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ADRENAL DISORDERS

Abstract #100

ACTH-SECRETING PHEOCHROMOCYTOMA

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Objective: We present a case of ACTH-producing pheochromocytoma, which is an extremely rare but important cause of ectopic Cushing's syndrome.

Case Presentation: A 56 year old female presented with 3 years of progressively worsening diabetes mellitus, hypertension, hypokalemia, facial swelling, insomnia, and irritability. Her blood pressure was 160/94, pulse was 98, and BMI was 36.5. She was noted to have typical Cushingoid features of moon facies, facial plethora, hirsutism, cervicodorsal and supraclavicular fat deposition, purple abdominal striae, and lower extremity edema. Serum sodium was 142 mEq/L and potassium was 2.7 mEq/L. Random serum cortisol was 101.9 ug/dL with ACTH of 299 pg/mL. Urinary free cortisol was 11,870 mcg/24 hrs.

She was hospitalized and received potassium repletion, spironolactone, and ketoconazole to treat her hypercortisolemia. Pituitary MRI revealed no abnormalities and other pituitary hormone levels were normal. CRH stimulation testing yielded a 10.4% rise in serum cortisol and 49.4% rise in ACTH. High-dose (8 mg) dexamethasone suppression testing resulted in a 2.7% decrease in serum cortisol. Together, these results were suggestive of ectopic ACTH secretion.

Abdominal CT revealed a 5.6 cm heterogeneous right adrenal mass with postcontrast enhancement of 4 Hounsfield units. Serum aldosterone, plasma renin activity, testosterone, and DHEAS were normal. Urine and plasma metanephrines were greater than 4 times the upper limit of normal. Right adrenalectomy was performed following the initiation of alpha and beta blockade. Pathology confirmed pheochromocytoma with positive ACTH staining.

The patient’s Cushingoid features rapidly improved; her diabetes mellitus, hypertension, and hypokalemia resolved; and her plasma metanephrines normalized. Glucocorticoid replacement was tapered over the ensuing 3 months with eventual recovery of her HPA axis and sustained normalization of her ACTH and cortisol.

Discussion: Pheochromocytoma is a rare source of ectopic ACTH production, with fewer than 30 cases described in the medical literature. This condition has protean manifestations and the clinical features of catecholamine excess may be obscured. Our patient had symptoms (hypertension, insomnia, irritability) that were initially attributed to hypercortisolemia, but may also have been due to her hyperadrenergic state. Recognition of her pheochromocytoma was critical to the implementation of preoperative measures to avert hypertensive crisis.

Conclusion: Our case adds to the small body of literature on this topic and underscores the need for clinicians to be alert to the possibility of pheochromocytoma in patients with Cushing’s syndrome.

Abstract #101

PREVALENCE OF INCIDENTAL ADRENAL ENLARGEMENT ON COMPUTED TOMOGRAPHY (CT) SCAN OF THE ABDOMEN AND SIZE OF ADRENALS IN RELATION TO THE SUBCUTANEOUS VERSUS VISCERAL FAT

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Objective: Adrenal enlargement can be an incidental finding and may be missed during routine reporting. Though its clinical significance is not known at this time, we aimed to evaluate the prevalence of adrenal enlargement on CT abdomen, preliminary to exploring the clinical significance.

Methods: After the approval of the Institutional Review Board, Using the VA computerized patient record system and with the help of the Data Support System, we retrieved the records of Veterans at Stratton VA Medical Center, who had a CT abdomen completed between January 2012 through December 2013. We reviewed all the images of the adrenals in the CT abdomen and measurements were carried out. The clinical information retrieved included age, sex, BMI, presence or absence of obstructive sleep apnea, depression, substance abuse, HTN, malignancy, and medications that alter electrolytes. Adrenal enlargement when present was classified as moderate or severe enlargement.

