156).After 4 days of HCG stimulation T was >26 & DHT increased to 725. Alpha fetoprotein 2.6 ug/l RR <=7),HCG <0/1 IU/l. Alpha imaging studies: atrophic rt. testis, hypoplastic seminal vesicles. Rt orchidectomy planned. Pt. B: 28-yrs.US findings: bilateral inguinal testes, had testicle resection, histology: intratubular germ cell neoplasia (IGCN), extensive tubular atrophy, absent spermatogenesis, multiple sertoli cell nodules, leydig cell hyperplasia. Malignant cells strongly positive for placental-like alkaline phosphatase (PLAP) & c-Kit. Two other brothers from same mother were reported w/ ambiguous genitalia, repair of hypospadias & orchidopexy. None of brothers born to step mother had similar problems.

Discussion: Classical AIS is inherited as X-linked. Affected 46,XY individuals are almost always infertile. The defect is due to mutation in androgen receptor. There is wide spectrum of AIS depending on the amount of residual receptor function. Clinical features range from phenotypic females w/ complete AIS, ambiguous genitalia in partial AIS to normal phenotypic male but w/ infertility in minimal AIS. AIS is associated with IGCN. IGCN cells are derived from primordial germ cells. Almost half of the testicular neoplasms are malignant, but transformation usually does not occur until after puberty. Two proteins, are over expressed; PLAP & c-kit receptor. A history of cryptorchidism is the best established risk factor for IGCN & invasive testicular cancer. Between 25 & 100% affected pts. may harbor IGCN. The optimal clinical Rx is uncertain because latent period for this precursor lesion to develop into malignant GCT is uncertain. In pts. who have female identity & who develop virilisation & have XY karyotype, testes should be removed earlier to preserve female phenotype & female gender identity.

Conclusion: A high percentage of pts. are known to have affected relatives, family screening at early life is important. AIS associated with cryptorchidism carries high risk of testicular tumor. These findings indicate the need for orchidectomy.
Abstract #909

XYY MALE WITH SARCOIDOSIS, HIGH PROLACTIN AND PRIMARY HYPOGONADISM

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Objective: We report a case of a man with primary hypogonadism with mildly elevated prolactin and XYY karyotype.

Case Presentation: A 60 year old man with inactive sarcoidosis presented with ejaculatory difficulty for six month with decline in libido over two years. Patient had previously been treated with solifenacin (Vesicare) for overactive bladder but there was no improvement in ejaculation or libido when solifenacin was stopped. He had not fathered any children and he denied history of testicular swelling or injury, breast enlargement, headache, change in size of feet or hands, or usage of steroids or opiates. Exam revealed an obese tall male with BMI=31, height=78 inches, male pattern baldness with abundant hair on chest. Genitalia exam showed normal size phallus and testicles. Initial workup showed low free testosterone and patient was started on testosterone patch by his urologist. Subsequent labs drawn after patient was started on testosterone showed a low free testosterone with high FSH, LH, and prolactin. Testosterone was stopped and 3 months later, repeat labs were consistent with primary hypogonadism with high prolactin. The rest of the hypothalamic-pituitary axis was normal. MRI showed deviation of the infundibulum to the left with normal pituitary. Karyotype showed 47 XYY.

Discussion: 47, XYY karyotype is a known cause of primary hypogonadism. The incidence is 1/1000 males. It can present as delayed puberty and accelerated growth but with normal body proportion by adulthood. It is associated with low IQ and aggressive behavior. Unlike 46, XX and 47, XXY (Klinefelters), androgen secretion in 47, XYY boys remains normal. The association of XYY with prolactinoma is rare. The mildly elevated prolactin in our patient could be secondary to an undetectable microprolactinoma or neurosarcoidosis.

Conclusion: Orchitis and Klinefelters are well known acquired and genetic causes of primary hypogonadism respectively. The role of karyotyping in primary hypogonadism is based on clinical suspicion. Our case demonstrates that karyotyping should be considered in patients with primary hypogonadism with high prolactin levels and normal body proportions. Testosterone replacement therapy should be considered in such patients. The role of dopamine agonists in patients with 47, XYY with high prolactin levels with or without radiologically evident prolactinoma is unknown.

Abstract #910

LEYDIG CELL TUMOR AND ENDOMETRIAL HYPERPLASIA: A RARE ASSOCIATION.

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Crittenton/WSU

Case Presentation: A 58-year-old postmenopausal woman presented with 6-year history of progressive hyperandrogenism. Initially, she noticed an abnormal hair growth on her face, neck, breast, back along with temporal balding. Physical examination revealed frontotemporal hair loss, shaved hair stubs on her face and neck with scattered terminal hair growth on her back and breast with increased muscle mass and clitoromegaly. Transvaginal US showed enlargement of both ovaries with the left (2.3 X 2.5 X 1.8) being larger than the right (1.6 X 1.1 X 2) and endometrial thickening of 13 mm. However, no sonographic evidence of a distinct ovarian mass. Hormonal profile in blood indicated excessive androgenic activity, in the form of elevated testosterone 460 ng/dl (normal range 6-25 ng/dl), free testosterone 95.5 pg/ml (0.6-3.8 pg/ml), DHEAS 137 mcg/dl (35-341 mcg/dl), estradiol 64.5 pg/ml (reference range is < 16.3 for postmenopausal women), LH 4.1 mIU/ml (12.4-70.5 mIU/ml), FSH 2.8 mIU/ml (48.6-143.9), cortisol 13.2 mcg/dl (4-27 mcg/ml). CT and subsequent MRI failed to show ovarian mass. Dilatation and curettage showed atypical complex hyperplasia, the patient underwent total hysterectomy and bilateral salpingo-oophorectomy. Gross histopathology revealed a left ovary that was enlarged with a well-circumscribed 1.5 cm tan solid mass. Microscopic histopathology of the mass showed benign Leydig cell tumor. No focal lesions were detected in the right ovary. Following the surgery there was a dramatic clinical and biochemical improvement.

Discussion: Sertoli-Leydig cell tumor is a rare ovarian neoplasm accounting for less than 0.2 % of ovarian tumors and the majority present at an average age of 25 years unlike our patient which is post menopausal and is almost always unilateral. Our patient has a pure Leydig cell tumor postmenopausally, that proved to be benign. Her endometrial hyperplasia might be due to aromatization of androgen to estrogen and/or the direct effect of elevated androgen on androgenic receptors in the endometrium, very few cases reported regarding coexistence of Leydig cell tumor and endometrial carcinoma which progressed from endometrial hyperplasia.
**Conclusion:** We believe that physicians should keep ovarian androgen secreting tumors in mind as a differential diagnosis of virilization in postmenopausal women and investigate for endometrial hyperplasia to prevent endometrial cancer.

**Abstract #911**

**SERTOLI CELL ONLY SYNDROME: A RARE CAUSE OF MALE INFERTILITY**

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University of Arkansas for Medical Sciences

**Objective:** We report a case of Sertoli cell only syndrome as a rare cause of male infertility. We emphasize the importance of testicular biopsy to determine the etiology of their infertility.

**Methods:** After informed consent, a chart review of the case was performed.

**Case Presentation:** A 39 year old healthy Caucasian man with no history of erectile dysfunction was referred to endocrinology for infertility. He was trying to achieve pregnancy with his partner for one year without success. He had no genital anomalies and went through puberty at a normal age. He denied tobacco and illicit drug use. He had normal sexual libido and was sexually active. Physical examination revealed normal male hair distribution with an adult male voice, a height of 185 cm and weight of 204 lbs. Bilateral testicular size was normal; there was no gynecomastia or breast tenderness. Laboratory evaluation revealed total testosterone levels of 143-189 (280-800ng/dl), free testosterone levels of 5.8-7.1 (8.7-25.1 pg/ml), Sex hormone binding globulin level of 10.1 (14.5-48.4 nmol/L), FSH level of 9.3 (1.5-12.4 mIU/ml), LH level of 4.8 (1.7-8.6mIU/ml) and prolactin level of 6.4 (4.0-15.2ng/ml). MRI sella showed no abnormality. Scrotal ultrasound showed left testicular size of 3.8x1.7x2.3cm, right testicular size of 4.1x1.5x2.6cm with mild right scrotal varicocele. Semen analyses showed complete absence of sperms. Chromosome analysis showed normal karyotype with no microdeletions on chromosome Y. Testicular biopsy showed pure sertoli cell only pattern with azoospermia in 100% of the tubules. He underwent varicocele repair without improvement in fertility. Human chorionic gonadotropin therapy was tried for two years which resulted in normalization of total testosterone level to post treatment level of 527 (260-1000ng/dl). On follow up semen analysis azoospermia was still persistent.

**Discussion:** Male factor accounts for approximately half the cases of infertility. Of these, men with azoospermia comprise about 15-20% of the total cases. The testicular pathology that is associated with non-obstructive azoospermia varies from markedly reduced spermatogenic activity seen on histological examination to spermatogenic arrest and total absence of germ cells or their products. This condition is referred to as Sertoli cell-only (SCO) syndrome or germ cell aplasia which is an uncommon presentation in 13-30% of the azoospermia patients. Chromosomal abnormalities account for only 15-20% of azoospermia and Sertoli cell only syndrome cases. Sertoli cell only syndrome with pure sertoli cell only pattern on histology is a rare cause of male infertility which should be recognized by endocrinologists and testicular biopsy be performed to confirm diagnosis.

**Abstract #912**

**KLINFELETER SYNDROME: IT IS NEVER TOO LATE TO DIAGNOSE AN EASILY MISSED CHROMOSOMAL DISORDER!**

Louna El-Zein, MD, Ali Rizvi, MD

University of South Carolina School of Medicine

**Objective:** To describe a case of Klinefelter Syndrome diagnosed at age 63, and review the literature.

**Case Presentation:** A 63 year old male was admitted to the hospital for chest pain. He had mild mental retardation and a history of deep vein thrombosis, pulmonary embolism, s/p Inferior vena cava filter placement, and chronic venous stasis. Endocrinology consultation was obtained because of acromegaloid features. The patient did not shave regularly because of slow facial hair growth and never had sexual intercourse. He was unmarried and had no biological children. He had eunuchoid body proportions. Height was 6’9”, leg to height ratio 0.59, torso to height ratio 0.44, and arm-span to height ratio 1.059. He appeared to have a speech impediment, with prominent gynecomastia, small testes (< 1 cm in length bilaterally), and sparse axillary, facial, and pubic hair. Laboratory evaluation revealed total testosterone level of 11 ng/dl [300-720 ng/dl] with free testosterone 1 pg/ml [47-244], LH 17 mIU/ml (1.2-10.8), FSH 48 mIU/ml(0.7-10.8), prolactin 13.4 ng/ml [2.5-17.4] and IGF-1=199 ng/ml (50-255), Pituitary MRI was normal. A karyotype of 47, XXY confirmed the clinical suspicion of Klinefelter Syndrome. The diagnosis was discussed with the patient and he received appropriate counseling.

**Discussion:** Klinefelter syndrome (47,XXY), the most common sex chromosome aneuploidy disorder in males, is caused by the presence of an extra X chromosome. It occurs in 1 in every 500 males in the general population. 3% of infertile males have Klinefelter syndrome and it is a frequent cause of hypogonadism. Features include small testes, increased arm span and lower extremity proportions.
length, gynecomastia, developmental delay, speech and language deficits, behavioral issues, learning disabilities, and infertility. About 10% of affected males are diagnosed prenatally, 25% at puberty and another 25% in late adulthood. Amazingly, almost two-thirds of affected individuals are never diagnosed. Of those diagnosed, fully 12% are found in the sixth decade of life, like our patient. Often the diagnosis is made fortuitously as a result of unrelated medical evaluations or hospital admissions.

**Conclusion:** In the appropriate clinical setting, a high index of suspicion should be maintained by health care professionals for the presence of Klinefelter Syndrome. Small testes, low testosterone, and elevated gonadotropins (hypergonadotropic hypogonadism) should prompt further clinical investigation for the disorder. Since the manifestations of the syndrome are often variable, a karyotype analysis should be ordered for confirmation. Early diagnosis and management is essential for minimizing morbidity and enhancing quality of life.

**Abstract #913**

**A CASE OF 46XXDSD: AMBIGUITY LIES WHERE?**

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**Objective:** A phenotypic male DSD in their teens are encountered with psychological trauma as a result of inadequate masculinization. Absence of SRY (SRY negative) presents with ambiguous genitalia at birth and presence of remnants of mullerian structures.

**Case Presentation:** 16 yr old male reported with poor testicular development and absence of moustache and beard. There was no consanguineous marriage of parents. Antenatal and postnatal period was uncomplicated. On examination Ht: 156 cm (25-50th % ile), MPH: 164 cm; US/LS 0.92 Vitals normal; SMR: GII, (bilateral testes scrotal, 06cc), AI, PI. No gynecomastia. Initial FSH, LH, Prolactin values were normal (7.32, 5.82 mIU/ml, 2.65 ng/ml). Total Serum Testosterone (8Am) was low (195.6ng/dl), started on Inj. Testosterone @100 mg I.M/ month with advice to regular follow up. However he reported after 16 months by which time he took 05 Inj. testosterone and was feeling better with increase in height of 4.7 cm, improvement in libido, size of testes (08cc), pubic hair (P 5); (SPL): 6 cm. not started shaving yet. His consultation this time was for development of bilateral gynaecomastia. Repeat FSH and LH were raised (20.7 and 15.8 mIU/ml). Serum Prolactin: 5.6 ng/ml; Total Serum Testosterone:334.5ng/dl. Further evaluation with karyotyping and FISH analysis revealed 46 XX chromosome and SRY negative.

MRI pelvis showed absence of Mullerian structures and normal presence of wolffian duct system.

**Discussion:** 46 XX male can be clinically divided into SRY-positive and the SRY-negative groups. SRY-negative group includes Ovotesticular -DSD and Testicular DSD. Testicular DSD is characterized by a full development of both gonads as testes without any evidence of ovarian tissue. In most cases of 46XX DSD, SRY gene is translocated to the short arm- end of the paternal X chromosome. Molecular analysis in our patient showed absence of SRY, a rare phenomenon in 46 XX male. Testicular DSD is characterized by a full development of both gonads as testes without any evidence of ovarian tissue. In most cases of 46XX DSD, SRY gene is translocated to the short arm-end of the paternal X chromosome. Molecular analysis in our patient showed absence of SRY, a rare phenomenon in 46 XX male. In absence of SRY protein, it is considered male phenotype can also be induced by excessive or absent actions of other determinants within the sexual differentiation cascade such as SOX9, DAX-1, Ad4BP/SF-1. WT1, GATA4, WNT4 FGFr9 and RSP01. His gender identity is male and received testosterone.

**Conclusion:** This case also highlights that there are other factors in male determination other than SRY protein.

**Abstract #915**

**46 XX WITH SRY GENE, A RARE CAUSE OF HYPOGONADISM IN ADULT MALE**

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**Objective:** To discuss an interesting case of male hypogonadism diagnosed with 46 XX gonadal dysgenesis

**Case Presentation:** A 65 yr old male, with post-traumatic stress disorder, bipolar disorder, under-socialized conduct disorder; aggressive type with inappropriate sexual behavior, polysubstance abuse, hepatitis C, HIV (HAART therapy), was referred to the Endocrine Clinic for evaluation and treatment of low testosterone levels with 15 yrs of erectile dysfunction and decreased libido. He has always shaved regularly, has had multiple sexual partners, lives with second wife, and claims to have 23 yr biological son. He was previously prescribed testosterone topical and injections and phosphodiesterase inhibitors with some clinical response. He is non-compliant with his medications and appointments. Physical examination: 52 kg, 165 cm phenotypic male, normal descended testicles, penis and other secondary sexual characteristics. Hormonal evaluation: Total testosterone 24 ng/dl (250 - 1100), free...
testosterone 1.8 pg/dl (35-155), LH 77 mI/ml (1-9), FSH 71 mIU/ml (1-18), prolactin 7ng/dl (2-18), compatible with Hypergonadotrophic hypogonadism. MRI-normal pituitary and DXA scan-osteoporosis. Karyotype analysis: 46, X, der(X), t(X-Y) (p22.3-p11.2), with florescence in situ hybridization (FISH) analysis confirming SRY translocation on the X chromosome. [nuc ish (DXZ1x2, SRYx1, Ycenx0)]; (female karyotype contradictory with the patient’s gender). The patient refused further imaging for remnant streak gonads.

Discussion: The incidence of 46 XX testicular disorder of sexual development is about 1 in 20,000. SRY gene on the Y chromosome is known to regulate gender phenotype. Translocation of SRY gene between Y and the X chromosome engenders a genetically female with male phenotype. Most individuals are identified early in life with a typical presentation of ambiguous genitalia, usually identified at birth, childhood, or in early adulthood. These patients are often shorter, can present with gynecomastia and also have low testosterone levels, azoospermia and infertility. Although most cases are identified earlier in life, this patient’s history and presentation (claims of having a biological child, including non compliance with medical care) delayed the diagnosis until late adulthood.

Conclusion: This case emphasizes the need for a comprehensive history and physical examination in all cases of hypogonadism and erectile dysfunction in order to establish the proper diagnosis. Therefore a karyotype analysis should be performed in all cases of primary hypogonadism despite the age of the patient.

Abstract #916

TRUE HAEMORPHRODITISM: HOW COMMON?

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Objective: The aim of this presentation is to highlight that we have cases of true haemorphroditism in our environment but high index of suspicion and detailed evaluation is needed to confirm the diagnosis.

Case Presentation: A 20yr old divorcee presented with complain of inability of her husband to penetrate, lump in the R labia, cyclical lower abdominal pains and absence of menstruation. Examination found a masculine young lady with a nasal ring, well developed breast, cliteromegaly (Penile like) and well developed R hemiscrotum with rugae containing a firm lump. No lump was palpable in the L labia or along the route of descent. No hisutism or hyperpigmentation. The vaginal pouch was about 3cm and ended blindly. Buccal smear show xy, CT scan shows a gonad in the pelvis L with L fallopian tube, & small uterus. Hormonal Assay-Testosterone 1.3 (0.2-0.8ng/L), 17 β estradiol 400 (130-350pg/ml), progesterone 22ng/ml (Luteal 2-25, Follicular 0.15-0.7ng/ml). Karyotyping, LH, FSH, HCG/HMC stimulation, Inhibin A,B and anti mullarian hormone assays could not be done. Patient had R Orchiecotomy, Vaginoplasty, Nerve sparing clitoral reduction and hysterectomy. The hysterectomy was done because the uterus was unicorneat with atrophic cervix. Samples for R testicular tissue and L ovary were sent for histology. Patient did well after surgery and is expected for follow up.

Discussion: True haemorrhproditism is rare worldwide. Diagnosis in a developing country like ours is usually made late due to child birth at home. Some cases are only diagnosed after marriage and marital disharmony due to detection of abnormal external genitalia by spouses or lack of penetration. There are also numerous challenges at confirming diagnosis in hospital because of limited investigative modalities like CT scans, MRI, Histology and karyotyping that are not available in most hospitals in developing countries.

Conclusion: This presentation shows that we have cases of intersex in our communities including the “rare” True haemorphroditism but some cases present only after marital disharmony.
Abstract #917

TURNER SYNDROME: COMMON, BUT NEGLECTED ENDOCRINE DISORDER

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UMDNJ

Objective: Turner syndrome affects one in 1,500 to 2,500 live-born females, with an average incidence of one in 2000. Yet it is a relatively neglected disease. Turners’ girls and women encounter premature ovarian failure secondary to chromosomal abnormality, and thus, are estrogen deficient.

Results: Girls and women with Turner Syndrome have short stature, subnormal bone mass, cortical bone thinning, and suffer from increased fracture risks. In addition, they also suffer from cardiovascular, immunological, and dermal abnormalities. The short stature responds well to timely administration of appropriate doses of recombinant human growth hormone and estrogen replacement therapies, by near normalizing their adult height and bone mass. However, if untreated they may end up with on average 20 cm shorter than age- and ethnicity-matched females. Turner Syndrome is associated with reduced apparent/areal bone mineral density. Cortical bone density is reduced at the femoral neck and at the radius with somewhat sparing of the trabecular bone till older age.

Discussion: In spite of having lower bone mineral density, current data do not justify Turner patients treating with anti-osteoporosis medications, unless they are postmenopausal, having osteoporosis or fractures. Most of the skeletal abnormalities can be corrected with physiological means: proper nutrition, adequate calcium and vitamin D, weight-bearing exercises, together with appropriate therapy with growth hormone and timely administration of estrogen replacement therapy, and corrections of other hormonal abnormalities if present. These would not only improve the final adult height, but also prevent future development of osteoporosis and fractures.

Conclusion: Achievement of the desired adult height and the female sexual characteristics, and normalizing the bone parameters is feasible in Turner patients with timely administration of recombinant human growth hormone and estrogen replacement therapies. However, less than 70% of girls and women with Turner Syndrome are currently been treated appropriately with hormonal therapies. Thus, the awareness needs to be improved among the endocrinologists and primary care physicians on optimum management of Turner patients.

Abstract #918

TUBERCULOUS EPIDIDYMITIS: AN UNEXPECTED FINDING DURING EVALUATION OF MALE HYPOGONADISM

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Objective: Endocrinologists rely primarily on biochemical data to determine the etiology of male hypogonadism, and because of this may be tempted to defer the genital exam due to patient or physician discomfort. We present the case of 52 year-old man with low testosterone who was found on exam to have a scrotal mass, leading to the important diagnosis of extrapulmonary tuberculosis.

Case Presentation: A 52 year-old man had complained of fatigue and low libido to his primary care physician. He was found to have low testosterone and was started on testosterone gel. When this did not improve his symptoms, he sought endocrine consultation. Physical exam demonstrated a firm right scrotal mass. An ultrasound demonstrated a 2.5 centimeter extra-testicular mass inferior to the right testicle. Orchiectomy was recommended as malignancy could not be excluded. Pathology demonstrated necrotizing granulomas of the epididymis and spermatic cord with fibrosis. AFB and fungal stain of the tissue was negative. The patient was referred to infectious disease and an interferon gamma release assay was positive for tuberculosis (TB). He denied systemic symptoms of TB and had no prior history of TB, though he did live in India until age 20. A chest X-ray (CXR) was negative. The patient was diagnosed with tuberculous epididymitis (TBE) and started on therapy with isoniazid, rifampin and pyrazinamide. Due to uncertainty about his diagnosis of testosterone deficiency, testosterone gel was withdrawn and his gonadal axis reevaluated. He was diagnosed with hypogonadotrophic hypogonadism. Prolactin was minimally elevated and pituitary MRI was normal. He was started on therapy with intramuscular testosterone.

Discussion: Extrapulmonary involvement is seen in ~20% of patients with TB, with the genitourinary system, most commonly the kidneys, representing a common site of involvement. TBE is seen in < 10% of patients. Patients with TBE may be asymptomatic or can present with a variety of symptoms including painful scrotal swelling. The differential diagnosis often includes malignancy. Diagnosis is made by biopsy or surgical pathology, with supporting tests including PCR, interferon gamma release assays, and ultrasound. CXR to exclude pulmonary
involvement should always be performed. TBE is treated with standard multidrug anti-TB regimens.

**Conclusion:** Our case demonstrates the importance of performing a genital exam in patients with male hypogonadism. The genital exam can demonstrate significant findings that may be related (e.g. small testes in Klinefelter’s syndrome) or unrelated (e.g. masses, hernia, varicocele) to the testosterone deficiency.
THYROID DISEASE

Abstract #1000

OVARIAN CANCER METASTASIS TO THYROID GLAND PRESENTING WITH DIFFUSE FDG UPTAKE ON PET SCAN IN A PATIENT WITH HASHIMOTO HYPOTHYROIDISM: A CASE REPORT

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Case Presentation: A 66-year old Caucasian female with history of Hashimoto’s hypothyroidism and ovarian serous papillary adenocarcinoma treated with total abdominal hysterectomy, bilateral salpingo-oophorectomy, chemotherapy and radiation therapy presented with metastatic disease. The patient had been receiving levothyroxine replacement therapy for the past 6 years. Serum TSH was 8.57 mcU/ml (0.4-4 mcU/ml), free T4 1.07 ng/dl and thyroglobulin antibody was 47 IU/ml (<40IU/ml). Surveillance FDG-PET scan demonstrated increased focal uptake in right neck and posterior to clavicular heads and diffuse increased uptake in both lobes of the thyroid. Maximum standardized uptake value (SUVmax) was 8.3 mg/dl and 7.6mg/dl in right and left thyroid lobes, respectively. Thyroid ultrasound revealed diffusely heterogeneous parenchyma without focal nodules. Biopsy of the cervical node and fine needle aspiration (FNA) of both thyroid lobes were positive for metastatic ovarian adenocarcinoma. Total thyroidectomy was performed. Thyroid gross examination revealed tan-pink micro nodular tissue that completely replaced the normal thyroid tissue. Final pathology diagnosis was metastatic bilateral serous papillary carcinoma with positive resection margins and bilateral chronic lymphocytic thyroiditis.

Discussion: Positron emission tomography (PET) is used for evaluation of metastatic cancer. FDG uptake in the thyroid gland is common. Focal lesions are suspicious for malignancy whereas diffuse uptake is often benign, associated with autoimmune thyroiditis and seldom does it represent thyroid cancer or require surgical intervention. Thyroid cancer presenting with diffuse FDG uptake or the thyroid gland being a site of metastasis is rare; but case reports have been documented. In a patient with diagnosis of Hashimoto hypothyroidism diffuse FDG uptake on PET scan is the expected finding and FNA is not mandatory. However, as seen in this patient, it is important to recognize that diffuse thyroid FDG uptake on PET scan does not exclude malignancy.

Conclusion: Focal FDG uptake on PET scan of the thyroid gland is highly suspicious for malignancy with an estimated risk ranging from 25-50% and FNA is recommended. Diffuse FDG uptake is a common finding in Hashimoto hypothyroidism and FNA is not mandatory. However, in a patient with history of non-thyroid metastatic cancer, a PET scan with diffuse uptake should probably prompt additional evaluation.

Abstract #1001

DIFFERENCES AND ASSOCIATIONS OF METABOLIC AND VITAMIN D STATUS AMONG SAUDI PATIENTS WITH AND WITHOUT THYROID DYSFUNCTION: A CASE-CONTROL STUDY

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Objective: In this cross-sectional case-control study we describe the differences and associations in the metabolic patterns of adult Saudis with and without thyroid dysfunction in relation to their vitamin D status.

Methods: A total of 99 consenting adult Saudis (52 controls, 47 cases) were included in this cross-sectional study. Anthropometrics were measured and fasting blood samples were taken ascertaining lipid and thyroid profile as well as PTH, 25(OH)D3 and calcium.

Results: Subjects with thyroid dysfunction had a significantly higher body mass index as compared to controls (p < 0.001). Circulating triglycerides was also significantly higher among the cases as opposed to controls (p = 0.001). A significant positive association between HDL-cholesterol and PTH (R = 0.56; p = 0.001) as well as a negative and modestly significant association between LDL-cholesterol and PTH (R = - 0.20; p = 0.04) were observed. FT3 was inversely associated with circulating 25 (OH) vitamin D3 (R = -0.25; p = 0.01).

Discussion: The main finding of this study is that aside from the conventional and expected differences in the expression of thyroid tests, including iodine and TPO-Ab, patients with thyroid dysfunction also exhibit obesity and elevated levels of triglycerides as compared to controls. One striking finding in this study is the higher mean 25(OH) vitamin D levels among patients with thyroid dysfunction as compared to controls. Our study has a few limitations. The cross-sectional nature of the study and the small sample size limits the findings of the study to at best, suggestive. Several major confounders were also not included. Gender difference cannot be elicited due to the big discrepancy between male and female subjects.

Conclusion: Patients with thyroid dysfunction possess several cardiometabolic abnormalities that include obesity and dyslipidemia. The association between PTH and cholesterol levels as well as the inverse association between vitamin D
status and FT3 needs to be reassessed prospectively on a larger scale to confirm present findings.

Abstract #1002

TYPE 2 MYOTONIC DYSTROPHY ASSOCIATED WITH FOLLICULAR THYROID CANCER

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Objective: Myotonic muscular dystrophy (MMD) is a multisystem disorder caused by unstable nucleotide repeat expansion. The endocrine system is commonly involved, in particular various thyroid diseases. We describe a male with MMD associated with three thyroid disorders; multinodular goiter, subclinical hyperthyroidism, and follicular thyroid cancer.

Case Presentation: A 64 year old male with past medical history of muscle weakness presents in a wheelchair for fine needle aspiration of a thyroid nodule. The patient first noticed to have proximal muscle weakness 20 years ago that gradually progressed. He became wheelchair bound for the past 8 years. He experienced complete heart block which require placement of pacemaker in 1987. He also had bilateral cataracts and sexual dysfunction. On physical examination the patient was bald, the thyroid gland was enlarged with multiple nodules. He had gynecomastia, and decrease muscle strength with muscle atrophy. Laboratory tests were significant for subclinical hyperthyroidism (TSH 0.19 mIU/mL, free T4 0.87 ng/dL), and hypogonadism (testosterone 184 ng/dL). Thyroid sonogram showed multinodular goiter, the largest nodule was 6.5 cm in right lobe. Fine needle aspiration revealed follicular lesion. Surgical pathology confirmed follicular thyroid cancer stage II B [T3 CN0PN0M0]. After surgery the patient received I131 ablation therapy and was maintained on levothyroxine suppression therapy. Unfortunately he passed away at home after choking a piece of meat.

Discussion: MMD results from unstable nucleotide repeat expansions CTG (in type 1) and CCTG (in type 2) which may predispose these patients to develop cancer. Daumerie et al studied the CTG triplet expansion of DMPK gene in a patient with type 1 MMD associated thyroid nodular disease and reported 7 times larger amplification was found in abnormal thyroid tissue compared to lymphocytes, suggesting that anomalies in the DMPK gene might contribute to thyroid dysfunction. Win et al studied cancer risk among 307 patients with MMD type 1 and type 2 and reported an increase risk of thyroid cancer and choroidal melanoma. They observed 6-fold increased risk of thyroid cancer compared with general population. However, Gadalla et al conducted larger multinational study including 1658 MMD patients and identified increased risks for cancers of the endometrium, brain, ovary, and colon, but not thyroid cancer. Conclusion: An association between MMD and thyroid cancer remains unclear. Cases of thyroid neoplasm (3 papillary, 3 medullary, 6 unknown type) associated with MMD have been reported in literature. We report the first case of follicular thyroid cancer in type 2 MMD.

Abstract #1003

ABRUPT ONSET OF MUSCLE DYSFUNCTION AFTER TREATMENT FOR GRAVES’ DISEASE

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Objective: To identify hypothyroid myopathy in patients with normal or near normal thyroid tests.

Case Presentation: Case of a 24 year old female with history of Graves’ disease treated with radioactive iodine 3 months before arrival to urgency, complaining of proximal muscle cramps, weakness, unable to tolerate physical activity for 2 weeks. At the physical examination she was presented with decreased strength in lower extremities, and increased relaxation phase of Achilles tendon reflexes, hard non pitting edema in both legs, and proximal muscle tenderness. Laboratory evaluation was significant for suppressed thyroid stimulating hormone, normal thyroid hormone levels, and increased creatinine kinase. There was no evidence of renal failure or rhabdomyolysis. After admission, intravenous normal saline was administered with transitory improvement of symptoms, and then creatinine kinase decreased. Improvement lasted for 7 days then symptoms relapsed. Creatinine kinase and thyroid stimulating hormone were in an increasing trend. Patient has already been placed on oral Levothyroxine. Then Levothyroxine was given intravenously, and after 3 days Creatinine kinase levels decreased with improvement of symptoms. Patient was discharged on Synthroid. Other tests performed were: Aldolase, myoglobin, EMG, MRI of both thighs (all normal). ANA positive, dsDNA and anti histone antibodies were negative. Four months after discharge patient developed symptoms of hyperthyroidism and suppressed thyroid stimulant hormone, with positive thyroid stimulant and blocking immunoglobulin’s. Propranolol was started and Synthroid was discontinued.
with no new symptoms suggestive of myopathy. In spite of an initial suppressed TSH, the diagnosis of hypothyroidism induced myopathy secondary to 131-I radiation therapy was made most likely due to an acute descend in thyroid hormone levels.

Discussion: Acute myopathy with onset during acute hypothyroidism following treatment of Graves’ disease is rare in adults with only three cases reported. The mechanism involving the myopathy is not yet well understood. In spite of an initial suppressed TSH the diagnosis of hypothyroidism induced myopathy secondary to 131-I radiation therapy was made most likely due to an acute descend in thyroid hormone levels.

Conclusion: Physicians should be aware that hypothyroid myopathy can be triggered by abrupt correction of hyperthyroidism and occur while TSH is still suppressed and with normal or normal to low values of thyroid hormones that are significantly lower than the pretreatment values. Hormone replacement leads to resolution of symptoms and normalization of muscle enzymes serum levels.

Abstract #1004

THYROTOXIC PERIODIC PARALYSIS - A CASE REPORT

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Objective: To present the thyrotoxic periodic paralysis, a rare case presentation.

Methods: A 25 year old male patient, who developed weakness of all 4 limbs having s/s of hyperthyroidism and hypokalemia is presented here as a rare entity.

Case Presentation: 25 yrs old male patient having increased sweating, palpitation, fever, weakness of 4 limbs 3 days ago withshooting pain in the legs while walking. No history of either respiratory, urinary problem, sensory loss in any limb, backache, involuntary movements, pain abdomen and drug intake, trauma or heavy exercise. His past history did not reveal any clinical illness. There was no history of similar illness in the family. On examination, he was conscious afebrile, anxious, had exophthalmos bilaterally. Pulse 94/min, BP 150/70 mmHg. Respiratory, CVS, neurological examination were normal. He had fine tremors of both hands, proximal weaksss in both arms and legs associated with diminished deep tendon reflexes bilaterally. His investigations was normal except Hyponatremia and hypokalemia (S. Na 126 meq/l, S. K 2.0 meq/ L), T3 246μg/dl, T4 18.1μg/dl, TSH 0.01μIU/ml. ABG, X-ray chest normal. USG of thyroid revealed altered echotexture with increased blood flow. ECG showed prolonged QT interval. A diagnosis of hypokalemic thyrotoxic periodic paralysis (HTPP) was made. The patient was put on IV potassium chloride (KCl) and within few hours, he improved. He started moving all 4 limbs next day. Power improved in all four limbs and reflexes returned to normal. He was also given tablet propranolol 3mg/kg body weight. At 3 mhs follow up, he was doing well.

Discussion: Patient usually present with clinical features of thyrotoxicosis and the attack is characterized by sudden recurrent transient episodes of muscle weakness that range from mild weakness to complete flaccid paralysis. Proximal muscles are affected more severely than distal muscles. Sensory function is normal. Peripheral nerve function is normal. Pathophysiology of TPP remain unclear. Hypokalemia occurs due to rapid and massive shift of potassium from the extracellular into intracellular compartment mainly into the muscles. this is probably due to increased Na/K -ATPase pump activity in patients of TPP. Treatment consists of emergent correction with IV KCl and management of thyrotoxic state along with ECG monitoring. Oral propranolol in dose of 3 mg/ Kg is given to reverse paralysis, hypokalemia and hypophosphetemia.

Conclusion: Early diagnosis and prompt treatment are important.

Abstract #1005

PAPILLARY THYROID CARCINOMA MASQUERADING AS A BENIGN MIDLINE CYSTIC LESION WITHOUT MALIGNANT INVOLVEMENT OF THE THYROID GLAND

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Objective: PTC is the most common type of thyroid cancer. Female to male ratio is estimated at 2.5:1 with most preponderance being seen during the fourth and fifth decade. The biggest risk factor is radiation exposure for treatment of childhood malignancy or environmental exposure. Family history of thyroid cancer in a first degree relative or history of a thyroid cancer syndrome can often be found. Importantly, isolated cervical node involvement without any clinical signs of thyroid involvement is also known. Lymph node metastasis may also undergo cystic degeneration making a diagnosis of thyroid cancer difficult especially when the primary focus cannot be identified in the thyroid. A cystic metastasis from PTC usually behaves as a very indolent lesion resulting in erroneous diagnosis as a benign disease process. We present a case of solitary submental nodule of soft tissue with PTC with
cystic degeneration without thyroid gland involvement on excisional biopsy.

**Case Presentation:** A 24-year old male presented with abdominal pain, weight loss, hyperdefecation, palpitations and a testicular mass. Physical exam revealed blood pressure of 138/84, pulse 142, temperature 100.4° F and respiration 16. He was cachectic. Skin was warm and moist. Eyes were normal without exophthalmus. Neck revealed a non palpable . He had prominent cervical chain lymphadenopathy. Lungs were clear and heart was rapid and regular. Abdomen was diffusely tender. Genital exam revealed an enlarged tender left testicle. Neurological exam revealed prominent tremor with brisk reflexes. Mental status was normal. Initial laboratory data included a thyroid stimulating hormone < 0.01 µIU/ML (0.3-4.5), free T3 11.0 NG/DL (1.7-4.2), free T4 8.95 (0.6-1.2), human chorionic gonadotropin (HCG) > 400,000 IU/L. Testicular ultrasound confirmed a left testicular mass. Chest x-ray showed diffuse bilateral nodules, and CT chest, abdomen, and pelvis showed numerous bilateral pulmonary masses and retroperitoneal lymphadenopathy in the region and extending into the common ILIAC region.

**Discussion:** His clinical presentation and abnormal thyroid function tests were consistent with thyroid storm with a score of 45 using the Burch and Wartofsky criteria (a score of >45 is highly suggestive of thyroid storm). He was also diagnosed with a metastatic testicular choriocarcinoma based on serum and radiological findings. The hyperthyroidism was treated with methimazole and propanolol and the metastatic testicular choriocarcinoma was treated with cisplatin and etoposide. After four cycles of chemotherapy his laboratory data revealed TSH 0.15 µIU/ML, free T4 0.88 NG/DL, and HCG 99.6 IU/L.

**Conclusion:** Both HCG and TSH share a common alpha subunit. Therefore, high levels of HCG can stimulate the TSH receptor of the thyroid gland and result in hyperthyroidism. This case demonstrates a very uncommon presentation of a presumably controllable malignancy. It is important for clinicians to be aware that although very rare, thyroid storm can be associated with testicular cancer if not recognized and treated promptly and can further compromise treatment of the underlying cancer.
Abstract #1007

HYPOTHYROIDISM REVEALED BY DILATED CARDIOMYOPATHY

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Objective: Aim: To report the case of a heart failure secondary to dilated cardiomyopathy incidentally found to have primary hypothyroidism.

Case Presentation: A 39 year old lady presented with a month’s history of recurrent episodes of chest tightness, breathlessness and paroxysmal nocturnal dyspnoea. There was also history of excessive sweating, heat intolerance and weight gain in the previous 6 months. An anterior neck swelling was noted at presentation. She had history of secondary infertility and uterine fibroids with menorrhagia which had worsened in the last 1 year. She was not previously known to have hypertension or diabetes however her blood pressure was elevated at presentation with persistently elevated diastolic readings. She had signs in keeping with congestive cardiac failure. ECG showed sinus tachycardia with non specific T wave changes. Echocardiography revealed an ejection fraction of 16%, global hypokinesia and dilated cardiac chambers, consistent with a diagnosis of dilated cardiomyopathy. Thyroid function test (TFT) result was in keeping with primary hypothyroidism (TSH- 7.31u/ml, FreeT4 - 6.7pmol/l, FreeT3 - 4.2pmol/l). She was commenced on L-thyroxine 50µg daily along with medications earlier prescribed for management of heart failure. Repeat TFT after 2 months showed normal thyroid function. Repeat echocardiography 5 months after presentation also showed an improvement in ejection fraction from 16% initially to 28.30%.

Discussion: Thyroid dysfunction is known to have major effects on the heart and cardiovascular system, but heart failure is reportedly rare in hypothyroidism due to lower oxygen demand in the peripheral circulation. Dilated cardiomyopathy is usually an idiopathic disease with poor prognosis. However, some cases have been found to be reversible with identification and treatment of the underlying aetiological factors. Although the diagnosis of hypothyroidism in this patient was incidental, it may have been a specific cause of the dilated cardiomyopathy. The addition of L-thyroxine to this patient’s therapy appears to have led to an improvement in her cardiac function. Thyroid hormone assay should therefore be performed in persons with dilated cardiomyopathy so as to help in determining possible causative factors thus aiding adequate treatment and recovery.

Conclusion: Thorough examination and investigations are important in persons with dilated cardiomyopathy in order to promptly identify and treat reversible causes such as hypothyroidism.

Abstract #1008

SUBACUTE THYROIDITIS PRESENTING AS TOXIC ADENOMA

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Objective: To describe a diagnostically challenging presentation of DeQuervain’s subacute thyroiditis (SAT) that mimicked toxic adenoma (TA) on radioactive iodine uptake (RAIU) scan.

Case Presentation: A 33-year-old Hispanic woman presented with anxiety, fatigue, hair loss, and mild neck pain. Labs showed TSH <0.01 mIU/L (0.5-5 mIU/L) and free thyroxine 2.4 ng/dL (0.8-1.8ng/dL). Examination revealed bilateral thyroid enlargement but no distinct nodules or bruit. The patient had no history of iodine exposure and no family history of thyroid disease. I-123 RAIU scan revealed a single, focal area of elevated I-123 uptake (12.7%) in the lower pole of the left thyroid and suppression of the remainder of the thyroid. Ultrasound revealed bilateral heterogeneity and mildly increased vascularity, but no discreet nodules; biopsy was not indicated. The patient was referred for I-131 radioablation. However, the patient did not present for treatment, due to travel obligations. Instead, she presented to us one month later, still reporting neck pain and fatigue. At that point, bloodwork revealed serum TSH 36.04 mIU/L and FT4 0.8 ng/dL, now consistent with the hypothyroid phase of SAT. Thus, I-131 therapy was no longer indicated. The patient followed up three months later; at that time, she was asymptomatic and euthyroid, consistent with the natural course of SAT.

Discussion: In patients presenting with thyrotoxicosis, a RAIU scan can distinguish SAT from TA; both conditions may present with thyrotoxicosis. SAT is thought to result from a viral infection, leading to thyroid inflammation and uniformly suppressed RAIU. An adenomatous nodule is thought to result from sporadic TSH receptor gene mutations and is classified as “toxic” if it hypersecretes T4. A TA appears “hot” on RAIU scan if it has elevated RAIU compared to the rest of the gland and the patient presents in a thyrotoxic state. This case depicts a rare presentation of DeQuervain’s SAT as a hot nodule. In our literature search, we saw
this presentation reported only four times. Investigators described three possible pathological mechanisms: a transient antibody-mediated process similar to that of neonatal Graves’ disease, coexisting SAT and TA, or an “incomplete” case of SAT that left a nodular area of the gland untouched.

**Conclusion:** Both TA and the acute thyrotoxic phase of SAT may present with thyrotoxicosis. A RAIU scan usually distinguishes the two conditions, but this case illustrates how the thyrotoxic stage of SAT may mimic TA on a 123-I RAIU scan by showing a hot nodule, instead of uniform thyroid suppression. Both TA and SAT should be considered in the differential diagnosis of patients presenting with thyrotoxicosis.

**Abstract #1009**

**PROPITHIOURACIL ASSOCIATED VASCULITIS**

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**Objective:** To present a rare side effect of propylthiouracil and review its diagnostic considerations.

**Case Presentation:** 32 yo female with Graves’ disease presented with a skin rash of 3 weeks duration. Skin exam was significant for numerous tender, hemorrhagic bullae with an erythematous base involving her bilateral lower legs and thighs. Medical history was significant for a pulmonary embolus 5 months ago. Medications prior to admission included warfarin, PTU, and atenolol. She underwent a skin biopsy which revealed brisk leukocytoclastic vasculitis with leukocytoclasis, neutrophilic infiltrate, and vessel wall damage. Fibrin thrombi were noted in small and medium vessels. Thyroid studies revealed TSH <0.005 MCU/ml (0.27-4.2), total T3 416 ng/dl (80-200), free T3 13.2 pg/ml (2.3-4.2) and free T4 1.6 mg/dl (0.9-1.8). Serologic work up revealed c ANCA <1:20, p ANCA <1:20 but atypical pANCA positive at 1:320. ANA, rheumatoid factor, MPO antibody, anti double-stranded DNA and PR-3 antibody were negative. D-dimer was positive at 2.48 mcg/ml (0-1.19), PTT was normal and antidiardiolipin IgM antibody positive at 39 MPL U/ml (0-12). The antidiardiolipin IgM antibody was also positive 5 months ago when it was drawn prior to anticoagulation for her pulmonary embolii. The atypical p ANCA and antidiardiolipin positivity suggested PTU induced vasculitis. PTU was promptly discontinued. High dose steroids were initiated and the patient underwent thyroidectomy. The skin lesions improved after PTU was stopped.

**Discussion:** Common side effects of PTU include leukopenia, agranulocytosis and abnormal liver function tests. A less common side effect, vasculitis, has been reported in the literature though its occurrence remains rare. As in our case, it is typically associated with ANCA positivity. The mechanism of the vasculitis remains poorly understood. Our patient was also found to be antidiardiolipin IgM positive. This unique combination of ANCA and antidiardiolipin IgM positivity has been associated with drug induced vasculitis particularly with antithyroid drugs. Though hyperthyroidism itself can lead to a hypercoaguable state, the presence of antidiardiolipin antibody warrants consideration for discontinuation of PTU therapy. As there have been fatal cases associated with PTU vasculitis, early recognition of this problem is crucial.

**Conclusion:** Patients with Graves’ disease are predisposed to a variety of autoimmune problems. This makes differentiating between drug induced side effects and Graves’ itself very challenging. Our case demonstrates the importance of maintaining a high level of clinical suspicion for PTU related side effects.

**Abstract #1010**

**THYROID METASTASES TO THE AXILLA: TWO RARE CASES OF PAPILLARY AND MEDULLARY THYROID CARCINOMA**

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**Objective:** Thyroid cancer metastatic to the axilla is an extremely rare event. Here we describe two patients, one with papillary thyroid carcinoma (PTC) and one with medullary thyroid carcinoma (MTC), who developed axillary lymph node (LN) metastases, and compare them to the few cases in the literature.

**Case Presentation:** Case 1 - A 56 year-old Bangladeshi female that initially presented with heat intolerance and weight loss underwent total thyroidectomy (TTx) and radioiodine therapy in 2004 for stage IV PTC (lung and bone metastases). She was treated in 2008-09 with vascular endothelial growth factor antisense, lapatinib, vinorelbine, and triapine for progression to the liver; then sorafenib in 2011-12 for spread to the chest wall. In 2012, screening mammography detected multiple masses, which subsequent magnetic resonance imaging revealed to be level I axillary LNs. Fine needle biopsy (FNA) demonstrated metastatic PTC with a corresponding
thyroglobulin (Tg) level of 1859. The patient underwent a right axillary node dissection with 2/28 positive LNs and post-Tg level of 583. Case 2 - A 59 year-old Hispanic male that presented with a painful, enlarging neck mass, weight loss and diarrhea underwent a TTx and bilateral modified neck dissection in 2011 for stage III MTC (37/63 lymph nodes positive). He was started on vandetanib, however, his calcitonin levels trended upwards from 687 to 989, at which time a positron emission tomography scan revealed a hypermetabolic LN in his left axilla. After two failed FNAs under radiologic guidance, an excisional left axillary LN biopsy showed metastatic MTC. A subsequent completion left axillary LN dissection revealed 14/40 positive LNs and a post-calcitonin level of 411. He has since recurred in supraclavicular LNs.

Discussion: There are only 12 other reports of axillary node metastases from thyroid cancer in the literature, 7 PTC, 2 mucoepidermoid carcinoma variants, and 1 each of follicular, MTC, and poorly differentiated mucin-producing adenocarcinoma. Most patients presented with large infiltrating tumors and widely metastatic disease at the time of diagnosis. However, the exact pathophysiology of metastatic spread to axilla region has yet to be established.

Conclusion: PTC and MTC metastases to the axilla are exceedingly rare, can occur in both males and females, and are indicative of late manifestations of widely metastatic disease. Surgical resection remains the standard of care, although these findings are often poor prognostic indicators.

Abstract #1011

PRIMARY HYPERPARATHYROIDISM IN A FIRST TRIMESTER WOMAN WITH HYPEREMESIS AND PANCREATITIS

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Case Presentation: A 31 year old G3P2 woman was admitted at 11 weeks gestation for refractory nausea and vomiting with hypercalcemia and mild pancreatitis. Labs revealed elevated serum calcium of 12.6mg/dL, PTH 103pg/ml, low phosphorus 1.6mg/dL, low normal 25-OH Vitamin D 25ng/ml, high 1, 25-OH Vitamin D 129pg/ml, creatinine 0.53, and high spot urine calcium of 29mg/dL, consistent with primary hyperparathyroidism. Thyroid ultrasound revealed 1x0.6x0.4cm right lower parathyroid adenoma. She was medically managed initially and discharged with plan for second trimester parathyroidectomy. However, follow-up calcium rose to 14.1mg/dL a few days later, and she was symptomatic; urgent parathyroidectomy was performed at 12 weeks gestation without maternal or fetal complications.

Discussion: Primary hyperparathyroidism during pregnancy is rare, comprising 0.5-1.4% of cases. Up to 80% of patients remain undetected due to masking of hypercalcemia by hypoalbuminemia secondary to plasma volume expansion. Presenting symptoms are often mistakenly ascribed to pregnancy. It is therefore essential to have a low index of suspicion for primary hyperparathyroidism during pregnancy, as early diagnosis and treatment lowers maternal and fetal complications. Maternal complications for moderate-severe cases (up to 65%) include hyperemesis, muscle weakness, nephrolithiasis, bone disease, mental status changes, hypercalcemic crisis and pancreatitis. Fetal complications (up to 80%) include miscarriage, postpartum neonatal tetany (due to fetal PTH suppression), permanent hypoparathyroidism, low birth weight, preterm delivery, intrauterine growth retardation and fetal demise. Complications are rare with mild asymptomatic hypercalcemia where medical management may be appropriate, postponing surgery until after delivery. Parathyroidectomy during second trimester is the therapeutic gold standard for symptomatic patients. It is considered safe and effective (as organogenesis is complete) with low risk of fetal loss. Severe cases need urgent surgery regardless of gestational age. Third trimester surgery allows for fetal parathyroid regeneration but its safety is under debate; one series showed 94% success. Women with known disease planning pregnancy should undergo parathyroidectomy prior to conception.

Conclusion: Primary hyperparathyroidism in pregnancy is rare but treatable. Surgery is the definitive treatment modality, safest in the second trimester. Some practitioners are willing to medically treat mild asymptomatic hypercalcemia; others advocate offering all patients surgical intervention. Treatment approach should be individualized, estimating the best outcome.
Abstract #1012

METASTATIC MICRO-PAPILLARY THYROID CANCER TO BONE, AN UNUSUAL CASE

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Objective: Papillary thyroid microcarcinoma (PTM) is defined as a papillary thyroid cancer <1.0cm in diameter. Although most PTM are localized, with favorable behavior, distant metastases can be seen occasionally. At the time of diagnosis, PTM is often found within the thyroid or spread to cervical lymph nodes. We present an unusual case of metastatic PTM to scalp, bone and dura.

Case Presentation: A 65 y/o female initially presenting to neurosurgery for a recurrent right temporal scalp mass and imaging that showed a 4.4 x 3.4cm tumor within the bone, extending into the dura with mass effect and outside to soft tissue. She was asymptomatic and physical exam was remarkable for a large, non tender, rubbery right temporal mass. Biopsy revealed papillary thyroid cancer with follicular features.

The patient underwent resection of the right temporal tumor with a craniectomy, cranioplasty and removal of the involved dura. Pathology confirmed papillary thyroid cancer with bone remodeling and extension into the dura and adjacent brain tissue. Pathology of subsequent total thyroidectomy discovered a 3mm PTM in the isthmus with negative margins and no capsular, thyroidal, lymphovascular or perineural extension; two recovered lymph nodes were negative for neoplasm. Thyroglobulin level after surgery, while on levothyroxine therapy, was undetectable.

After completing ten cycles of adjuvant external beam radiation, tumor growth stabilized.

Discussion: Thyroid microcarcinoma is papillary in 85% of the cases and is usually an incidental finding in thyroidectomy samples. Micropapillary carcinomas are slow growing tumors; distant metastasis is very rare, mainly because it predominantly invades regional lymphatic tissue. Less common metastatic sites for non-incidental PTM are submandibular/salivary glands, lungs, skeleton and brain. Distant metastasis is associated with a worse prognosis. Our patient presented with bone, dura, and brain metastasis without lymph node invasion, yet the tumor retained histological features of papillary thyroid cancer.

Conclusion: Papillary microcarcinoma may be aggressive with multifocal disease found in about one third of the tumors, spread to local lymph nodes in 30%, extrathyroidal invasion in 20% and distant metastases in 3% along with higher relapse rates. This suggests that histologically similar papillary thyroid cancers may have different gene mutations that regulate aggressiveness and metastatic properties. Future genotyping studies in thyroid cancer are essential to explain why certain thyroid tumors acquire aggressive metastatic traits.

Abstract #1013

A CASE OF PROPYLTHIOURACIL (PTU) INDUCED ANTINEUTROPHIL CYTOPLASMIC ANTIBODY (ANCA) POSITIVE CUTANEOUS VASCULITIS IN A HISPANIC WOMAN

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Objective: To report a case of PTU- induced cutaneous vasculitis associated with antimyeloperoxidase (MPO)-ANCA and anti-proteinase (PR3)-ANCA.

Case Presentation: A 40 year old Hispanic woman presented with a painful rash of 3 weeks duration, which started on her legs but gradually spread upward. She had been diagnosed with Graves’ disease in January 2011, with a high free T4 (4.54 ng/ml, (0.80-1.80)), undetectable TSH (<0.004 uIU/ml) and positive anti-TPO and anti-thyroglobulin titers. Since then she had been hospitalized 4 times for recurrent thyrotoxicosis with high output cardiomyopathy and medication noncompliance. She also had bipolar disorder, hypertension and possible methimazole (MMI) allergy. She was currently on PTU 100mg TID, and 4 days prior to admission had been given SSKI in preparation for thyroidectomy. She denied any flu-like symptoms or arthralgias. Her other medications were Aripiprazole, Carvedilol and Ranitidine. On examination, she was afebrile with BP 110/68 mm Hg and HR 110 beats/minute. She had diffuse thyromegaly without bruit and no ophthalmopathy. Skin showed tender papules and non blanchable, purpuric lesions bilaterally over her calves, thighs, buttocks and abdomen and a necrotic lesion on her left ear. Her TSH was <0.01 uIU/ml (0.27- 4.20), free T4 1.11ng/ml (0.93-1.70) and total T3 0.85 ng/ml (0.80-2.0). CBC, metabolic panel and urinalysis were normal. She had elevated levels of p-ANCA 1:640, anti-MPO 49.7 U/ml (0.0-9.0) and anti-PR3 36.0 U/ml (0.0-3.5). Previous records revealed that her c-ANCA, p-ANCA and atypical p-ANCA had been negative in February 2011. Skin biopsy was consistent with neutrophilic vasculitis. PTU was stopped and solumedrol was begun: the skin lesions
slowly regressed. She was not a candidate for radioiodine ablation due to recent KI intake; hence was referred for thyroidectomy. 

**Discussion:** ANCA-positivity is often present in patients treated with PTU, and is less common with MMI. The development of vasculitis, however, is a rare, but well-documented side-effect, which seems to be more common in Oriental patients. The majority of patients with PTU-induced vasculitis are positive for MPO-ANCA; however our patient was also positive for PR3-ANCA. Positivity to both MPO-ANCA and PR3-ANCA has been infrequently reported, and such patients may be more likely to develop overt clinical vasculitis. Although there can be multi-organ involvement, our patient only displayed skin involvement. Mechanisms for ANCA-positivity and vasculitis caused by PTU are not well defined.

**Conclusion:** We report a rare case of PTU induced cutaneous vasculitis with antibodies against both MPO-ANCA and PR3-ANCA in a Hispanic woman.

Abstract #1014

**THYROID TEST ABNORMALITIES ASSOCIATED WITH CHRONIC USE OF QUETIAPINE**

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**Case Presentation:** Quetiapine is an atypical antipsychotic commonly used in psychiatric patients due to presumed more favorable side-effect profile. We report three adult male patients with schizophrenia and depression who developed abnormal thyroid function tests after administration of Quetiapine. All three patients had normal thyroid tests prior to initiation of treatment. Patient A had been on Quetiapine since 2004 with doses ranging from 400 to 800 mg daily, with the maximum dose consumed consistently since 2008. Thyroid function tests were within the normal range up to 2010 when low circulating FT4 concentration of 0.54 ng/dL (n: 0.76-1.46) associated with borderline high TSH levels 4.42 µlU/mL (n: 0.48-3.96 µlU) was observed. Since then, while FT4 levels have remained minimally lower than the normal range, circulating TSH concentrations have been variably normal to minimally elevated (3.5 to 4.9µlU/mL). Similar pattern of thyroid function tests abnormalities were detected in patients B and C after receiving Quetiapine in lower doses ranging from 25 to 200 mg/day. More specifically, patient B was on relatively low doses of Quetiapine (25-75 mg) for close to a year prior to the first encounter of increased TSH level (7.6 µU/mL) accompanied by decreased serum FT4 concentration (0.75 ng/dL). Follow-up in this patient while on Quetiapine doses of 50-100 mg/day for the past 2 years has revealed FT4 levels minimally below the lower limit of normal (0.58-0.73ng/dL) with serum TSH concentration in the normal range or marginally elevated (2.36-5.72 µlU/mL). Patient C was on Quetiapine for over 2 years at a 200 mg dose for the most part before an increased TSH level of 7.36 µU/mL was documented. While the FT4 level was normal at that point, measurements during a follow-up period of over one year have demonstrated low levels (0.68-.73 ng/dL) with continuing minimally high TSH concentrations.

**Discussion:** Quetiapine-induced thyroid function test abnormalities in these 3 subjects are for the most part characterized by marginally decreased FT4 in concert with borderline increases in TSH, suggestive of a state of central hypothyroidism. These changes appear to be more treat-duration rather than dose dependent.

**Conclusion:** The present cases and limited previous reports cannot conclusively differentiate between Quetiapine-induced nonspecific thyroid test abnormalities versus Quetiapine-provoked hypothyroidism. Such predicament can only be rectified by future prospective studies.

Abstract #1015

**JUSTIFICATION FOR SCREENING TYPE 2 DIABETES PATIENTS FOR PRESENCE OF OVERT OR SUBCLINICAL HYPOTHYROIDISM**

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**Objective:** Thyroid disease is common in general population & prevalence increases with age. Subclinical hypothyroidism & overt hypothyroidism are recognized risk factors for atherosclerotic cardiovascular disease, hyperlipidemia, low grade inflammation & hypercoagulability. Type 2 diabetes(T2DM) is a major risk factor for atherosclerosis & cardiovascular disease. As diabetes & hypothyroidism are independent risk factors for the same disease process, it is possible that patients suffering from both these disease entities may have a compounded risk. Our study is an effort to investigate the proposed association between these two disease entities and to identify the factors that increase the risk of this association.

**Methods:** A cross sectional study in a tertiary care hospital in Kolkata, India. 1485 patients, 20-70 years old, attending Endocrinology & Diabetes clinic, were studied.
between January to April, 2012, for 4 months. 1059 patients had T2DM (624 males, 435 females), 426 (96 males, 330 females) had hypothyroidism only. TSH, FT4 were measured using electrochemiluminescence immunoassay. Anti thyroid peroxidase (TPO) antibody measured in all patients with raised TSH, using enzyme linked immunosorbent assay. Baseline characteristics between the groups were compared with Student’s “t” test. Chi-square test was used to analyze association between T2DM & hypothyroidism. Logistic regression analysis was applied to identify association between hypothyroidism & the patient characteristics in the study group.

**Results:** 1485 patients, 720 males (48.48%), 765 females (51.51%), mean age 46 ± 9.4 years. Of 1059 patients with T2DM -- 435 females (41.08%), 624 males (58.92%). Of the 426 patients with hypothyroid only, 96 males (22.53%), 330 females (77.46%). In the entire group, 231 patients (93 males (40.25%), 138 females (59.74%) had T2DM & hypothyroidism coexisting together. This is 15.56% of the total group having both hypothyroid and T2DM associated together. 2x2 Chi square test was used to look for association of T2DM & hypothyroidism & independence value of Chi square was rejected, thereby proving association of T2DM & hypothyroidism. Logistic regression analysis recognized the association between female gender (P = 0.031) & hypothyroidism (P = 0.011) more strongly when compared with males.

**Discussion:** Thyroid dysfunction may have physiological effects. Subclinical hypothyroidism can raise serum LDL cholesterol & worsen dyslipidemia. Since T2DM patients are at high risk for atherosclerosis & cardiovascular diseases, diagnosis and treatment of thyroid diseases is important.

**Conclusion:** Hypothyroidism & T2DM may coexist. Screening patients with T2DM for hypothyroidism may be justified to treat cardiovascular risks.

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**SEVERE HYPOTENSION ASSOCIATED WITH CALCIUM CHANNEL BLOCKADE IN THYROID STORM: A CASE REPORT**

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**Objective:** Congestive heart failure (CHF) and atrial fibrillation (AF) are common cardiac manifestations of thyroid storm. We describe a case of heart failure and AF due to unrecognized thyroid storm treated with an intravenous calcium channel blocker (CCB), with subsequent severe hypotension.

**Case Presentation:** A 60 year old woman, with no pre-existing medical conditions, presented to the emergency department complaining of palpitations and dyspnea on exertion of several weeks duration. She was afebrile, with blood pressure (BP) initially 124/68 mmHg, and heart rate 207 beats per minute. Examination revealed a thin leathargic woman with a diffuse goiter, distended neck veins, and irregular heartbeat. Electrocardiogram showed AF with a rate of 191 beats per minute. Chest X-ray showed pulmonary vascular congestion, and CT scan was negative for pulmonary embolism. Intravenous dilitiazem and heparin were started, followed by a rapid decrease in her BP to 70/30 mmHg. 2D echocardiogram showed an ejection fraction of 20-25%. Dilitiazem was discontinued and dopamine was started for BP support. Thyroid function tests showed TSH was 0.1 mIU/mL (0.36-5.8), and free T4 was 6.25 ng/dL (0.89-1.76). Hepatic dysfunction was present, manifested by increased prothrombin time and transaminase levels. Burch-Wartofsky score was >45, highly suggestive of thyroid storm. Propylthiouricil (PTU) and hydrocortisone were started, and metoprolol was substituted once her BP was stabilized. A rapid improvement in her symptoms was noted. Thyroid ultrasound showed a diffusely enlarged gland; thyroid stimulating immunoglobulin was 427% (0-139). Repeat echocardiogram two weeks after admission showed an ejection fraction of 40-45%. She was discharged home on methimazole, metoprolol and coumadin, with scheduled follow-up for radioactive iodine ablation once euthyroid.

**Discussion:** Cardiac dysfunction and arrhythmia are common manifestations of thyroid storm, even in the absence of preexisting cardiac disease. Beta-blockers are often used to suppress the cardiac manifestations of thyrotoxicosis, although cases have been reported of cardiovascular collapse following their use. Our review of the literature found no reports of adverse effects of CCB in thyroid storm. In our case, severe hypotension developed, likely from impaired myocardial contractility and further decreased cardiac output. This suggests that CCB should be used with caution in thyroid storm, especially if CHF is present.

**Conclusion:** Use of CCB can cause hemodynamic deterioration in thyroid storm and heart failure, and should be used with extreme caution.
Abstract #1017

RARE CASE OF THYROTOXIC PERIODIC PARALYSIS IN CAUCASIAN MALE

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Objective: To describe a case of thyrotoxic periodic paralysis in a Caucasian male.

Methods: Clinical Case Presentation

Case Presentation: A 26 year old Caucasian male was brought to the emergency room for sudden onset of bilateral lower extremity weakness and inability to walk after he woke up in the morning. He had 2 episodes of vomiting before coming to the hospital, ate pizza in dinner the day before and was doing fine when he went to sleep. He did complain of generalized fatigue going on for 4 to 6 weeks, increased appetite but no weight changes. He works as an accountant and denied tobacco usage or alcohol abuse. No history of illicit drug abuse or any herbal medications/supplements intake. On examination, he was alert, awake and oriented, BP 153/80 and heart rate was 148/min. He was diaphoretic and warm. Thyromegaly and tremors were noted. Neurological exam showed power 3/5 in bilateral lower extremities with preserved sensation and brisk reflexes. EKG showed sinus tachycardia. Serum potassium was 2.4, magnesium 1.5 with normal renal function and negative urine drug screen. Thyroid function test revealed TSH < 0.02, FT4 4.3 and FT3 18.8, thyroid stimulating immunoglobulin 446 and anti-TPO > 1000. He was given intravenous potassium, magnesium, hydrocortisone and admitted for further monitoring. He was started on beta-blocker and Propylthiouracil. He was discharged in 2 days with normal electrolytes and no focal deficits but still had tremors. Later on had radioiodine ablation for Grave’s disease and started on Levothyroxine as outpatient.

Discussion: Thyrotoxic periodic paralysis (TPP) is more frequently seen in males; especially Asian population. The prevalence is estimated to be 0.1-0.2% in Caucasians. Despite a higher incidence of hyperthyroidism in women, over 95% of cases TPP occur in men. Thyroid hormone, insulin, epinephrine increase adrenergic response causing intracellular shift of potassium by upregulation of Na/K-ATPase leading to hypokalemia and paralysis of skeletal muscles. Hypokalemia is secondary to intracellular shift of potassium and not total body depletion. Any event associated with an increased epinephrine or insulin release precipitates the paralysis. Treatment involves beta blockers to prevent the intracellular shift of potassium and phosphate by stabilizing the Na/ K-ATPase and anti-thyroid treatment with medications and radioiodine therapy or surgery.

Conclusion: Though TPP is rare in Caucasian population, it should be kept as a differential diagnosis in a previously healthy individual presenting with sudden onset of paralysis and hypokalemia. It has a good prognosis if identified and treated in a timely fashion.

Abstract #1018

AUTOIMMUNE HYPOTHYROIDISM CONVERTED TO HYPERTHYROIDISM: IS IT A COMMON PHENOMENON?

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Objective: Graves’ disease and Hashimoto’s thyroiditis are the two autoimmune spectrum of thyroid disease. Cases of conversion from hyperthyroidism to hypothyroidism have been reported but conversion from hypothyroidism to hyperthyroidism is very rare although reported.

Case Presentation: A 36 yrs old female presented with a 3 months history of Easy fatigability, cold intolerance, polymenorrhagia, constipation and weight gain in 2005. On examination she had bradycardia and dry skin. Thyroid gland was palpable, mostly diffuse but some nodular feeling at upper pole of left lobe. Clinical suspicion of primary hypothyroidism was made than confirmed by TSH of greater than 50 uIU/ml (0.4-4.2uIU/ml) with FT4 value of less than 0.30 ng/dl and positive thyroid antibody titre. Thyroxine was started at a dose of 100 mcg/ day. Gradually the requirement of thyroxine decreased and from end of 2005 onwards she maintained her TSH within normal range on 50 mcg/day of thyroxine. In the beginning of 2008 the dose was further reduced to 25 mcg/day but again towards the end of 2009 thyroxine dose was increased to 50 mcg/ day because of slightly increased TSH of 8.86. Slightly more than a year later she presented with weight loss of 3 kg with a feeling of anxiety and associated tremors of hands. TSH at this time was less than 0.005 with a FT4 of 2.4 confirming the state of thyrotoxicosis. Thyroxine was stopped and patient was observed intermittently over a period of 6 months. She remained clinically and biochemically hyperthyroid with a repeat TSH of <0.005 and an FT4 of 2.66. Thyroid scintigraphy with technetium 99 showed done at this stage showed an increased homogenous tracer uptake. Finally she was started on Carbimazole in mid of 2011 and remains on it till to date.

Discussion: Primary Hypothyroidism is permanent most of the time but occasionally it may reverse.
Certain mechanisms have been postulated behind this. One mechanism is the presence of different autoantibodies that includes thyroid stimulating antibodies, thyroid stimulation blocking antibodies and the response of thyroid gland to these antibodies. It has been suggested that the thyroid cells are damaged due to an autoimmune mechanism that results in increase in pituitary TSH secretion. This fails to keep the patient euthyroid as TSH blocking antibodies also render TSH ineffective. The transition from TSH blocking antibodies to thyroid stimulation antibodies may be the cause of hyperthyroidism.

**Conclusion**: This case demonstrate that high index of suspicion should be there if a patient with primary hypothyroidism develop persistent symptoms of hyperthyroidism. Otherwise it can be missed easily considering it as an over replacement with thyroid hormone.

**Abstract #1019**

**THE RENAL FUNCTION OF HYPERTHYROID PATIENTS IN NIGERIA**

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Lagos State University Teaching Hospital

**Objective**: Renal impairment occurs in a wide range of diseases. The effect of hyperthyroidism on renal function of these patients is a poorly reported aspect of thyrotoxicosis especially in Nigeria. This study is to determine the renal function of hyperthyroid patients.

**Methods**: This is a prospective case-control study in which 40 hyperthyroid patients whose ages ranged from 21-50 years with clinical (Wayne’s score > 19) and biochemical features of thyrotoxicosis 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. Statistical analysis using SPSS 17 package was carried out. p value ≤ 0.05 was taken to be significant.

**Results**: There was a female to male ratio of 4:1 in the hyperthyroid group. The mean weight of the hyperthyroid group was significantly lower than the control group p=0.000 and 0.008 respectively. Urinary calcium/creatinine ratio and estimated glomerular filtration rate (GFR) were significantly elevated in the hyperthyroid compared to the controls, p = 0.02 and 0.002 respectively, however there was no significant difference between mean albumin/creatinine excretion of the hyperthyroid and controls , (p = 0.8).

**Discussion**: Our study showed that hyperthyroid subjects had reduced levels of 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 This study also showed that the mean albumin/creatinine ratio was < 20µg/mg in the hyperthyroid group.

**Conclusion**: Hyperthyroid patients in Nigeria had reduced serum creatinine, hypercalcuria and increased GFR compared with control but a normal albumin creatinine excretion rate therefore thyrotoxicosis was not a significant risk factor for renal impairment in this study.

**Abstract #1020**

**DISCREPANCY IN THYROID STATUS OF PREGNANT WOMEN OF MANIPUR, INDIA**

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Regional Institute of Medical Sciences

**Objective**: To find the thyroid status of pregnant women of Manipur, India by comparing the trimester specific range as published by American Thyroid Association (ATA) guidelines with the non-pregnant/laboratory reference range.

**Methods**: A total of 377 patients with a distribution of 110,149 and 118 among the trimesters were included in the study. TSH, TT4, and TT3 were analyzed using Advia Centaur Siemens by Chemiluminescence assay. The results were tabulated using trimester specific ATA guidelines and non-pregnant/laboratory reference range. The patients were divided into those having overt hypothyroidism, subclinical hypothyroidism and overt hyperthyroidism.

**Results**: One patient, each in first and second trimester had overt hypothyroidism when trimester specific reference range as published by American Thyroid Association (ATA) guidelines with the non-pregnant/laboratory reference range.

**Results**: One patient, each in first and second trimester had overt hypothyroidism when trimester specific reference range (ATA) and laboratory reference were followed. The prevalence of subclinical hypothyroidism as per ATA guidelines were 34.4, 31.5 and 30.5 % in the respective trimesters. The prevalence of subclinical hypothyroidism on taking into account the non-pregnant reference range were 3.6, 2.6 and 6.8% in the respective
trimesters. 35.4, 28.8 and 23.7% among the trimesters were misdiagnosed as normal patients when non-pregnant reference was used. Further, when the non-pregnant reference range was used, 1% of normal patients were misdiagnosed to be having subclinical hyperthyroidism. None of the patients had overt hyperthyroidism in both the reference ranges.

**Discussion:** Maternal hypothyroidism during first half of pregnancy is harmful to embryo-foetal brain development, thereby intellectual retardation in the offspring. Foetus does not completely establish its own thyroid functions until 20 weeks of pregnancy and the developing fetus depends on the maternal thyroxine for the normal brain development. A large number of pregnant patients were misdiagnosed as having normal thyroid function when non-pregnant reference range was followed in our study. hCG which has a structural similarity with TSH has intrinsic thyrotrophic activity. A high serum hCG levels during pregnancy cause thyroid stimulation. Normal suppression of TSH during pregnancy is often misdiagnosed as subclinical hyperthyroidism. If non-pregnant reference is used, there is potential failure to identify women with early hypothyroidism because of suppressed TSH.

**Conclusion:** Thus we conclude that trimester specific reference range should be used to interpret the thyroid hormones in pregnancy to avoid the misdiagnosis, as thyroid hormones are necessary for the normal fetal brain development.

**Abstract #1021**

**HIGH PREVALENCE OF THYROID DYSFUNCTION IN PREGNANT WOMEN IN EASTERN INDIA**

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**Objective:** Screening for thyroid disorders in pregnancy is controversial with current guidelines recommending targeted screening. There is wide geographic variation in prevalence of hypothyroidism during pregnancy, varying from 2.5% in west to 10-13% in Asia. We evaluated thyroid hormone status in pregnant women attending tertiary care Hospital in Eastern part of India.

**Methods:** This cross sectional, prospective study included 378 consecutive pregnant women attending ANC clinic of a tertiary referral center irrespective of gestational age. fT4, TSH and Anti TPO Antibody were measured using CLIA after a detailed history & physical examination.

**Results:** 378 pregnant women with mean age of 21.4 ± 4.4 years and mean gestational period of 19.0 ± 8.1 weeks were recruited in the study. Mean fT4 & TSH was 1.12 ± 0.2 & 3.05 ± 5.78 for patients in 1st, 1.03 ± 0.21 & 2.62 ± 1.74 for patients in 2nd and 12 ± 0.2 & 3.08 ± 2.13 for patients in 3rd trimester. 7 patients (1.85%) had preexisting hypothyroidism. Using semester specific cut-offs, 8 patients (2.1%) had overt hypothyroidism while 116 patients (30.68%) had subclinical hypothyroidism. 13 patients had low fT4 Inspite of TSH being in normal range. 41 patients (10.84%) were positive for Anti TPO antibodies. 4 patients had TSH < 0.4, all in the first trimester.

**Discussion:** We report a very high prevalence of hypothyroidism (predominantly subclinical) from India compared to rest of world. This is in concurrence with recent data from other centers in India and may reflect under diagnosis of hypothyroidism in developing countries like India. Selective referral of pregnancy with history of bad obstetric outcome to tertiary centre may have also caused bias. The other possible explanations include increased iodine intake in diet, goitrogens in diet & micronutrient deficiency. Ethnic Indian cut offs values for TSH are not yet available.

**Conclusion:** The prevalence of overt (3.96%) and subclinical (30.68%) hypothyroidism in pregnancy may be much higher in Eastern India than the western world. We recommend consideration of universal screening of hypothyroidism in pregnancy in areas with high prevalence as targeted screening may miss many cases.

**Abstract #1022**

**PERCEPTIONS AND ATTITUDES OF PATIENTS AT THE TIME OF DIAGNOSIS WITH HYPOPARATHYROIDISM**

Nandini Hadker1, Jacqueline Egan1, Hjalmar Lagast2, Bart Clarke3

1. Trinity Partners, 2. NPS Pharmaceuticals, 3. Mayo Clinic Rochester

**Objective:** Hypoparathyroidism (hypoPARA) is a rare and complex endocrine disorder characterized by absent or abnormally low levels of parathyroid hormone. Research has largely focused on clinical aspects of the condition, but research exploring its impact on patient (pt) lives is limited. The goal of this study was to capture the recall of the perceptions and attitudes of pts when they were diagnosed. To the authors’ knowledge, this is the most comprehensive study measuring the burden of illness in hypoPARA pts conducted to date.

**Methods:** A 30-minute, web-based instrument was developed with input from pts, clinical experts, and
the Hypoparathyroidism Association to assess the clinical, social, and economic burden of hypoPARA. The majority of the participants were invited from the Hypoparathyroidism Association member list. Qualifying participants were ≥18 yrs old, diagnosed with hypoPARA for ≥6 mos, and residents of the US. A total of 374 pts completed the survey.

**Results:** Mean respondent age was 49 y. 85% respondents were female. On a 7-point Likert scale, where 1 is “Strongly Disagree” and 7 is “Strongly Agree,” 56% (208/374) strongly agreed (rated 6-7) with feeling unprepared to manage the condition, 47% (176/374) with feeling fearful, and 48% (180/374) with feeling mismanaged. Self-reported “severe” hypoPARA pts were statistically more likely to strongly agree with feeling fearful and mismanaged (52%, 59/114 and 54%, 62/114) compared to self-reported “mild” pts (35%, 28/80 and 39%, 31/80; P<0.05). Pts with postoperative hypoPARA were statistically more likely to strongly agree with feeling unprepared (60%, 175/293) and mismanaged (54%, 157/293) at the time of diagnosis compared to pts with other etiologies (41%, 33/81 and 28%, 23/81; P<0.05). The study also found pt understanding of hypoPARA was low at the time of diagnosis. 41% (153/374) strongly agreed that hypoPARA was not believed to be a very serious condition and 33% (123/374) strongly agreed that their hypoPARA was only a temporary condition. Additionally, pts reported having to see an average total of 6 physicians for the condition before selecting their current managing physician. Referrals to specialists, lack of physician knowledge, and inadequate treatment were the most cited reasons for having to consult multiple physicians.

**Discussion:** The research illustrates that at diagnosis pts are fearful of, poorly informed about, and inadequately prepared to manage their hypoPARA. Also, pts appear to need consultation with several physicians regarding their hypoPARA before they chose an appropriate physician.

**Conclusion:** These findings suggest the need for more education about and greater awareness of hypoPARA among both pts and physicians.

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**Abstract #1023**

**AN INTERESTING CASE OF GRAVES’ DISEASE IN A PATIENT FOLLOWING MORE THAN A DECADE OF HYPOTHYROIDISM**

Muhammad Mahmood, Henry Driscoll

Joan C. Edwards School of Medicine, Marshall University

**Objective:** We describe a patient with hypothyroidism who developed Graves’ disease with hyperthyroidism.

**Case Presentation:** A 55 year-old white man with type 2 diabetes mellitus was evaluated in endocrinology for undetectable TSH of <0.02 micro IU/ml (reference range, RR: 0.35 - 5.5) and elevated free thyroid hormone levels, free T4: 2.4ng/dl (RR: 0.9 - 1.7); free T3: 9.6pg/ml (RR: 2.3 - 4.2). Records review he was diagnosed with hypothyroidism on routine pre-operative screening for right hemicolectomy thirteen years earlier. He took oral levothyroxine replacement of 100 micrograms daily. TSH ranged 0.5-4.2 microIU/ml on this dose until fifteen months prior when TSH became suppressed. Subsequently TSH was persistently undetectable, and free thyroid hormone levels were high. Levothyroxine dose was gradually lowered and then discontinued 4 months earlier by the primary care physician. On evaluation, he was having palpitations, heat intolerance, unintentional loss of over 30 lbs and constant fatigue. He was tachycardiac with warm sweaty hands. There was no lid lag or lid retraction. His skin showed vitiligo. Off levothyroxine, TSH was still undetectable, FT4 was 1.88ng/dl; FT3 was 8.3pg/ml. 24 hour radioactive iodine uptake scan showed homogenously increased uptake of 44%(Normal uptake: 10-30%). Thyroid ultrason showed a heterogeneous thyroid gland with increased blood flow on doppler. Thyroid peroxidase antibody was 92 IU/ml (RR: 0-34). Trab (Thyroid receptor antibody) was 11.86 IU/l (RR: 0 - 1.75). Thyroglobulin antibody was absent. Methimazole 20mg daily was started and pt was scheduled to return in 8 weeks.

**Discussion:** Although the incidence of thyroid illness varies in different races, hypothyroidism is more common than hyperthyroidism. Hashimoto’s thyroiditis and Graves’ disease, different manifestations of autoimmune thyroid illness, are the leading cause of hypothyroidism and hyperthyroidism respectively. Switches between these two disorders have been described owing to autoimmune destruction of thyroid gland (hyperthyroidism to hypothyroidism), shift from TSI (thyroid-stimulating immunoglobulins) to TBII (thyrotropin-binding inhibitor immunoglobulin) in hyperthyroidism to hypothyroidism, and very rarely shift of TSI to TBII in hypothyroidism to...
hyperthyroidism. Both TSI and TBII are thyroid receptor antibodies or Trab.

**Conclusion:** In our patient we do not have baseline autoantibody titers. However, it is likely that the hyperthyroid state is due to stimulating Trab. His thyroid gland was still functional after twelve years of suppression. This case of transformation illustrates the need for regular follow up of hypothyroid patients to prevent life threatening complications of hyperthyroidism.

**Abstract #1024**

**FREE T4 OR TSH IN PREGNANCY!**

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**Objective:** Controversy exists over the choice of tests for screening for thyroid disorders in pregnancy. In non pregnant, TSH measurement may be enough in most of patients due to inverse, log-linear relationship between serum thyroid stimulating hormone (TSH) and free T4 (fT4). This is due to the hypothalamic-pituitary-thyroid feedback loop and may be altered in pregnancy. The aim of the study is to describe the relationship between serum TSH and free T4 in pregnant women and to see if measurement of TSH alone may be enough for screening.

**Methods:** This cross sectional, observational prospective study included 378 pregnant women in different periods of gestation attending antenatal clinic of a tertiary referral center. Free T4, TSH and Anti TPO Antibody were measured using CLIA for all the patients after a detailed history & physical examination.

**Results:** The relationship between TSH and fT4 in pregnancy was not log-linear as traditionally described. Infact we could not find any relationship between TSH and free T4 even after complex analysis.

**Discussion:** The relationship between TSH and free T4 in pregnancy has always been controversial. Thyroid physiology in pregnancy is affected by multitude of physiological and exogenous factors. Serum free T4 may be lower while TSH level varies according to gestation period. The net effect may be unpredictable. It may be better to estimate both free T4 and TSH for all pregnant women (as per recent ATA/AACE recommendation) undergoing Thyroid screening than TSH alone (as per Endocrine society recommendation).

**Conclusion:** The relationship between TSH and fT4 is not log-linear in pregnancy. Both free T4 and TSH should be measured in all pregnant women undergoing thyroid hormone screening.

**Abstract #1025**

**NODULE CHARACTERISTICS OF PAPILLARY AND FOLLICULAR THYROID CANCER ON THYROID ULTRASOUND, IS THERE A DIFFERENCE?**

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**Objective:** Evaluate characteristics of thyroid nodules on ultrasound for patients with thyroid cancer and determine if these characteristics are predictive of papillary versus follicular thyroid carcinoma.

**Methods:** We performed retrospective, observational study on patients with diagnosis of papillary and follicular carcinomas as demonstrated by surgical pathology. Patients were seen at University of Florida, Jacksonville endocrinology clinics between January 1, 2010 and February 29, 2012.