Results or Case Report: 338 CT scans of the abdomen where reviewed, and 158 records were excluded as they did not meet the criteria. Most of the subjects where men. Subjects with incidentalomas (N=30) reported were not included in the
statistical analysis. The mean age of the subjects was 66 ± 13 with mean BMI of 29.5 ± 7.0. Among 50 subjects with adrenal enlargement, 39 subjects had bilateral enlargement and 11 had unilateral enlargement. The prevalence of adrenal enlargement was 14.8%. Only 11 (22%) of the 50 adrenal enlargements were reported. Subjects with incidental adrenal enlargement had a higher prevalence of hypertension (p < 0.001) and electrolyte abnormalities (p < 0.001). Adrenal enlargement positively correlated with BMI (r = 0.17; p < 0.01), visceral fat (r = 0.15; p < 0.01), and subcutaneous fat (r = 0.19; p < 0.01).

Conclusion: Since adrenal enlargement is more common in those with higher BMI, hypertension and electrolyte abnormalities, and correlates with both visceral and subcutaneous fat, it may be worth studying the benefit of hormonal evaluation to explore clinical relevance.

Abstract #102

CRISES PREVENTION MEASURES IN PATIENTS WITH ADRENAL INSUFFICIENCY-ARE THEY BEING FOLLOWED?

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MSU

Objective: Subjects with adrenal insufficiency (AI) are at risk for developing adrenal crisis. It has been estimated that approximately 8% of patients with AI are hospitalized annually for adrenal crisis and only a few receive crises prevention education and have access to emergency glucocorticoid (GC) kits. Proper education prevents episodes of adrenal crisis. Aim of our study was to determine if education for prevention of adrenal crisis was being provided to patients with AI.

Methods: Data was collected from patients with AI from March 2009 through March 2014 by a retrospective chart review. Age, gender, causes of AI, GC dose, monitoring for hyponatremia and hyperkalemia, postural blood pressure, crises prevention education for GC dose adjustments during stress, MedicAlert ID and parenteral GC kit provision were recorded.

Results: There were 85 patients with AI, 33 (38.8%) with primary and 52 (61.2%) with secondary AI. Mean age was 55.8 years. There were 29 males and 56 females. 23 out of 85 patients (27%) had postural blood pressures checked of which 5 (21.7%) were positive. 77 out of 85 patients (90.6%) had monitoring done for electrolytes. The calculated replacement dose for steroids was 15-20 mg of hydrocortisone or its equivalent based on body surface area. Out of these 85 patients on steroids, there were 41 patients (48.2%) on doses above 20mg/day. Only 57 out of 85 patients (67.1%) had received steroid dose adjustment instructions and 29 out of 85 patients (34.1%) had Medic Alert ID. Only 17 out of 85 patients (20%) were given access to emergency parenteral GC kits.

Discussion: The preventive strategies for adrenal crisis in AI patients are not being consistently followed. Patient education is key for having a successful prevention strategy for adrenal crisis in patients with AI. We, as endocrinologists, have a responsibility to ensure that all patients with AI have Medic Alert ID and access to life saving emergency GC kits. Patients and families should receive adequate education about parenteral steroid administration and steroid dose adjustments in stressful situations.

Conclusion: Patients and their families are not being provided education related to prevention of adrenal crisis and osteoporosis. We are introducing an automated electronic alert in our electronic medical records to determine if this will improve adherence to these preventive measures.

Abstract #103

EVALUATION OF ADRENAL ADENOMAS & INCIDENTALOMAS IN A UNIVERSITY BASED ENDOCRINE PRACTICE: A RETROSPECTIVE REVIEW

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Objective: With increasing use of imaging modalities, more incidental adrenal masses are being discovered. Professional societies including AACE recommend that those adenomas deserve baseline biochemical work-up; and if found to be benign and nonfunctioning, will need follow-up imaging and laboratory testing. To our knowledge, it is not known what proportion of these adenomas are getting appropriate baseline and follow-up work-up.

Our study was designed to look at patients with adrenal adenomas, managed at a University based endocrine practice and study their characteristics and management strategies.