**Results:** Sixty four nodules were included in the study. Papillary thyroid cancers comprised 60.9% (n = 39) and 32.8% (n = 25) were follicular thyroid cancers. African Americans comprised 34.4% (n = 22) and Caucasian comprised 54.7% (n = 35), other various ethnic origins 10.9% (n = 7). There was a statistical significant difference when comparing age, mean age of patients was 43.05 years old (range: 19-74) in papillary thyroid cancer group and 52.2 years old (range: 30-76) in the follicular thyroid cancer group (P value 0.018). In addition there was a statistical significant difference when comparing age, mean age of patients was 43.05 years old (range: 19-74) in papillary thyroid cancer group and 52.2 years old (range: 30-76) in the follicular thyroid cancer group (P value 0.018).

**Discussion:** Given all of the above variables that we examined we found that patients with follicular thyroid cancer were older than those with papillary thyroid cancer. Isoechoic nodules were found to be present more in follicular thyroid cancer. Microcalcifications, hypoechoic nodules and abnormal lymph nodes on pathology were found to be present more in papillary thyroid cancer.
Conclusion: There are differences in nodule characteristics of papillary and follicular thyroid cancer. This recognition may enrich patient discussion about treatment planning prior to surgery.

Abstract #1027

AN UNUSUAL CASE OF A SUBCENTIMETER FOLLICULAR VARIANT PAPILLARY THYROID CANCER PRESENTING AS A SOLITARY LARGE ILIAC BONE METASTASIS AND REVIEW OF LITERATURE

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Objective: We present an unusual case of a microscopic follicular variant papillary thyroid cancer that presented as a large solitary iliac bone distant metastasis. A literature survey was also performed.

Case Presentation: 57-year-old previously healthy male presented to the emergency room for left groin pain following a ground level fall. Left hip x-ray showed a large lytic lesion in the left iliac bone. A subsequent pelvic MRI confirmed the presence of a large 6.2 x 8.1 cm enhancing mass in the left iliac bone that expanded to the inner and outer pelvic regions. Biopsy of the mass surprisingly suggested metastasis from thyroid carcinoma. The biopsy specimen stained positive for thyroglobulin and other thyroid markers. A whole body Tc99 bone scan identified the left iliac osseous lesion without additional sites of uptake. Ultrasonogram of the thyroid which was conducted to identify a primary tumor, revealed a 1.08 x 0.76 x 0.71 cm right lobe hypoechoic nodule with peripheral calcification without internal blood flow. FNA of the thyroid nodule yielded inadequate specimen due to peripheral calcification. Total thyroidectomy was performed. Thyroidectomy specimen revealed two foci of follicular variant papillary thyroid cancer. One focus measured 4 mm and the other focus measured 1 mm within the left and the right thyroid lobes respectively. The lesions were completely excised without apparent extra-thyroidal or lymph nodes involvement. Therapeutic I 131 ablation was administered following complete surgical excision of the iliac bone mass. BRAF mutation testing is pending.

Discussion: Papillary thyroid carcinoma commonly exhibits intra-glandular, extra-thyroidal, and lymph node spread. Follicular variant cancers are reported to exhibit variable aggressive behavior, and rarely do they present with bony distant metastases at the time of diagnosis. Distant metastases are encountered rarely with primary cancers that are < 2cm or when extra-nodal invasion is absent. To our knowledge, this is one of kind case in which a sub-centimeter thyroid cancer presented with a large single distant bone metastasis.

Conclusion: This case demonstrates two important findings. Firstly, that there is no definite correlation between the size of the primary tumor and the size of the distant metastasis. Secondly, there is considerable variation in the clinical aggressiveness of follicular variant papillary thyroid cancer. Factors predicting aggressive behavior amongst these cancers require further studies. BRAF mutation is pending in our case.

Abstract #1028

UTILITY OF RADIO-ISOTOPE SCANNING IN SUBCLINICAL HYPERTHYROIDISM: A RETROSPECTIVE AUDIT

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Objective: We attempted to study the use of radio-isotope scanning in patients with sub clinical hyperthyroidism (SCH) with suspected endogenous disease and find the relationship of findings with serum thyrotropin (TSH) levels.

Methods: A retrospective audit of 30 patients with biochemical SCH for whom a radio-isotope scan was requested. Each patient had a baseline thyroid function with/without antibody screening and then had an Iodine 123 radio-isotope scan. The results were interpreted for an etiological diagnosis and comparisons were made in relation to their baseline TSH. (grade I- TSH 0.1-0.4 mU/L and grade II- TSH < 0.1 mU/L)

Results: 30/84 patients had true biochemical SCH amongst all the request made for Iodine 123 uptake scan. 24 patients (80%) were females with mean age of 60.95±15.91 years whereas the males were slightly older (65.23 ± 17.28 years). 21 patients had grade I and 9 had grade II disease. Thyroid antibodies were only positive in 6 patients (Anti-TPO - 2 patients, TRAB - 2 patients) On 1123 scanning, nodular pattern of uptake was predominant and was found in 16 patients (8 solitary nodule and 8 multi-nodular) whereas diffuse uptake was noted in 12 patients and the remainder was indeterminate. Nodular disease was more predominant when patients had grade II disease (14 patients) and was also found in the higher age group (mean age 70.12 ± 12.13 years) as compared to the diffuse uptake group (mean age 51.16 ± 15.87 years). Percentage (%) uptake in relation to serum TSH levels also showed a higher uptake in patients with grade II disease.
**Abstract #1029**

**A HEART BREAKING STORM**

*Edgar Torres Garcia*

University District Hospital of Puerto Rico

**Objective**: To report a case of a woman who presented with cardiac involvement attributed solely to hyperthyroidism in the absence of any other causative factors and the importance identifying these complications and achieving prompt euthyroid state.

**Case Presentation**: 33 y/o female patient without previous history of systemic illness who presented, after computer tomography with IV contrast was performed, with worsening tremors, palpitations, sweaty hands and anxiety; requiring hospitalization. De novo hyperthyroidism complicated by thyroid storm was diagnosed. Afterwards patient was lost to follow up. Three years later she presented for evaluation at outpatient clinics with menstrual irregularities, dysphagia, irritability, hair loss and muscle cramps. Laboratory results were remarkable for suppressed thyroid stimulating hormone level with radioiodine ablation therapy. She was again lost to follow up, but presented months later complaining of shortness of breath and worsening dyspnea, requiring several visits to emergency departments and admissions where a diagnosis of congestive heart failure was done. Right and left heart catheterization showed normal coronary vasculature, but decreased systolic function and high cardiac output with pulmonary artery hypertension. Throughout the course of illness, uncontrolled thyroid condition persisted and further attempts for radioablation therapy were interrupted. 2D echocardiogram showed global hypokinesia, moderate left ventricular and bilateral atrial enlargement with mitral, tricuspid and pulmonary valve regurgitation with elevated pulmonary artery pressure (EF 40%). In absence of ischemic heart disease or other precipitating risk factors patient was diagnosed with Thyrotoxic Heart Failure.

**Discussion**: Despite, well established associations between the heart and the thyroid, including congestive heart failure, it has been superficially documented and described in medical literature with few population based studies on this now called “Thyrotoxic Heart Disease”. In addition, a consensus for establishment of its definition remains in debate.

**Conclusion**: Clinicians should keep in mind these cardiac manifestations when evaluating a patient with history of hyperthyroidism and symptoms suggestive of heart disease; because it has been described that the restoration of the euthyroid state leads to the reversal of the cardiac dysfunction.

**Abstract #1030**

**GRAVES’ DISEASE: TYPICAL GONE ATYPICAL**

*Jillian Douglas¹, Omolola Olajide²*


**Objective**: Graves’ disease usually presents with common symptoms and signs that are distinctive. Atypical manifestations of hyperthyroidism are increasingly being recognized. The lack of knowledge of the association between these findings may lead to a delay or misdiagnosis, or result in unnecessary investigations.

**Case Presentation**: We present a 50 year old female admitted for angina, dyspnea, orthopnea, nausea, vomiting, and palpitations. She had a previous diagnosis of atrial fibrillation which became uncontrolled with a rapid ventricular rate. During her hospitalization she developed abdominal pain. A CT abdomen showed uncontrolled with a rapid ventricular rate. During her hospitalization she developed abdominal pain. A CT abdomen showed severe cardiomegaly with global and right ventricular hypokinesia, moderate left sided and bilateral atrial enlargement with mitral, tricuspid and pulmonary valve regurgitation with elevated pulmonary artery pressure (EF 40%). In absence of ischemic heart disease or other precipitating risk factors patient was diagnosed with Thyrotoxic Heart Failure.
negative. She was diagnosed with congestive hepatopathy and right sided heart failure attributed to Graves’ disease.

Discussion: The atypical manifestations of Graves’ disease presents a broad spectrum of clinical and biochemical findings. Hepatic injury is thought to result from the hypermetabolic state which causes hypoxia in the perivenular regions increasing oxygen demand without an increase in blood flow. Thyroid hormones may also have a direct toxic effect on hepatic tissue.

Conclusion: Graves’ disease may present with atypical and under-recognized symptoms. Awareness about this is prudent to avoid misdiagnosis and unnecessary investigations.

Abstract #1031

PSEUDOMALABSORPTION OF LEVOTHYROXINE: A FACTITIOUS DISORDER

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University of Texas Medical Branch

Objective: To emphasize the clinical recognition of pseudomalabsorption of Levothyroxine in patients with resistant hypothyroidism.

Case Presentation: A 36 year-old female presented to our endocrine clinic with persistent hypothyroidism despite being on Levothyroxine 1100mcg daily. She had typical symptoms and signs of hypothyroidism including fatigue, weight gain, dry skin, hair loss, constipation, cold intolerance, slow mentation, puffy face and peripheral edema. Her labs showed TSH of 220 (0.45-4.70 uIU/ml), free T4 < 0.07 (0.78-2.20 ng/dl), free T3 0.3 (2.4-4.2 pg/ml) and TPO antibodies of 53.5 (0.0-3.9 IU/ml). She reported compliance with Levothyroxine, taking it on an empty stomach with no other medications. She had no symptoms or signs of any gastrointestinal, liver, pancreatic or heart disease. Her previous records showed that she switched multiple providers in the past. Review of her outside labs ranging over the past few years showed that she was persistently hypothyroid, the only occasion when her thyroid function tests were normal was when she was pregnant. The presence of normal thyroid function tests only during the pregnancy raised the possibility that the patient was compliant with levothyroxine medication only during her pregnancy. A diagnosis of factitious disorder with nonadherence to Levothyroxine called pseudomalabsorption of levothyroxine was suspected and the patient was advised to have levothyroxine absorption test for which she failed to show up and was lost to follow up.

Discussion: Patients with persistent hypothyroidism despite being on large doses of Levothyroxine should be evaluated for any dietary or drug interferences or malabsorption due to gastrointestinal, liver, pancreatic or heart disease. However noncompliance to levothyroxine referred to as pseudomalabsorption of Levothyroxine remains a common cause and can be diagnosed with an oral Levothyroxine absorption test. The test is performed by supervised oral administration of 1000mcg of Levothyroxine followed by measuring Free T4 levels showing incremental increases. Treatment includes once a week supervised oral or parenteral Levothyroxine administration.

Conclusion: Pseudomalabsorption of Levothyroxine, a factitious disorder with noncompliance to levothyroxine should be suspected in patients with persistent hypothyroidism despite being on large doses of Levothyroxine.

Abstract #1032

MEDULLARY THYROID CANCER AND AUTOIMMUNE THYROID DISEASE - A RARE ASSOCIATION

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Objective: Although the association between thyroid cancers deriving from follicular cells and Hashimoto’s thyroiditis is documented in the literature, the coexistence of medullary thyroid carcinoma (MTC) and an autoimmune thyroid disease is relatively rare. We present three patients with this association, out of 24 patients diagnosed with MTC in our clinic (12.5%).

Case Presentation: Patient 1. A 62 years old woman diagnosed several years before with Graves disease was diagnosed in 2012 with multinodular goiter, with a large nodule with microcalcifications and irregular shape. The patient has two children with Graves disease (one also with rheumatoid arthritis) and a girl with systemic lupus erythematosus. Hormonal work-up showed serum calcitonin > 2000 pg/mL (normal < 4.8 pg/mL), normal thyroid and adrenal function, low vitamin D and moderately elevated PTH with normal serum calcium (secondary hyperparathyroidism). CT scan showed bilateral adrenal hyperplasia and small mediastinal lymph nodes. She underwent total thyroidectomy and the diagnosis of MTC with metastatic adenopathy was confirmed. A calcitonin of 160 pg/ml persisted after surgery. Patient 2. A 61 years old women diagnosed 20 years before with Graves disease, then with autoimmune
hypothyroidism. She had an adrenal tumor discovered in 2009 and a thyroid nodule in 2012. She had high blood pressure since 2006 with paroxysms, tachycardia and sweating since 2011. She has elevated TPO and thyroglobulin antibodies, high free plasma metanephrines 374 pg/ml (10-90), normetanephrines 2033 pg/ml (15-80) and chromogranin A suggestive for pheochromocytoma, elevated calcitonin 176 pg/ml (<4.8) suggestive for MTC (multiple endocrine neoplasia type IIa). PTH and calcium were normal. She underwent right adrenalectomy then thyroidectomy. The patient has a son with Graves disease and an asymptomatic daughter (Patient 3), 32 years old, in whom screening revealed MTC: a thyroid nodule with microcalcifications, elevated calcitonin 282 pg/ml (N<13), normal adrenal and parathyroid function. She has also an euthyroid chronic autoimmune thyroiditis and underwent thyroidectomy. Genetic screening for RET mutations performed by direct sequencing of exons 10, 11 and 13 of RET gene was negative in the first patient and is pending in the last 2 patients.

Discussion: Both sporadic and familial MTC have been associated with chronic thyroiditis in our patients. It is debated whether lymphocyte infiltration may predispose to the onset of MTC or whether it is a defense against the tumor.

Conclusion: We presented a rare association between thyroid autoimmune disease and medullary thyroid cancer. It is not known if this association influences the prognosis.

Abstract #1033

THYROID DISORDERS IN NORTHERN NIGERIA - A PRELIMINARY REPORT OF CLINICAL PATTERNS AND COMPLICATIONS

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Objective: Thyroid disorders represent the second most common endocrine condition in Nigeria. Data on the clinical pattern of thyroid diseases in Northern Nigeria is scanty, hence the need for this study. We aim to describe the clinical pattern of thyroid diseases and their complications in Kano.

Methods: In a prospective study spanning 24 months at Aminu Kano Teaching Hospital and Murtala Mohammed Specialist Hospital Kano, thyroid patients attending the endocrine clinics were evaluated. Clinical data obtained include demographic characteristics, anthropometry, type and complications of thyroid disease.

Results: A total of 113 patients comprising of 87(77%) females and 26(23%) males were evaluated. The female: male ratio was 3.4:1. The mean age of the patients was 30.54±12.37 years; females 28.3±7.62 years and males 41.0±14.33 years. The mean BMI of the patients was 18.1±3.31 Kg/m2 (range 15.3 - 21.4 Kg/m2). There were 6(5.3%) with simple (euthyroid) goiter, 56(49.6%) with Grave’s disease, 38(33.6%) with Toxic Multinodular goiter, 2(1.8%) Thyroid cancer, 9(7.9%) Primary Hypothyroidism, 2(1.8%) Drug-induced hypothyroidism. The complications of thyroid diseases found were Thyroid ophthalmopathy 33(51.6%), systemic arterial hypertension 16(25.0%), atrial fibrillation 3(4.7%), sinus tachycardia 6(9.4%), sinus bradycardia 2(3.1%), and Congestive Cardiac Failure (CCF) 4(6.3%).

Discussion: In keeping with observations by Ogbera et al from South-West Nigeria, most thyroid disorders are seen in young females with a predominance of Graves disease over the other forms. We observe a pattern of late hospital presentation by most patients probably accounting for the high proportions of complications of thyroid diseases in our setting. The use of Amiodarone for cardiac arrhythmias in two patients who defaulted follow up visits to the cardiology clinic resulted in drug-induced hypothyroidism.

Conclusion: Grave’s disease is the predominant form of thyroid disease in Kano and is seen mainly in females. Cardiovascular disease especially systemic hypertension and congestive cardiac failure are the main complications seen in our thyroid patients. Late presentation accounts for the complications observed.
Abstract #1034

GRAVES' OPHTHALMOPATHY IN PATIENTS WITHOUT HYPERTHYROIDISM

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University of Texas Medical Branch

Objective: To increase awareness that Graves' ophthalmopathy (GO) can occur in patients without current or prior hyperthyroidism.

Case Presentation: A 53 year old female diagnosed with hypothyroidism in 2009, on Synthroid 125 mcg daily, presented in 2011 with increased tearing and change in appearance of her eyes with bulging. On physical exam she had mild proptosis bilaterally. Her labs showed normal TSH of 1.51 (0.45-4.70 uIU/ml), normal free T4 of 1.00 (0.78-2.20 ng/dl), elevated TPO antibodies of 435 (0-100 WHO units), elevated TSI of 403 (<110 %) and elevated TRAb of 24 (<=1.75 IU/l). Her CT orbits showed mild exophthalmos. She was treated with selenium and local measures.

A 60 year old male diagnosed with hypothyroidism in 2006, on Synthroid 88 mcg daily, presented in 2011 with double vision with lateral gaze and change in appearance of his left eye. On physical exam, he had left eye proptosis with left 6th cranial nerve deficit. His labs showed TSH of 3.61 (0.45-4.70 uIU/ml), normal free T4 of 0.97 (0.78-2.20 ng/dl), elevated TPO antibodies of 870 (0-100 WHO units) and negative TSI and TRAb. CT orbits showed mild exophthalmos. Six months later he presented with tearing and bulging of his right eye with worsening double vision and later progressed to have conjunctival edema, erythema and tunnel vision. His TPO antibodies increased from 870 to 2816 WHO units, TSI increased from 105 to 302% and TRAb remained negative. He was treated with oral steroids, selenium and local measures with subsequent improvement.

Discussion: GO is the most common extrathyroidal manifestation of Graves' disease, but it may even occur in patients without current or prior hyperthyroidism. About 5% of patients with GO are euthyroid or hypothyroid with low or absent TRAb as early diagnosis and treatment of mild eye disease can prevent progression to sight threatening GO.

Conclusion: GO should be considered in patients who present with eye symptoms even if they are euthyroid or hypothyroid with low or absent TRAb as early diagnosis and treatment of mild eye disease can prevent progression to sight threatening GO.

Abstract #1035

SAFETY AND TOLERABILITY OF RECOMBINANT HUMAN PARATHYROID HORMONE (RHPTH[1-84]) FOR THE TREATMENT OF ADULTS WITH HYPOPARATHYROIDISM: THE REPLACE STUDY, A RANDOMIZED, DOUBLE-BLIND, PLACEBO (PBO)-CONTROLLED STUDY

Dolores Shoback1, Tamara Vokes2, Michael Mannstadt3, Bart Clarke4, Hjalmar Lagast5, John Bilezikian6


Objective: Hypoparathyroidism is a complex endocrine disorder, characterized by hypocalcemia and hyperphosphatemia, due to absent or low levels of parathyroid hormone (PTH). Current management is limited to control of symptoms and biochemical indices, often with large amounts of calcium (Ca) and active vitamin (Vit) D (calcitriol or 1-alpha calcitriol), which can result in short and long-term complications.

Methods: This 24-week study assessed the safety and efficacy of rhPTH(1-84) plus optimized supplementation (oral Ca and active Vit D) vs optimized supplementation alone and PBO. During the optimization period, Ca and active Vit D doses were adjusted to achieve and maintain baseline serum Ca between 8.0−9.0 mg/dL for 2 wks. Patients (pts) received 50 μg/d rhPTH(1-84) or PBO; dose escalation, up to 75 and then to 100 μg/d of rhPTH(1-84), was permitted if active Vit D and oral Ca could be further reduced while normalizing or maintaining serum Ca level ≥ baseline. Adverse events (AEs) were monitored throughout the study.

Results: 134 completed the optimization period and were randomized (2:1) to receive rhPTH(1-84) (n=90) or PBO (n=44): 6 (7%) pts who received rhPTH(1-84) and 7 pts (16%) who received PBO discontinued treatment; 1 discontinuation in the rhPTH(1-84) group occurred due to treatment-related AEs. By the end of treatment, 81 (90%) pts in rhPTH(1-84) and 42 (96%) pts in PBO group reported ≥1 AE. Treatment-emergent AEs that occurred 10% more frequently in the rhPTH(1-84) than the PBO group were hypocalcemia (38% vs 23%), paraesthesia (34% vs
23%), and vomiting (12% vs 0). Serious AEs occurred in 5 (6%) and 2 (5%) pts in the rhPTH(1-84) and PBO groups, respectively; only 1 serious AE (hypercalcemia requiring brief hospitalization) in the rhPTH(1-84) group was considered treatment-related. During the 4-week post-treatment follow-up period, 52 (58%) pts in the rhPTH(1-84) group and 19 (43%) pts in the PBO group experienced AEs; 5 (6%) pts in the rhPTH(1-84) group experienced a serious AE (hypocalcemia [n=3], hypercalcemia [n=1], pancreatitis [n=1]) compared with 2 (5%) pts in the PBO group (hypocalcemia [n=1], dehydration [n=1]).

Discussion: Primary biochemical endpoints were met (Clarke et al, AACE 2013). When rhPTH(1-84) was withdrawn, an expected rebound in AEs including hypocalcemia was observed. The practitioner should ensure that adequate supplementation and frequent clinical and biochemical monitoring are implemented if rhPTH(1-84) therapy is interrupted.

Conclusion: Treatment of hypoparathyroidism with rhPTH(1-84) was well tolerated.

Abstract #1036

IMPROVEMENTS IN MINERAL HOMEOSTASIS BY RECOMBINANT HUMAN PARATHYROID HORMONE (RHPTH [1-84]) TREATMENT IN ADULTS WITH HYPOPARATHYROIDISM: THE REPLACE STUDY, A MULTICENTER, PLACEBO-CONTROLLED, RANDOMIZED CLINICAL TRIAL

Bart Clarke1, Michael Mannstadt2, Tamara Vokes3, Dolores Shoback4, Hjalmar Lagast5, John Bilezikian6


Objective: In hypoparathyroidism, mineral homeostasis is disrupted due to absent or low levels of parathyroid hormone (PTH). Current management is directed to symptom control with large doses of oral calcium (Ca) and active vitamin (Vit) D, which can result in short and long-term toxicity. This study assessed the effect of replacement therapy with rhPTH(1-84) on mineral homeostasis.

Methods: After a defined optimization period with Ca and active Vit D (calcitriol or 1-alpha calcitriol) supplementation to achieve stable serum Ca levels of 8.0-9.0 mg/dL, patients (pts) were randomized to rhPTH(1-84) 50 μg/d or placebo (PBO) in addition to continuing the optimized Ca and Vit D supplements for 24 wks. Both Ca and active Vit D were actively down-titrated as doses of rhPTH(1-84) were advanced to 75 and then to 100 μg/d if needed, during the next 8 wks. The primary efficacy variable was a composite endpoint of ≥50% reduction in need for Ca and active Vit D at Wk 24 while maintaining serum Ca levels ≥ baseline. Changes in serum Ca, phosphate (PO4), bone mineral density (BMD) and bone turnover markers (BTMs) were also assessed.

Results: 134 pts were randomized (2:1) to rhPTH(1-84) (n=90) and PBO (n=44). At Wk 24, 48/90 (53%) pts in the rhPTH(1-84) group and 1/44 (2%) pts in the PBO group met the primary endpoint (P<0.001). In the rhPTH(1-84) group, serum Ca levels remained near or above baseline throughout treatment (mean change -0.13 mg/dL), despite substantial reductions in active Vit D and Ca doses. By contrast, the PBO group experienced an initial decline in serum Ca levels, followed by a rise (mean change -0.28 mg/dL) as supplementation was increased toward baseline doses. During the first 12 wks where drug titration and planned supplement reductions were taking place, mean urinary Ca excretion declined in the rhPTH(1-84) pts despite increase in mean serum Ca; conversely both mean Ca excretion and mean serum Ca declined in the PBO group. There was a greater decrease in mean serum PO4 values in the rhPTH(1-84) group (-0.5 mg/dL) vs PBO (-0.1 mg/dL) throughout treatment (P<0.003). At Wk 24, 1 PBO pt and no rhPTH(1-84) pts had a Ca-PO4 product >55 mg2/dL2. There was a decrease towards normal in Z-scores in the rhPTH(1-84) group compared to a worsening in the PBO group; scores for total hip and hip femoral neck were significantly improved in the rhPTH(1-84) vs PBO (P<0.001). There were significant increases from baseline in all BTMs for rhPTH(1-84) vs PBO (P<0.001). rhPTH(1-84) was generally well tolerated.

Conclusion: In pts with hypoparathyroidism, rhPTH(1-84) simulated the beneficial effects of endogenous PTH by improving mineral homeostasis.
Abstract #1037

A TWO-YEARS MULTICENTER RANDOMIZED TRIAL OF LASER ABLATION VERSUS FOLLOW-UP FOR THE TREATMENT OF COLD THYROID NODULES.

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Objective: To compare clinical and ultrasound (US) changes induced in benign thyroid nodules by US-guided laser ablation (LA) versus follow-up and to assess side effects and efficacy of the technique in different centers.

Methods: Two hundred consecutive patients were referred to four different thyroid centers and randomly assigned to a single LA treatment (Group 1) or follow-up (Group 2). Entry criteria: solid thyroid nodule with a volume > 5 and < 18 ml, repeated benign cytological findings, normal thyroid function, no thyroid gland treatment. Group 1: LA was performed with a 1.064 nm neodymium yttrium-aluminum garnet laser with 2 fibers and an output power of 3 watts. Energy delivery was 3600 Joules for nodules up to 13 ml and 7200 for nodules larger than 13 ml. Volume and local symptoms changes were evaluated 1, 6, 12 and 24 months after LA. Side effects and complications were registered.

Results: A progressive nodule volume reduction was found at 6, 12 and 24 months (delta median volume vs baseline -50.7%, -57.3% and -60.9% p<0.001, respectively). A reduction > 50% was observed in 73.6% of cases (p=0.001). The 24-month mean volume reduction in the different centers was 41.6%, 63.2%, 61.5% and 58.7%. The presence of pressure symptoms complain decreased from 31% to 1% of cases (p=0.000). The procedure was well tolerated. One case of self-resolving vocal cord paresis was reported. In Group 2 volume showed a 12.9% increase at 24 month. Local symptoms did not change significantly.

Discussion: LA procedure was performed on outpatients, was rapid (30 minutes) and fairly well tolerated. Volume reduction was progressive until 12 month and remained stable until 24 month. The cost of disposables was about $400 for each procedure. Efficacy and side effects were similar in different centers.

Conclusion: A single LA induces a significant shrinkage of thyroid nodules and the improvement of local symptoms without relevant complications.

Abstract #1038

AN OFFICE BASED EVALUATION OF GENE EXPRESSION CLASSIFIER USE IN THYROID NODULES

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Objective: To determine the impact of a gene expression classifier technique on typical office based endocrine practice

Methods: We pooled data from three practice locations in different areas of the United States. A total of 750 thyroid nodules were evaluated in 653 adult patients. All specimens were obtained using similar ultrasound guided fine needle aspiration technique of thyroid nodules of at least 1 cm in size. Liquid based cytology, and cellular material for genetic analysis was submitted for analysis. All cytology was interpreted by a single team of cytopathologists. Indeterminate cytology results were reflexively submitted for GEC analysis to Veracyte for GEC testing which was classified benign, or suspicious. Patients with indeterminate cytology and benign GEC were generally observed per ATA guidelines, and suspicious GEC markers were referred for surgery.

Results: Benign cytology was demonstrated in 77% of the nodules biopsied. Malignant or suspicious cytology was found in 3.7 % of the nodules. 17 percent of biopsied nodules had non diagnostic cytology (AUS, FLUS, etc) prompting gene classifier testing. Of the molecular classifiers run, 50 % were suspicious, 46.75% were benign, and 3.25% yielded insufficient genetic material for evaluation. Of the 50% suspicious GEC markers, referred for surgery, 48% had malignancy confirmed on final pathology. GEC markers suspicious for medullary carcinoma were obtained in .5 percent of total aspirates and confirmed at surgery. Six suspicious GEC marker patients (.8%) are awaiting surgery and one has declined operation.

Discussion: Thyroid nodules are common in adults, but only a small fraction is malignant. Fine needle aspiration biopsy of nodules to obtain cytology specimens has been the most sensitive and specific tool available for diagnosis,
but 10-30% of cytology obtained is not clearly benign or malignant. Common practice has dictated that most indeterminate nodules are referred for excision. A high proportion of these prove to be benign. To determine the impact of a new commercially available gene expression classifier technique on the management of indeterminate cytology results we pooled the FNA results of three practices over approximately one year. A significant reduction in the number of diagnostic surgeries in patients with indeterminate cytology results appears possible.

**Conclusion:** Use of a GEC in an office setting can reduce the number if patients referred for diagnostic surgery when indeterminate cytology results are obtained by FNA. Our results appear similar to those published in registration studies. A possible limitation is the limited amount of control data available to establish a false negative rate for this technique.

**Abstract #1039**

**AN INDEPENDENT STUDY OF A GENE EXPRESSION CLASSIFIER (AFIRMA™) IN THE EVALUATION OF CYTOLOGICALLY INDETERMINATE THYROID NODULES: COST ANALYSIS**

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**Objective:** Between 10 and 25% of thyroid FNA cytology samples prove indeterminate, requiring surgery for diagnosis. We have performed an independent assessment of a novel Gene Expression Classifier (GEC; Afirma™, Veracyte Inc., San Francisco, CA), which is available to recategorize these samples. We now report the impact on cost-effectiveness of the GEC when applied to these samples.

**Methods:** Mayo Clinic began using the GEC in May 2011, collecting nucleic acid samples using Veracyte’s published protocol. GEC testing was offered selectively to patients with indeterminate cytology in whom surgery was not otherwise indicated. Patients with a benign GEC were offered ultrasound follow-up as an alternative to surgery. We determined the cost of surgery and follow-up based on 2010 Medicare reimbursement and Physician Fee Schedules, and used a Medicare reimbursement rate of $3200 for the Afirma assay, to allow direct comparison with previous publications.

**Results:** We biopsied 1112 nodules from 863 eligible patients, of which 89 were cytologically indeterminate. Afirma GEC samples were available on 77 of these nodules. Clinical assessment led to a decision to operate on 18 of these patients, in whom no GEC was therefore requested, while 59 patients agreed to GEC analysis. No results were obtained from 6 samples (10.2%), while 13 (24.5%) were GEC-benign; 3 patients in this group chose surgery, while the remaining 10 patients chose follow-up. We have operated on 32 (80%) of the 40 GEC-suspicious nodules. The average cost of assessment, treatment and follow-up using an algorithm that incorporates Afirma was $11,749.09, compared to $10,898.81 without Afirma, an estimated incremental cost per patient of $850.28.

**Discussion:** Our experience with the GEC has shown a lower than expected rate of GEC-benign samples and a lower PPV in GEC-suspicious nodules, a result of the low risk of malignancy in the nodules we have selected for GEC. The reduced PPV alters the cost-benefit of the assay, causing an incremental cost of $850 per patient, rather than the cost savings of $1,453 suggested by an earlier analysis. Based on the predicted improvement in quality of life of 0.07 quality adjusted life years (QALY), the cost per QALY of the GEC would be $12,150.

**Conclusion:** When applied to samples with a low rate of malignancy, the Afirma GEC may slightly increase health care costs. Nevertheless, the cost per QALY remains well within usually accepted limits for value to the healthcare system. Our data again emphasize the importance of ongoing real-world studies of the performance and cost-benefit of this and other molecular adjuncts to thyroid cytopathology.

**Abstract #1040**

**LANGERHANS CELL HISTIOCYTOSIS OF THE THYROID**

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Mayo Clinic

**Case Presentation:** A 23 year old female with history of hypothyroidism was found to have a thyroid nodule. She underwent ultrasound (US) guided fine needle aspiration and cytology was consistent with a benign nodule. The patient had a repeat thyroid US 2 years later and the nodule had increased in size. Surgery was recommended and the patient underwent a near total thyroidectomy. Pathology: Histology showed a nodular and circumscribed proliferation of cells with clear cytoplasm bounded by dense collagen sclerosis. The background thyroid parenchyma showed chronic lymphocytic thyroiditis with numerous secondary lymphoid follicles. The clear cells showed uniform histiocytoid morphologic features characterized by abundant clear-to-granular cytoplasm, kidney bean-shaped nuclei with longitudinal nuclear grooves, small
nucleoli, and indistinct cell borders. Accompanying these clear cells were numerous eosinophils with foci of Charcot-Leydin crystal deposits. The histiocytic proliferation showed expression of CD68, CD1a and S-100. Histological analysis was consistent with Langerhans cell histiocytosis (LCH) and lymphocytic thyroiditis on both thyroid lobes. Follow up: After surgery the patient had a brain MRI which demonstrated minimal enhancement and subtle questionable enlargement of the pituitary infundibulum at the level of the median eminence which could represent LCH infundibular involvement. A skull X-ray and bone scan were within normal limits. The patient is still under routine follow up.

Discussion: LCH is a multisystem disease characterized by an abnormal proliferation of Langerhans cells. Thyroid involvement in LCH has been rarely reported. The diagnosis is challenging because the clinical picture is highly variable. Patients present with diffuse or nodular thyroid enlargement. Thyroidal pain and obstructive symptoms are unusual. Patients are euthyroid initially but may have biochemical signs of primary hypothyroidism or hyperthyroidism. The diagnosis is based on histopathologic findings. Immunoreactivity for S-100 protein, CD1a, and Langerin confirms the diagnosis. For patients with thyroid LCH additional investigation (CT chest, bone scan, bone marrow aspiration) is suggested to distinguish isolated from multisystemic cases. Treatment of LCH of the thyroid is controversial. Surgery is recommended for isolated thyroid LCH but no specific guidelines exist regarding management. Chemotherapy with or without radiotherapy has also been performed.

Conclusion: LCH of the thyroid is very rare. The diagnosis is confirmed by the distinct morphologic appearance of the histiocytes as well as their characteristic expression of S100 and CD1a via immunohistochemistry.

Abstract #1041

HYPERTHYROIDISM, A REVERSIBLE CAUSE OF PULMONARY HYPERTENSION

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Objective: To highlight the association between hyperthyroidism and pulmonary hypertension.

Case Presentation: A 39 year-old female was admitted for fatigue, edema and abnormal liver function tests. She had been diagnosed with thyrotoxicosis and treated with potassium iodide. On exam she had scleral icterus, a systolic heart murmur and edema. Her labs showed suppressed TSH 0.009 mIU/ml (0.4-4.7) with elevated free T4 6.18 ng/dl (0.58-1.76) and total T3 3.22 ng/dl (0.6-1.81). Her liver function tests showed elevated alkaline phosphatase 238 U/L (45-129) and total bilirubin 6.4 mg/dl (0.3-1.2). Ultrasound of the liver revealed evidence of congestion. Echocardiogram showed severe tricuspid regurgitation, elevated systolic pulmonary artery pressures at 45 mmHg, and impaired right ventricular function. Elevated pulmonary pressures (38/18 mmHg) were confirmed with right heart catheterization. Methimazole was started for hyperthyroidism and furosemide and carvedilol for heart failure. After 5 months of methimazole, improvement in tricuspid regurgitation and a decrease in pulmonary artery systolic pressure to 35 mmHg was seen on repeat echocardiogram. Her TSH remained suppressed but her free T4 (1.1 ng/dl) and total T3 (1.47 ng/dl) were normal.

Discussion: Pulmonary hypertension is increasingly recognized in association with hyperthyroidism. The increase in right ventricular pressures due to increased pulmonary blood flow without a decrease in pulmonary vascular resistance results in peripheral edema and can produce passive congestion of the liver occasionally progressing to jaundice and hepatic failure as in our patient. Treatment of hyperthyroidism can normalize the right atrial and right ventricular pressures and improve tricuspid regurgitation. In two studies of 87 patients with hyperthyroidism from either Graves disease or toxic multinodular goiter screened with transthoracic echocardiogram, 43 of the 87 (49%) had asymptomatic pulmonary hypertension and many of them had tricuspid regurgitation. After at least 7 months of therapy, 33 (77%) of these patients had resolution of their pulmonary hypertension on repeat echocardiogram.

Conclusion: Hyperthyroid patients may have pulmonary hypertension that improves or resolves with treatment of the hyperthyroidism. An echocardiogram should be considered in any hyperthyroid patient with dyspnea, edema, or abnormal liver function tests. Conversely, thyroid function tests should be part of the evaluation of patients diagnosed with pulmonary hypertension.
Abstract #1042

ASSESSMENT OF FINE NEEDLE ASPIRATE SAMPLING OF THYROID BIOPSIES IN AN ACADEMIC CENTER WITH EARLY ADOPTION OF BEDSIDE EVALUATION BY CYTOPATHOLOGY

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Objective: Fine needle aspiration (FNA) with ultrasound guidance is the preferred method for evaluation of thyroid nodules. The addition of rapid bedside evaluation by pathology to evaluate the adequacy of specimens has been recently added at some sites and has been present at our institution for twelve years. In certain studies of FNA without ultrasound guidance, up to 20% of FNA biopsies yield inadequate material for diagnosis, with that number dropping to 5% with the addition of bedside ultrasound with experienced ultrasound operators. The Nation Cancer Institute recent recommendation state that a documented unsatisfactory sample rate (<10%) is a conservative measure of proficiency. A recent meta analysis demonstrated that rapid on-site evaluation by cytopathology increased adequacy rate on samples by as much as 9% as compared to sites without bedside cytopathologists.

Methods: All fine needle aspirations preformed with bedside thyroid ultrasound in the presence of a pathologist (resident or attending) performed at the Regional Medical Center at Memphis over a twelve year period were examined. Age, race, sex, nodule size, and location, as well as pre-FNA thyroid function tests were noted. FNA results were classified as benign, atypical with undetermined significance, follicular neoplasm/suspicious for follicular neoplasm, suspicious for malignancy, or malignant. The bedside ultrasound and actual FNAs were performed by either endocrinology staff or fellow, however slide preparation and review was entirely performed by pathology staff. Those found to have incidental thyroid cancer on surgical pathology in areas not biopsied were excluded.

Results: Of the 86 patient who underwent FNA under ultrasound guidance and bedside pathologist review, 5 or 5.8% were found to be unsatisfactory with an adequacy rate of 94.2%. 64 (79.2%) were benign, 4 (4.6%) atypia with undetermined significance, 8 (9.4%) were follicular neoplasm or suspicious for follicular neoplasm, 3 (3.7%) was Suspicious for Malignancy, and 2 (2.3%) were found to be malignant. All unsatisfactory samples had their initial referring ultrasound at outlying facilities.

Discussion: Our results show that the FNAs performed both under ultrasound guidance and with rapid on-site evaluation by cytopathology demonstrated a low unsatisfactory sample rate, consistent with recent studies in the area of bedside evaluation by cytopathology. Conclusion: The institution’s early adoption of bedside analysis by pathology staff has kept the unsatisfactory sample rate well above the standards set by the National Cancer Institute.

Abstract #1043

A CASE OF MOYA-MOYA DISEASE AND THYROTOXICOSIS

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Objective: 1. To describe a case of hyperthyroidism with inter-current Moya-Moya Disease. 2. Discuss connection between Moya-Moya and Hyperthyroidism.

Case Presentation: A 32 y/o Hispanic male with a history of hyperthyroidism not compliant on his tapazole therapy presented to the hospital with confusion, fever and sinus tachycardia. Physical exam elicited ocular proptosis, lid lag, bilateral tremors on arm extension, and a diffusely enlarged smooth thyroid with a bruit. He was found to have a free T4 of 6.97 ng/dL, total T3 of >8.0 ng/mL and TSH of <0.01 uIU/mL. Burch-Wartofsky score found to be 35 included tachycardia, nausea and delirium. CT scan of the head found a suspected sub-acute infarct in the right frontal lobe. He was started on therapy for severe thyrotoxicosis with impending thyroid storm, including propranolol, PTU, SSKI and hydrocortisone. Thyroid U/S showed a diffusely enlarged and heterogeneous gland with increased vascularity throughout the gland. MRI confirmed recent brain infarct. MRA of the cerebral vessels showed narrowing of the internal carotid arteries, and “puffed smoke appearance” of collateral vessels suggesting a Moya-Moya Disease pattern of occlusion. His clinical symptoms did improve but to achieve euthyroidism he required very large doses of PTU and subsequent change to methimazole 20mg TID. He required bilateral carotid by-pass with pre-operative dilemmas included adequate beta-blockade for tachycardia control. He had a successful surgical outcome and was subsequently discharged on methimazole and propranolol therapy.

Discussion: Moya-Moya (MM) is a cerebrovascular disease resulting in progressive occlusion of the bilateral internal carotid arteries. This results in formation of a collateral network of vessels at the brain base resulting in a “puffed-smoke” appearance on imaging. Weak collateral vessels develop which may result in cerebral infarctions
or hemorrhage. There have been few case reports of intercurrent MM and thyrotoxicosis. Some have involved acute cerebral events in patients with MM when aggravated by a thyrotoxic state. The direct link between these conditions is unclear, and multiple mechanisms have been proposed. Studies have shown increased carotid artery stiffness in Grave’s Disease and a hyperdynamic circulation seen in the thyrotoxic state which can both cause aggravation of the ischemic condition seen in MM. Another possibility is an auto-immune link as other autoimmune diseases have been associated with MM (i.e. SLE).

**Conclusion:** Moya-Moya Disease can be associated with hyperthyroidism, though the exact mechanism of this link is unclear. It should be considered in the differential diagnosis when assessing thyrotoxic patients with neurological deficits.

**Abstract #1044**

**COURSE AND MANAGEMENT OF SUBCLINICAL HYPERTHYROIDISM IN AN ACADEMIC CENTER AND EFFECT ON VENTRICULAR FUNCTION**

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**Objective:** Subclinical hyperthyroidism (SCH), defined as a low TSH with normal free T4 and free T3, is a common condition with an estimated prevalence of about 1%. The course of SCH is variable; therefore there are considerable differences in practice patterns. We sought to determine the course and management of patients with SCH in an academic practice and evaluate the effect of treatment vs. no treatment on left ventricular function.

**Methods:** All patients with a diagnosis of SCH from 2003 to 2011 were identified from electronic medical records at Michigan State University. Data regarding demographics, co-morbid conditions, treatment modality were collected and the patients were followed longitudinally. The decision to treat or not treat SCH was made by individual physicians.

**Results:** Eighty seven patients with SCH were identified of which 31% were men. Mean age was 56.4 years (SD ±15.9). Mean follow up was 36.7 months (SD ±33.9). Twenty (23%) patients were treated and 67 (77%) were not treated. Atrial Fibrillation (AF) was present on diagnosis in 4 patients of which 3 were untreated (2 were not treated due to age >80 years while SCH resolved in the other). Osteoporosis was present by history in 7 patients (6 untreated). Bone Mineral Density was available in 22 patients and showed osteoporosis in 1 out of 6 treated and 4 out of 16 untreated patients. Of the 67 untreated patients, SCH resolved spontaneously in 37 (55.2%), remained persistent in 27 (40.3%) while 3 (4.5%) developed overt hyperthyroidism. None of the untreated patients developed AF on follow up. Of the 20 treated patients, 16 were treated with thionamide drugs and 4 underwent surgery. Eight treated patients had echocardiograms of which 3 demonstrated diastolic dysfunction and the rest were normal. Fifteen untreated patients had echocardiograms with systolic dysfunction in 2, diastolic dysfunction in 1 and left ventricular hypertrophy in 4. All the untreated patients with ventricular dysfunction except 1 were hypertensive. Although the number of echocardiograms were small compared to the group size, there was no difference in the presence of diastolic (p=0.10) or systolic (p=0.52) dysfunction between the treated and untreated groups.

**Discussion:** SCH resolved spontaneously in majority of the untreated patients (55.2%) in our study and only 4.5% developed overt hyperthyroidism. None of the untreated patients developed AF during the follow up period which averaged 36.7 (0.5 to 136) months.

**Conclusion:** Our study, although limited by small sample size, suggests that most patients with SCH either revert to normal or remain persistently in SCH and demonstrates no difference in ventricular function between the treated and untreated groups.

**Abstract #1045**

**RAPIDLY GROWING THYROID MASS IN A IMMUNOCOMPROMISED YOUNG MALE ADULT**

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**Case Presentation:** We describe a 20 year-old man diagnose with a myelodysplastic syndrome (MDS), admitted to our hospital due to pancytopenia, and fever of undetermined origin after myelosupression with chemotherapy. Disseminated Aspergillosis was suspected after he developed skin, and lung involvement. A rapidly growing mass was detected on the left neck area by the patient, during hospitalization. Physical examination
revealed a diffusely enlarged non tender palpable mass in the left thyroid lobe. Laboratory data showed normal thyroid function (TSH: 1.07 µU/mL; Total T4: 6.37 µg/dL); with negative blood cultures for fungal pathogens. Chest CT demonstrated a right middle lobe nodular infiltrate measuring 2.5 x 2.3 x 1.9 cm, and a thyroid ultrasound reported a 3.7 x 2.5 x 2.9 cm oval heterogeneous structure, suggestive of an abscess versus a hematoma. Fine needle aspiration of the thyroid revealed invasion of septate fungal hyphae suggesting Aspergillosis. He was treated aggressively with amphotericin B and voriconazole.

Discussion: Fungal pathogens are increasingly encountered on immunocompromised patients. Fungal thyroiditis is a rare occurrence. In the last decade, of the different infectious thyroiditis reported, only 12% were fungal; most likely due to the unique features of the thyroid gland. Infection is difficult to diagnose; since more than 50% of patients do not exhibit clinical or laboratory manifestations of thyroid dysfunction. Usually these patients have a fatal outcome; for this reason is rarely diagnosed antemortem. Early diagnosis of invasive thyroid Aspergillosis is a challenge on immunocompromised patients; and usually the diagnosis and treatment is delayed. Frequently the fungal infection is first revealed at autopsy.

Conclusion: To our knowledge, this is the 10th case reported in the literature in an adult were the diagnosis of fungal invasion to thyroid was able to be performed antemorten by fine needle aspiration biopsy. Aspergillus thyroiditis is difficult to diagnose without biopsy, but should be considered in the differential diagnosis of any thyroid nodule, mass or abscess, particularly in patients with conditions causing immunodeficiency, such as MDS.

Abstract #1046

FOLLICULAR THYROID CARCINOMA PRESENTING WITH ENDOBRONCHIAL METASTASES

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Objective: Endobronchial metastases from follicular thyroid carcinoma are rare. We report a patient with distant metastases to endobronchial tissue of lungs from follicular thyroid carcinoma.

Case Presentation: A 79-year old male presented with dyspnea, chest pain and weight loss. Physical examination revealed an emaciated patient with a BMI of 16.7 kg/m2. Vital signs were within normal limits. CT chest revealed multiple lung nodules. Subsequently, bronchoscopy demonstrated an endobronchial nodule in the right upper lobe. Pathological evaluation of the nodule revealed neoplastic cells that stained positive for thyroglobulin (TG), thyroid transcription factor-1 (TTF-1) and cytokeratin-7, consistent with metastatic follicular thyroid carcinoma. Endocrine consultation was requested and further evaluation revealed a firm fixed right thyroid nodule with irregular borders. His thyroid function tests were normal. Thyroid ultrasound revealed a 2.3x2.2x1.8 cm right thyroid solid nodule. Fine needle aspiration of the nodule revealed follicular cells. The patient subsequently had total thyroidectomy and neck exploration. Thyroid gland pathology revealed a nodule with features of high-grade follicular thyroid carcinoma. Nuclear imaging scans 5 days after the radioactive iodine therapy demonstrated multiple foci of activity in lungs and neck consistent with metastatic thyroid cancer.

Discussion: We report a rare case of follicular thyroid carcinoma that presented with endobronchial metastases. Follicular thyroid carcinoma (FTC) metastasizes primarily by hematogenous route. Distant metastases occur in 15% of FTCs, typically to bones, brain and lungs (usually as nodular lesions in lung parenchyma). Endobronchial metastases as in our patient are extremely rare and usually imply a poor prognosis. Pathogenesis of endobronchial lesions formation may involve direct invasion from parenchymal lesion, direct extension of mediastinal lesions, transbronchial aspiration, direct lymphatic spread and/or direct metastasis via the bronchial artery.

Conclusion: We suggest that patients with signs and symptoms of malignancy and diagnosis of pulmonary nodules of unknown etiology should undergo examination of the thyroid gland to identify those subjects who may be at risk for metastatic thyroid cancer.

Abstract #1047

MICROPAPILLARY THYROID CANCER WITH LUNG METASTASIS: AN UNUSUAL PRESENTATION

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Objective: We present a rare case of micropapillary thyroid cancer with lung metastasis.

Case Presentation: A 60-year-old army Veteran was referred for evaluation of metastatic papillary thyroid cancer. He was found to have a 3 cm left hilar mass on CT chest done for chronic cough. Transbronchial biopsy of the lung mass was negative for malignancy; however pretracheal lymph nodes showed metastatic papillary carcinoma. He denied Agent Orange or radiation...
He smoked 2 packs cigarettes daily for 40 years. No personal or family history of thyroid disease. Physical examination demonstrated no thyromegaly or nodules. Laboratory data showed TSH of 1.44 IU/ml (0.5-5). Thyroid ultrasound revealed benign appearing subcentimeter nodules without lymphadenopathy. PET scan demonstrated a hypermetabolic area corresponding to the lung mass. A left upper lobectomy was performed and pathology showed metastatic papillary thyroid cancer. Immunostaining was negative for thyroglobulin and PAX 8 mutation but positive for NAPSIN, CD57, and HBME. Subsequently he underwent total thyroidectomy. Pathology showed multifocal subcentimeter papillary microcarcinoma, one cystic and follicular and the other, sclerotic and follicular variant without capsular or vascular invasion. Due to absence of residual disease on whole body uptake and PET CT scan, ablation therapy was deferred. His thyroglobulin levels trended down on levothyroxine suppressive therapy, last level being 0.8 (5-25ng/dl). Repeat PET scans were negative but follow up thyroid ultrasound showed residual tissue with subcentimeter lymph nodes and chest CT showed a 7mm nodule, both of which are being monitored radiologically.

Discussion: Incidence of papillary thyroid carcinoma has risen, however whether it is due to an actual increase or overzealous surveillance is unclear. They are often multifocal. Among patients undergoing modified radical neck dissection, up to 80% have lymph node metastases. 2-10% have metastases beyond the neck at the time of diagnosis. Among such, two-thirds have pulmonary and one-fourth skeletal metastasis. Microcarcinomas usually have a benign course. In contrast, large tumors have higher chances for local lymph node and distant organ metastasis. Factors predicting poor outcomes are large tumor burden, age, male sex, more than 1 nodal or bilateral mediastinal lymph node involvement and presence of BRAF or VEGF mutation. Sclerosing and tall cell variants are aggressive but less common forms.

Conclusion: Micropapillary thyroid cancers presenting with large lung metastasis are unusual. Distinction between a second lung primary and metastatic thyroid carcinoma can be difficult as in this case due to absence of thyroglobulin stain and PAX8 mutation.

Abstract #1048

EPIDEMIC OF THYROID NODULES. HOW ARE THEY BEING FOUND?

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Objective: Thyroid nodules are epidemic. Over the past seven years the discovery of thyroid cancer has doubled with an estimated 56,000 cases diagnosed in the US in 2012. Paralleling this increase in cancer, the number of biopsies performed in the US has increased to 450,000 per year. We sought to evaluate how nodules were detected, and whether a correlation exists between method of detection and rate of malignancy.

Methods: We reviewed medical records of 200 consecutive cases referred for thyroid nodule. The mode of discovery of the nodule was determined from medical records. Additional information reviewed included size and number of nodules, whether a biopsy was performed, and if biopsied, whether benign or malignant.

Results: Of the 200 cases, 67 (33.5%) were found on other imaging studies, including 35 CT scans, 15 MRI studies, and 8 carotid US studies. 75 (37.5%) were found on physical examination. Twenty-four (12%) were initially found by the patient. 34 (17%) cases were found when a thyroid ultrasound was ordered for other reasons, such as abnormal thyroid function tests. Biopsy was performed in 141 (70%) cases and not in 59 (30%). In 42 cases biopsy was not performed, due to the nodule not meeting current guidelines for biopsy, based on size and lack of suspicious ultrasound features. In 2 cases no nodule was present.

Discussion: 12 of the 141 biopsies were surgically confirmed as cancer. Of these 12 cases seven (58%) were found on physical examination, and 3 (25%) were detected by the patient. Thirty-two (22%) cases were found when a thyroid ultrasound was ordered for other reasons, such as abnormal thyroid function tests. Biopsy was not performed in 4 cases due to age and co-morbidities. Two patients had a benign biopsy prior to consultation. Biopsy was not performed in 9 cases due to the presence of Hashimoto’s thyroiditis without suspicious nodules. In two cases no nodule was present.

Conclusion: Of 200 consecutive referrals for thyroid nodules, 37.5% were found on physical examination, and
33.5% were found incidentally on other imaging studies. While prior studies have suggested that the mode of discovery has no impact on the probability of the nodule being malignant, this study found a much higher rate of cancer in cases found by physical examination (9%) compared to those detected incidentally on other imaging studies (1.5%).

Abstract #1049

10 YEARS OBSERVATION ON MORTALITY AMONG PATIENTS PRESENTING AS THYROCARDIAC EMERGENCY

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**Objective:** To find out the pattern and factors for mortality in patients hospitalised with thyrocardiac disease.

**Methods:** 68 patients in age group of 26 to 74 years were studied through their case records, admitted in hospital from September 2002 to August 2012. All these patients had final diagnosis as Thyroid storm (n=16), Myxedema coma (n=13), Atrial fibrillation with thyrotoxicosis (n=36), Severe Pericardial effusion with Myxedema coma (n=3).

Their clinical history, drug history, radioactive iodine therapy, iodinated contrast use, amiadarone therapy and duration & treatment of thyroid disease and associated illness, need for mechanical ventilatory support, detail evaluation of laboratory results, thyroid function tests, adrenocorticol reserve, sepsis panel and other investigations were analysed in detail.

**Results:** Mortality observed was 6.3% among patients with thyroid storm, 15.3% in Myxedema coma, 2.7% in atrial fibrillation. There was no mortality among patients with severe pericardial effusion. Mortality group has associated illness- agranulocytosis in thyroid storm, uncontrolled diabetes mellitus in Atrial fibrillation and myxedema coma. Fungal sepsis, Bacterial urosepsis, Peritonitis were also observed in mortality group. Survival group had liver cirrhosis, renal cell carcinoma and myocardial infarction in three patients with thyroid storm.

**Discussion:** Thyroid disease is one of the common endocrine disorder seen in general population as well as in endocrine clinic. However the sole cardiac manifestation in thyroid disorder is rare and includes atrial fibrillation and other arrhythmias in patients with thyroid storm. Other rare cardiac presentation of thyroid disorder is cardiac tamponade and pericardial effusion. Thyroid hormones also have positive and negative regulation of gene coding for various cardiac proteins. During the last ten years, we reviewed morbidity and mortality among hospitalised patients due to thyrocardiac disease. During this period we observed 16 cases of thyroid storm, 13 patients with myxedema coma, 36 patients with atrial fibrillation and 3 patients with severe pericardial effusion.

**Conclusion:** 10 years Mortality observed was 6.3% in patients with Thyroid Storm while in Myxedema Coma, it was 15.3%. There was no mortality in patients with severe Pericardial Effusion with Myxedema. Diabetes mellitus and sepsis were observed as common associated illness in mortality group. Methimazole induced agranulocytosis in one patient with Thyroid Storm was observed in mortality group.

Abstract #1050

CONCOMITANT GRAVES’ DISEASE AND PRIMARY HYPERPARATHYROIDISM

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UMDNJ-RWJMS

**Objective:** To describe a case of concomitant Graves’ disease and primary hyperparathyroidism presenting with hypercalcemia.

**Case Presentation:** A 71-year-old African American woman with a past medical history of hypertension, colon cancer, and anxiety disorder was admitted to the hospital with generalized fatigue, polyuria, polydipsia, and poor appetite for a few weeks. On examination, she was anxious. BP was 118/68 mm Hg, HR was 108 bpm, RR was 14, and she was afebrile. Extra-ocular muscles were intact. She was noted to have mild proptosis. The thyroid was normal in size, non-tender, and without bruits. Cardiovascular examination was notable for a 2/6 systolic ejection murmur. The pulmonary, abdominal, and neurologic examinations were unremarkable. There was trace bilateral lower extremity edema. Laboratory values showed a serum calcium of 12.3 mg/dL (8.6-10.4), albumin of 3.6 g/dL (3.5-4.8), intact PTH of 37 pg/mL (15-65), PTH related peptide of 0.2 pmol/L (<2), 25OH vitamin D of 65 ng/mL (30-74), TSH of 0.01 uIU/mL (0.45-4.50), and free T4 of 7.1 ng/dL (0.82-1.77). 1-23 uptake and scan of the thyroid showed 20% and 44% homogeneous uptake at 4 and 24 hours, respectively. Thyroid ultrasound showed a multi-nodular goiter with a dominant 1.8 cm complex hypechoic nodule in the right lower lobe with mild vascularity and no microcalifications. The patient was diagnosed with hypercalcemia related to hyperthyroidism. She received intravenous hydration and was started on methimazole and propranolol. Prior to discharge, the serum calcium improved to 11.2 mg/
ABSTRACTS — Thyroid Disease

dL (8.6-10.4) and free T4 improved to 5.53 ng/dL (0.82-1.77). Two months later, she was treated with 25.9 mCi of I-131. Although the free T4 normalized to 1.58 ng/dL (0.82-1.77), the serum calcium remained 10.4-10.7 mg/dL (8.6-10.4). Repeat labs revealed serum ionized calcium of 5.9 mg/dL (4.5 - 5.6), intact PTH of 65 pg/mL (15-65), 24-hour urinary calcium of 166.4 mg (100-300), and 25OH vitamin D of 46.4 ng/mL (30-74), which is consistent with primary hyperparathyroidism.

Discussion: The occurrence of Graves’ hyperthyroidism with primary hyperparathyroidism is rare. In our case, the diagnosis of Graves’ disease is suggested by low TSH, high free T4, and high diffuse I-123 uptake. The diagnosis of primary hyperparathyroidism is suggested by high calcium and non-suppressed intact PTH levels.

Conclusion: Hypercalcemia in Graves’ hyperthyroidism, particularly in older patients, should warrant a thorough investigation for concomitant primary hyperparathyroidism. Combined thyroidectomy and parathyroidectomy may be considered after hyperthyroidism is under control.

Abstract #1051

ATYPICAL PRESENTATION OF HURTHLE CELL FOLLICULAR THYROID CARCINOMA IN AN ELDERLY PATIENT

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Objective: To report a case of metastatic thyroid cancer in an elderly patient who presented with hip pain.

Case Presentation: 70 year old female who complained of persistent left sided hip pain during a recent hospitalization for syncope. She had history of DM, HTN and breast cancer s/p lumpectomy and RT in 2003. Initial syncope workup was negative; however she was noted to have an abnormal gait on exam. Hip x-rays were normal. MRI demonstrated a 5.0 x 2.9 x 2.3 cm lesion in the proximal Lt femur that was replaced the bone marrow. Findings were confirmed by CT and Bone scan. Biopsy of the lesion demonstrated Hurthle cell follicular thyroid carcinoma (HCC). Initial labs showed thyrotropin (TSH) 2.89mIU/ml (nl: 0.55-4.78), free thyroxine (FT4): 1.1ng/dl (nl:0.86-1.76), thyroglobulin: 23102ng/dl (nl: 0.73-84), Thyroglobulin Ab: < 20 IU/ml (nl:0-40). Thyroid ultrasound showed a 4.4 x 2.0 x 2.4 cm mass within the Lt lobe with no abnormal lymph nodes. Neck MRI confirmed these findings. She underwent total thyroidectomy and final pathology demonstrated HCC in the Lt lobe and a 0.5 cm papillary carcinoma in the Rt lobe. Post-surgery labs showed TSH 26.52mIU/ml, FT4: 0.7ng/dl, thyroglobulin 6330ng/dl. Low Dose I131 (2mCi) scan showed small area of uptake in the thyroid bed and no uptake in the Lt femur. Patient was started on levothyroxine. Following administration of recombinant thyrotropin she was given 250mCi of I131. Post treatment scan showed focal area of uptake in the thyroid bed but no uptake in the Lt femur. She received localized RT to the Lt hip after stabilization with intramedullary rods. The patient was referred to oncology to discuss further treatment options.

Discussion: HCC represents 3% of thyroid cancers. The clinical course is usually aggressive, especially in elderly patients. Initial presentation in this population commonly includes symptoms related to distant metastases. Our patient presented with hip pain and abnormal gait due to a metastatic lesion. Features such as decreased I131 avidity and late recurrence are associated with poor prognosis. Management of metastatic, I131 resistant HCC is challenging. Palliative external beam RT is recommended by current guidelines. Further modalities of treatment such as tyrosine kinase inhibitors are currently being studied in this population.

Conclusion: Metastatic HCC can present late in the course of the disease with atypical symptoms. Treatment options for this aggressive disease are presently limited. Newer therapeutic modalities including the use of tyrosine kinase inhibitors may prove beneficial in patients with advanced HCC.

Abstract #1052

ELEVATED POST-OPERATIVE THYROGLOBULIN LEVELS IN A PATIENT WITH FOLLICULAR THYROID CANCER AND A HISTORY OF GRAVES’ DISEASE — CHRONIC STIMULATION DUE TO TSI & TRAB, OR A FALSE ELEVATION?

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Case Presentation: A 60yo man with history of uncontrolled DM1, vitiligo, Graves’ disease treated with radioactive iodine (RAI), and Graves’ ophthalmopathy, presented with a palpable 4 cm left thyroid mass. Ultrasound revealed a 5.1 cm thyroid nodule, and fine-needle aspiration biopsy was suspicious for a follicular neoplasm. He underwent a total thyroidectomy; pathology revealed a 5.8 cm encapsulated follicular thyroid carcinoma with extensive...
vascular invasion. Seven weeks later, he received 208 mCi 131-I after thyrogen stimulation, and a post-ablation whole body scan showed a focus in the neck. A chest CT showed several subcentimeter pulmonary nodules. Thyroglobulin (Tg) 1 month postoperatively was 350 ng/dl (nl 0.73-84 ng/dl), TSH 12.35 mIU/ml (nl 0.55-4.78 mIU/ml), anti-Tg <20 IU/ml (nl 0-40 IU/ml). With TSH suppression to 0.06 mIU/ml, Tg reached a nadir of 288 ng/dl six months postoperatively. Thyroid stimulating immunoglobulin (TSI), TSH receptor antibody (TRAB) and thyroid peroxidase antibody (TPO Ab) were persistently elevated. PET/CT was negative. Nine months after thyroidectomy, Tg increased to 402 ng/dl, TSH <0.03 mIU/ml, anti-Tg <20 IU/ml. Neck CT and ultrasound revealed no evidence of disease, and repeat chest CT revealed stable pulmonary nodules. The patient is undergoing active surveillance with levothyroxine suppressive therapy.

Discussion: In the setting of well-differentiated thyroid cancer, Tg after total thyroidectomy with or without RAI can be used as a tool to monitor recurrence. There have been reports of increased aggressiveness of thyroid cancer in patients with Graves’ disease. However, in these patients, the presence of TSI and TRAB may cause an elevated Tg level, due to stimulation of subclinical disease that does not correlate with the amount of disease present. Alternatively, the Tg elevation may be false, due to interference of TSI and TRAB with the Tg assay. The etiology of an elevated Tg level in patients with Graves’ must be understood, to avoid excessive TSH suppression with thyroxine, or repeated doses of RAI to achieve euthyroglobulinemia. Aggressive therapy should be reserved for structural evidence of progressive disease on cross sectional imaging.

Conclusion: Elevated Tg levels after thyroidectomy in patients with Graves’ disease may be due to chronic stimulation of subclinical disease by TSI or TRAB, or due to interference of these antibodies with the Tg assay. Careful monitoring and imaging follow up is needed to avoid unnecessary therapy in these patients.

Abstract #1053

**IS THYROID NODULAR SIZE >3CM PREDICTIVE OF MALIGANCY BASED ON FINAL SURGICAL PATHOLOGY?**

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**Objective:** To evaluate the predictive value of nodular size (greater than 3 cm in diameter) in identifying malignancy based on final surgical pathology. If a predictive value does exist, determine whether thyroid nodular size alone, can be used as a predictor of malignancy and thus guide surgical therapy.

**Methods:** A retrospective, observational study was performed on patients with diagnosis of nontoxic multinodular or uninodular goiter that were seen at University of Florida, Jacksonville endocrinology clinics and underwent surgical intervention between January 1, 2010 and February 29, 2012. Incidence of malignancy based on surgical pathology for nodules > 3 cm versus nodules < 3 cm were examined.

**Results:** One hundred and eight thyroid nodules were included in this study. 38.9% (n=42) of nodules were greater than 3 cm and 61.1% (n=66) were less than 3 cm. Of the 42 nodules greater than 3 cm, 53.4% (n=22) were malignant. Of the 66 nodules less than 3 cm, 63.6% (n=42) were malignant. There was no statistically-significant difference in malignancy rates between nodules greater than 3 cm and nodules less than 3 cm (p=0.246, Chi-square test). The odds ratio of being malignant was 1.59 (95% CI: 0.72,3.49) for those nodules less than 3 cm compared to those greater than 3 cm.

**Discussion:** Nodules greater than 3 cm did not have statistically-significant higher rates of malignancy compared to less than 3 cm. Higher rates of malignancy were found in nodules less than 3 cm. Although not statistically significant, this finding may warrant further investigation with larger samples on malignancy rates in smaller nodules and their associated characteristics.

**Conclusion:** Thyroid nodules greater than 3 cm have similar risk of malignancy compared to those less than 3cm.
Abstract #1054

INCIDENTAL PAPILLARY THYROID MICROCARCINOMA IN A THYROGLOSSAL DUCT CYST: IS IT A PRIMARY TUMOR OR METASTATIC DISEASE?

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Objective: To report the case of a young woman who presented with papillary thyroid carcinoma arising incidentally from a thyroglossal duct cyst, and to review current recommendations for management and treatment dilemmas.

Case Presentation: 18 y/o woman who presented with a 3 cm painless neck mass in the anterior aspect of the neck. Neck CT scan revealed findings suggestive of a thyroglossal duct cyst (TGDC) and the patient underwent surgical resection of the mass. Histopathological examination showed a 0.5 cm papillary thyroid carcinoma arising from the thyroglossal duct cyst. The tumor showed surrounding fibrosis and calcifications without lymphovascular invasion with resection margins free of tumor. On physical examination there was no evidence of goiter or cervical lymphadenopathy. Thyroid function tests were within normal limits. Thyroid sonogram post TGDC resection showed a thyroid gland with normal echogenicity without abnormal focal lesions. No risk factors identified, such as family history of thyroid cancer or history of radiation exposure during childhood.

Discussion: The thyroglossal duct arises during the embryologic development of the thyroid, but usually vanishes during early fetal life. Failure to disappear can result in a cyst, duct or even in ectopic thyroid tissue. TGDC is the most common congenital neck mass. However the development of a malignancy in the TGDC is rare, with only approximately 200 cases reported in the literature. Currently, there is no consensus regarding postoperative management in these patients. Typical papillary thyroid microcarcinoma usually responds well to treatment and the definite therapy is surgical resection without thyroid stimulating hormone suppression therapy or radioiodine ablation therapy. However, it is still controversial whether an incidentally found lesion in a TGDC is a metastatic lesion versus a primary site tumor, challenging the current management. Recently, several authors have proposed stratification into low, moderate and high risk groups according to risk factors.

Conclusion: Papillary thyroid carcinoma arising from TGDC is a very rare condition usually found incidentally. It is important to remember that before making the decision of which patients should undergo total thyroidectomy and/or further managements, individual risk stratification should be done and long-term follow up should be mandatory.

Abstract #1055

NODULE CHARACTERISTICS AND THE INCIDENCE OF THYROID MALIGNANCY WHEN COMPARING INDETERMINATE AND NON-DIAGNOSTIC CYTOLOGY ON FINE NEEDLE ASPIRATION

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Objective: Evaluate the nodule characteristics and the incidence of malignancy of thyroid nodules with undetermined finding and non-diagnostic findings on fine needle aspiration.

Methods: We performed retrospective, observational study on patients with diagnosis of nontoxic multinodular or uninodular goiter that were seen at University of Florida, Jacksonville endocrinology clinics and underwent fine needle aspiration (FNA) between January 1, 2010 and February 29, 2012. Nodules with FNA that resulted in indeterminate cytology and non-diagnostic findings were included only. Variables examined included internal content of the nodule, margins, echogenicity, presence of microcalcifications, vascularity, and number of nodules, shape and presence or absence of abnormal lymph nodes on surgical pathology.

Results: Twenty one nodules were identified. Nodules with indeterminate cytology comprised 61.9% (n=13) versus 38.1% (n=8) for non-diagnostic nodules on FNA. When comparing both groups, there was no statistical significant difference in echogenicity, echotexture, internal content, margins, microcalcifications, vascularity, and number of nodules. There was no statistical significant difference in the rate of malignancy on surgical pathology when comparing indeterminate and non-diagnostic nodules (P value 1).

Discussion: Determination of certain characteristics of thyroid nodules on ultrasound that are associated with
risk of having indeterminate or non-diagnostic cytology, may help in guiding the treatment plan of thyroid nodule. In our study we did not find any difference in thyroid nodules characteristics for both groups. Furthermore we did not find any difference in the malignancy rates for both groups. However, the malignancy rate was higher (40%) than what has been reported in literature (10 - 30%) and this could be related to the small sample size. 

**Conclusion:** There was no statistical significant difference in the nodule characteristics and malignancy rates between indeterminate and non-diagnostic nodules on fine needle aspiration. However, we found a higher rate of malignancy of the two groups but this could be secondary to small sample size.

**Abstract #1056**

**THYROIDECTOMY IN A TWO-YEAR OLD FOR GRAVES’ DISEASE**

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**Objective:** The most common cause of hyperthyroidism in children is Graves’ disease. Treatment includes medical therapy with anti-thyroidals, radioactive iodine, or surgery, with medical therapy most often employed as a first-line treatment. We present the case of a two-year-old male with Graves’ disease unresponsive to medical therapy who underwent near-total thyroidectomy. To our knowledge this is the youngest patient reported in the literature to undergo thyroidectomy for Graves’.

**Methods:** A literature search was performed to evaluate the use of thyroidectomy for Graves’ disease in children.

**Case Presentation:** The patient presented to his pediatrician in April 2011 as a two-and-a-half-year-old male with hyperactivity, excitability, severe diarrhea, and diffuse neck enlargement noted by his family. His lab workup was consistent with Graves’ disease, with an undetectable TSH and a total T4 level of 31.2 mcg/dL (normal <10.5). His mother had Graves’ and his father’s family had a history of Graves’. Over a two-month period, the patient was treated with various combinations of methimazole,atenolol, prednisone, and saturated solution of potassium iodide (SSKI). Despite this he continued to have intractable symptoms, and it became apparent that he was not taking most of his medicines as an outpatient. He was admitted to a pediatric inpatient unit and under careful observation his thyroid function was better controlled. Because the medical regimen could not be reliably maintained in the outpatient setting it was decided the patient should be operated upon. We performed a near-total thyroidectomy without complication. Final pathology demonstrated a 27g thyroid consistent with treated Graves’ disease. His post-operative course has been unremarkable, and his thyroid function has been normalized with L-thyroxine.

**Discussion:** Medical management of Graves’ is the first-line treatment in children. Two other options include radioactive iodine and surgery. Radioactive iodine is avoided in the young because of fears of future infertility and the development of cancer.

**Conclusion:** Typically children are managed medically until they are old enough to undergo radioactive iodine therapy. However, surgery remains an effective option in intractable cases, even in the very young.

**Abstract #1057**

**GRAVES’ DERMOPATHY APPEARING MANY YEARS AFTER TREATMENT FOR GRAVES’ DISEASE**

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**Case Presentation:** An 83 year-old female presented with painful recurrent lumps on the dorsum of her feet and lower extremities since the age of 60. She had a past history of Graves’ disease diagnosed at age 44. Following 8 years of treatment with propylthiouracil, she developed thyroid storm. This was treated successfully with radioactive iodine and she has, since been maintained on daily levothyroxine. Physical exam revealed exophthalmos, acropachy, and bilateral indurated nodules on dorsum of both feet and lower extremities. Lab studies revealed TSI 4980 (Range < 150 % of normal), TBI 49.1 U/L (Range <1.0 U/L), TSH 1.6 uU/mL (Range 0.40-4.0 uU/mL), free T4 1.53 ng/dL (Range 0.80-1.80 ng/dL). A previous biopsy of the skin nodules had revealed mucin deposits, consistent with Graves’ dermopathy. Treatment was initiated with Clobetasol 0.05% applied nightly under occlusive dressing. Within 1 month, she had marked improvement.

**Discussion:** Dermopathy occurs in less than 5% of patients with Graves’ disease. Autoimmunity against the TSH receptor is responsible for mediating excess production of glycosaminoglycans and is the suspected pathogenic mechanism. Most patients with Graves’ disease gradually lose TSH-receptor autoimmunity and resolve dermopathy after medical treatment with propylthiouracil or surgical resection. Loss of TSH receptor activity after radioiodine therapy is less common.
Conclusion: In this patient, TSH receptor autoimmunity persisted and may have played a role in mediating new onset dermopathy many years after treatment. Cognition of this peculiar late presentation may aid in the expeditious diagnosis and treatment of Grave’s dermopathy.

Abstract #1058

EXCELLENT CORRELATION BETWEEN CYTOPATHOLOGIST-INDEPENDENT RAPID ONSITE EVALUATION AND FINAL CYTOPATHOLOGICAL EVALUATION OF THYROID FINE NEEDLE ASPIRATION (FNA) IN AN ENDOCRINE OFFICE SETTING

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Objective: Recent studies have emphasized the role of rapid onsite evaluation (ROSE) in thyroid FNA, many showing that ROSE has decreased the number of non-diagnostic aspirates with potential cost savings. This has led to its increased use in the clinical settings and more endocrinologists are utilizing this procedure in the office. We retrospectively investigated the accuracy of ROSE performed by a single office-based ECNU-certified endocrinologist for specimen adequacy in thyroid FNA and compared the findings with published literature

Methods: Data were collected from the electronic medical records of 102 consecutive patients with ultrasound-guided FNA of 175 nodules, performed by a single endocrinologist from March 1, 2010 to March 31, 2011. Smears prepared on site included at least 2 air dried slides. The needle was rinsed into CytoLyt solution for Thin Prep evaluation. Each procedure was given a final adequacy rating of adequate or inadequate based on ROSE by the endocrinologist. At the end procedure location of nodule, size, flow and status of specimen adequacy were noted. Agreement on specimen adequacy between onsite, and final assessment and non-diagnostic rates were calculated.

Results: During the study period, 102 patients (90 women and 12 men; mean age 54 years) underwent FNA of 175 nodules. The average size of the nodule was 1.7 cm. Among 146 specimens that were interpreted as adequate onsite, 142 (97.3%) remained concurrent at the time of diagnosis. Four (2.7%) were changed to non-diagnostic by cytopathologist. Out of 29 specimens which were evaluated as inadequate on site, 3 (10.3%) were changed to adequate by cytopathologist. The final calculation identified 145 (82.9%) as adequate and 30 (17.1%) as inadequate. Overall, 96% level of agreement (final versus onsite) regarding specimen adequacy was achieved.

Discussion: Potential benefits of ROSE include fewer passes once adequacy is confirmed and a potential for increased adequacy by performing more passes if otherwise. Our study showed excellent correlation between ROSE and cytopathological findings. The time and expense of ROSE especially with a cytopathologist in attendance had limited its utility in some settings. Cytotechnologists have been resorted to as an alternative source of technical skills, but current lack of reimbursement limits this alternative.

Conclusion: To our knowledge, this is first study to evaluate specimen adequacy for FNA performed solely by an endocrinologist with ROSE in an office based setting, without the use of cytopathology specialists or technicians. The results on adequacy were comparable or even better, when compared to published data on other physicians performing FNA with ROSE.

Abstract #1059

RHABDOMYOLYSIS AND RENAL FAILURE WITH HYPOTHYROIDISM

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Objective: To present a case of rhabdomyolysis and renal failure as rare complications of hypothyroidism that highlights the importance of assessing thyroid function in patients with myalgia.

Case Presentation: A 60-year-old African-American male presented to his primary care physician with a 1-month history of gradually progressing myalgia, most severe in both arms and legs. He denied any trauma, strenuous activity, seizures, or use of alcohol and drugs, including cocaine. He had a history of toxic multinodular goiter, was treated with 25.1 mCi of iodine-131 six months earlier, and lost follow-up with his endocrinologist after that. Musculoskeletal examination was unremarkable. Initial investigations revealed elevated creatinine phosphokinase (CPK) of 4,050 U/L (20-200 U/L), creatinine 2.2 mg/dL (0.5-1.4 mg/dL), baseline creatinine 1.2 mg/dL, and transaminases slightly elevated. Thyroid stimulating hormone (TSH) was not checked. Repeat laboratory tests after 4 weeks showed even higher CPK of 7,559 U/L, creatinine still elevated at 2.2 mg/dL, and transaminases slightly higher than before. He was sent to the emergency room, where his TSH was found to be elevated at 83 uIU/mL (0.4-4.0 uIU/mL). Free T4 was <0.40 ng/dL (0.71-1.51 ng/dL). Patient was diagnosed with hypothyroidism, rhabdomyolysis, and renal failure. He was treated with levotyroxine 125 mcg daily and intravenous fluids. Repeat laboratory tests 2 weeks later
showed improving CPK at 677 U/L, creatinine of 1.5 mg/dL, and TSH of 25 uIU/mL. After 6 weeks of treatment, the myalgia resolved, TSH was 1.19 uIU/mL, CPK was 193 U/L, creatinine was 1.3 mg/dL, and liver enzymes were normal.

**Discussion:** Hypothyroidism is a common disorder, yet presentation can be highly variable. Muscle symptoms such as myalgia, weakness, easy fatigability, and cramps are prevalent and can be prominent during rapid onset of hypothyroidism after surgery or iodine 131 therapy. However, rhabdomyolysis is rare, and only a few cases with severe hypothyroidism have been reported in the literature. The exact mechanism is unclear, but both impaired glycogenolysis and impaired mitochondrial oxidative metabolism have been implicated. Our patient developed rhabdomyolysis and acute renal failure because of overt hypothyroidism. He did not have any other precipitating factors, such as strenuous exercise or lipid-lowering drugs. Along with aggressive hydration, correction of the underlying hypothyroidism is key. After thyroxine replacement, his myalgia, rhabdomyolysis, and acute renal failure resolved.

**Conclusion:** This case highlights the importance of evaluating for and treating thyroid disorders in patients with muscle complaints and/or unexplained increase in CPK concentration.

Abstract #1060

**AUTOIMMUNE THYROID DISEASE AND STIFF-PERSON SYNDROME**

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Ochsner Clinic Foundation

**Case Presentation:** A 23-year-old African-American female presented with a 1-day history of painful spasms of both legs. She also complained of palpitations, hot sensation, and anxiety. On examination, she was afebrile, alert and oriented but anxious, had thyromegaly, lid lag, fine tremor. Reflexes are brisk with shortened relaxation phase. She had rigidity of lower back and both lower extremities along with episodes of painful muscle spasms of lower extremities bilaterally. Her TSH was <0.010 uIU/mL (0.4-4.0 uIU/mL), Free T4 was 2.97 ng/dL (0.7-1.51 ng/dL), free T3 was 4.4 pg/mL (2.3-4.2 pg/mL), thyroid peroxidase antibodies were 131.5 IU/mL (0-6 IU/mL), thyroid-stimulating immunoglobulins 423% (<140%). She was diagnosed with thyrotoxicosis from autoimmune thyroid disease and treated with beta blocker, propylthiouracil (PTU) and then potassium iodide. PTU was later changed to methimazole because her liver enzymes were increasing. Stiff-person syndrome (SPS) was suspected, glutamic acid decarboxylase antibodies (GAD Abs) were ordered, and Neurology was consulted. She was treated with diazepam and baclofen with mild improvement in her symptoms. Her GAD Abs were very high 1,612 H (≤0.0 nmol/L), supporting the diagnosis of SPS. After a 5-day course of intravenous immunoglobulin, she had significant improvement in rigidity and muscle spasms. She was able to participate in physical therapy and was sent to an inpatient rehabilitation facility.

**Discussion:** Autoimmune thyroid disease is characterized by the presence of antibodies against thyroid peroxidase, thyroglobulin, and TSH receptors. These patients have an increased frequency of other autoimmune diseases. SPS is a very rare neurological disorder with an estimated prevalence of about 1-9 per 1,000,000 persons that is characterized by fluctuating stiffness and spasms, predominantly in the lower back and proximal lower extremities. SPS has been associated with other autoimmune diseases such as autoimmune thyroid disease and type 1 diabetes mellitus. The pathophysiology of SPS is unclear but is thought to result from immune-mediated loss of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA). Glutamic acid decarboxylase is the key enzyme in synthesis of GABA. In about 60% of patients with SPS, anti-GAD antibodies are present in very high titres (50-500 times the levels found in type 1 diabetes) and help in the diagnosis of this disorder. The symptoms of SPS decrease with the use of GABA agonists such as benzodiazepines and baclofen. Many patients require immunosuppression with IV immunoglobulin, corticosteroids, or plasmapheresis.

**Conclusion:** This case highlights the importance of investigating for coexisting autoimmune diseases.

Abstract #1061

**PREVALENCE OF THYROID FUNCTION TESTING IN PATIENTS WITH NEWLY DIAGNOSED HYPERCHOLESTEROLEMIA AT BOSTON MEDICAL CENTER**

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**Objective:** Guidelines from the American Association of Clinical Endocrinologists, American Thyroid Association, and National Cholesterol Education Program recommend screening for hypothyroidism as a secondary cause of hypercholesterolemia. The extent to which primary care providers apply these guidelines is unknown. Our objective is to determine the rate of thyroid function screening in
patients with newly diagnosed hypercholesterolemia at Boston Medical Center’s (BMC) primary care clinics.  

Methods: This is a retrospective chart review of patients ages ≥18 years with a total cholesterol ≥200 mg/dL and/or LDL cholesterol ≥160 mg/dL who presented to BMC’s General Internal Medicine or Family Medicine clinics for routine care from 2003-2011. Patients who had previously taken lipid-lowering agents or thyroid medications were excluded. The proportion of patients with serum thyroid function testing obtained within six months prior to or following the initial elevation of total and/or LDL cholesterol was determined. From this subset, the proportion of patients with abnormal serum thyroid stimulating hormone (TSH) and the proportion in whom levothyroxine and/or an antilipemic agent was subsequently initiated were ascertained.

Results: There were 8795 patients (55% women; mean age 53 ± 12 [SD] years; 45% African-American, 24% Caucasian, 16% Hispanic) with a new diagnosis of hypercholesterolemia within the study period. Serum TSH was obtained in 4349 (49.5%) patients, 225 (5.2%) of whom had a TSH concentration >5 µIU/mL. Of all patients who had TSH screening, 151 (3.5%) had a TSH concentration 5-10 µIU/mL, and 74 (1.7%) had a TSH concentration >10 µIU/mL.

Discussion: Approximately half of the primary care patients with newly diagnosed hypercholesterolemia at our institution receive thyroid function screening. Of those in whom a TSH was obtained, only a small subset (5.2%) had hypothyroidism.  

Conclusion: Although testing rates were low, these findings demonstrate that only a small proportion of patients with newly diagnosed hypercholesterolemia have hypothyroidism.

Abstract #1062  

RAPID REVERSAL OF SEVERE HEART FAILURE AFTER PLASMAPHRESIS IN A PATIENT WITH THYROTOXICOSIS-INDUCED DILATED CARDIOMYOPATHY AND THYROID STORM  

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Objective: To describe a drastic effect of plasmapheresis (PP) on severe heart failure due to thyrotoxicosis-induced dilated cardiomyopathy (TIDC) and thyroid storm.

Case Presentation: A previously healthy 22 yo man was admitted with a 5-day history of SOB and fever. On admission, his vitals were T’ 100 °F, RR 30, HR 200, BP 116/87 and he was intubated for respiratory failure. He was also noted to have AFib with RVR of 170 at EKG, cardiomegaly, pulmonary edema and right pleural effusion at Chest XR, and dilated LV and severe LV systolic dysfunction (LVSD) with LVEF 10.5% at Echo. TFT was consistent with Graves’ hyperthyroidism (TSH <0.01, NR 0.35-5.5 µIU/mL; FT4 4.3, NR 0.89-1.76 ng/dL; TT3 256, NR 76-81 ng/dL; TSI 546, NR<140%). He was started on PTU, iodine, steroid and beta-blocker for thyroid storm and inotropes, digoxin and diuretics for cardiogenic shock. DC cardioversion and radiofrequency ablation were attempted for AFib without success. Liver enzymes went up (ALT 2354, NR 10-40 U/L; AST 3581, NR 8-40 U/L) following hypotensive episodes. Therefore PTU was stopped on day #2 and he received daily PP on day #3 for 3 consecutive days. There was drastic improvement in clinical, biochemical and cardiac parameters immediately after 3 days of daily PP. Pre- vs 1 day post-PP data were: FT4 2.5 vs 0.9 ng/dL, TT3 83 vs 34 ng/dL, TSI 546 vs 369%, max HR 154 vs 99, max BP 124/92 vs 151/61, LVEF 10.5 vs 42% (NR 60-100%). There was also dramatic improvement in pulmonary edema and pleural effusion at Chest XR. Therefore he underwent total thyroidectomy on day #10, was extubated on day #11 and was discharged home on day #23. There was a complete reversal of TIDC and LVSD 12 days after PP and 7 days after thyroidectomy. Pre- vs 12 days post-PP echo data were: LVIDd (left ventricular internal dimension at diastole) 6.89 vs 5.44 cm (3.8-5.7), LVIDs (left ventricular internal dimension at systole) 5.86 vs 3.67 cm (2.2-4) and LVEF 10.5 vs 60.4%.  

Discussion: Severe LVSD due to TIDC is a rare manifestation of hyperthyroidism. There were several case reports describing reversal of LVSD and TIDC with anti-thyroid medications, thyroidectomy or radioiodine treatment. However, to our best knowledge, there has been no previous report of rapid and beneficial effect of PP on LVSD. Another observation was that there was a striking and complete reversal of LVSD and TIDC 12 days after euthyroidism in our case though it took from several weeks to several months in all previous reports. Early achievement of euthyroidism with PP and thyroidectomy in our case may have accelerated the recovery.

Conclusion: Plasmapheresis may be an effective option to rapidly improve severe LVSD in patients with heart failure due to TIDC and thyroid storm.
Abstract #1063

ATYPICAL (CALCITONIN-NEGATIVE) MEDULLARY THYROID CANCER: THE SEVENTH REPORTED CASE

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Objective: To report a case of a 79-year-old woman with an atypical medullary thyroid carcinoma with minimal (<5%) calcitonin expression.

Methods: We describe the patient’s clinical findings and laboratory test results, as well as the gross and histopathological features and immunohistochemical staining characteristics of her tumor. We also review the literature describing atypical medullary thyroid carcinomas with little or no calcitonin expression.

Case Presentation: This 79-year-old woman was noted to have an enlarging right thyroid mass. Fine needle aspiration biopsy revealed atypia of undetermined significance. We discussed the option of rebiopsy versus thyroidectomy. The patient opted for surgery and underwent a total thyroidectomy as well as right lower parathyroidectomy for incidentally discovered hyperparathyroidism. Pathologic examination revealed mild hyperplasia of the right lower parathyroid. The right thyroid mass showed morphologic appearance highly suggestive of a medullary thyroid carcinoma, as well as strong and diffuse staining for synaptophysin and chromogranin. However, the tumor cells were essentially negative for CEA and calcitonin. Including the present case, we identified 7 cases of so-called “atypical” medullary thyroid carcinomas with little or no calcitonin expression.

Discussion: This report describes the seventh documented case of a medullary thyroid carcinoma with little calcitonin and CEA expression. The differential diagnosis of a tumor with these immunohistochemical and pathologic features includes well-differentiated neuroendocrine tumors of the thyroid including paragangliomas, intrathyroidal parathyroid tumors, primary oat-cell carcinomas of the thyroid, or metastatic neuroendocrine tumors. As the traditional tumor markers calcitonin and CEA are not secreted by these atypical medullary thyroid cancers, postoperative surveillance for recurrence or metastatic disease is dependent upon periodic neck ultrasonography and other cross-sectional imaging.

Conclusion: Atypical medullary carcinoma of the thyroid without calcitonin expression presents a diagnostic challenge, and the lack of tumor marker production makes surveillance for disease recurrence difficult as well.

Abstract #1064

TRANSCRIPTOMICS AND PROTEOMICS AS ANALYTICAL TOOLS FOR DIFFERENTIAL PREDICTION AND PROGNOSIS OF EPITHELIAL THYROID CANCER

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Objective: To search for new molecular markers for prediction and prognosis in epithelial thyroid tumors

Methods: 1-Tumor samples. Surgical snap-frozen specimens were obtained from all volunteer patients with papillary carcinoma (PC), follicular adenoma (FA), and follicular carcinoma (FC), recruited since January 2010. 2-Validation of a previously reported genetic signature (Oncogene 2008;6:1554-61) was performed by real time-polymerase chain reaction (qRT-PCR) and microfluidic card (low density micro-array; Applied Biosystems; SDS203 package; Data AssistTM v3.0). 3-Post-transcriptomic research. Proteomics was carried out by two-dimensional difference gel electrophoresis (DIGE). Protein extracts were labelled with cy2, cy3 or cy5 and 2D-PAGE was performed. Differential analysis was done using software Decyder (GE Healthcare) and SameSpots (Progenesis). Proteins of interest were identified by MALDI-TOF MS/MS, ESI-MS/MS (QTOF) using Mascot search engine.

Results: 1-Differential gene expression for PTC: A) Overexpression of genes PTPRN2, and TWIST1. B) Underexpression of ANLN, PRC1, and RRM2. 2-Differential Expression for FTC: A) Overexpression of APLP2, PPAP2B, SIAH1. B) Underexpression of CEP55. 3- Proteomic profiling revealed that 208 out of 800 detected and matched spots, exhibited changes in the expression with a statistical significance (ANOVA p< 0.05) and 120 proteins were successfully identified by MALDI-TOF MS/MS, ESI-MS/MS (QTOF) using Mascot search engine.

Conclusion: Atypical medullary carcinoma of the thyroid without calcitonin expression presents a diagnostic challenge, and the lack of tumor marker production makes surveillance for disease recurrence difficult as well.
Discussion: Poorly differentiated thyroid tumors are responsible for most thyroid cancer patient deaths. The analysis of the genetic signature as potential predictor of worse prognosis, identified 9 genes as potential new biomarkers, which will be confirmed by western blot or immunohistochemistry. The proteomic approach permits us to compare hundreds of proteins in a single experiment under quantitative and reproducible conditions. 2D-DIGE analysis showed differentially expressed proteins by distinct epithelial thyroid tumors.

Conclusion: 1- Results of this investigation may allow for better characterization of the differential gene expression profile in PTC and FTC. 2- This research may also contribute to the knowledge of the dedifferentiation process of epithelial thyroid tumors and the identification of new therapeutic targets in the future.

Abstract #1065

STRAIN RATIO CALCULATION - DIAGNOSTIC VALUE IN MALIGNANT UNINODULAR THYROID CANCER

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Objective: To evaluate the diagnostic value of strain ratio, measured with elastography, in identifying thyroid malignancy. Elastography measures tissue elasticity, after applying an external force, and scores tissue elasticity in a qualitative manner, but also measures directly the strain ratio. In the literature, strain ration higher than 4 or 5 are considered predictive for malignancy.

Methods: Retrospective study of 105 cases, mean 51.2±5.1 years, 89 females and 16 males, diagnosed with uninodeular goiter with volume higher than 0.5 ml. Enrolment period: January 2011- June 2012. All cases underwent surgery after complete evaluation. Extemporaneous and post surgical histopathological exam was performed in all cases. Strain ration was measured with a HITACHI EUB 7500 HV machine, with 6-13 MHz variable frequency linear probe, Hitachi Medical System Tokyo, Japan.

Results: We identified 13 cases (12.38%) with thyroid malignancy: 1 undifferentiated thyroid carcinoma, 1 case with follicular cancer and 11 cases with papillary carcinoma (8 follicular variant, 3 simple papillary carcinoma). From the benign cases, 78/92 cases had strain ration lower than 3, 10 cases had values between 3 and 4, and 4 cases had values higher than 4. 12 out of 13 carcinoma cases had strain ration values higher than 4, with a mean of 5.45±1.15, the remaining 1 case having a score between 3 to 4. As a diagnostic tool in identifying malignancy, higher strain ration had: a sensitivity of 92.3%, specificity of 95.65%, PPV = 75% with a very high NPV = 98.88%. Low levels of strain ration are highly predictive for benign lesion : VPP= 98.7%, with a lower negative predictive value = 53.8%.

Discussion: The strain ratio, calculated by the computer, helps the diagnostic value of real time sonoelastography. The physician gives by self assessment a Ueno score, from 1 to 5. The strain ratio is a much more objective criteria in differentiation binging versus malignant nodules.

Conclusion: The use of strain ratio value, add diagnostic value in identifying malignant thyroid nodules.

Abstract #1066

SUBCLINICAL HYPOTHYROIDISM IN RELATION TO METABOLIC SYNDROME AND ITS COMPONENTS

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Objective: To study the association between subclinical hypothyroidism and metabolic syndrome and its components.

Methods: All patients routinely attending the National Center for Diabetes, Endocrinology, and Genetics’ clinics (Amman- Jordan) during the period between February and June 2012 were eligible for inclusion in the study. A total of 1037 patients were consecutively enrolled in the study: 523 with MetS (424 female, 99 male, mean age: 50.5±11.0) and 514 without MetS (423 female, 90 male, mean age: 48.5±11.5).

Results: A total of 108 cases (10.4%) with SCH were observed of whom 75 (14.3%) with MetS and 33 (6.4%) without MetS (P=0.0001). Female gender (0.02) and triglycerides above 150 mg/dl (P=0.0001) were associated with significant increase in the prevalence of SCH.

Discussion: Our study showed that about one in every seventh patient with MetS had SCH and, there was positive correlation between SCH and TG, after adjusting for gender and age and Hba1c, the correlation still existed.

Conclusion: The high prevalence of SCH in patients with MetS (14.3%) suggests a need for investigating the presence of SCH during the care of MetS patients.
Abstract #1067

ELEVATED TROPONINS IN A PATIENT WITH GRAVES’ DISEASE - THYROTOXICOSIS INDUCED MYOCARDIAL INFARCTION?

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John H Stroger Jr Hospital of Cook County

Objective: Describe the rare presentation of thyrotoxicosis induced acute myocardial infarction (AMI).

Case Presentation: 49 year old female with Graves’ disease for 7 years who presented with left sided chest pain and dyspnea on exertion. She was not compliant with her Methimazole. On admission, her vital signs were normal. Physical examination showed elevated JVP, mild orbitopathy and large, diffuse, non-tender thyroid gland. Laboratory data showed a TSH of <0.015 mIU/ml, FT4 4.75 ng/dl and FT3 9.53 pg/ml. Troponins were elevated to 2.530 ng/ml trending to 5.390 ng/ml and her EKG had no ST elevations. Telemetry overnight showed paroxysmal atrial flutter. A recent cardiac catheterization (5 months before admission) had shown no evidence of coronary artery disease. An echocardiogram showed normal ejection fraction and no regional wall motion abnormalities. The cause of her elevated troponins was considered to be thyrotoxicosis-induced AMI. She was restarted on methimazole and propranolol without any chest pain recurrence. At follow up, she was euthyroid, with no cardiopulmonary symptoms and she opted to undergo radioactive iodine ablation.

Discussion: Thyrotoxicosis has been frequently associated with cardiovascular abnormalities. Cardiac arrhythmias and congestive heart failure are very common manifestations of thyrotoxicosis. Angina pectoris has been reported to occur in 0.5%-20% of patients with thyrotoxicosis and there has been few reports (10 cases) of thyrotoxicosis induced AMI either due to a thrombotic event or due to vasospasm. Almost all cases of AMI have been reported in Grave’s disease. Both hyper- and hypothyroidism are known to be associated with coagulation abnormalities. Thyrotoxicosis also increases sensitivity to norepinephrine and/or a blunted response to nitric oxide mediated vasodilatation in the coronary arteries causing coronary vasospasm. This two mechanisms are the main considerations in our patient, however a repeat angiogram was not performed at the time of this event so we could not conclude which of them was the cause of her AMI. However, the fact that she was treated with beta-blockers without any complications suggests new thrombosis as the most likely etiology.

Conclusion: Thyrotoxicosis is a rare and poorly understood cause of AMI with current theories suggesting vasospasm and the prothrombotic state of thyrotoxicosis as causative mechanisms.

Abstract #1068

SEVERE HYPOTHYROIDISM INDUCED BY FLAXSEED OIL CAPSULES: A CASE REPORT

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Objective: Flaxseed is a commonly used dietary supplement. It contains cyanogenic glycosides, which can cause hypothyroidism. We report a case of severe hypothyroidism after flaxseed use.

Case Presentation: A 27yo man saw his Internist for follow-up of hypercholesterolemia. Three months before he was told of high cholesterol 334 mg/dl. He denied any significant past medical history or medication use. Routine laboratory values were significant for thrombocytopenia, transaminitis, renal insufficiency, and a TSH >150 mIU/l (0.4-4.5). Repeat tests confirmed these findings. He was referred to Endocrinology. He had also noted fatigue, hair loss on legs and scalp, myalgias, hoarseness, dry skin, and increased bleeding with shaving. Due to the multiple, disparate laboratory abnormalities and the lack of association of transaminitis and thrombocytopenia with hypothyroidism, he was questioned on the use of dietary supplements. He admitted to starting a daily regimen of flaxseed oil after the diagnosis of hypercholesterolemia. Physical exam was significant for a 35 gram heterogeneous thyroid gland, decreased eyebrows and leg hair. Additional tests: T3 <25 ng/dl (76-181), free T4 0.1 ng/dl (0.8-1.8). Thyroid peroxidase antibodies >1000 IU/ml (>35) and thyroglobulin antibodies 900 IU/ml (<20). 24 hr urine iodine was normal. 24 hr RAIU was 0.2%. Thyroid ultrasound revealed a small thyroid gland. The flaxseed oil was stopped. He was prescribed levothyroxine 150 mcg daily. After 2 months the prothrombin time, platelet count, creatinine, T3, free T4 and liver function tests were normal. The TSH decreased to 5.80 mIU/l. He felt much more energetic with significantly less myalgias, and his eyebrows were growing back. Levothyroxine was increased. On follow up one year later, he is maintained euthyroid on levothyroxine 200mcg daily.

Discussion: The use of dietary supplements and herbal medications is not always reported by patients, so the clinician should be specific when obtaining a history of medication use. This is especially important when the laboratory abnormalities do not correlate with the severity of the clinical picture. Flaxseed contains cyanogenic glycosides which are converted to thiocyanate by the liver. Thiocyanate is a competitive inhibitor of the sodium-
iodine symporter in the thyroid and has been associated with thyroid dysfunction in humans, and necrosis in rats.

Conclusion: It is important to include supplements when taking a history of medication use. The appearance of multiple laboratory abnormalities, particularly in a patient who is not acutely ill, should prompt investigation of dietary supplement use. Flaxseed supplements may be associated with thyroid destruction and severe hypothyroidism.

Abstract #1069

CLINICAL AND SUBCLINICAL HYPOTHYROIDISM IN TYPE 2 DIABETIC PATIENTS WITH MICROVASCULAR AND MACROVASCULAR COMPLICATIONS

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Objective: This study has been designed to find out frequency and association of clinical and subclinical hypothyroidism in type 2 diabetic patients with microvascular and macrovascular complications.

Methods: This cross sectional study was carried upon 227 (female= 152, male=75) type 2 diabetic patients purposely selected in the department of Endocrinology, Bangladesh Institute of Research and Rehabilitation in Diabetes, endocrine and Metabolic Disorders (BIRDEM), Dhaka, Bangladesh, during the period of December 2009 to November 2010. Pregnant or patient with sever co-morbid conditions were excluded. Statistical analysis was analyzed by SPSS programme.

Results: FT4 and TSH were studied in 227 diabetics. Frequency of hypothyroidism was 30.4% having significantly low FT4 and high TSH than the euthyroid subject. As 95% Confidence Interval FT4 and TSH were [(10.17 to 11.47) Vs (13.72 to 14.34) in pmol/L] and [(6.47 to 11.84) Vs (1.75 to 2.08) in uIU/ml]). But the frequency hypothyroidism was significantly high for subjects with complication of diabetes (n 156) in contrast to that for subjects without complication of diabetes (n 71) (34.6% vs 21.1%; p 0.041). Among the hypothyroid diabetic subjects (n 69), 58% (n 40) were sub clinical hypothyroid. The other variable of the study included age, BMI, SBP, DBP, serum Hemoglobin, fasting plasma glucose, HbA1c%, serum creatinine, CCR, serum total cholesterol, Serum triglyceride, serum HDL and serum LDL. The 54 hypothyroid subjects with complication of diabetes did not differ from 15 hypothyroid subjects without complication of diabetes (sig. 0.147) by logistic analysis where 14 study variable including two thyroid hormones included as covariate (sig. > 0.066). The 40 sub clinical hypothyroid subjects with diabetes was different from the rest of the 29 hypothyroid subjects with diabetes (sig. 0.000) by logistic analysis and among the 14 study variable serum FT4, serum Hb, HbA1c and serum Cholesterol had influenced the difference significantly (sig. < 0.028).

Discussion: This study documented frequency of hypothyroidism among type 2 diabetes as 30.4% in Bangladesh and this figure is signally higher among the diabetic with complication(s) - 34.6%. Clinical and biochemical feature among the hypothyroid do not differ on presence or absence of diabetic complication. Four biochemical parameters namely HbA1c, serum Hb, serum Cholesterol and serum FT4 were found to be determinant of sub clinical hypothyroidism in hypothyroid and type 2 diabetic subjects.

Conclusion: This hospital-based cross-sectional study documented not only the coexistence of primary hypothyroidism with type 2DM but also emphasized on importance of screening of hypothyroidism.

Abstract #1070

AUTOANTIBODIES DURING TREATMENT WITH PEGINFERON AND RIBAVIRIN

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Case Presentation: A 52 year old African American female with chronic hepatitis C type 1A infection presented to the endocrine clinic with thyroid stimulating hormone (TSH) of 0.013 mIU/L and free thyroxine (T4) of 3.72 ng/dl. She had been treated with interferon Pegasys 180 mcg/wk + Ribavirin 100 mg/day for 14 weeks. Prior to beginning therapy, she had normal thyroid function test. Treatment was stopped because she was symptomatic, with loose stools and heart palpitations. Thyroid peroxidase (TPO) antibodies was 586.8 IU/ml and thyroid stimulating immunoglobins (TSIg) antibody was 4.4 IU/ml. Thyroid scan showed a low uptake. She was treated with prednisone and propanolol for thyroiditis. Several days after beginning these medications, the patient was hospitalized for new onset diabetic ketoacidosis. After six months of being off interferon therapy, Glutamic acid decarboxylase antibody (GAD) was 37.2nmol/l, Insulin antibody was negative, Islet cell antibody > 1:8, Islet cell IgG autoantibody > 80, Serum C peptide was 1.5. ng/ml. Fourteen months after having stopped interferon, TPO antibodies was 317.4 IU/ml and TSIg was 1.9 IU/
ml. More than two years after stopping interferon therapy, GAD antibodies was still present at 19.4nmol/l, C-peptide 0.1ng/ml, with glucose of 256mg/dl. She has been treated with insulin since onset.

**Discussion:** Chronic infection with hepatitis C virus is a significant public health problem due to complications including end-stage liver disease as well as hepatocellular carcinoma. The standard of treatment is limited to the combination of pegylated interferon (PEG) and ribavirin (RBV). The treatment duration and ribavirin dosage depends on the viral genotype, and treatment guidelines recommend a combination of PEG with RBV 48 weeks for HCV genotype 1. Patients receiving PEG and RBV therapy for chronic hepatitis C may experience side effects. Type 1 interferon has immunomodulatory properties. The following case exemplifies a unique presentation of two autoimmune disorders manifesting simultaneously.

**Conclusion:** It would be beneficial to screen patients prior to interferon therapy for diabetes mellitus and thyroiditis.

**Abstract #1071**

**THYROTOXIC PERIODIC PARALYSIS. A CASE REPORT**

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**Objective:** To describe a case of thyrotoxic periodic paralysis in a Peruvian patient with no personal history of hyperthyroidism.

**Methods:** We abstracted the clinical chart and reviewed the pertinent medical literature.

**Case Presentation:** A Hispanic 33-year-old man was admitted because of complete flaccid paralysis. His personal and family history was negative for thyroid disorders. He complained of previous episodes of muscle weakness, which affected more severely the lower limbs. These episodes were mild and transient. Before admission, he was eating a lot of carbohydrates, ingesting alcohol, and doing exercise. Physical examination showed a diffuse goiter (4N), without exophthalmos or pretibial myxedema. Sensory function was not affected and deep tendon reflexes were absent. On admission, glucose, creatinine, urea, calcium, and sodium were normal; however, potassium was 2 mEq/L, TSH 0.004 μU/mL, and free thyroxine was >6 ng/dl. He was diagnosed with thyrotoxic periodic paralysis and started treatment with potassium chloride iv, propranolol, and thiamazole. He was discharged without complaints, potassium was 4.84 mEq/L, and thyroid peroxidase antibodies were positive.

**Discussion:** Thyroid periodic paralysis (TPP) is an alarming and potentially lethal complication of hyperthyroidism characterized by muscle paralysis and hypokalemia. TPP is more prevalent in Asian populations, although it can occur in any ethnicity. TPP occurs more frequently in men than in women. The clinical presentation includes flaccid paralysis, signs of thyrotoxicosis and hypokalemia during the paralytic crisis. Hypokalemia reflects an increased influx of the ion to the intracellular compartment. During TPP, immediate supplementation with potassium chloride is warranted to prevent major cardiopulmonary complications. Oral propranolol ameliorates the paralysis.

**Conclusion:** TPP is an infrequent complication of thyrotoxicosis. Early diagnosis and prompt treatment with supplementation of potassium prevents life-threatening cardiovascular complications associated with hypokalemia. Definitive treatment is adequate control of hyperthyroidism.

**Abstract #1072**

**MANAGEMENT CHALLENGES IN THE CARE OF PATIENTS WITH THYROID STORM AT A TERTIARY HOSPITAL IN SOUTH-WEST NIGERIA**

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**Objective:** To describe 2 patients who presented with thyroid storm at the university college hospital, Ibadan and the challenges encountered in their management.

**Methods:** An analysis of the case records of patients presenting to the medical wards of the university college hospital, Ibadan with a primary diagnosis of thyrotoxicosis was made over a period of 12 months from June 2011 to June 2012. Two patients with thyroid storm were identified from the records and their management challenges presented.

**Case Presentation:** This case report presents 2 female patients with thyroid storm and thyrotoxic heart disease. Both patients presented with heart failure and hepatic dysfunction. Their clinical management and outcome was hampered by various factors such as: 1. Poor drug compliance in the early stages of the disease. 2. Delay in making a clinical and biochemical diagnosis of thyrotoxicosis. 3. Delay in commencement of effective antithyroid drugs such as carbimazole, propranolol and lugol’s iodine. 4. Lack of available space for care in the medical intensive care unit. 5. Severe financial constraints and poor social support for one of the patients. 6. Multi-organ failure.
**Discussion:** Thyroid storm is an acute medical emergency which may be precipitated by trauma, surgery and systemic illness especially sepsis. Its pathogenesis remains poorly understood but may be due to a rapid increase in thyroid hormone levels due to the precipitating factors. The diagnosis is clinical and is aided by the Burch and Wartofsky criteria with a score of greater than 45 strongly suggestive. The 2 cases reported had scores of 95 and 90 respectively. Both cases presented with thyroid storm complicated by thyrotoxic heart disease and hepatic dysfunction. The management challenges encountered in the care of both patients occurred due to delay in recognizing the diagnosis of thyroid storm, late referral to the endocrinology team, lack of intensive care facilities at the admitting hospital and severe financial handicap of both patients. These challenges eventually led to both patients developing liver failure with encephalopathy and both died after 9 and 21 days of admission respectively.

**Conclusion:** The clinical management of thyroid storm is very difficult with a high mortality in settings where patients lack access to early diagnosis, effective medications and ICU support. A high index of suspicion, early referral to an endocrinologist and management in an intensive care unit should help to reduce the current high mortality we currently face in the management of patients with thyroid storm. Also appropriate social support should be provided by governments in resource poor countries for the care of these patients to reduce overall mortality.

**Abstract #1073**

**A CASE OF LYMPHANGIOMYOMATOSIS (LAM) PRESENTING WITH NECK SWELLING DUE TO AGGRESSIVE MULTIFOCAL PAPILLARY THYROID CARCINOMA**

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**Objective:** To report a rare case of LAM associated with papillary thyroid carcinoma.

**Case Presentation:** A 55 yo female with PMH of gastric bypass surgery presented with a 3-month history of neck swelling. She did not have any FH of thyroid cancer and denied any history of external radiation therapy. CT neck revealed several small nodules at both thyroid lobes, several enlarged cervical lymph nodes and a large nodule at left thyroid lobe. She underwent total thyroidectomy and right modified neck dissection followed by radioactive iodine therapy. Pathology report showed an invasive papillary carcinoma at isthmus, invasive multifocal papillary carcinoma at right lobe with metastasis in 3 cervical lymph nodes. Incidentally, she was noted to have multiple thin walled cysts throughout both lungs with small apical left pneumothorax at CT neck during initial evaluation for neck swelling, that was strongly suggestive of LAM. These findings were confirmed with HRCT chest. Further evaluation revealed 4.3 cm mass at left kidney and multiple soft tissue densities within the retroperitoneum at CT abdomen for which she underwent left nephrectomy. The pathology and immunohistochemical staining results of renal mass and periaortic lymph node biopsy were consistent with angiomyolipoma.

**Discussion:** LAM is a very rare progressive disease of women, characterized by proliferation of abnormal smooth muscle cells that leads to progressive cystic destruction of the lung resulting in pneumothorax and respiratory failure. The diagnosis is suggested by the clinical presentation, CT chest findings and abdominal angiomyolipomas. There are two forms of LAM: sporadic LAM and Tuberous Sclerosis Complex (TSC)-associated LAM. Both forms are caused by mutations in the tuberous sclerosis genes. LAM is considered a benign tumor and it is often associated with angiomyolipoma in the kidneys, and an increased frequency of meningioma. Association with uterine perivascular epithelioid cell tumor has also been reported. There have been only 3 reported cases of papillary thyroid carcinoma in cases with sporadic LAM, one patient at autopsy and two patients several years after external radiation therapy to the head and neck area. In our case, there was no known major risk factor for thyroid cancer and she did not have any skin lesion or characteristic features of TSC. Although the association of these two diseases may be coincidence, the possibility of a relationship between LAM and thyroid carcinoma is intriguing and deserves further investigation.

**Conclusion:** We describe a rare patient with LAM presenting with neck swelling due to aggressive multifocal papillary thyroid carcinoma.

**Abstract #1074**

**THYROTOXIC VOMITING. A CASE REPORT**

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**Objective:** To report a case of a woman with recent diagnosis of hyperthyroidism that developed intractable vomiting related to thyrotoxic state.
Methods: We abstracted the clinical chart and reviewed the pertinent medical literature.

Case Presentation: A 76-year-old woman with a 6-week history of nausea, vomiting, palpitations, weight loss, and heat intolerance was admitted in the Emergency room. Her medical history included type 2 diabetes, hypertension, cholecystectomy, and recent diagnosis of hyperthyroidism. Her family history for thyroid disorders was negative, and her regular treatment included metformin, losartan, methimazole and bisoprolol. On admission, her blood pressure was 130/80 mmHg, heart rate was 120 beats per minute, respiratory rate was 28 breaths per minute, and oral temperature was 39°C. Physical examination revealed an enlarged thyroid gland (3N), moderate edema in the lower limbs, and abdomen was painful on palpation. Laboratory results showed normal glucose, creatinine, electrolytes, calcium, urea, and magnesium. However, liver transaminases were elevated, TSH was 0.004 μIU/dL (normal range 0.3 - 5), free thyroxine was 2.40 ng/dL (normal range 0.8 - 2), and triiodothyronine was 279 ng/dL (normal range 89 - 190). She was started with iv saline, omeprazole, and dimenhydrinate. Further work-up showed that abdominal ultrasound, abdominal computed tomography, and endoscopy were normal. Next day, treatment was begun with propranolol 40 mg three times a day and methimazole 30 mg once a day. After ten days, the patient was discharged from the hospital without complaints.

Discussion: Hyperthyroidism results from overproduction of hormone by thyroid itself, Graves’ disease being the most common cause. The manifestations depend on the severity of the disease, the age of the patient, the presence or absence of extrathyroidal manifestations, and the specific disorder producing the thyrotoxicosis. The classical gastrointestinal manifestations of thyrotoxicosis are rapid intestinal transit, increased frequency of semiformed stools, and weight loss from increased caloric requirement or malabsorption. Anorexia, nausea, and vomiting are uncommon but may occur with severe disease. It was postulated that nausea and vomiting are related with aperistalsis and a marked diminution in upper gastrointestinal motility due to hypomagnesaemia. On the other hand, there are no evidence of hypermetabolism of the central nervous system; however, like another endocrine conditions, vomiting could be induced by stimulation of the chemical trigger zone.

Conclusion: Hyperthyroidism should be considered in differential diagnosis of unexplained vomiting. Treatment with beta blockers and antithyroid drugs seems to stop vomiting.

Abstract #1075

VITAMIN D STATUS IN AUTOIMMUNE HYPOTHYROIDISM

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Objective: To investigate vitamin D status in patients with autoimmune hypothyroidism.

Methods: The study group consisted of 100 patients with newly diagnosed Hashimoto’s thyroiditis and 100 subjects as the control group. Parameters of calcium metabolism, thyroid function tests and 25(OH) vitamin D levels were measured.

Results: Mean age of the study study groups was 33.4 ± 4.8 years with female: male= 72: 28. Vitamin D insufficiency/ deficiency (25 (OH) D < 30 ng/ml) rate was significantly higher in the Hashimoto’s group compared with the control subjects (75 % vs 20%, p<0.0001). In the Hashimoto group, mean 25(OH) vitamin D levels were significantly lower compared with the control group (12.5±7.0 vs 22.3±7.9 ng/mL, p<0.001). The study group revealed higher Anti TPO levels in patients vitamin D deficiency 25 (OH) D < 20 ng/ml than patients with vitamin D insufficiency group (25 (OH) D < 30 ng/ml) [650.4 ± 35.4 IU/ml vs 340.3 ± 65.4 IU/ml, p, 0.001]. Serum vitamin D level was inversely correlated with the Anti TPO levels (r = - 0.30, p = 0.007).

Discussion: Vitamin D is involved in immune system and, in particular, on T cell-mediated immunity. Vitamin D receptor is profoundly present in the immature immune cells of thymus and the CD8. Low vitamin D level gives rise to a variety of autoimmune disorders including type 1 diabetes, hypothyroidism.

Conclusion: The higher vitamin D deficiency rates besides lower vitamin D levels in the Hashimoto group together with the inverse correlation between vitamin D and AntiTPO suggest that vitamin D deficiency may have a role in the autoimmune process in Hashimoto’s thyroiditis.
Abstract #1076
FREE THYROID HORMONE LEVELS ARE ASSOCIATED WITH ALL CAUSE MORTALITY AND CARDIOVASCULAR MORTALITY IN CAUCASIANS

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Objective: The LURIC study (Ludwigshafen Risk and Cardiovascular Health Study) is a large prospective cohort study. 3316 patients with German ancestry 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 from all causes and from cardiovascular causes. Thyroid hormone function has been discussed to be associated with cardiovascular effects. Therefore we examined whether alterations in thyroid function were associated with long-term prognosis in patients of the LURIC Study.

Methods: We examined 2507 subjects with angiographic CAD and matched controls in which CAD had been ruled out by angiography. Subjects with overt thyroid disease and those receiving medication were not included as well as patients receiving medication with direct influence on thyroid metabolism like Lithium and Amiodarone. Only data of those subjects who had a full set of thyroid hormones were included. Participants of the LURIC study were classified into quartiles according to TSH, fT4 and fT3 levels. We used the COX proportional hazards model to examine the association between thyroid hormone levels and mortality from all causes or cardiovascular causes. Multivariable adjustments were also carried out.

Results: Our findings show that patients with fT4 levels over 18 pmol/l have the highest mortality from all causes: HR 1.52, (CI 95% 1.25-1.85) and from cardiovascular causes: HR 1.77 (CI 95%,1.38-2.27) Patients with the lowest fT3 Levels (1.1-4.2 pmol/l) have the highest mortality from all causes and from cardiovascular causes: HR 1.00 with decreasing HRs up to the forth quartile with fT3 ≥5.4 pmol/l HR 0.47 (CI 95% 0.36-0.61). These findings were robust against adjustment for age and sex.

TSH showed no correlation with all cause mortality or cardiovascular causes. Patients in our study were exclusively Caucasians of German ancestry. We therefore suggest that control of free thyroid hormone levels may be especially important in long term prognosis of Caucasian patients. Our findings may furthermore help to interpret results of other cohort studies with mixed ethnic origin like the COLORADO study.

Conclusion: High fT4 and low fT3 levels in Caucasians undergoing angiography are related to mortality from cardiovascular causes and from all causes.

Abstract #1077
HEMORRHAGE IN METASTATIC LYMPH NODE AFTER ABLATIVE RADIOACTIVE IODINE THERAPY FOR PAPILLARY CARCINOMA - A RARE COMPLICATION

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Case Presentation: A 34-year-old Caucasian female underwent total thyroidectomy and central neck dissection for papillary carcinoma. Tumor was 5 cm with extension into perithyroidal tissue, 9/18 lymph nodes were positive, T4N1M0. Patient was treated with 149.6 millicuries of radioactive iodine (RAI) 6 weeks after surgery following withdrawal of thyroid hormone. Pretreatment TSH was 148 mIU/L. Pretreatment scan revealed small to moderate uptake in right neck and posttreatment scan was read as large amount of uptake in right neck. Three weeks following RAI, patient presented with painful right-sided neck swelling and dysphagia. On examination, trachea was deviated to left due to a tender palpable right neck mass. Ultrasound revealed a 10 cm cystic mass, 12 ml of bloody fluid was aspirated with relief of symptoms. Cytology was non-diagnostic. Patient underwent a modified right lateral neck dissection. Pathology reported 7/46 positive lymph nodes at levels 3 and 5. Large cystic mass was 8x4x1 cm and was positive for papillary carcinoma.

Discussion: In this patient, hemorrhage occurred in residual metastatic thyroid tissue in lateral neck lymph nodes. Only two similar cases have been reported in literature- 1) mediastinal hemorrhage following RAI for thyrotoxicosis caused by retrosternal thyroid tissue and 2) hemorrhage in brain metastases following RAI for treatment of metastatic papillary carcinoma. Possible pathophysiology includes increased vascularity of thyroid metastases and possibly stimulation of growth induced by the TSH stimulation prior to ablative therapy. The temporal relationship between RAI and hemorrhage into metastases is highly suggestive of causality.
Conclusion: Clinically significant metastatic lymph node hemorrhage post radioiodine therapy has been reported here for the first time. Pretreatment scan indicating significant residual disease should warrant closer surveillance or possibly consideration for additional surgery prior to treatment with radioiodine.

Abstract #1078

RARE AND UNUSUAL METASTASES OF WELL-DIFFERENTIATED THYROID CANCERS: A SYSTEMATIC REVIEW

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Objective: A systematic review of the literature was performed to compile all cases of thyroid cancer metastases to unusual locations and compare pathological, radiological and laboratory data, as well as their outcomes.

Methods: A systematic review of 3 bibliographic databases (MEDLINE, EMBASE, Cochrane Collaboration) was performed. Medullary carcinoma, thyroid lymphoma and poor or non-differentiated thyroid cancers were excluded. 630 studies were reviewed.

Case Presentation: There were 47 case reports and 2 case-series identified. End-organ metastatic sites included the meninges, cerebrum, pancreas, skin, orbits, soft tissue and muscle tissue, kidneys, endobronchium, thyroid gland, parotid gland, adrenal gland, ovaries, gastrointestinal tract, breast, liver, penis, heart and spleen. Median age was 63 with a female:male ratio of 1.4:1. In the entire cohort, 63% were papillary, 32% follicular, and 2% Hurthle cell thyroid cancers. Histopathology subgroup analysis however showed follicular thyroid cancer metastases to be 80% and 83% in the meninges and orbits, respectively. Positron emission tomography and 131-Iodine scans revealed hypermetabolic foci 100% and 92% of cases, respectively. Disease-free interval was highly variable, ranging from simultaneous presentation to 516 months after initial presentation of primary thyroid cancer. Patients were treated by surgical metastasectomy (67%), external beam radiation (48%), chemotherapy (15%), or radioiodine ablation therapy (RAI; 61%). 131-Iodine scans were positive in 45% of RAI-treated patients.

Discussion: Well-differentiated thyroid cancer usually remains localized to the thyroid. However, a minority present with distant metastases, commonly to lung, bone and lymph nodes. Rare sites of end-organ distant metastases have been reported in the literature. There is a need for the clinical manifestations and outcomes of these unusual metastases to be compiled for analysis in one cohort.

Conclusion: This is the first systematic review to catalogue tumor metastases of well-differentiated thyroid cancers to rare end-organ locations. Clinicians should consider these rare sites of metastases in the absence of the more common extra-cervical disease recurrence locations. Establishing a comprehensive database network to record these unusual metastases would allow treating physicians to gain additional insight so as to improve upon the diagnosis, prognosis and treatment of rare metastatic thyroid cancers. Furthermore, the implementation of a centralized tumor bank would allow for a molecular profile to be defined and therefore enhance our understanding of metastatic thyroid tumor biology.

Abstract #1079

A RARE CASE OF HYPOPIGMENTED THYROID ADENOMA IN A BLACK THYROID

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Case Presentation: A 36-year-old female was found to have palpable thyroid nodules. Ultrasound of her thyroid showed multiple, bilateral nodules. An FNA of the dominant left lobe nodule showed a follicular lesion of undetermined significance, and the patient decided to undergo a total thyroidectomy. At operation, the thyroid appeared dark black in color, with multiple palpable nodules. Following thyroidectomy, gross examination of the thyroid revealed a 6-gram left thyroid lobe with a well-circumscribed pink-tan nodule with surrounding black parenchyma. The final pathologic diagnosis was a follicular adenoma with small, bilateral colloid nodules. On microscopic examination the nodule did not contain pigment, but the surrounding parenchyma contained brown-black granules in the cytoplasm of the follicular cells and dark grey to black, amorphous pigment within the colloid. On further discussion with the patient we found that she had taken minocycline chronically for severe acne.

Discussion: Tetracycline and its derivatives are widely used as broad-spectrum antibiotics. It is known that these antibiotics can lead to discoloration of various tissues in the body. The pigment is thought to be a byproduct of the degradation of tetracycline in the lysosome, and closely resembles melanin in composition. There have been reports that the same pigment can be found in microscopic amounts in grossly normal thyroids. It has also been hypothesized, but remains unclear, that build
up of this pigment increases the risk of papillary thyroid cancer. Some recommend that an incidentally discovered black thyroid should be resected due to the risk of future neoplastic change.

**Conclusion:** This patient’s chronic use of minocycline likely resulted in the black color of the thyroid. It is interesting that the adenoma did not contain the pigment that was distributed throughout the rest of the gland. Whether this pigment leads to neoplastic change remains unclear, however this case adds new data to the growing body of literature on black thyroid.

**Abstract #1080**

**CANCER GENE PROFILING IN BENIGN AND MALIGNANT FOLLICULAR LESIONS OF THE THYROID GLAND**

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**Objective:** Thyroid nodules are common, identified in 5% to 10% of the population. Pre-operative fine needle aspiration (FNA) is a tool that may be used to distinguish benign from malignant lesions. However, when the cytology is inconclusive (demonstrating follicular cells,) patients may be subjected to repeat FNA or even an unnecessary surgical intervention to rule out malignancy. Examining follicular thyroid lesions and their FNA samples for differential expression of particular genes implicated in oncogenesis may lead to identification of biomarkers that can stratify follicular lesions into benign or malignant neoplasms. Thus, a panel of biomarkers could potentially be used as a diagnostic tool in pre-operative clinical evaluation.

**Methods:** Patients undergoing surgical intervention for follicular lesions identified on pre-operative FNA with a post-operative diagnosis of follicular thyroid adenoma (FTA) or follicular thyroid carcinoma (FTC) were included in this study. Thyroid tissue from these lesions was collected prospectively at the time of definitive surgery. Samples were then subjected to quantitative reverse transcription polymerase chain reaction (qRT-PCR) using a PCR array profiler which includes 84 previously identified genes involved in transformation and tumorigenesis. RT²² Profiler PCR array data analysis software (SABiosciences) was used for ∆∆Ct fold-change calculations. Gene expression was normalized to the average expression of 5 housekeeping genes (B2M, HPRT1, RPL13A, GAPDH, ACTB).

**Results:** A total of 19 patients were included in this study: 10 had FTA and 9 had FTC on post-operative pathology. Females constituted the majority of patients in all groups (74%), and the mean age of the entire group was 52.4 years. Of the 84 genes analyzed, 32 genes in the FTC samples had 2 fold up-regulation or greater relative to the FTA samples. Three out of the 32 genes reached statistical significance: CCNE1, NME4, and EPDR1, (p= <0.05).

**Discussion:** Initial screening for genetic markers identified three potential candidates that may be able to distinguish FTC from FTA. These markers have been implicated in cell cycle control, cell growth, and cell adhesion.

**Conclusion:** Our preliminary data demonstrate the potential for genetic discrimination using qRT-PCR that may be a valuable diagnostic tool in the clinical setting to guide the treatment of patients with indeterminate follicular lesions from FNA samples.

**Abstract #1081**

**IMPACT OF HYPOPARATHYROIDISM ON PATIENT’S EMPLOYMENT STATUS, SOCIAL RELATIONSHIPS, AND PERSONAL LIFE IN THE PARADOX STUDY**

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**Objective:** Hypoparathyroidism (hypoPARA) is a rare and complex endocrine disorder. The goal of this study was to quantify the impact of hypoPARA on patients (pts) and explore its effect on pts’ employment status, social relationships, and personal lives.

**Methods:** A 30-minute, web-based instrument was developed with input from clinical experts, the Hypoparathyroidism Association, and pts to assess the clinical, social, and economic burden of hypoPARA. Pts were invited to participate primarily via Hypoparathyroidism Association’s member list. To qualify for the study, pts had to be ≥18 yrs old, diagnosed with hypoPARA for ≥6 mos, and residents of the U.S. A total of 374 pts completed the survey.

**Results:** The mean age of the 374 pts was 49 yrs and mean time with hypoPARA was 13 yrs. Of the total respondents, 85% were female and 78% suffered from postsurgical hypoPARA. 45% (167/374) reported that hypoPARA significantly interfered with their lives in the last 12 mos on a 7-point Likert scale. More pts who described their condition as severe (30%; 114/374) reported a greater degree of interference (72%; 82/114; P≤0.05). 20% (75/374) of pts had a change in employment.
status following hypoPARA diagnosis. The number of unemployed patients increased from 1% to 5% following diagnosis (5/374, 18/374, P≤0.05). 72% (13/18) of currently unemployed pts attributed their status to hypoPARA. In terms of the impact on their personal life, 85% (317/374) reported that hypoPARA has prevented them from doing household activities, with 62% (233/374) reporting a daily or weekly impact. Physically-demanding optional activities, such as exercising, gardening, and pursuing hobbies, were the most affected. Pts also reported that hypoPARA can be a socially alienating condition. On a 7-point Likert scale, where 1 is “Strongly Disagree” and 7 is “Strongly Agree,” 72% (263/367) of respondents strongly agreed (rated 6-7) that it is hard for family and friends to understand the condition and 52% (192/370) strongly agreed that their family has experienced stress due to the condition. Additionally, 57% (211/369) of pts strongly agreed that the lack of familiarity with hypoPARA is a source of stress.

Discussion: To the authors’ knowledge, this is the largest and most comprehensive study conducted to measure the burden of illness in pts with hypoPARA.

Conclusion: The results show that hypoPARA has a significant, multidimensional impact on pts’ lives beyond clinical symptoms. HypoPARA affects pts’ social and personal life, employment status and family. Given the significant impact of the condition revealed by this study, more research appears to be needed to better understand the impact of hypoPARA on pts’ lives.

Abstract #1082

NUMBER OF THYROID ULTRASOUND GUIDED FINE NEEDLE ASPIRATIONS (UGFNAS) PERFORMED OR YEARS OF CLINICAL EXPERIENCE DOES NOT CORRELATE WITH TECHNICAL PROFICIENCY ACROSS MULTIPLE SPECIALTIES OR INSTITUTIONS

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Objective: Ultrasound Guided Fine Needle Aspiration (UGFNA) is the standard of care in managing thyroid nodules.1-6 Several specialties perform thyroid FNAs with variable levels of formal training and clinical experience.2 Non-Diagnostic (ND) specimens vary in the literature from <1 to >20% and by reporting specialty.2,3,7 Several studies have investigated factors contributing to low ND rates - a surrogate marker of proficiency in the procedure.7-11 We surveyed various physicians regarding their UGFNA technique and compared this data with their measured ND rates from our database to identify variables that best correlate with proficiency across various clinical practices in the US. To our knowledge, this is the first study of UGFNA technique across multiple specialties in both community and academic settings throughout the US.

Methods: An email survey on UGFNA technique was sent to 351 physicians; 97 completed the survey (28% survey response rate). Kappa testing and logistical regression was utilized to detect differences in ND rates with a power of 80% (i.e. able to detect a 0.5% difference).

Results: Number of self-reported UGFNAS performed and years of experience did not correlate with ND rates (p-value = 0.87). Self reported ND rates did not correlate with actual ND rates, with the poorest correlations for those with high ND rates (>10%). 70% of the high ND group over-estimated their technical proficiency. None of the 19 variables directly related to UGFNA technique tested; alone or in combination, were predictive of any difference in ND results.

Discussion: Previous studies showed some correlation between proficiency and UGFNA technique or experience; however these studies were either meta-analyses of individual institutional experiences or limited to a single specialty or a small number of sites.7-11 In contrast, our multi-specialty/institutional study failed to show any clear variable(s) which correlated with proficiency. We found that physicians were not accurate in estimating their own ND rates. We suggest physicians obtain their actual ND rates to help them better gauge their performance and modify UGFNA technique if necessary.

Conclusion: One explanation of our findings is that low ND rates are related to a combination of multiple variables. As such, we propose that UGFNA training should be customized to the practitioner rather than a one-size fits all approach. A prospective study examining the correlation between customized training and pre- and post-training ND rates would be valuable.

Abstract #1083

AUTOIMMUNE THYROIDITIS WITH HYPOTHYROIDISM INDUCED BY SUGAR SUBSTITUTES

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Objective: Increase in consumption of sugar-substitutes is being observed over the last few decades. We are presenting a case of Hashimoto’s hypothyroidism induced by high intake of beverages containing sugar-substitutes, which resolved completely with the elimination of these products from diet.
Case Presentation: A 52 year old female with a history of consumption of high dose of artificial sweeteners was diagnosed with Hashimoto’s hypothyroidism in 2008. On presentation her TSH (Thyroid Stimulating Hormone) was 12.2 mIU/L (normal: 0.4 - 4.5), Free-T4 0.5 ng/dl (normal: 0.58 - 1.64) and Anti TPO Ab (Anti-Thyroid Peroxidase Antibody) 196 IU/ml (normal: <35). Treatment with Levothyroxin 0.75 mg/day normalized her TSH, which remained between 1.23 mIU/L and 2.16 mIU/L during the following 3 years. She was also ruled-out for other autoimmune disorder. Due to weight gain the patient reduced, and eventually stopped taking the sweeteners in February 2012. This was followed by unanticipated drop in her TSH to 0.005mIU/L. The TSH remained suppressed despite reduction in Levothyroxin dose to 0.5 mg and complete discontinuation of Levothyroxin was achieved with fully normal TSH and Anti-TPO antibody <20 IU/ml (normal: <35) TSI (thyroid stimulating immunoglobulin) 113% (normal less than 140%) TBII (Thyrotropin Binding Inhibiting Immunoglobulins) <6.0% (normal: <16%). She remained clinically euthyroid without any treatment during subsequent follow-up visits.

Discussion: The sugar-substitutes are attributed with large number of health related side effects in animal studies, ranging from obesity to various malignancies. Nonetheless, not much is known about the human implications of these findings considering the phenomenon of excessive consumption of sugar-substitutes being relatively new. In our case it may either be a rare idiosyncratic or more generalized reaction to high intake of artificial sweeteners. Formaldehyde, a metabolite of aspartame is reported to be associated with Type IV delayed hypersensitivity. Large control studies should be done to confirm this association.

Conclusion: This case emphasizes that in all patients diagnosed with Hashimoto’s Thyroiditis, intake of sugar-substitutes should be inquired. If found positive, discontinuation of intake and close follow-up of thyroid function test should be done.

Abstract #1084

MALE PATIENT WITH NECK MASS: ECTOPIC CANCER VS METASTASIC DISEASE

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Case Presentation: Case of 33 y/o male patient, Traffic policeman, with an unremarkable past medical history, who after being run over by a car, was found incidentally with a cystic nodular right neck mass by MRI of cervical spine. Physical examination revealed a mildly tender right neck mass. He was clinically and biochemically euthyroid. Denied history of neck irradiation. No family history of thyroid disease or thyroid cancer. Excisional biopsy of right neck mass showed metastasic well differentiated papillary carcinoma of thyroid gland at lymph node. Total thyroidectomy with right modified neck dissection was performed. Histopathological report disclosed no evidence of malignant tumor within the thyroid gland (papillary cancer) as well as sixteen right lymph nodes obtained from surgery. One month after surgery, Thyroglobulin levels were elevated, 133.61 ng/ml (nv: 5-25 ng/mL ) with negative antthyroglobulin antibodies (Thyroglobulin antibodies: 11.8 uU/ml nv: 0-4.11). Thyroid scan and Whole Body Scan showed evidence of functional thyroid tissue remnants; this appears to be a right thyroid lobe. Also, a faint visualization of a smaller focus in the left thyroid bed region was seen. Thyroid ultrasound showed two right medial neck nodules. Fine needle aspiration biopsy of neck nodules were reported positive for metastasic thyroid papillary carcinoma. Radiodine ablation therapy was given.

Discussion: Initially, incidental Right neck mass with diagnosis of metastasic papillary carcinoma of thyroid gland, but after a total thyroidectomy without evidence of metastasis in thyroid gland, a malignant transformation of an heterotope thyroid tissue, is the most likely diagnosis. The possible explanation is related to embryology process.

Conclusion: Ectopic Thyroid tissue is a rare entity with an incidence of 1 in 300.000. An ectopic thyroid gland in the region of the submandibular gland, intra-trachea or laterally is very rare. Malignant transformation of ectopic thyroid tissue is an uncommon event; only 43 cases have been reported. Only 10 of those cases were papillary carcinoma. The incidence of cervical Lymph node metastasis...
Abstract #1085

A FATAL CASE OF RECURRENT RADIOIODINE RESISTANT PAPILLARY THYROID CANCER

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Objective: To report a treatment (Radio-Iodine) resistant case of Papillary Thyroid Cancer (PTC)

Case Presentation: 72 year old Male was diagnosed with Papillary Thyroid Cancer (Stage 4, T4,N1B, M0) in 1994 and underwent total thyroidectomy followed by Radio-Iodine ablation and was placed on thyroxine suppression therapy. Post ablation scan was negative. He was then being followed using thyroglobulin levels. 6 years later in 3/2000 his thyroglobulin levels rose and he received RAI Ablation for recurrence in thyroid bed. Post ablation scan was negative. 16 years later in 8/2010 his thyroglobulin levels rose again and workup revealed 2 pulmonary nodules, one of which was iodine avid, FDG negative and other was non iodine avid but FDG positive on PET scan. This PET positive but iodine negative nodule was confirmed by biopsy to be Metastatic Thyroid cancer. Shortly there after patient developed systemic metastasis to brain and bones that were treated with radiotherapy. Systemic chemotherapy with Sunitinib (Tyrosine Kinase inhibitor) was started as patient had non-Iodine avid lesions. Patient continued to deteriorate rapidly and died 2 weeks later.

Discussion: PTC usually has a very good prognosis but infrequently can have aggressive course with resistance to conventional treatments. Tumors with Radioiodine resistance do not accumulate radio iodine and have poor prognosis. Standard of therapy for these tumors has not been established and phase II trials are underway involving molecular agents targeting the enzymes involved in Thyroid cancer development. Few drugs like Sorafenib, Sunitinib have yielded partial response.

Conclusion: Our Patient had a fatal course with a stage-4 locally advanced cancer to begin with and multiple recurrences in thyroid bed, lung, brain, bone. He had developed radioiodine resistant cancer and did not respond to standard therapy.

Abstract #1086

UNIVERSAL VERSUS TARGETED SCREENING FOR HYPOTHYROIDISM AMONG EGYPTIAN PREGNANT WOMEN

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Objective: To determine the prevalence of hypothyroidism among pregnant Egyptian women and to study the efficacy of universal versus targeted high-risk screening among pregnant Egyptian women.

Methods: TSH, fT3, fT4 and anti TPO antibodies were checked for 168 pregnant women who were attending for their regular antenatal check up at obstetric outpatient clinic of Ain-Shams University hospital (tertiary care hospital). They were subdivided to high risk for developing thyroid disease (women with family or personal history of thyroid disease, type 1 DM or other autoimmune disease, positive for thyroperoxidase antibodies, women with previous therapeutic head or neck irradiation, history of miscarriage, preterm delivery, placental abruption, hypertension with pregnancy or preeclampsia) and low risk group and also subdivided according to gestational age into 1st, 2nd and 3rd trimester groups.

Results: Low-risk group and high risk group included 125 (74.4%), and 43 (25%) women, respectively. Using the trimesteric and normal population cut off values for thyroid functions, 94 women (56%) and 75 (44.6%) of the studied population had hypothyroidism, respectively. There was no significant difference in the prevalence of hypothyroidism between high risk group (60.5%) and low risk group (54.4%, p value 0.7) and also between 1st, 2nd and 3rd trimester groups (50.6%, 60.4% and 63.45, respectively, p value 0.33).

Discussion: Maternal hypothyroidism during pregnancy may cause hazards to the mother and the foetus. Consensus guidelines recommend screening thyroid functions only for pregnant women with high risk to develop thyroid disease. But unfortunately, no previous studies were concerned about the screening of thyroid dysfunction among Egyptian pregnant women and scanty studies were done in the Middle East. The current study and that by Alkafajie et al 2012 that was done in Jordan showed high prevalence of hypothyroidism among pregnant women. In our study the prevalence was comparable in low risk and high risk groups. Negro et al., 2012 also confirmed that case finding alone fails to detect the majority of pregnant women with thyroid disease.
Conclusion: There is high rate of hypothyroidism among the studied Egyptian pregnant women and universal screening for hypothyroidism in our population could avoid missing large number of patients.

Abstract #1087

DIAGNOSTIC VALIDITY OF THYROID ULTRASONOGRAPHY IN THYROID NODULES

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Objective: A thyroid ultrasound scan is recommended in the assessment of any suspected thyroid nodule. The ultrasound characteristics of nodules have been shown to be useful in assessing their malignant potential. The aim of this study is to determine diagnostic validity of thyroid ultrasound in differentiating benign & malignant thyroid nodule.

Methods: It was cross sectional study, conducted at Aga Khan University Hospital Karachi from August 2011-July 2012. All patients of either gender with thyroid nodules referred for ultrasound thyroid and FNAC were included. Patients with known thyroid malignancy, pure cystic lesion, indeterminate, non-diagnostic, suspicious finding in cytology without subsequent surgery were excluded. Ultrasonography was performed by radiologists with Toshiba US machines. The ultrasound parameters were assessed and compared with FNAC results in all nodules. Diagnostic validity of each ultrasound feature was calculated. Study was approved from Ethical Review Committee of Hospital.

Results: Total 101 patients were included in the study on this basis of availability of ultrasound images, pathology report and after exclusion. Mean age of patients was 43 ±13 Years (Range 15-73 Years) and n=81(80%) were females. Among 101, n=96 benign and n=5 nodules were malignant on histocytopathology. The sensitivity & specificity of each ultrasound feature in predicting malignancy were: microcalcification, 80% 68%; hypoechogenicity, 80% 52%; ill defined lobulated margin, 40% 96%; solid, 80% 40%; taller than wider, 50% 63% respectively. Each US feature have negative predictive value ranges from 95-98%.

Discussion: This study evaluated the diagnostic validity of various ultrasound features in thyroid malignancy in thyroid nodules. Our results are comparable with other studies done so far. Microcalcification, hypoechogenicity, solid consistency, ill defines margins are the predictor of malignancy in thyroid nodules.

Conclusion: Identification of microcalcification, hypoechogenicity & solid with ill defined margins thyroid nodules on ultrasound is helpful in diagnosing thyroid malignancy and warrants urgent diagnostic biopsy.

Abstract #1088

REVERSIBLE THROMBOCYTOPENIA - THE PLEIOTROPIC EFFECT OF HYPOTHYROIDISM

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Objective: The literature regarding an association between thyroid disease and immune thrombocytopenic purpura (ITP) suggests that autoimmune thyroid disease is a frequent finding in patients with ITP. A strong association between other systemic autoimmune diseases and autoimmune thyroid disease is also well known. We describe a case in which the most likely cause for thrombocytopenia was profound hypothyroidism and treatment of the hypothyroid state normalized the platelet count.

Case Presentation: A 54-year-old male presented to the emergency department with generalized weakness that was worsening for the past 2 months. On physical exam, he was pale, hypotensive (80/50 mm hg) and bradycardic (55/min). Complete blood count showed pancytopenia with WBC count of 1.4 K/uL, platelet count of 25 K/uL and hemoglobin of 8.1 g/dL. B12 and folic acid deficiencies, along with hepatitis and human immunodeficiency virus infections were ruled out. He was not on any regular medications. The bone marrow biopsy showed a normocellular marrow with megakaryocytes that were morphologically normal. The complete chemistry and coagulation profile were normal, except for hyponatremia (Na-128 mEq/L). A presumptive diagnosis of adrenal insufficiency was considered. After cosyntropin administration, cortisol levels at 0 and 45 minutes were found to be 13.9 and 14.1, respectively. He was started on cortisone 25 mg in the morning and 12.5 mg in the evening. After starting this steroid regimen, the leucopenia and anemia gradually improved but thrombocytopenia persisted. To evaluate for other potential polyglandular autoimmune endocrinopathies, TSH, free T4, thyroid autoantibodies, FSH, LH and prolactin levels were ordered. TSH and free T4 were found to be abnormal at 88.0 uIU/ml and 0.07 ng/dl, along with a positive antibody to thyroglobulin of 378 IU/mL. He was started on synthroid 50 mcg and the platelet count showed gradual improvement over a period of 8 weeks.

Discussion: Thrombocytopenia resulting from an autoimmune process accompanied by hypothyroidism...
can be effectively treated with levothyroxine. This case showed that it was the medical management of profound hypothyroidism that was ultimately successful for resolving the thrombocytopenia and that steroid regimen alone was insufficient to accomplish this task. We postulate that the most likely mechanism is probably improved platelet survival as a result of reduced platelet “autoimmunity”, rather than increased platelet production. **Conclusion**: Medical management of profound hypothyroidism can be successful in resolving thrombocytopenia in patients with autoimmune disease.

**Abstract #1089**

**NORMOKALEMIC THYROTOXIC PERIODIC PARALYSIS: A RARE ENTITY**

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**Case Presentation**: Thyrotoxic periodic paralysis (TPP) is a rare complication of hyperthyroidism. It is most commonly associated with Graves’ disease but may occur with any etiology of thyrotoxicosis. It is characterized by transient, recurrent episodes of flaccid muscle paralysis affecting proximal muscles more severely than distal muscles and is almost always associated with hypokalemia. There have been very few reported cases of TPP associated with normokalemia. Here we present the case of a 41 year old Asian man with TPP and normokalemia. The patient had no significant past medical history and presented to the emergency department with an episode of bilateral lower extremity and proximal upper extremity weakness that lasted about 5 hours upon waking up and resolved spontaneously. He did not have any sensory disturbances. He reported another episode of lower extremity paralysis upon awakening two weeks prior that lasted about ten minutes. His review of systems was positive for increasing fatigue with exercise, intermittent diarrhea, unintentional weight loss of 10 pounds in the past three months, heat intolerance, occasional palpitations, anxiety, and hand tremors. His physical examination was remarkable for tachycardia, a diffusely enlarged thyroid gland with small palpable nodule on the right, presence of a thyroid bruit, normal neurological exam, and a fine hand tremor. His laboratory studies were significant for a normal potassium level of 3.9, thyroid stimulating hormone (TSH) of less than 0.005, and free thyroxine (T4) elevated at 3.90, normal MRI of the brain and lumbar puncture studies. His thyroid uptake scan was consistent with Graves’ disease and he was started on propranolol and methimazole which resolved his symptoms. **Discussion**: Most cases of TPP are associated with hypokalemia. This case is very unusual in that the patient was found to have normal potassium levels during his attack. The degree of hypokalemia during an attack is variable. The etiology of hypokalemia in TPP is thought to be due to rapid influx of potassium into the muscles during the attacks. Some theories suggest that thyroid hormone can directly stimulate sodium-potassium adenosine triphosphatase (Na-K ATPase) activity leading to exaggerated potassium influx into muscles. In addition, β-adrenergic stimulation increases Na-K ATPase activity, which can lead to the development of hypokalemia. However, the etiology of normal potassium in TPP is unknown. **Conclusion**: Thyrotoxic normokalemic periodic paralysis should be kept in mind as a cause of acute muscle weakness to avoid missing a treatable and curable condition. Symptoms of TPP usually resolve once hyperthyroidism is treated appropriately.

**Abstract #1090**

**THYROTOXICOSIS HYPOKALEMIC PERIODIC PARALYSIS IN A PATIENT WITH CROHN’S DISEASE**

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**Objective**: Incidence of thyrotoxicosis periodic paralysis in patients with inflammatory bowel diseases is significant. Here we describe a case of thyrotoxicosis hypokalemic periodic paralysis due to severe channelopathy in a patient with Crohn’s disease. **Case Presentation**: A 35-year-old female with a history of hyperthyroidism and Crohn’s disease presented to the emergency department with generalized weakness, inability to walk, palpitations, nausea, and diarrhea for four days. This is her third episode in the past one year. The patient had been compliant on methimazole for hyperthyroidism. She had a history of partial small bowel resection at age thirteen secondary to Crohn’s disease and had her last flare up of the disease two years prior to admission. She was not currently on any medications for Crohn’s. On admission, the patient did not have any abdominal tenderness and a rectal exam failed to reveal blood. She was
tachycardic with features of thyrotoxicosis. Labs revealed a raised free T4 (6.53 ng/dl) and low TSH (<0.05 uIU/mL), confirming hyperthyroidism, which is associated with severe hypokalemia (K+: 2.2 mEq/L). She was admitted with thyrotoxicosis hypokalemic periodic paralysis. She was started on methimazole and propranolol. Aggressive oral and intravenous potassium replacement was initiated. Subsequently, a low magnesium level was found, which was also replaced. The patient recovered within three days with advice follow-up to the endocrinology clinic.

**Discussion:** Several published reports of epidemiological studies show a relationship between thyrotoxicosis and inflammatory bowel disease. Patient’s with a history of Crohn’s disease frequently present with severe complications of thyrotoxicosis as periodic paralysis. Genetic and environmental etiologies may contribute to the coexistence of these diseases. Specifically, both conditions have been linked to genetic mutations in genes that code for ion channels, L-type calcium channel α1-subunit and potassium inward rectifier across cell membranes. This channelopathy is responsible for severe hypokalemia with periodic paralysis.

**Conclusion:** Here we present a case of thyrotoxicosis hypokalemic periodic paralysis in a patient with Crohn’s disease.

Abstract #1091

**FNAC DIAGNOSIS OF THYROID NODULE WITH ITS CLINICAL CORRELATION**

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**Objective:** To investigate the frequency of malignancy and cellular aberration detected by fine needle aspiration cytology (FNAC) in euthyroid nodules and its correlation with clinical findings.

**Methods:** 150 (M:21, F:129) euthyroid nodular goiter attending endocrine OPD were recruited for this study. After clinical risk stratification FT4, TSH, USG, Isotope scan and FNAC of thyroid nodules were performed. Findings were categorized into malignant, suspicious, benign and indeterminate on the basis of cellular character. For statistical analysis Chi-square tests were done. Multiple regression analysis was done to see the independent significance of various factors for thyroid nodular malignancy.

**Results:** Recent changes of size (14.7%), pain in the nodule (4%) and dysphagia (6%). In 45.3% it was solitary; the rest (54.7%) had multinodular goiter. Enlarged regional lymph node was found in 12.7% patients. Frequency of malignant (10%) character was highest in cold nodules followed by uniform (5.6%), patchy (4%) and partially cold (1.6%) while none in hot nodules. About 17% of the nodules showed cellular aberration and 4.7% were clearly malignant whereas 124 (82.7%) were benign. Of the malignant, 4 were solitary and 3 were multinodular; which were 10 and 9 among the suspicious ones. A significant number (77%) among the malignant/suspicious nodules fell into moderate to high risk category (p<0.001), while 23.1% of the FNAC proven malignant/suspicious nodules were of low risk category. Enlarged lymph nodes (p<0.001), increased diameter of nodules of more than 4 cm (p=0.039) and recent changes in nodular size (p=0.042,) were independently and significantly related to cellular aberration.

**Discussion:** Noduler goiter is a common endocrine problem. Thyroid nodules are important for their malignant potential. In our study we have found strong co-relation with the FNAC findings but a good number clinically low risk categories also have cellular aberration. Similar results also found in other studies.

**Conclusion:** FNAC is a useful tool for cellular diagnosis of thyroid nodules. Clinical suspicion for malignancy strongly correlates with the FNAC findings.

Abstract #1092

**FAT IN THE THYROID-A RARE CASE OF THYROID HÜRTHLE CELL ADENOLIPOMA**

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**Objective:** While follicular adenomas are often seen by endocrinologists, it is quite unusual to encounter a thyroid lesion containing lipid. Pathologists frequently see a few adipocytes within fibrous septae, within the capsule, and surrounding blood vessels but rarely find mature adipose between thyroid follicles. A review of the literature revealed less than a dozen cases of adenolipoma or thyrolipoma. Here we report what we believe is the first case of a Hürthle cell adenolipoma.

**Case Presentation:** This is a 60 year old woman with a history of hypertension and hyperlipidemia who was referred to Endocrinology with the complaint of a visible left-sided neck mass for the past three years. She denied obstructive symptoms and had not noted any significant change in the mass over the past several years. Full thyroid function tests were within normal limits and her ultrasound revealed a multinodular goiter with a dominant 2.4 cm complex nodule on the left. Ultrasound-guided fine needle aspiration of the dominant nodule was suspicious for a Hürthle cell neoplasm. She underwent a
hemithyroidectomy and the pathology showed a Hürthle cell adenolipoma. Post-operatively, she developed mild hypothyroidism and is currently stable on a low dose of levothyroxine. It has now been several years and there has been no recurrence.

**Discussion:** Although adipose tissue is not commonly seen in thyroid lesions, it has been reported in thyroid lipomatosis, amyloid goiter, papillary thyroid carcinoma, thyroid adenoma and normal thyroid tissue. Even though fatty infiltration is known to occur with ageing in the thymus, pancreas, parathyroid and breast, this is not a finding seen in association with ageing and the thyroid. Adenolipoma of the thyroid is an encapsulated nodule containing both follicular cells and mature adipose. This patient was found to have a Hürthle cell adenolipoma and is believed to be the first case in the literature. She presented with a neck mass as was reported in other cases of adenolipoma of the thyroid. It is not well understood how adipose tissue becomes incorporated in thyroid lesions. It has been hypothesized that adipose can be included during embryonic development of the thyroid. Unfortunately, this would not explain adipose in acquired lesions (excluding the surrounding parenchyma). It has also been proposed that intralcsional lipids may result from metaplasia of stromal fibroblasts or represent neoplasia of mixed epithelial-mesenchymal tumors.

**Conclusion:** This case is presented here because of its rare occurrence. Endocrinologists should know these benign lesions and should be treated as such.

**Abstract #1093**

**PARATHYROID CARCINOMA PRESENTING AS SEVERE HYPERPARATHYROIDISM**

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Vanderbilt University Medical Center

**Case Presentation:** A 36-year-old man lost to follow up six years ago after presenting with mild hypercalcemia but normal PTH presents to ER with fatigue, weight loss, nausea, vomiting, constipation, neck pain, a right neck mass, and bilateral non-healing humerus fractures from a fall three months prior. Labs drawn on admission revealed high calcium of 17.4 mg/dL, PTH 1769 pg/mL and creatinine 2.42 mg/dL. Neck CT and ultrasound showed a 2.9 x 4.4 x 5 cm mass adjacent to right inferior thyroid pole, which matched the intense uptake in Sestamibi parathyroid scan. He underwent urgent en-bloc resection with right thyroid lobectomy and parathyroidectomy. Pathology confirmed a 5cm parathyroid carcinoma extensively invading into thyroid with multifocal lymphovascular invasion. Surgical margins and right level 6 lymph nodes were negative for cancer. Post-op course was complicated by hungry bone syndrome, treated with calcium and calcitriol. Post-op PTH dropped to 13 pg/mL, but trended up to 409 pg/mL 5 months later, with low normal calcium 8.9 mg/dL and creatinine 2.68 mg/dL. Extensive imaging (ultrasound, CT, 18-F PET, bone scan, parathyroid scan) did not reveal cancer recurrence. PTH dropped back down to 124 pg/mL after adding cinacalcet. HRPT2/CDC73 gene testing is pending.

**Discussion:** Parathyroid carcinoma is a rare cause of primary hyperparathyroidism (0.75-2%) often secondary to an inactivating mutation of the HRPT2 (CDC73) tumor suppressor gene. Presentation differs from benign hyperparathyroidism by large neck mass, very high calcium and PTH, renal insufficiency (84%) often with nephrolithiasis (56%) and bone disease with features of subcortical bone resorption, bone pain, and pathologic fractures. Diagnostic criteria rely on pathologically confirmed local invasion of contiguous structures, positive lymph nodes or distant metastases. The best treatment is en-bloc surgical resection. Adjuvant radiation and chemotherapy generally have poor results and are mostly reserved for unresectable disease. Anti-PTH immunotherapy has also shown promise with refractory disease. As recurrence is common, patients require lifelong surveillance with careful and frequent biochemical evaluation to differentiate between recurrence and other factors that elevate PTH, including hungry bone syndrome, renal failure, and parathyroid resistance.

**Conclusion:** Primary hyperthyroidism due to parathyroid carcinoma is rare, usually presenting with neck mass, very elevated calcium and PTH, renal insufficiency and bone disease. En-bloc surgical resection is the first-line and best therapy. Surveillance PTH monitoring can be complicated by secondary hyperparathyroidism due to vitamin D deficiency and renal insufficiency.
Abstract #1094

THYROIDECTOMY AFTER RADIOIODINE THERAPY FOR THE TREATMENT OF HYPERTHYROIDISM DUE TO GRAVES’ DISEASE AND TOXIC MULTINODULAR GOITER: A SINGLE ENDOCRINE SURGEON’S EXPERIENCE

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Objective: Graves’ disease and toxic multinodular goiters (TMNGs) are two of the most common causes of hyperthyroidism. Treatment options include antithyroid medications, radioiodine therapy, or thyroidectomy; the latter two options being the only ones that can provide definitive treatment. The reported incidence of recurrent hyperthyroidism after radioiodine therapy varies between 3-15%. Factors associated with increased risk of radioiodine failure include male gender, presence of goiter, and severity of hyperthyroidism, among others. Such patients eventually require surgical intervention to eradicate their hyperthyroidism. The purpose of our study was to describe demographic parameters and clinical outcomes of thyroid surgery after failed radioiodine therapy for the treatment of hyperthyroidism.

Methods: Between July 2004 and March 2012, a total of 31 thyroidectomies after radioiodine therapy (ROI) were performed by a single, experienced endocrine surgeon at Scott & White Memorial Hospital. A retrospective chart review was undertaken to evaluate demographic and clinical outcomes of these procedures.

Results: The mean age at operation was 52.8 years (range 16-83). There were 6 men and 25 women. The mean body mass index (BMI) was 43.2 (range 19-57). The mean thyroid gland size was 27.2 cm (excluding lobectomies). Mean operating time was 186 min for total thyroidectomy (range 135-385 min), and 138 min for thyroid lobectomy (range 80-175 min). Estimated blood loss (EBL) was 123 ml for total thyroidectomy, and 61 ml for thyroid lobectomy. There was one (3.2%) permanent recurrent laryngeal nerve (RLN) injury, and no temporary (stretch) injuries to the RLN.

Discussion: An analysis of our early experience reveals a slightly increased risk of permanent RLN injury for thyroidectomy after radioiodine therapy for Grave’s disease and toxic multinodular goiter.

Conclusion: Thyroidectomy after radioiodine therapy is a technically challenging, but safe and effective treatment for hyperthyroidism secondary to Graves’ disease and toxic multinodular goiter. It is imperative that such procedures be undertaken by an experienced endocrine surgeon, to ensure good outcomes with low complication rates.

Abstract #1095

METHIMAZOLE HEPATOXICITY: IS IT A “GRAVE” SITUATION IN PATIENTS WITH GRAVES’ DISEASE?

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Objective: Following the recent FDA restrictions to Propylthiouracil (PTU) prescription, Methimazole (MMI) has become the principal anti-thyroid medical treatment for hyperthyroidism, except in rare, selective situations. In this report we present the case of a patient with Graves’ disease in whom treatment with MMI led to severe cholestatic hepatitis, a rare adverse effect.

Case Presentation: A 44 year old female was seen for evaluation of recent-onset mildly symptomatic hyperthyroidism. On physical exam, she was clinically euthyroid, with a pulse rate was 80 beats/min. Her thyroid was diffusely enlarged to approximately 2 times normal with no nodules or bruits. She had normal reflexes and no tremors. Laboratory data showed a TSH of <0.01 uIU/ml (0.35-5.50), free T4 of 1.71 ng/dl (0.80-1.80), free T3 of 4.2 pg/ml (2.3-4.2), TRAb of 5.15 IU/L (0.00-1.75). Thyroid radiiodine uptake value was 14.1% at 4 hours and 37.8% at 24 hours (normal 35%). Her CBC and liver function testes were normal except for a ALT of 49 U/L (2 - 45) which was thought to be due to hyperthyroidism. She was started on MMI 10 mg TID. Three weeks later, the patient called the office to report that she developed yellowish discoloration of the eyes, darkening of her urine, joint pain, and itching. Laboratory data showed an AST of 189 U/L (10-40), ALT of 472 U/L (2-45), alkaline phosphatase of 283 U/L (1-120) and a total bilirubin of 5.9 mg/dl (0.2-1.2). Additional studies showed a negative viral hepatitis screen. Abdominal ultrasound showed no liver abnormalities. MMI was discontinued and her symptoms resolved quickly. Her liver function tests normalized in 2 weeks. She was started on levothyroxine, and has continued to do well on follow up. The case was reported to the FDA, in view of the extreme rarity of this adverse event.

Discussion: In contrast to PTU associated hepatic
necrosis, MMI can cause liver injury which is typically characterized by serious cholestatic dysfunction. The mechanism by which MMI causes acute liver injury is unknown but is likely due to an immunological reaction to a metabolic product of its metabolism. Typically MMI associated cholestasis has been associated with higher dose and older age. So far there have been no reports of MMI associated liver transplantation. In most cases that have been reported, the average duration of methimazole therapy before onset of hepatotoxicity is between 2-8 weeks.

**Conclusion**: Clinicians should always advise patients about the risk of hepatotoxicity associated with MMI, even though it is extremely rare. Compared to PTU, liver toxicity has been associated with better outcomes.
**LATE BREAKING**

**Abstract # 1100**

**ULTRASOUND-GUIDED THERMAL ABLATION FOR LARGE BENIGN THYROID NODULES: RADIOFREQUENCY ABLATION (RFA) VS LASER (LA) ABLATION**

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**Thyroid Disease**

**Objective:** To match a single session of ultrasound (US)-guided (US-G) thermal ablation therapy with laser (LA) vs Radiofrequency (RFA) in patients with large benign thyroid nodules.

**Methods:** One-hundred-and-eight consecutive outpatients with a symptomatic and cytologically benign thyroid nodule were randomized to a LA (N=54; mean±SD age 51±11.3) or RFA procedure (N=54; an±SD age 47±13.3) and followed up after one, three and six months. Compressive and cosmetic complaints were rated on a visual 10 cm analogue scale (VAS, 0-10). Percutaneous LA was performed with a solid-state laser source operating at 1064 µm, by inserting in a cranio-caudal approach 2-4 optic fibers into thyroid tissue through 21G Chiba needles, with a power output of 2-4 Watts. Mean total energy delivered was 9,624 Joules. Percutaneous RFA was carried out using a cool-tip 18G electrode needle powered by a 1,200kHz generator with an output of 35-55 Watts. Needle was inserted through a trans-isthmic approach and continuously moved within the thyroid nodule. Mean total energy delivered was 60,122 Joules.

**Results:** Carbonization, seen at US as a hypechoic irreversible mark, was observed in all patients after LA but not after RFA. Data are expressed as mean±SD of LA vs RFA procedure. Nodule volume were: baseline 39.3±22.5 ml vs 40.4±27.2 ml (P=n.s); 1 month after procedures 31.9±19.3 ml vs 28.9±23.6 (P<0.03), 3 months after ablation 27.8±18.7 vs 26.6±25.1 ml (P<0.04); 6 months after procedures 22.6±15.6 vs 16.9±13.9 ml, (P<0.01). Baseline compressive symptoms were (VAS) 5.1±1.4 vs 5.3±1.9; after 6 months were 2.5±1.1 vs 0.8±0.9 (P<0.01). TSH and thyroid hormone levels were unaffected in both groups.

**Discussion:** This is the first report showing the effectiveness of a single session LA or RFA therapy in large (>30) benign thyroid nodules. In previous studies, other authors used several LA cycles to obtain a 65% volume reduction in a series of patients with large (mean 53 ml) thyroid nodules. On the other hand, RFA has not been used in large nodules yet. Direct comparison between LA and RFA showed superior efficacy of the latter. Volume reduction of large benign thyroid nodules was greater, faster, and more homogeneous after RFA than LA therapy. Furthermore RFA permitted to deliver greater energy and to obtain larger ablations without carbonization.

**Conclusion:** Percutaneous US-G RFA is a new, valid treatment for rapid decompression of large benign thyroid nodules in a single session.

**Abstract # 1101**

**IMPACT OF SEVERE HYPOGLYCEMIA ON HEALTH-RELATED QUALITY OF LIFE (HRQOL) IN INSULIN-TREATED PATIENTS WITH TYPE 1 OR TYPE 2 DIABETES**

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**Hypoglycemia**

**Objective:** In this post-hoc meta-analysis, we examined whether severe hypoglycemia impacts on health-related quality of life (HRQoL) in insulin-treated patients with type 1 (T1D) or type 2 diabetes (T2D).

**Methods:** All open-label, randomized, treat-to-target phase 3a trials (26 or 52 weeks’ duration) in which once-daily insulin degludec and insulin glargine were given and HRQoL recorded (T1D: 1 trial; T2D: 5 trials) were eligible for inclusion. Severe hypoglycemia was defined as an episode requiring third-party assistance. HRQoL was assessed at baseline and end-of-trial via the Short Form 36 (SF-36; v2) questionnaire. Scores for patients who experienced one or more episodes of severe hypoglycemia and those who experienced no severe hypoglycemia were compared using ANCOVA.

**Results:** 11.9% (74/621) of T1D patients had at least one episode of severe hypoglycemia vs. 1.7% (57/3346) of T2D patients. Patients reporting severe hypoglycemia had significantly lower (worse) social functioning scores of -2.30 [-4.27; -0.34] and -2.69 [-4.99; -0.38] for T1D and T2D respectively, compared with those experiencing no severe hypoglycemia, p<0.05. Severe hypoglycemia was also associated with a significantly lower role-physical score of -2.30 [-4.27; -0.34] and -2.69 [-4.99; -0.38] for T1D and T2D respectively, compared with those experiencing no severe hypoglycemia, p<0.05. Severe hypoglycemia was also associated with a significantly lower role-physical score of -2.16 [-3.88; -0.44] in T1D, p<0.05 (similar but borderline significant in T2D, 2.19 [4.39; 0.00]). Mental health scores (-2.39 [-4.73; -0.05]) and general health scores (-2.65
ABSTRACTS – Late Breaking

EMPAGLIFLOZIN (EMPA), A SODIUM GLUCOSE COTRANSPORTER 2 (SGLT2) INHIBITOR FOR 90 WEEKS PROVIDES SUSTAINED GLYCEMIC CONTROL AND WEIGHT LOSS IN PATIENTS WITH TYPE 2 DIABETES (T2DM)

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Prediabetes/Diabetes Mellitus

Objective: To assess the effect of EMPA on glycemic control and weight in patients with T2DM.

Methods: A randomized, open-label 78-week extension study investigated EMPA or metformin IR (MET) as monotherapy and EMPA or sitagliptin (SITA) as add-on to MET in patients with T2DM who completed one of two 12-week, randomized, controlled trials. We present data at week 90 in patients who were randomized in the preceding trials to EMPA 10 mg, 25 mg or MET as monotherapy (n=81, 82 and 80, respectively) or EMPA 10 mg, 25 mg or SITA as add-on to MET (n=71, 70 and 71, respectively).

Results: Adjusted mean (SE) changes from baseline in HbA1c were -0.51 (0.09), -0.60 (0.09) and -0.64 (0.09)% with EMPA 10 mg, 25 mg or MET monotherapy, and -0.61 (0.10), -0.74 (0.10) and -0.45 (0.10)% with EMPA 10 mg, 25 mg or SITA as add-on to MET, respectively. Adjusted mean (SE) changes in fasting plasma glucose (FPG) were -32.4 (3.0), -28.1 (3.0) and -25.9 (3.0) mg/dL with EMPA 10 mg, 25 mg or MET monotherapy, and -23.3 (3.8), -31.8 (3.8) and -11.7 (3.8) mg/dL with EMPA 10 mg, 25 mg or SITA as add-on to MET, respectively. Over 90 weeks, ≥1 adverse event (AE) was reported by 58–61% and 68% of patients on EMPA or MET monotherapy, and 70–80% and 69% of patients on EMPA or SITA as add-on to MET, respectively. Changes in eGFR over 90 weeks were small and comparable across groups.

Discussion: EMPA led to clinically meaningful reductions in HbA1c, FPG and weight. The percentage of patients with ≥1 AE was similar on EMPA, MET and SITA.

Conclusion: EMPA 10 mg or 25 mg for 90 weeks provided sustained glycemic control and weight loss, and was well tolerated in patients with T2DM.

PREDX FINGER STICK: DIABETES RISK STRATIFICATION OF PREDIABETIC PATIENTS FROM CONVENIENTLY COLLECTED CAPILLARY BLOOD

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Prediabetes/Diabetes Mellitus

Objective: To develop and validate quantitative biomarker assays for use in the PreDx test from samples collected using a finger stick (FS) capillary blood collection method.

Methods: The PreDx test combines results from seven <i>in vitro</i> diagnostic assays, age and gender into a numeric score that stratifies patients by 5-year likelihood of developing type 2 diabetes. We sought to develop and validate PreDx test methods using FS blood samples collected on ADx100 serum separator collection cards. Each of the assays for glucose, HbA1c, insulin, adiponectin, ferritin, CRP and IL2Rα was modified to use sample extracted from the card. Assays were validated for precision and accuracy using CLSI guidelines. FS blood assays were calibrated to the corresponding venous blood assays using 75 to 80 matched FS blood and venous blood samples and validated by comparing assay results and PreDx scores in a separate matched set. Glucose values were evaluated using Clarke Error Grid Analysis (EGA). PreDx clinical performance was assessed <i>in silico</i> in the Inter99 cohort by adjusting the analytical variance of the venous blood assay for each analyte to match the variance of the corresponding FS blood assay.

Results: The FS blood assays showed good overall precision comparable to that of the venous blood assays; CVs ranged from 2.4% for HbA1c to 11.3% for adiponectin. After calibration, PreDx values from a set of...
matched samples showed excellent 1:1 agreement across the PreDx range, with an overall slope of 0.997 (95% CI 0.916 to 1.078) and intercept of -0.048 (-0.206 to 0.110) by Deming regression. EGA classified 98% of glucose values within zone A. Comparing simulated PreDx FS scores to the PreDx venous scores measured in the Inter99 study, there were no significant differences (p ≥ 0.05) in AUC, positive predictive value or sensitivity. As with PreDx venous, performance of PreDx FS was significantly better at predicting development of diabetes than fasting glucose by AUC and other measures.

**Discussion**: Capillary blood offers many logistical advantages but presents analytical challenges. Through careful development and validation, assays were modified to use FS blood and produce results with comparable accuracy and precision to the corresponding venous assays. The PreDx score generated using FS blood assays demonstrated accuracy and precision similar to that generated from venous blood. Differences in analytical performance had little impact on the PreDx clinical performance in the Inter99 cohort.

**Conclusion**: This work demonstrates that high quality quantitative PreDx test results can be obtained using the convenience of a FS blood collection device.

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**Abstract # 1104**

**HIGHER RATES OF CONFIRMED HYPOGLYCEMIA ARE ASSOCIATED WITH GREATER WITHIN-SUBJECT VARIATION IN FASTING PLASMA GLUCOSE IN PATIENTS WITH TYPE 1 OR TYPE 2 DIABETES: A META-ANALYSIS**

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**Hypoglycemia**

**Objective**: In this post-hoc meta-analysis of insulin-treated patients with type 1 (T1D) or type 2 diabetes (T2D), we investigated whether there is an association between hypoglycemia rate and the extent to which pre-breakfast blood glucose varies from day to day.

**Methods**: This patient-level meta-analysis included all open-label, randomized, treat-to-target phase 3a trials (26 or 52 weeks’ duration) in which once-daily insulin degludec (IDeg) was compared with insulin glargine (IGlar) in T1D (2 trials) and T2D (5 trials). Within-subject variability (CV%) in self-measured pre-breakfast plasma glucose (PG) (measured using blood glucose meters calibrated for PG) was determined from 3 consecutive daily measurements made in the final week (week 26 or 52) of each trial. CV% was compared between those patients with a rate of confirmed hypoglycemia (PG <56 mg/dL or severe) within the upper quartile (Top 25%) and those outside this range (Bottom 75%) using a linear mixed model, which allows for heterogeneity in the residual variance for each group.

**Results**: For patients with T1D, the CV% ratio – top 25% / bottom 75% – was 1.33 [1.20; 1.46] for IDeg and 1.25 [1.07; 1.42] for IGlar. In T2D, the ratio was 1.50 [1.43; 1.58] for IDeg and 1.46 [1.36; 1.56] for IGlar. Among insulin-experienced patients with T2D receiving basal insulin plus oral antidiabetic therapy (BOT), the ratio was 1.33 [1.25; 1.41] for IDeg and 1.46 [1.34; 1.57] for IGlar. For insulin-naive patients with T2D in whom BOT was initiated in the trials, the ratios were 1.33 [1.24; 1.42] (IDeg) and 1.49 [1.35; 1.63] (IGlar). Similar results were observed in patients with T2D on basal–bolus therapy with ratios of 1.65 [1.50; 1.79] (IDeg) and 1.65 [1.40; 1.91] (IGlar). In both IDeg and IGlar, estimated day-to-day variability in pre-breakfast PG was significantly higher for patients with the highest rates of confirmed hypoglycemia (Top 25%) than those with lower rates (Bottom 75%), regardless of diabetes type or T2D treatment history, p<0.05%.

**Discussion**: With both IDeg and IGlar, higher rates of confirmed hypoglycemia are associated with greater within-subject variation in fasting blood glucose in patients with T1D and T2D.

**Conclusion**: Reducing within-subject variation in fasting blood glucose, in patients with diabetes, may lower the incidence of hypoglycemia.
Abstract # 1105

METABOLIC PROFILING OF PATIENTS WITH CHRONIC CRITICAL ILLNESS: EXPLORATORY DATA ANALYSIS OF 150 PATIENTS

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Other

Objective: Chronic Critical Illness (CCI) designates a unique subset of patients surviving acute critical illness but requiring prolonged mechanical ventilation and tracheostomy. Outcomes in this population are poor with only about 50% liberated from the ventilator, high morbidity and mortality, and poor quality of life in survivors. Little data is available regarding endocrine-metabolic care specifically in the CCI population.

Methods: This is a retrospective case series of patients admitted to The Mount Sinai Hospital Respiratory Care Unit (RCU) from September 2009-December 2010. RCU patients are cared for by a multidisciplinary team, including an endocrinologist, with protocol-driven care applied to glycemic control, nutrition, and other metabolic variables (e.g. bisphosphonates, calcium, vitamin D). A database was created with demographic, clinical, biochemical and outcome data recorded.

Results: At RCU discharge, ventilator status was classified as (1) alive and off the ventilator (n=79, 52.7%), (2) alive and on the ventilator (n=49, 32.7%), or (3) expired (n=22, 14.7%); p<0.0001. 72 subjects (48%) expired within one year of hospital admission. The mean number of days to target nutritional energy goals (20-25 kcal/kg/day) in this cohort was 0.9±2.3 days. Median energy and protein intakes of enteral nutrition were 23.7 kcal/kg/day and 1.1 g/day, respectively, at RCU admission (n=130) and 25.9 kcal/kg/day and 1.4g/day at RCU discharge (n=83). The mean blood glucose for this cohort was 140.2 mg/dL (BSD=34.9; WSD=35.2) on admission and 130.1 mg/dL (BSD=27.5; WSD 25.4) after 120 hours in the RCU; p=0.0170. The hypoglycemia (<70 mg/dL) and severe hypoglycemia (<40 mg/dL) rates were 2.86% and 0.37%, respectively. Pamidronate was administered as a treatment for bone hyper-resorption in 32 patients (21%), with a calcium/vitamin D protocol administered in 107 patients (71%).

Discussion: Our RCU cohort demonstrates that protocol-driven care can achieve metabolic goals in a CCI population. Optimized glycemic control was achieved safely (i.e. low rates of hypoglycemia and severe hypoglycemia), with a subcutaneous insulin protocol. Nutritional optimization, with attainment of energy and protein targets early in the RCU stay, is likely an important factor in the management of safe glycemic control. Future goals of this research are to correlate metabolic variables with outcomes in the CCI population (e.g. ventilator liberation, mortality) and devise a predictive model to guide selection of patients for aggressive vs. palliative care and preserve economic resources.

Conclusion: Metabolic variables may play a role in the outcomes of a CCI population and require further study.

Abstract # 1106

TO STUDY THE ASSOCIATION BETWEEN PLASMA HOMOCYSTEINE AND MICROVASCULAR AND MACROVASCULAR COMPLICATIONS IN TYPE 1 DIABETES MELLITUS

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Prediabetes/Diabetes Mellitus

Objective: To study the association between plasma homocysteine and microvascular and macrovascular complications in type 1 Diabetes Mellitus.

Methods: This study was carried out from Nov ’2011 to Nov ’2012. The cases are 31 patients with Type1 Diabetes Mellitus with one or more micro vascular / macro vascular complications. Controls were 31 patients with Type1 Diabetes Mellitus without any vascular complications. Plasma total homocysteine was measured by Chemiluminescence Micropartide Immunoassay. Complications were diagnosed as Retinopathy by Fundus examination, neuropathy by nerve conduction study, coronary heart disease by ECG and nephropathy by microalbuminuria (Random spot urine sample for albumin–creatinine ratio). Between case and control group no significant difference in mean age, duration of diabetes, HbA1c, and vitamin B12 and folate level.

Results: The mean plasma homocysteine was higher in case group as compared to control group. (14.27
Patients with non proliferative retinopathy have higher plasma homocysteine as compared to patients without retinopathy, but this is statistically non significant. (12.58±3.92 vs. 11.22±3.05, P-value > 0.05). Patients with proliferative retinopathy have statistically significant higher plasma homocysteine as compared to patients without retinopathy (18.64±4.41 vs. 11.22±3.05, P-value < 0.01). Patients with microalbuminuria have higher plasma homocysteine as compared to normoalbuminuric patients. (15.60 ± 4.61 vs. 11.50± 4.59, P-value < 0.05) Patients with neuropathy have higher plasma homocysteine as compared to patients without neuropathy. (15.77±5.09 vs.13.05±4.54, P-value > 0.05).

Discussion: Above finding suggests that homocysteine might play an important role in the pathogenesis of vascular complications in type 1 diabetes. The biological mechanism for the interaction between diabetes and elevated plasma homocysteine on vascular complications is still not well understood, although proposals include oxidative stress, endothelial damage and decreased nitric oxide bioavailability.

Conclusion: In Type 1 Diabetes Mellitus: Plasma homocysteine level is higher in patients with vascular complications as compared to patients without these complications. Proliferative retinopathy and microalbuminuria significantly associated with Plasma homocysteine level, but non-proliferative retinopathy and neuropathy does not show significant association.

Abstract # 1107

SUCCESSFUL INTEGRATION OF AACE GUIDELINES AND EMR BEST PRACTICE ALERTS IMPROVES DIABETES CONTROL

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Prediabetes/Diabetes Mellitus

Objective: Translation of best practices in diabetes management has been challenging with half of patients failing to achieve goals for glycemic, blood pressure or lipid control. Sentara medical group (SMG) encompasses 144 primary care providers caring for 29,000 persons with diabetes. In an effort to improve delivery of diabetes care and adherence to treatment goals a transformation of care team was assembled to engage providers by providing best practice alerts (BPA) and treatment recommendations driven by Epic® electronic medical record (EMR). A high risk BPA was developed for HbA1c > 9% and/or lack of statin use. Moderate risk BPA was developed for HbA1c 7.1 to 8.9%. BPAs were coupled with smart order sets to facilitate medication changes and/or referrals to specialty care.

Methods: A transformation of care team was assembled and tasked with adapting AACE guidelines for the management of diabetes into clinical care pathways for patients with HbA1c > 9%. Strategies included BPA alerts linking providers to insulin order sets as well as recommendation for lipid lowering with a statin. The clinical care package was piloted in two primary care practices and one endocrine site prior to integrating into the EMR system wide. Data presented represent results for the system during a 10 month interval.

Results: Our intervention yielded marked improvements in attaining goal HbA1c ≤ 7.0 for the total SMG population (8.5 % improvement with additional 1390 patients at goal) and a reduction in values ≥ 9% ( 13% improvement with 891 fewer patients at risk). Overall there was an increase in use of statins in diabetic patients with a system wide improvement of 3% in obtaining LDL cholesterol less than 100 mg/dL. One practice site improved attainment of goal LDL cholesterol by 100%.

Discussion: These data suggest clinically significant improvements in metabolic parameters important to diabetes control can be achieved by implementation of an EMR driven BPA. Order sets and referral options delivered at the point of care in real time likely facilitate the health care provider attending to appropriate diabetes management while managing acute complaints. The institution of AACE guidelines facilitated by BPAs has helped to develop a diabetes management culture in tune to improving quality care.

Conclusion: Adoption of quality improvement projects by providers using electronic medical records improves metabolic parameters; critical to the prevention of diabetic complications. The intervention described is low cost and effective. Ongoing analysis will assist in estimating both cost savings and avoidance of diabetes associated hospitalizations.
Abstract # 1108
THE QUANTIFICATION OF DIABETIC RISK REDUCTION DURING A 12-WEEK MEDICALLY SUPERVISED WEIGHT LOSS PROGRAM.

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Serotonin-Plus Weight Loss Program, Burke, VA, United States.

Prediabetes/Diabetes Mellitus

Objective: To assess the change in PreDx DRS after 12 weeks of participation in the Serotonin-Plus Weight Loss Program in patients who are at risk for development of T2DM.

Methods: All new patients entering the Serotonin-Plus Weight Loss Program who have not already been diagnosed with type 2 or type 1 diabetes mellitus will be offered entry to the study. During their first visit, they will have a (10 hour fasting) PreDx DRS test performed. The patient will then proceed through the Serotonin-Plus Weight Loss Program 12-week protocol and on the last visit, will have the fasting PreDx DRS test performed. The results will be reviewed by an independent statistics expert.

Results: 34 patients’ (22 female, 12 male) results were analyzed. Diabetes risk, as defined by the PreDx Score, was reduced from an average of 6.66% to 3.51% over the course of the 12-week Serotonin-Plus Weight Loss Program. This represents a 47.2% reduction in diabetes risk among this sample. Additionally, the diabetes risk scores were found to decrease from 5.15 to 3.24 over the course of the study, which represents a 37.09% reduction. Finally, the risk of diabetes in comparison to the general population was found to decrease from a mean of 2.4317 to 1.0236 over the course of the study, which represents a 57.91% reduction. Additionally, by the end of the study, patients had a risk of diabetes nearly equal to the general population.

Discussion: The monetary costs of diagnosing and treating diabetes mellitus and the associated co-morbidities are measured in the hundreds of billions of dollars yearly worldwide. Developing and supporting aggressive weight loss programs will be paramount to achieving the saving of lives and money. This interim study results demonstrate that in a fairly brief period of time (12 weeks) the risk of a “pre-diabetic” developing frank diabetes drops tremendously. With further weight loss intervention, this risk reduction will be even more pronounced. Obviously, the major challenge is to develop systems and strategies to reduce the recidivism rates to ensure that the affected people do not return to old habits, regain weight and go back to the same diabetes risk they had previously. Long-term behavioral modification, life-style changes and support for the patients when they leave a formal weight loss program are paramount to the success in keeping the diabetes risk much lower.

Conclusion: The study results demonstrate that a medically supervised weight loss program can help reduce diabetic risk by almost 50% in just 12 weeks. By reducing diabetic risk, we can ultimately save many lives, and we can also reduce the high healthcare costs that are spent on treating diabetes each year.

Abstract # 1109
RESPONSE TO SITAGLIPTIN THERAPY IN A PATIENT WITH NEWLY DIAGNOSED CYSTIC FIBROSIS-RELATED DIABETES MELLITUS: A CASE FOR DDP-4 INHIBITOR USE IN CFRD.

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Prediabetes/Diabetes Mellitus

Objective: Cystic fibrosis-related diabetes (CFRD) is a major co-morbidity affecting 40-50% of adult cystic fibrosis (CF) patients. Insulin injection is the recommended treatment for CFRD. Risk of hypoglycemia is high in many of these patients when treated with insulin, especially in the early stages. The rational approach in such patients may be an effective oral agent with little or no risk of hypoglycemia.

Methods: We report the case of a middle-age man with history of CF and impaired glucose tolerance (IGT) and subsequent diabetes, and then started on Sitagliptin, a DPP-4 (dipeptidyl peptidase-4) inhibitor. We describe the progression to CFRD and the use of a DPP-4 inhibitor to control his BG and the response to treatment.

Case Presentation: A 45-year old man with history of CF (+delta 508 gene) and IGT presented for diabetes screening. An OGTT was done: Fasting, 30-min, 60-min, 90-min and 2-hr BG values were 77 mg/dl, 170 mg/dl, 218 mg/dl, 131 mg/dl and 57 mg/dl respectively; HBA1C was 5.8%. Follow-up OGTT in 1 yr: FBG was 102 mg/dl; 2-hr value of 204 mg/dl diagnostic of diabetes; BG values at 30, 60 and 90 min, were 256 mg/dl, 327 mg/dl and 362
mg/dl respectively. HBA1C was 6.0% with an estimated glucose average of 125 mg/dl. CGMS (Continuous Glucose Monitoring System) demonstrated postprandial hyperglycemia with virtually every meal. Sitagliptin 100 mg daily orally was prescribed. The 2-hr postprandial BG trended towards normal range; fasting BG normalized; and HBA1C was 5.6% after 6 months of therapy; no hypoglycemia was observed. Follow-up CGMS showed resolution of BG excursions that were present prior to initiation of therapy.

Discussion: Spontaneous hypoglycemia is common in CF patients, even without CFRD; occurs both in the fasting state, and postprandially in relation to delayed and disordered insulin secretion. Insulin-induced hypoglycemia also occurs in CFRD as in any patient on insulin therapy, further increasing the risk of hypoglycemia, especially in the early stage. CF patients do not have a good glucagon response to hypoglycemia. An incretin-based therapy that is void of hypoglycemia is a reasonable approach. DPP-4 inhibitors fulfill both conditions; and unlike GLP-1 agonists, they are weight neutral and are administered orally, hence the ideal choice in this scenario. Sitagliptin has been shown to reduce blood glucose excursions following glucose load or meal without causing hypoglycemia. This CFRD patient has clearly benefited thereof.

Conclusion: Glycemic control was achieved with Sitagliptin in this CFRD patient with predominant postprandial hyperglycemia, and the treatment was not complicated with hypoglycemia. DPP-4 inhibitors may have an important role in the early treatment of CFRD.

Abstract # 1110

A NOVEL MOUSE MODEL OF METASTATIC THYROID CARCINOMA USING ADIPOSE STEM CELLS

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Thyroid Disease

Objective: The main aim was to produce an established metastatic human thyroid carcinoma model.

Methods: We used thyroid cancer K-1 cell line (harbors heterozygous mutation in B-Raf V600E) and Adipose Stem Cells (ADSCs) to create this model. We had four groups of severe combined immunodeficient mice, with each group consisting of four mice. The first group was injected subcutaneously in the flank with (K-1 cell line + ADSCs), while the second group was injected with only k-1 cell line. The last two groups were both orthotopically injected; the third group was injected with (k-1 cell line + ADSCs), and the fourth group was injected with k-1 cell line only

Results: Concomitant injection of ADSCs produced larger thyroid tumors and consistent metastatic disease in both flank and thyroid orthotopic groups (p<0.05 for both). Gross tumor metastasis and histopathologic features of high-grade neoplasms (atypia, nuclear pleomorphism, and high nuclear to cytoplasmic ratio) were noticed in lungs. Here we establish a novel orthotopic metastatic thyroid carcinoma model using ADSCs.

Discussion: In view of the recent massive effort to present new treatments for radioiodine resistant metastatic thyroid cancers, scientists have been searching for the best in vivo model to evaluate different kinds of chemotherapeutics. This model can assess the feasibility of many new chemotherapeutics used for the management of radioiodine resistant metastatic thyroid cancers.

Conclusion: This novel model of advanced human thyroid cancer is theoretically possible, simply reproducible, valuable tool to evaluate new surgical and medical interventions on the primary tumor and other organs metastasis.

Abstract # 1111

LONG TERM EFFECTS OF ENHANCED EDUCATION AND COORDINATION OF CARE (PATIENT CENTERED MEDICAL HOME MODEL) IN DIABETIC PATIENTS

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Prediabetes/Diabetes Mellitus

Objective: The aim of this study was to assess the impact of a Patient-Centered Medical Home (PCMH) model of care on diabetes management with regard to blood sugar control, LDL cholesterol, microalbuminuria and blood pressure control over a period of 3 years.

Methods: 92 consecutive diabetic patients (mostly uninsured or underinsured) were enrolled in our PCMH pilot at resident continuity clinic starting January 2009 to December 2009 and were followed longitudinally until January 1, 2012. Only patients who had been seen by a physician at least once per year were included. Demographic data, blood pressure and laboratory values were entered into the CDEMS registry. As part of PCMH model of care, assigned nurses provided pre and post visit assessment of current status of patients’ diabetes and associated comorbidities, and reviewed goals of care.
Nurses were also responsible for coordinating referrals and clarifying the plan of care until the next follow up visit. Of this cohort we reviewed retrospectively a random sample of 30 patients; values of hemoglobinA1c, LDL and microalbumin were recorded at the enrollment into the PCMH, at 6 months and at the end of study. The values were compared using paired t-test. The blood pressure flow sheet was reviewed and the percentage of measurements within goal (<140/90) was recorded.

**Results:** Compared to enrollment, the HbA1c dropped significantly at 6 months (p= 0.040, CI 0.040-1.622) and this effect sustained at the end of the study (p= 0.020, 95% CI 0.159 to 1.730). LDL cholesterol did not reach statistically significant change at 6 months (p= 0.672), but dropped significantly by the end of the study (p= 0.032, 95% CI 1.81 to 37.89). Microalbuminuria did not change statistically during the study period. BP control varied: 21.2% of patients had all BP values within goal, while 54.5% of patients had more than 75% of their BP within goal, and 84.8% were controlled on more than 50% of visits.

**Discussion:** The PCMH is a model of practice in which a team of health care professionals, coordinated by a personal physician, works collaboratively to provide high levels of care, access and communication, enhanced patient education, and care coordination and integration. In our clinic this model of care resulted in significant long term, sustained improvement in Hba1c and LDL cholesterol. BP control varied: 21.2% of patients had all BP values within goal, while 54.5% of patients had more than 75% of their BP within goal, and 84.8% were controlled on more than 50% of visits.

**Conclusion:** Recognising DbCM and taking measures for its early detection and preventing its progression is likely to have significant benefit in morbidity mortality and financial burden of disease. Retinopathy is a very specific and well recognised easily screened microvascular complication of diabetes. Using retinopathy as a surrogate marker will improve the awareness of DbCM and lead to its early detection. The health and economic benefits of this simple association are likely to be very fruitful.
Abstract # 1113

TESTICULAR GERM CELL TUMOR: AN UNUSUAL CAUSE OF HYPERTHYROIDISM IN A YOUNG MALE

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Thyroid Disease

Case Presentation: A 25 year-old Caucasian male with no prior medical history was admitted to the hospital with hemoptysis. A CT angiogram of the chest performed to evaluate for a pulmonary embolism showed no evidence of a pulmonary embolism, however showed numerous lung lesions concerning for metastases of unknown origin. He was transferred to our ICU and on initial examination, he was tachycardic with a heart rate of 134. Thyroid function tests were obtained: TSH <0.01 mU/L (0.6-3.3), free thyroxine (FT4) 4.98 ng/dL (0.71-1.40), free thryonine (FT3) 9.58 pg/mL (2.32-6.09). Thyroid gland on exam was not enlarged and there were no audible bruits. Physical exam revealed a firm right testicular mass. Scrotal ultrasound revealed a large, complex right mass measuring 3.4 x 2.1 x 3.1 centimeters. Tumor markers were obtained: alpha fetoprotein 725.42 ng/mL (0-10.0), beta hCG 836,080 u/L (0-5), lactate dehydrogenase 3734 U/L (338-610). He was started on methimazole 30mg daily and atenolol 50mg twice daily on hospital day #2. He underwent right orchiectomy on hospital day #2 with pathology revealing a non-seminomatous mixed germ cell tumor. Pathology also showed syncytiotrophoblastic giant cells and nodules of necrosis that stained positive for beta hCG consistent with choriocarcinoma. Chemotherapy with cisplatin, ifosfamide and etoposide commenced on hospital day #3. He tolerated the chemotherapy well and was discharged home on hospital day #9. He was continued on methimazole 30mg daily upon discharge. Sixteen days after initial presentation, tests showed a TSH of 0.50 mIU/mL (0.6-3.3), free thyroxine of 1.11 ng/dL (0.71-1.40) and methimazole 30mg daily. Thyroid function tests remained within normal limits after cessation of methimazole and lowering of beta hCG levels.

Discussion: Germ cell tumors account for 95% of malignant testicular tumors and many of these tumors produce high amounts of hCG which can result in thyrotoxicosis. The pathophysiolocial mechanism behind hCG-induced hyperthyroidism is likely the ability of hCG to activate the TSH receptor. Since the first case of hCG-induced hyperthyroidism in males in 1964, studies have shown the prevalence of hyperthyroidism in men with hCG levels >50,000 IU/L to be upwards of 50%.

Conclusion: Hyperthyroidism due to hCG-secreting testicular carcinomas should be considered in men presenting with atypical thyrotoxicosis. Successful treatment with chemotherapy and lowering of hCG levels can result in return of normal thyroid function and quick cessation of antithyroidal medication.

Abstract # 1114

A COMPARATIVE STUDY OF FACTORS INFLUENCING PARATHYROID GLAND ACTIVITY IN PRIMARY VERSUS TERTIARY HYPERPARATHYROIDISM OF CHRONIC RENAL FAILURE

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Other

Objective: To determine intraglandular PTH (IGPTH) concentration in tertiary hyperparathyroidism (THPPT) of chronic renal disease (CKD) & contrast w/ that of primary hyperparathyroidism (PHPPT) of adenoma.

Methods: PTH assay was done in wash liquid after fine-needle aspiration bx under ultrasound (US) along w/ cytological exam of aspirated cells.

Results: US guided alcohol ablation of parathyroids was undertaken as therapeutic measure in both pts. Pt. A: 80-yrs old man had a 2.7x1.0x 1.2 cm (volume 1.68 Cm3) Lt inferior parathyroid adenoma. labs:Serum Ca++ 2.7 mmmol/L RR: 2.1-2.55), PO4 0.69 mmol/l(RR:0.8-1.45),creatinine 74 umol/l(RR::45-96),eGFR >60 ml/min/1.73 m2, PTH 176 ng/l; (RR: 10-65), Vit D D3: 6nmol/l(RR: 50-150). He had multiple comorbid conditions precluding neck surgery. Pt. B: 32-yrs old lady w/ x-linked hypophospatemic osteomalacia & THPPT of CKD (S creatinine 211, GFR 20, vit D3: 33 nmol/l, S Ca++: 2.72, increased S PO4 1.86, despite high PTH(2345 hg/l) & high FGF 23 (6130 RU/ml: RR:< = 180). This set up provided w/ chance to explore effect of elevated FGF 23 on parathyroid hyperplasia of CKD. She previously had PTHX & implantation of 1/2 gland in Lt forearm. Whole body parathyroid scan: the only parathyroid tissue located in Lt forearm. US guided ablation of gland measuring 1.78x 0.7xx 0.847 (volume 0.545 cm3) was done. Cytology confirmed parathyroid tissue, immuno +ve for PTH. The IGPTH & peripheral PTH concentrations were 96,000
ng/l & 303 respectively in THPPT & were 61,700 & 176 respectively in PHPPT (IGPTH was 156% & peripheral PTH was 172% higher in THPPT). These data correlated w/ following variables: lower gland volume in THPPT (32%), higher SPO4 in THPPT (38%), higher Scratinine in THPPT (172 %), decreased eGFR in THPPT (186 %), low Vitamin D in PHPPT, Similar S Ca++ concentrations, & high S FGF23 in THPPT.

Discussion: Our data indicate that secretory function of smaller hyperplastic parathyroid tissue in CKD is quite vigorous compared to larger adenoma of PHHPT. The over activity of smaller gland in THPPT appears to be driven by decreased renal status. However, multiple factors that underpin CKD potentially influence parathyroid over activity include high S PO4, creatinine, FGE23. Under physiological conditions, FGF23 acts directly on parathyroid to decrease PTH synthesis & secretion. Our data supports the notion that in CKD elevated FGF 23 fail to suppress PTH secretion. In CKD parathyroid resistance to FGF23 may be caused by decreased expression of Klotho–FGFR1 complex in hyperplastic parathyroid.

Conclusion: Our data provide insights into the role of FGF23 in mineral homeostasis & its direct interaction on parathyroid, focusing on pathophysiology of THPPT of CKD.

Abstract # 1115

DIFFERENTIAL DIAGNOSIS OF HYponatreMIA: NORMAL PRESSURE HYDROCEPHALUS ACCOMPANIED BY A SYNDROME OF INAPPROPRIATE ADH SECRETION.

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Pituitary Disorders/Neuroendocrinology

Objective: To prompt clinicians to consider the syndrome of inappropriate antidiuretic hormone secretion (SIADH) in the differential diagnosis of hyponatremia in patients with idiopathic normal pressure hydrocephalus (NPH). Methods: A case report of an elderly woman with the clinical and radiological features of NPH accompanied by hyponatremia is presented. The authors report their findings from an extensive workup of the hyponatremia. Case Presentation: A 78-year old woman was being evaluated for hyponatremia. She had presented with one-year history of urinary incontinence, also chronic gait disturbance and decline in cognitive function, which constitute the classic triad of NPH; brain MRI showed ventriculomegaly and other features consistent with this syndrome. Serum sodium was 129 mEq/L with serum osmolality of 270 mOsm/kg; urine osmolality 167 mOsm/kg and sodium 65 mmol/L. Serum uric acid was 3.1 mg/dl and urea level was 5 mg/dl. Other metabolic workup was negative; renal, adrenal and thyroid functions were normal. Cardiac workup was negative. Chest and brain imaging results were negative for occult malignancy. SIADH was diagnosed. Interestingly, ADH level was 6.2 pg/ml. A conservative treatment was started based on patient’s preference, with moderate improvement in hyponatremia.

Discussion: Clinical diagnosis of NPH is based on the presence of the classic triad of gait disturbance, urinary incontinence and cognitive function impairment. It is associated with ventriculomegaly typically in the absence of elevated cerebrospinal fluid pressure. The import of this rare entity found in the elderly, first reported by Hakim and Adams in 1965, is the potential for the clinical abnormalities to abate or resolve with treatment. Theoretically hyponatremia may occur in NPH; however up to date only one associated case of SIADH has been described in the literature. Hyponatremia due to SIADH in a patient with NPH is thought to result from the mechanical pressure on the hypothalamus from the third ventricle. Chronic hyponatremia, by itself even in mild form, is known to be associated with increased rate of falls. A case of an elderly woman with typical clinical features and brain imaging consistent with NPH accompanied by hyponatremia due to SIADH has been presented. Although, the patient refused any consideration of a shunt placement or any invasive procedure, condition somewhat remained stable with conservative management of the SIADH and concomitant clinical problems. Conclusion: Recognition of occurrence of SIADH in NPH, though an extremely rare metabolic manifestation of the neurological disorder, only one case having been reported in the literature, is important for the appropriate management of the associated hyponatremia.
Abstract # 1116

**MASSIVE PULMONARY THROMBOEMBOLISM AS A COMPLICATION OF DIABETIC KETOACIDOSIS**

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**Prediabetes/Diabetes Mellitus**

**Objective:** To present a case of massive pulmonary thromboembolism in the setting of diabetic ketoacidosis in a newly diagnosed diabetic.

**Case Presentation:** A 57 year old man with no significant past medical history was admitted for syncope. On the day of admission, patient was jogging in the park, when he suddenly felt dizzy and fell on the ground. He denied any chest pain, palpitations, shortness of breath, involuntary movements, tongue bite, bowel or bladder incontinence or any similar episode in the past. However, he reported polyuria, polydipsia and weight loss of 20 lbs in past 6 months as well as blurred vision since 2 months. He denied nausea, vomiting, abdominal pain, diarrhea, history of recent travel and sick contacts. He had a 10-pack year history of smoking, without a history of illicit drug use and was taking no medications. Family history was positive for type II diabetes in mother. On initial physical exam, he was obese, his temperature was 98.3°F, respiratory rate was 20 breaths/min, pulse was 107/min and blood pressure was 132/82mmHg. Neck exam was notable for acanthosis nigricans. Rest of the systemic examination was normal. Lab evaluation revealed the following: serum glucose 767mg/dl, arterial pH 7.3, anion gap 35, BUN 35mg/dL, serum creatinine 2.4mg/dL, creatine kinase 824units/L, ketonemia and ketonuria. CBC was remarkable for WBC count of 13300/mcL. Liver enzymes, amylase, lipase and serum electrolytes were normal. His HbA1C was 19.9%. Initial EKG was notable for sinus tachycardia and poor R wave progression. Echocardiogram showed a dilated and hypokinetic right ventricle. CT angiogram was remarkable for extensive emboli in both pulmonary arteries and extending throughout the lungs. Protein C and free protein S levels were low at 43% and 20% respectively.

**Discussion:** Studies have shown that systemic prothrombotic changes occur during diabetic ketoacidosis which include endothelial activation, increased levels of fibrinogen, decreased levels of free protein S and protein C activity; as is the case in our patient. Increased levels of vWF antigen and activity also confer to the hypercoagulable state in DKA. Hyperglycemia-induced oxidative stress is responsible for enhanced peroxidation of arachidonic acid to form biologically active isoprostanes, which represents an important biochemical link between impaired glycemic control and persistent platelet activation. Furthermore, it causes confrontational changes in the vascular endothelial cells that change their hemodynamic profile and result in a prothrombotic state.

**Conclusion:** Healthcare professionals must be aware of this rare but life-threatening complication of thromboembolic phenomenon in patients with DKA and newly diagnosed diabetes.

Abstract # 1117

**AN UNUSUAL CASE OF REFRACTORY HYPOTHYROIDISM SOLELY RESPONSIVE TO PARENTAL LEVOTHYROXINE**

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**Thyroid Disease**

**Case Presentation:** There are very rare cases in literature of refractory hypothyroidism that responded to only parental doses of levothyroxine in which no other cause of malabsorption could be identified. Here, we are presenting a 46 year-old female with refractory hypothyroidism status post thyroidectomy who responded selectively to parental doses of levothyroxine.

**Discussion:** The mainstay treatment for hypothyroidism is oral levothyroxine sodium (LT4). The dosage is generally 1.6-μg/kg bodyweight (3). The amount of absorption of oral thyroxine is the key to obtaining successful treatment. The absorption of oral thyroxine is generally between 70-80% of the administered dose and takes place at the intestinal level. (1) The absorption amount does not differ if a patient is euthyroid or hypothyroid. (2) In certain studies, it has been shown that 20% of T4 is absorbed at the level of the duodenum, 40% in the upper jejunum and the remaining 40% in the lower jejunum. (1) Despite administering appropriate or higher doses of levothyroxine in some patients they are still unable to reach a euthyroid state. Such rare cases need to be further evaluated and there are many differentials to be considered such as (1) poor patient compliance (2) states requiring an increased need for thyroxine and (3) malabsorption disorders. In the study of refractory hypothyroidism, there are very few cases that respond only to parental levothyroxine after ruling out all other possible causes of malabsorption. In the following case, we present a 46 year-old female who solely responded to parental levothyroxine in whom no cause of malabsorption could be identified.
Abstract # 1118

EFFECTIVE AND SAFETY OF LINAGLIPTIN IN HISPANIC/LATINO PATIENTS WITH TYPE 2 DIABETES: POOLED ANALYSIS FROM SIX RANDOMISED PLACEBO-CONTROLLED PHASE 3 TRIALS

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Prediabetes/Diabetes Mellitus

Objective: Hispanic/Latino groups in the Americas are disproportionately affected by type 2 diabetes (T2D). Its prevalence in this population is almost twice that of non-Hispanic/Latino whites, and they have a raised risk of related complications; yet these patients are often diagnosed late, inadequately treated, and thus less likely to achieve or maintain glucose targets. They are also less likely to start or to adhere to insulin therapy. Given the burden of T2D in Hispanic/Latino groups and that they are the fastest growing and largest ethnic minority in the US, it is important to assess new T2D therapies in this population. By pooling data from a large clinical development program, we assessed the safety and efficacy of linagliptin, an oral, dipeptidyl peptidase-4 inhibitor, in Hispanic/Latino patients.

Methods: This retrospective analysis identified self-reported Hispanic/Latino subjects from 6 randomized, double-blind, placebo-controlled, parallel-group trials of linagliptin as monotherapy or add-on to various glucose-lowering regimens, in North and South America (NCT00601250, NCT00602472, NCT00819091, NCT00954447, NCT00798161, NCT00740051). Two studies were 18 wks, and 4 were 24 wks in duration.

Results: Of 745 Hispanic/Latino patients identified; 478 received linagliptin 5 mg/day and 267 placebo. Mean (SD) baseline characteristics were similar in linagliptin and placebo groups: age, 57.4 (10.0) and 56.8 (9.7) years; BMI, 30.3 (5.0) and 31.4 (4.6) kg/m2; HbA1c, 8.25 (0.85) and 8.23 (0.92)%; fasting plasma glucose (FPG), 161.4 (46.3) and 156.1 (44.4) mg/dL. Overall, 69% had T2D for >5 years. Those on linagliptin had significantly greater reductions from baseline at wk 24 in HbA1c (placebo-adjusted mean change [95% CI]: 0.58% [−0.74, −0.42]; P<0.0001) and FPG (placebo-adjusted mean change [95% CI]: −14.1 mg/dL [−22.0, −6.3]; P=0.0004). Linagliptin had an overall favorable safety profile with adverse events (AEs) in 66.5% on linagliptin, and 68.9% on placebo. Fewer patients on linagliptin had drug-related AEs (14.6% vs. 18.4% with placebo). Investigator-defined hypoglycemia incidence was slightly lower in those on linagliptin (17.4%) vs. placebo (21.0%). Both linagliptin and placebo were weight neutral.

Discussion: In this analysis of Hispanic/Latino patients with T2D, linagliptin significantly improved glycemic control and was well-tolerated with a low hypoglycemia risk and no weight gain. As many Hispanic/Latino patients resist starting insulin, the availability of effective oral antidiabetes therapies is therefore of particular value for this group.

Conclusion: This analysis supports linagliptin as a useful oral T2D therapy option in Hispanic/Latino patients.

Abstract # 1119

EFFECTIVE AND SAFETY OF LINAGLIPTIN IN INDIVIDUALS WITH LONG-STANDING TYPE 2 DIABETES (≥10 YEARS)

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Prediabetes/Diabetes Mellitus

Objective: A rising prevalence of type 2 diabetes (T2D), alongside increased life expectancy, has led to increased numbers with long-term T2D, which is associated with a raised risk of related complications and markedly reduced β-cell function. While less stringent glycemic goals may be appropriate, effective oral antidiabetes options remain limited for this group. Using pooled data, we assessed linagliptin, an oral, dipeptidyl peptidase (DPP)-4 inhibitor, in people with a reported T2D duration of ≥10 yrs.

Methods: Two 24-wk, randomized, placebo-controlled trials of linagliptin 5mg QD as monotherapy or add-on to T2D regimens (NCT01194830: black/African Americans; NCT01084005: age ≥70 yrs) captured data on T2D duration ≥10 yrs. Safety analyses included all those treated; full analysis set (FAS) included those with relevant measurements.

Results: Of 475 Hispanic/Latino patients identified: 478 received linagliptin 5 mg/day and 267 placebo. Mean (SD) baseline characteristics were similar in linagliptin and placebo groups: age, 57.4 (10.0) and 56.8 (9.7) years; BMI, 30.3 (5.0) and 31.4 (4.6) kg/m2; HbA1c, 8.25 (0.85) and 8.23 (0.92)%; fasting plasma glucose (FPG), 161.4 (46.3) and 156.1 (44.4) mg/dL. Overall, 69% had T2D for >5 years. Those on linagliptin had significantly greater reductions from baseline at wk 24 in HbA1c (placebo-adjusted mean change [95% CI]: 0.58% [−0.74, −0.42]; P<0.0001) and FPG (placebo-adjusted mean change [95% CI]: −14.1 mg/dL [−22.0, −6.3]; P=0.0004). Linagliptin had an overall favorable safety profile with adverse events (AEs) in 66.5% on linagliptin, and 68.9% on placebo. Fewer patients on linagliptin had drug-related AEs (14.6% vs. 18.4% with placebo). Investigator-defined hypoglycemia incidence was slightly lower in those on linagliptin (17.4%) vs. placebo (21.0%). Both linagliptin and placebo were weight neutral.

Discussion: In this analysis of Hispanic/Latino patients with T2D, linagliptin significantly improved glycemic control and was well-tolerated with a low hypoglycemia risk and no weight gain. As many Hispanic/Latino patients resist starting insulin, the availability of effective oral antidiabetes therapies is therefore of particular value for this group.

Conclusion: This analysis supports linagliptin as a useful oral T2D therapy option in Hispanic/Latino patients.
Late Breaking ABSTRACTS – Late Breaking ABSTRACTS

and placebo arms was 70.8 (9.6) and 66.6 (10.2) yrs; BMI was 29.2 (4.6) and 31.1 (5.2) kg/m². The most common background regimens in the FAS were metformin (32.3%) or metformin and sulfonylurea (30.7%); 20.8% were on insulin. Baseline mean (SE) HbA1c was 8.07 (0.08)% for linagliptin (n=116) and 8.33 (0.14)% for placebo (n=72). By wk 24, those on linagliptin had significantly greater HbA1c reductions (placebo-adjusted mean change [95% CI]: −0.66% [−0.95, −0.38]; P<0.0001). Mean (SE) baseline fasting plasma glucose was 157.3 (3.7) mg/dL for linagliptin (n=115) and 168.8 (7.1) mg/dL for placebo (n=74); the placebo-adjusted mean change [95% CI] at wk 24 was −15.5 mg/dL [−29.6, −1.3]; P=0.0323. Linagliptin was well tolerated, with drug-related adverse events in 21.3% of linagliptin, and 16.3% of placebo safety sets. Investigator-defined hypoglycemia incidence was higher for linagliptin (25.4%) vs. placebo (12.5%). However, no severe hypoglycemia occurred with linagliptin. Moreover, in those with no background sulfonylurea, the difference in hypoglycemia incidence between linagliptin and placebo was <1%

Discussion: The extent of glucose lowering was similar to that in linagliptin trials that largely included patients in earlier disease stages, suggesting β-cell independent effects of linagliptin significantly impacted glucose control. Thus, we propose that regulation of glucagon release from pancreatic α-cells may be relevant for hyperglycemia control in patients with long-term T2D.

Conclusion: To our knowledge, this is the only available data set of a DPP-4 inhibitor in this challenging group and we show that linagliptin significantly improved hyperglycemia with good overall tolerability.

Abstract # 1120

COEXISTENCE OF TOXIC MULTINODULAR GOITER AND STRUMA OVARI IN A HYPERTHYROID PATIENT

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Thyroid Disease

Objective: To report the rare case of a woman with hyperthyroidism due to toxic multinodular goiter and concomitant struma ovarii.

Case Presentation: 29 y/o woman, diagnosed with hyperthyroidism on 2009. She presented with weight loss, tachycardia, dysphagia, hoarseness, sweating, tremors and anxiety. Physical exam showed an anxious woman; heart rate 99bpm, blood pressure 103/57, diffuse non-tender goiter, no exophthalmos, fine tremors and hyperreflexia. Thyroid function tests were: TSH 0.002 mIU/L and total T4 23.4 µg/dL. She was started on methimazole 30mg daily and propranolol 10mg twice daily, which was increased to methimazole 50mg daily and propranolol 80mg daily by her primary care physician. Thyroid scan was compatible with a diffuse toxic goiter. Referral for radioiodine ablation therapy was given but patient was lost to follow up for several years. She returned to clinics using the same medical therapy, still clinically hyperthyroid with TSH < 0.001 mIU/L, Free T4 3.43 ng/dL and Free T3 11.00 pg/ml despite high dose methimazole and propranolol. Patient had visited the emergency room due to left lower quadrant pain. Workup showed bilateral pelvic masses. She underwent surgical resection of a large (10cm x 7.5cm x 7cm) left adnexal mass and a wedge resection of right ovary. Pathology report revealed a left mature cystic teratoma, and a right monodermal cyst with colloid and mature follicles, suggestive of normal thyroid tissue and consistent with struma ovarii. Whole body radioiodine uptake study was ordered to assess functionality of thyroid and pelvic tissue. Thyrotropin receptor antibodies were ordered to rule out Grave’s disease.

Discussion: Struma ovarii is a rare ovarian teratoma in which thyroid tissue constitutes more than 50% of the tumor. Hyperthyroidism is present in less than 5-8% of patients. The concomitant presentation of goiter in a hyperthyroid woman with struma ovarii is extremely rare. Coexistence of Graves’ disease and struma ovarii has rarely been reported. However toxic nodular goiter with parallel formation of thyroid autonomy in an ovarian teratoma has few or none cases reported in the literature. This woman had a thyroid scan with increased tracer trapping and heterogeneous distribution, suggestive of toxic multinodular goiter. Thyroid antibodies and radioiodine uptake study will help to identify etiology of thyroid disease and assess functionality of struma ovarii.

Conclusion: All though very rare, hyperthyroidism difficult to control with high dose antithyroid medications, may have coexisting etiologies of hormone overproduction. We report the unusual case of uncontrolled hyperthyroidism due to toxic multinodular goiter and concomitant struma ovarii.
Abstract # 1121

RESOLVING PCOS WITH GLP1 ANALOGS

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Reproductive Endocrinology

Objective: PCOS is an insulin resistant syndrome. Early intervention treatment of NON-DIABETIC woman with PCOS, using a GLP1 analog, to resolve amenorrhea, infertility, insulin resistance and restore normal pituitary/ovarian axis.

Methods: Methods: 5 drug naive F patients with either: infertility, amenorrhea, oligomenorrhea, hirsutism with PCOS referred by OB/GYN. Patients consented for off label use GLP1 therapy. All patients were ruled out for thyroid disease, GH or cortisol excess, had lab and US findings consistent with PCOS. Patient 1 : 18 yo F, BMI 34, oligomenorrhea, acanthosis nigracans, FBS 93, HgA1C 5.7%, fasting insulin level 191. Pt was started metformin 500mg titration and GLP1 therapy. Pt 2: 16 yo F, BMI 21, hirsutism, oligomenorrhea, mild elevation testosterone, FBS 92, HgA1C 5.7%, fasting insulin 22. Placed on GLP1 therapy. Pt 3: 33 yo woman seeking fertility, BMI 32, FBS 97, HgA1C 5.4%, Fasting Insulin 37. Placed on GLP1 therapy. Pt 4: 40 yo F seeking fertility, BMI 32, FBS 98, HgA1C 5.8%, insulin level 3. Was placed on metformin, and GLP1 analog therapy. Pt 5 44 yo F with premature ovarian failure, BMI 35, c/o hot flashes and dizzy spells. FBS 88, HgA1C 5.6%, Fasting insulin 29. Placed on metformin titration and GLP1 agonist therapy.

Case Presentation: Pt 1: at 6 weeks experienced 31 pound weight loss, FBS 82, HgA1C 5.2% and fasting insulin of 7. Menses resumed after 5 weeks and at 3 months had 2 menses with correction of LH and FSH. Pt 2: In 2 months resumed regular menses, FBS 78, HgA1C 5.4%, insulin level 3. Not on metformin. Pt 3: in 2 months had 12 pound weight loss, return of menses, fasting glucose 81, HgA1C 4.8% and fasting insulin 5 (at 3 months was pregnant). Changed to metformin, GLP1 eliminated Pt 4 in 2 months, lost 18 pounds, FBS 81, HgA1C 4.7% and insulin level <2. Had one period. Has not conceived. Pt 5 seen at 6 weeks, lost 27 pounds, FBS 76, HgA1C 5.2% and fasting insulin <2, resumed menses week 5 of therapy with resolution of hot flushes and dizzy spells.

Discussion: The pituitary/ovarian axis was restored in these 5 patients with different causes of ovarian dysfunction. Patients reported significant improvements in weight, activity, sense of well-being.

Conclusion: Current ADA guidelines call for life style changes and consideration for metformin therapy once diagnosed with “pre-diabetes.” Insulin resistance occurs well before the diagnosis of pre-diabetes and can manifest in other conditions, namely PCOS. Treating individuals with PCOS with GLP1 analogs may restore normal pituitary/ovarian axis by decreasing insulin levels, and restoring euglycemia.

Abstract # 1122

IDENTIFYING RISK FACTORS FOR SEVERE HYPOGLYCEMIA IN HOSPITALIZED PATIENTS

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Hypoglycemia

Objective: Few of the deleterious effects of hypoglycemia in hospitalized patients include increased rates of mortality, longer length of stay, and increased need for mechanical ventilation. Our primary objective was to identify the risk factors associated with severe hypoglycemia in hospitalized patients.

Methods: A total of 5026 diabetic hospitalized patients’ 2010 electronic medical records were reviewed to identify those patients that developed severe hypoglycemia (BG <40 mg/dL). Additional information obtained included age, sex, A1C, diagnoses of chronic kidney disease (CKD), cirrhosis, sepsis, CHF and previous hypoglycemia while in the hospital, defined as a blood glucose <70 mg/dL. Chi-square tests were performed to assess for statistical significance. Adjusted logistical regression was used to determine the risk factors for hypoglycemia in the hospital.

Results: Out of 5026 diabetic patients included in our review, 81 experienced severe hypoglycemia (1.6%). Statistically higher proportions of CKD (69.1% vs. 46.9%, p<0.001), CHF (48% vs. 28.5%, p<0.001), sepsis (49.3% vs. 12.4%, p<0.001), insulin use (45.7% vs 26.04%, p =0.000), type 1 diabetes (21% vs 5.1%, p=0.009) and cirrhosis (14.8% vs. 7.1%, p=0.009) were seen in the hypoglycemic group vs. the non-hypoglycemic group respectively. In addition, 84% of patients who experienced an episode of severe hypoglycemia in the hospital (BG<40 mg/dL), had a previous episode of hypoglycemia (BG <70 mg/dL). Among patients who experienced severe hypoglycemia, 2.2% were 65 years
old or younger, whereas 1.2 % where older than 65 (p < 0.01). In multivariate analysis, all variables that were significant in the bivariate analyses were included and the ones that were still significant in the multivariate analyses were retained in the model. The odds ratio for type 1 DM, sepsis, previous hypoglycemia, insulin use was 3.43 (95% CI 1.81, 6.49), 2.64 (95% CI 1.6, 4.35), 46.08 (95% CI 24.76, 85.74), 1.65 (95% CI 1.02, 2.69) respectively.

Discussion: We identified type 1 DM, insulin use, sepsis and previous episode of hypoglycemia as risk factors for severe hypoglycemia in hospitalized patients. Identifying these risk factors at the time of admission and appropriately adjusting the dose of insulin and blood glucose target will help reduce the frequency of severe hypoglycemia in hospitalized patients.

Conclusion: Iatrogenic hypoglycemia is a major barrier to achieving optimal glycemic control in hospitalized patients. Identification of risk factors, appropriate monitoring and early treatment will reduce morbidity and mortality associated with hypoglycemia.

Abstract # 1123

PARATHYROID CYSTS(PC) FOUR UNUSUAL CASE PRESENTATIONS AND PEI THERAPY

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Thyroid Disease

Objective: To make physicians aware of the possible PC bleed that can be serious and even descend into the upper chest. PC can be mistaken for a thyroid cyst. Patient had 10 years of draining the large PC before having PEI therapy.

Methods: Ultrasound for location of the PC. Clear fluid and Parathyroid hormone PTH needle washout for definitive diagnosis N= PTH < 10.0. USC Thyroid Lab. Ultrasound guided PEI for therapy. 200 proof ethanol for injection.

Case Presentation: Case #1 36 Y/O F with tender left neck in the thyroid area. US: 0.6 ml oval mass in inferior left parathyroid area. bloody fluid removed. PTH needle washout positive 120,300. The bleed resolved without therapy. The PC decreased to 0.3 ml and the fluid became clear. 6 year observation no change or new bleed. Definitive therapy surgery or PEI with any new bleed. Case # 2 60 Y/O F with 5 year history large visible ‘thyroid cyst’. The fluid was discarded. The cyst recurred and caused local symptoms. US: Large cyst in the thyroid with clear fluid and PTH positive at 68.5. Intrathyroidal PC was treated with ethanol on two occasions with complete resolution. Case# 3 36 Y/O F ten years of drainage therapy for the large PC. Refused surgery and PEI until the 10 th recurrence. PTH washout was 68.1 and 13 ml clear fluid removed. 6 cc of ethanol injected. 3 month resolved. Case #4 32 Y/O F with a thyroid nodule. US revealed a small inferior PC confirmed by clear fluid and elevated PTH. Observation only for 6 years.

Discussion: 1. Bleeding in a rare complication of soft pliable PC and if they are large have been described to bleed into the chest. Large PC are more likely to have significant bleeds and should have definitive therapy. Delayed treatment after 10 years of drainage only could have ended badly if a large bleed happened during the 10 years before the PEI. 2. Ectopic PC located in the thyroid and called a thyroid cyst needs a diagnosis made by clear fluid and PTH needle washout. 3. Recurrence of a large PC needs definitive therapy by surgery of PEI and should not be treated by many years of just draining the cyst. 4. Incidentally found small PC that are stable over many years can be followed without therapy unless there are symptoms or a bleed occurs.

Conclusion: Teaching points Bleeding from a PC can cause symptoms and even severe problems from hemorrhage into the chest. Ectopic PC can be hiding in the thyroid as a ‘thyroid cyst’. 3. Small PC found during thyroid nodule evaluation can be followed and only treated if a hemorrhage occurs. 4.Multiple simple drainage for recurrent large PC is to be condemned as a therapy method. The risk of a bleed of a large PC make PEI or surgery a definitive answer.

Abstract # 1124

CONCOMITANT DIABETES HAS A NEGATIVE IMPACT ON AVERAGE AST AND ALT LEVELS AND ON AST TRENDS IN HCV+ PATIENTS OVER 12 MONTHS: RESULTS FROM A NATIONAL DATABASE

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Prediabetes/Diabetes Mellitus

Objective: Both diabetes and the hepatitis C virus (HCV) are independently associated with raised liver function tests (LFTs), however, the impact of concomitant diabetes and HCV infection on LFTs is not known. We compared aspartate aminotransferase (AST) and alanine transaminase (ALT) levels in patients with HCV infection and diabetes mellitus.
aminotransferase (ALT) levels in HCV+ patients with diabetes (PWD) versus nondiabetic HCV+ patients (NDPs) to assess the correlation of diabetes status with AST and ALT levels in HCV+ patients, including overall values and changes over a 1-year period.

**Methods:** Over 120,000 patients in a national laboratory database (Medivo Inc., NY) were tested for AST or ALT between January 1 and December 31, 2012. We used ICD-9 diagnostic codes to identify a subset of >3,740 HCV+ patients, and to divide this group into PWD vs. NDP cohorts. >485 PWD and >3,255 NDP were tested for AST and ALT at least once. 215 PWD and 868 NDP were tested for AST and ALT exactly twice. We assumed that both PWD and NDP were similar in other relevant variables, e.g. HCV treatment status and disease duration. ANOVA was performed to test for a difference in average AST and ALT levels in these populations. Multiple regression analysis was performed to determine how the 2 AST and ALT results changed in these populations over 1 year.

**Results:** The average AST and ALT levels in HCV+ patients were significantly higher in PWD than in NDP (mean AST values 61.9 IU/L vs. 56.2 IU/L, p=0.018, and mean ALT values 67.79 IU/L vs. 60.66 IU/L, p=0.024). Among HCV+ patients tested twice over 1 year, NDP saw a significant improvement in AST levels (59.21 to 56.19 IU/L, P<0.001) but no significant change in ALT levels (60.92 to 55.60 IU/L, p=0.22). In contrast, PWD had no significant changes in either AST (60.05 to 61.9 IU/L, p=0.22) nor in ALT (64.92 to 62.26 IU/L, p=0.17).

**Discussion:** Our analysis shows that HCV+ PWD have significantly higher levels of average AST and ALT than HCV+ NDP. Also, while HCV+ NDP showed improvement in AST, HCV+ PWD did not show improvement in either AST or ALT results over a 1-year period.

**Conclusion:** From this analysis, concomitant diabetes appears to have a negative correlation with LFTs in HCV+ patients. Additional vigilance in monitoring LFTs may be warranted in patients with both HCV and diabetes. Further studies to assess causes for differences in behavior of LFTs for these populations are recommended.

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**Abstract # 1125**

**DIGITAL CAMERAS VERSUS PAPER DIARIES FOR FOOD LOGGING IN OBESE TYPE 2 DIABETIC PATIENTS: A RANDOMIZED, CROSSOVER FEASIBILITY STUDY**

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**Prediabetes/Diabetes Mellitus**

**Objective:** Technology-based food logging may confer better adherence and outcomes than paper diaries (PD) in obese patients with type 2 diabetes (T2DM). Digital cameras (DC) for food logging have not been thoroughly examined in this population. Primary objectives of this study were to compare DC versus PD on a) patient adherence and b) short-term glycemic control. The secondary objective was to assess perceived clinical utility of these methods among physicians caring for diabetic patients.

**Methods:** This randomized, crossover study at UMHS ran from January thru March 2013. Inclusion criteria were T2DM, age 18-70, BMI>30, and hemoglobin A1c (HbA1c) 7.5-9. Pregnancy was excluded. Patients were randomized to a DC or PD week first, crossing over for the second week. Strict adherence (SA) was defined as 21 entries, with at least 2 entries per day for 7 days. Mild adherence (MA) was 21 entries, with at least 2 entries per day for at least 5 days. Minimum participation (MP) was at least one week of mild adherence. The internet-based physician survey was administered in January thru February, 2013. Adherence was analyzed by McNemar’s exact or paired t-testing. Change in glucose/checks from baseline between methods was compared using generalized estimating equations to fit a multivariable linear regression model controlling for treatment sequence effect.

**Results:** 17 patients were randomized to DC (with 1 loss) and 16 to PD first (with 2 losses). There were no differences in age, HbA1c, BMI, sex, or insulin (not shown). Overall adherence (SA +MA, 61% for each method) and SA (42.4% DC versus 57.6% PD, p=0.45) did not differ. There was no mean difference in number of weekly entries (DC-PD) (2.5, 95%CI -1.4-6.4, p=0.20). There were borderline significant differences when only
Abstract # 1126

EFFECT OF THE MEDITERRANEAN AND STANDARD HYPOLIPEMIC DIET ON PARAMETERS OF METABOLIC SYNDROME

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Prediabetes/Diabetes Mellitus

Objective: The aim of this study was to explore the effect of Mediterranean diet (MD) and Standard hypolipemic diet (SHD) on parameters of metabolic syndrome in obese patients in a randomized controlled study.

Methods: 124 subjects with a body mass index (BMI) above 30 kg/m2 were recruited from the outpatient Clinic of Department of endocrinology, diabetes and metabolism disorders at Dubrava University Hospital in the period from November 2008 to February 2013, and were randomly assigned to either MD or SHD. All subjects received education on their diet during one-week stay in the Daily hospital. Parameters of metabolic syndrome (waist circumference, blood pressure, glucose level, triglycerides and HDL) were obtained at the baseline (day 1) and at each subsequent visit (after 7 days, 1, 3, 6 and 12 months). Data were entered into SPSS version 20.0 (SPSS Inc, Chicago, III) for analysis.

Results: During 12 months period, significant decrease was observed for both diets, for waist circumference (mean decrease was 7.00 cm in MD group (P<0.05) and 5.65 cm in SHD group (P<0.05)), and for glucose (mean decrease was 0.52 mmol/L for both groups (P<0.05)). Significant increase in the HDL cholesterol value of 7.12% (P<0.05) was induced by the MD group, whereas slight (3.06%), though insignificant increase was observed by the SHD group.

Discussion: However, when comparing the two diets, significant difference was not found for any of the explored parameters.

Conclusion: During 12 months period, both diets showed beneficial effects on waist circumference and glucose level. MD showed higher beneficial influence on HDL cholesterol than SHD what supported previous study results.

Abstract # 1127

A COMPARISON OF MEDITERRANEAN AND HYPOLIPEMIC DIETS IN WEIGHT REDUCTION MANAGEMENT

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Prediabetes/Diabetes Mellitus

Objective: The aim of the study was to explore the effect of Mediterranean diet (MD) and Standard hypolipemic diet (SHD) on weight reduction in obese patients.

Methods: Patients at the outpatient Clinic of Department of endocrinology, diabetes and metabolism disorders at the Dubrava University Hospital were randomly assigned to either MD or SHD. Both groups received counseling and education from two dietitians, two clinical pharmacists and two endocrinologists during the initial week at the Daily hospital. Weight, height and waist circumference were obtained at the baseline (day 1), after 7 days, 1, 3, 6 and 12 months of the dietary program. Data were entered into SPSS version 20.0 (SPSS Inc, Chicago, III) and analyzed.

Results: Eighty-four (67.7%) out of 124 randomized patients completed the 12-month program. After 12 months of diet intervention, both groups had a significant decrease in body weight, body mass index (BMI) and waist circumference. Mean decrease in body weight, BMI and waist circumference for the MD group was:

- 7.35 kg (p<0.001),
- 2.55 kg/m2 (p<0.001)
- 7.00 cm
(p<0.001), respectively, while for SHD group these values were: 5.98 kg (p<0.001), 2.18 kg/m³ (p<0.001) and 5.65 cm (p<0.001), respectively. There was no significant difference in weight reduction between the two diets. Number of patients who accomplished a target decrease of more than 7.5% of the initial body weight, was similar for MD and SHD groups, 18.2% and 18.9%, respectively.

**Discussion:** There were more successful patients during the first 6-months of the program with 33.3% participants in MD group and 39.6% in SHD group accomplishing the same target decrease of more than 7.5% of the initial body weight.

**Conclusion:** Both diets showed beneficial effect on weight reduction with no significant difference between them. The comparison between 6- and 12-month results implies the need for better management of a long term weight reduction.

Abstract # 1128

**EFFECT OF AMERICAN GINSENG ON ARTERIAL STIFFNESS IN SUBJECTS WITH WELL-CONTROLLED TYPE-2 DIABETES AND HYPERTENSION**

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**Lipid/Cardiovascular Disorders/Hypertension**

**Objective:** The aim of this study was to explore the effect of American ginseng (AG) treatment on peripheral blood pressure (BP) and arterial stiffness, measured by augmentation index (AI), in subjects with well-controlled type 2 diabetes and concomitant hypertension.

**Methods:** Using a double-blind, randomized, placebo-controlled, parallel design, each participant received either the selected AG root preparation (10% extract) or placebo at the dose of 500 mg/meal = 3 g/day for 12 weeks as an adjunct to their usual anti-diabetic therapy (diet and/or medications). BP and AI were measured by applanation tonometry at baseline and after 12 weeks of treatment. A total of 64 individuals with well-controlled essential hypertension and type 2 diabetes (gender: 22 M: 42 F, age: 63.1 ± 9.27 years, systolic/diastolic BP: 145.4 ± 10.81/ 84.8 ± 8.03 mmHg, HbA1c: 7.0 ± 1.31%, FPG: 8.1 ± 2.31 mmol/L) completed the study.

**Results:** Compared to placebo, 3 g of AG significantly lowered radial AI by 5.25% (P=0.041) and systolic BP by 11.72% (P<0.001), and no significant effect was observed with diastolic BP.

**Discussion:** The present study was the first to demonstrate that AG can generate favourable effects on pulse wave reflection and systolic BP.

**Conclusion:** The selected AG treatment showed convincing preliminary long-term clinical efficacy when administered as an adjunct to usual antihypertensive and antidiabetic therapy.

Abstract # 1129

**LONGTERM EFFECT OF AMERICAN GINSENG EXTRACT (PANAX QUINQUEFOLIUS L.) ON GLYCEMIC CONTROL IN PATIENTS WITH TYPE 2 DIABETES**

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**Prediabetes/Diabetes Mellitus**

**Objective:** The objective of the present study was to test the efficacy and safety of supplementation with the selected American ginseng extract (AG) as an adjunct to their usual anti-diabetic therapy (diet and/or medications).

**Methods:** Study was double-blind, randomized and placebo-controlled. Each participant received either the selected AG preparation (ethanol extract) or placebo (500 mg/meal = 3 g/day) for a period of 12 weeks. Outcomes included measures of efficacy (glycated hemoglobin (HbA1c)-primary, fasting plasma glucose (FPG), fasting plasma insulin (FPI), and HOMA); safety (liver and kidney function); and compliance (returned capsules and body-weight). Seventy-four participants with well-controlled type 2 diabetes (sex: 28 M: 46 F, age: 62.9±9.49, BMI: 32±5.3, HbA1c: 7±1.3), randomized to either intervention (n= 35) or control (n=39) group, completed the study.

**Results:** There was no change in the primary endpoint, HbA1c. Nevertheless, there was a trend toward lower HbA1c by 0.84% (P=0.836) compared to placebo. Furthermore, the participants remained well-controlled (HbA1c = 7.12%) throughout. The selected AG treatment
also decreased FPG, FPI and HOMA by 4.42, 11.54 and 18.84%, respectively, with no significant between-treatment difference (P=0.947, P=0.373, P=0.489, respectively).

Discussion: Safety and compliance outcomes remained unchanged.

Conclusion: Although clinical efficacy, as assessed by HbA1c, was not demonstrated, 12 weeks of supplementation with the selected AG treatment maintained good glycemic control in people with well-controlled type 2 diabetes without adverse effects.

Abstract # 1130

ENDOCRINOLOGISTS ORDER SIGNIFICANTLY MORE HBA1C TESTS PER PATIENT WITH DIABETES PER YEAR THAN PRIMARY CARE PHYSICIANS, REGARDLESS OF PATIENT AGE; PCPS IN THE STROKE BELT ORDER SIGNIFICANTLY FEWER TESTS THAN PCPS IN OTHER STATES: RESULTS FROM A NATIONWIDE

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Prediabetes/Diabetes Mellitus

Objective: To assess the use of a lab results database (Medivo Inc., New York, NY) to review population-level datasets, we reviewed HbA1c testing patterns for endocrinologists vs. primary care physicians (PCPs), using different demographic and geographic criteria. We analyzed testing frequency, patient age and practice zip codes.

Methods: We analyzed endocrinologists’ and PCPs’ HbA1c order rates for patients with diabetes (PWD) in the nationwide Medivo Database Repository between Jan 1 - Dec 31, 2012. During this year, 2,562 physicians (180 endocrinologists and 2,382 PCPs) ordered a total of 171,697 HbA1c tests for 39,556 PWD. ANOVA was performed to compare HbA1c order rates between the two physician groups and across age groups. For the regional analysis, we created a second dataset by identifying zip codes for endocrinology vs. PCP practices where tests had been ordered. ANOVA was performed to compare HbA1c test rates/patient/yr in the CDC-defined Stroke Belt zip codes to all other zip codes.

Results: The physician-level dataset shows that endocrinologists order significantly more HbA1c tests per patient per year than PCPs (3.24 tests/pt/yr vs. 2.61 tests/pt/yr, p<0.001). Age does not impact this difference. Endocrinologists order significantly more tests than PCPs for patients both <65 years (p<0.001) and ≥65 years (p=0.03). The zip code-level dataset shows regional differences were small, about 0.1 tests/pt/yr fewer in the Stroke Belt for both physician groups. Endocrinologists’ trend toward a lower testing rate but not at a significant level (p=0.06), while PCPs’ lower testing rate achieves significance (p=0.004).

Discussion: Per PWD, endocrinologists order significantly more HbA1c tests than PCPs across all ages. Region did not impact endocrinologists’ ordering rates, but PCPs in the Stroke Belt order significantly fewer tests than those elsewhere.

Conclusion: Research based on a large, nationwide laboratory results database can provide valuable insights on differences in clinical indicators between specialties and between regions. Further studies to track adherence to guideline recommendations on testing across specialties, regions and patient populations are recommended.

Abstract # 1131

ENDOCRINOLOGISTS AND PRIMARY CARE PHYSICIANS TEST CREATININE, AST AND ALT AT SIMILAR RATES IN PATIENTS WITH DIABETES; HOWEVER, THE RATE OF ABNORMAL CREATININE AND ALT TEST RESULTS VARIES BETWEEN SPECIALTIES. PATIENTS WITH DIABETES HAVE A SIGNIFICANTLY HIGHER CREATININE LEVEL:

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Prediabetes/Diabetes Mellitus

Objective: Renal and liver disorders are common in diabetes. We analyzed data in a national laboratory database (Medivo Inc., NY) to compare the frequency of serum creatinine, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) tests by endocrinologists vs. primary care physicians (PCPs). We analyzed the rates of abnormal test results in patients with diabetes (PWD) vs. nondiabetic patients (NDP), and compared the rate of abnormal results in PWD between the 2 physician groups.

Methods: The database includes 218 endocrinologists and 3,420 PCPs who ordered these tests at least once in 2012. >612,261 patients were tested for serum creatinine, AST, ALT, and creatinine and ALT in PWD and or nondiabetic patients (NDP), and compared the rate of abnormal results in PWD between the 2 physician groups.

Results: The physician-level dataset shows that endocrinologists order significantly more HbA1c tests per patient per year than PCPs (3.24 tests/pt/yr vs. 2.61 tests/pt/yr, p<0.001). Age does not impact this difference. Endocrinologists order significantly more tests than PCPs for patients both <65 years (p<0.001) and ≥65 years (p=0.03). The zip code-level dataset shows regional differences were small, about 0.1 tests/pt/yr fewer in the Stroke Belt for both physician groups. Endocrinologists’ trend toward a lower testing rate but not at a significant level (p=0.06), while PCPs’ lower testing rate achieves significance (p=0.004).

Discussion: Per PWD, endocrinologists order significantly more HbA1c tests than PCPs across all ages. Region did not impact endocrinologists’ ordering rates, but PCPs in the Stroke Belt order significantly fewer tests than those elsewhere.

Conclusion: Research based on a large, nationwide laboratory results database can provide valuable insights on differences in clinical indicators between specialties and between regions. Further studies to track adherence to guideline recommendations on testing across specialties, regions and patient populations are recommended.
Abstract 

ABNORMAL ISLET CELL COMPOSITION IN LIRAGLUTIDE-TREATED ZDF RATS

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Prediabetes/Diabetes Mellitus

Objective: The ultimate treatment goal of diabetes is to preserve and restore islet cell function. Treatment of certain diabetic animal models with incretins has been reported to preserve and possibly enhance islet function and promote islet cell growth. The studies reported here detail islet cell anatomy in animals chronically treated with the incretin, liraglutide. Our aim was to analyze quantitatively and qualitatively islet cells from diabetic animals treated with vehicle (control) or liraglutide to determine whether normal islet cell anatomy is maintained with pharmaceutical treatment.

Methods: We harvested islets from liraglutide-treated ZDF rats to examine their structure and function. Twelve-week old Zucker Diabetic Fatty (ZDF) rats were assigned to 3 groups: 1) liraglutide-treated diabetic, 2) vehicle-treated diabetic, 3) lean non-diabetic. Liraglutide was given SC twice daily for 9 weeks.

Results: As expected, liraglutide treatment reduced body weight by 15% compared to the vehicle-treated animals, eventually to levels that were not different from lean controls. At the termination of the study, blood glucose was significantly less in the liraglutide-treated rats compared to vehicle treated controls (485.8 ± 22.5 and 547.2 ± 33.1 mg/dl, respectively). Insulin content/islet (measured by immunohistochemistry) was 34.2 ±0.7 pixel units in vehicle-treated rats, and 54.9 ± 0.6 in the liraglutide-treated animals. Liraglutide did not preserve normal islet architectural. There was a decrease in the glucagon-positive area/islet and in the α-cell numbers/area with liraglutide treatment (6.5 cells/field), compared to vehicle (17.9 cells/field). With an increase in β-cell numbers, the β- to α-cell ratio was statistically higher in the liraglutide-treated rats (24.3 ± 4.4) compared to vehicle (9.1 ± 2.8). Disrupted mitochondria were more commonly observed in the α-cells (51.9 ± 10.3 % of cells) than in the β-cells (27.2 ± 4.4%) in the liraglutide-treated group.

Discussion: While liraglutide enhanced or maintained growth and function of certain islet cells, the overall ratio of α- to β-cells was increased and there was an absolute reduction in islet α-cell content. There was selective disruption of intracellular α-cell organelles, representing an uncoupling of the bihormonal islet signaling that is required for normal metabolic regulation.

Conclusion: Confirmation of such anatomic changes in humans may suggest abnormal islet cell function and could offer insight into the development of nesidioblastosis in patients after roux-en-y surgery.
Abstract # 1133

RACIAL-ETHNIC DISPARITIES IN THE PREVALENCE OF OBESITY AND REPRODUCTIVE DYSFUNCTION IN WOMEN WITH PCOS FROM A DIVERSE HIGH RISK URBAN POPULATION

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Reproductive Endocrinology

Objective: Our objectives were: 1) To determine the prevalence of reproductive (irregular menses, oligomenorrhea, amenorrhea, infertility) and hyperandrogenic (acne, hirsutism) disorders in women with polycystic ovary syndrome (PCOS) in an urban clinic population of diverse race-ethnicity; 2) To determine if the prevalence of these disorders varies by race-ethnicity, and 3) To determine if obesity is associated with the prevalence of these disorders.

Methods: PCOS cases (n=1159) and the presence of reproductive and hyperandrogenic (HA) disorders were identified through Boston University Medical Center’s (BUMC) clinical research database by ICD9 code. Race-ethnicity was determined by self-report: Black (B: n=393, 34%), Hispanic (H: n=184, 16%), White (W: n=325, 28%), or Other (O: Asian/Pacific Islander/Native American/Middle Eastern; n=257, 22%). Comparisons across groups were done with Chi2/Fischer Exact tests, alpha<0.05.

Results: Mean (±SD) age was 33±8 years with BMI 35±9 kg/m2. 40% were obese (n=458). Prevalence of reproductive disorders was: Irregular menses 20%, Oligomenorrhea 9%, Amenorrhea 18%, Infertility 14%. Prevalence of HA disorders was: acne 11%, hirsutism 12%. Black women had the highest prevalence of reproductive and HA disorders: Irregular menses: B 31%, H 18%, W 13%, O 14% (p<0.0001); Oligomenorrhea: B 12%, H 8%, W 6%, O 9% (p=0.05); Amenorrhea: B 26%, H 20%, W 15%, O 10% (p<0.0001); Infertility: B 19%, H 16%, W 7%, O 12% (p<0.0001); Hirsutism: B 17%, H 10%, W 11%, O 8% (p=0.003); Acne: B 14%, H 7%, W 11%, O 9% (p=0.04). Black women had the highest rates of obesity: B 48%, H 44%, W 33%, O 31% (p<0.0001) but the prevalence of reproductive and HA disorders did not vary with obesity in any group.

Discussion: PCOS, the most common endocrine disorder in reproductive age women, presents with a variety of phenotypes due to complex interactions between environmental and genetic influences. Black and Hispanic women are at a disproportionately high risk of obesity and PCOS. There is little data on differences in the reproductive dysfunction characteristic of PCOS in different race-ethnicities. The prevalence of reproductive and HA disorders varied by race-ethnicity in women with PCOS at BUMC. Black women had the highest rates of reproductive and HA disorders as well as obesity. However, obesity was not associated with reproductive disease in any group.

Conclusion: Clinicians should be aware of racial-ethnic disparities in reproductive and HA disorders in women with PCOS. Black women may have a higher symptom burden than women in other groups. Furthermore, racial-ethnic differences in reproductive dysfunction may be indicative of similar disparities in metabolic disease in women with PCOS.

Abstract # 1134

PRIMARY HYPOTHYROIDISM PRESENTING AS RAISED INTRACRANIAL TENSION

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Thyroid Disease

Objective: Description of an Unusual Clinical Scenario

Case Presentation: KD, 35 year old Asian Indian Hindu female presented with headache, nausea and vomiting, behavioural changes, memory impairment, cognitive impairment. Routine neurological workup under category Dementia unknown origin by neurologist. MRI head ventricular dilatation changes observed interpreted as Normotensive Hydrocephalus. Routine referral to internist/endocrinologist for anaemia (Hb 8 gms/dl) and hypercholestrolaemia (Serum cholesterol 280 mg/ml) revealed significant hypothyroidism, TSH 120 mU/L, (ECLIA), FT3 1.30 pg/ml and FT4 0.50 ng/dl. AntiTPO antibodies 800 IU/L. No goitre. No Hyponatraemia. No papilloedema. Patient had no history of head injury/tuberculosis/unusual postpartum bleeding. Menstrual history unremarkable. 2 children aged 3 and 7 years. EKG showed low voltage complexes and bradycardia. On Thyroxine replacement therapy gradually escalated to 200 ug daily, she showed marked clinical improvement. TSH normalised to 3 mU/L. Headache, nausea, vomiting and behavioural/cognitive changes regressed. MRI continued to show dilated lateral ventricles.
Abstracts – Late Breaking

Late Breaking Abstracts – Late Breaking

2.1% vs. 12.1, 2.3%, p=0.6) or BMI (32.7, 6.1 vs. 32.8, 6.2, p=0.96). The A1c at 4 months was not significantly different in the oral agent and insulin treatment arms (6.5, 1.1% vs. 6.1, 0.6% respectively). At 4 months, the majority of patients from each treatment arm were no longer on pharmacologic agents.

Discussion: Rates of remission with intensive glycemic control were 45% in new onset African-Americans with type 2 diabetes. The rates were similar with either insulin or oral antidiabetic agents with short-term follow-up in contrast to Asians in whom insulin achieved higher rates of remission. These rates of remission are similar to previous data using insulin treatment alone in African-American patients. Our study is limited by a small number of patients and a higher dropout rate in insulin compared to the oral agent treatment arms. Nevertheless, the goal of remission is a viable treatment target in new onset patients presenting with severe hyperglycemia.

Conclusion: Remission is achievable in nearly half the patients regardless of the type of treatment and may be an important concept in reducing the high complication rates in African-Americans.

Abstract # 1136

THINK OUTSIDE THE BOX: PANHYPOPHYSITIS WITH MASKED DIABETES INSIPIDUS UNVEILED BY GLUCOCORTICOID REPLACEMENT

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Pituitary Disorders/Neuroendocrinology

Objective: We present a case where a patient presented with glucocorticoid deficiency-associated hyponatremia with unveiling of central Diabetes Insipidus (DI) after glucocorticoid replacement.

Case Presentation: A 59-y/o male presented with an 18 month h/o progressive bifrontal headaches and lethargy. MRI of the brain revealed stalk thickening, diffuse enlargement of the pituitary gland, and homogeneous enhancement of gadolinium contrast medium. Endocrine assessment revealed pan-hypopituitarism, with low serum cortisol, gonadotrophs, testosterone, thyroid hormone (T4), and thyroid-stimulating hormone. Other remarkable lab. abnormality was hyponatremia (Na of 121 at presentation). His symptoms improved after replacement with hydrocortisone while his serum Na levels went up to 148 (Normal 133-144) along with polyuria. Desmopressin suppression test was positive and he was diagnosed with...
DI. He was placed on desmopressin nasal spray along with thyroxine and testosterone. At 18 month F/U, the patient remained well with improved headaches and lethargy.

**Discussion:** Hypophysitis are a group of inflammatory lesions affecting the pituitary gland and pituitary stalk. Lymphocytic hypophysitis (LYH) is the most frequent form of chronic pituitary inflammation. LYH can manifest with compression symptoms, hypopituitarism, diabetes insipidus or hyperprolactinemia. The imaging study of choice is MRI. Treatment includes replacement of the functional pituitary deficiency and the use of corticosteroids at high doses. Surgical treatment is reserved for patients unresponsive to conservative therapy. Low serum ACTH and undetectable serum cortisol levels accounted for the initial presentation of hyponatremia that was caused by a lack of negative feedback from glucocorticoids on secretion of ADH and ACTH-RH from the spared paraventricular nucleus (PVN). Inhibition of glucocorticoid on ADH secretion from PVN was reestablished after steroid replacement unveiling central DI. In our patient water diuresis and hypernatremia after glucocorticoid therapy was well depicted. Hypothyroidism rarely causes marked hyponatremia. However, hypothyroidism in combination with secondary adrenal insufficiency could have contributed to our patient’s hyponatremia. But glucocorticoid replacement without thyroxine was able to increase the patient’s Na, indicating that hypothyroidism did not have an important role in the genesis of his hyponatremia.

**Conclusion:** This case highlights how panhypophysitis behaves in terms of water balance since ACTH and ADH impairment may have opposite influences on water balance. In conclusion, lymphocytic hypophysitis may feature a concealed central DI caused by glucocorticoid deficiency-associated hyponatremia.
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