Methods: We retrospectively looked at the medical records of patients managed between 2009 and 2013. Using ICD 9 diagnostic codes of 227.0, 255.8 and 239.7, we identified 101 patients. On careful review, 80 patients were found to have adrenal adenomas and included in the study. Data was collected including demographic information, imaging, laboratory testing, management and follow-up.
Results: Of the 80 patients studied, 60 (75%) were females. The mean age was 61 years. CT scan was used as initial imaging in 75 (94%). Biochemical testing was performed in 58 (73%), which included cortisol axis in 48 (83%), mineralocorticoid axis in 45 (78%) and catecholamines in 46 (79%). Follow up imaging was done in 70 (88%), at an average interval of 36 months. Follow-up biochemical testing was done in 28 of 58 (48%) at an average interval of 25 months. These were, cortisol axis in 19 (68%), mineralocorticoid axis in 22 (79%) and catecholamines in 17 (61%). Of the 35 patients who had complete baseline and follow-up data, 25 were found to be nonfunctioning (71%) and 10 (29%) functioning (3 cortisol, 5 aldosterone, 1 catecholamine secreting and 1 combined cortisol/aldosterone). Of the 25 nonfunctioning ones, 24 (96%) were observed and 1 (4%) had adrenalectomy. Of the 10 patients with functioning adenomas, 6 were managed with medications (5 aldosterone secreting; 1 combined aldosterone and cortisol secreting), 1 had surgery (catecholamine secreting) and 3 were observed.

Discussion: The AACE incidentaloma guidelines, recommend that all incidentalomas have to undergo biochemical evaluation. If they are benign and non-functioning, it is recommended to do follow-up imaging in 3-6 months as well as biochemical testing annually. Our study is showing that not all patients are getting the recommended management plan, and when they do the time interval is much longer than is recommended.

Conclusion: Our single center retrospective review of patients with adrenal adenomas & incidentalomas revealed that a significant proportion of them may not be getting appropriate testing and follow-up as recommended by major professional societies.

Abstract #104

RADIOFREQUENCY ABLATION OF LIVER METASTASES IN ECTOPIACTH PRODUCING NEUROENDOCRINE TUMOR RESULTED IN CLINICAL AND BIOCHEMICAL RESOLUTION OF CUSHING’S SYNDROME

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Objective: Ectopic ACTH secretion (EAS) accounts for 20% of ACTH dependent Cushing’s syndrome. Lung carcinoma and neuroendocrine tumors are the leading causes. Surgical resection of the primary tumor is optimal therapy; however in cases of metastatic tumors a surgical approach may not be feasible. For nonresectable tumors therapeutic options to control the hypercortisolism include adrenal enzyme inhibitors, bilateral adrenalectomy or treatment of metastasis by ablation. We present a case of severe Cushing’s syndrome caused by bronchial carcinoid tumor with liver metastasis with resolution following radiofrequency ablation (RFA).

Case Presentation: A 57 year old male presented with 6 months of uncontrolled hypertension, 50 pound weight gain, new onset diabetes, and edema. Initial laboratory revealed a serum cortisol of 91.5 mcg/dL, ACTH 198 pg/mL, and 24 hour urinary free cortisol of 7820 mcg. Pituitary MRI showed no abnormalities and inferior petrosal sinus sampling confirmed a non-pituitary source of ACTH. Octreotide scan revealed no abnormal uptake. CT scan revealed a left lower lobe peribronchial nodule and 2 right lobe liver masses (3.5 cm and 1.5 cm) all which were metabolically active on PET. Liver biopsy showed moderately differentiated neuroendocrine carcinoma. When ketoconazole 1200 mg/day resulted in persistently high cortisol and no clinical improvement, alternative treatments were considered. Surgery was considered high risk and unlikely curative, therefore RFA of the hepatic metastasis was undertaken. 2 weeks after RFA his serum AM cortisol decreased from 38.8 mcg/dL to 5.0 and ACTH from 232 pg/mL to 59. 3 months after RFA 24 hour urinary free cortisol decreased to 10 mcg. His signs and symptoms of Cushing’s syndrome resolved.

Discussion: Curative surgical treatment for EAS has been reported between 12- 46%. Adrenal enzyme inhibitors including ketoconazole and adrenolytic agents are options for cortisol control in preparation for surgery or in patients where surgery is not feasible or curative. Medical therapy response rate has been reported between 53-88%. EAS with high ACTH and cortisol levels may be less likely to respond or normalize with medical therapy. Treatment of the primary tumor or metastasis with RFA or other ablative procedures has shown response rates of 50-96% over 4-18 months.

Conclusion: Treatment of EAS from a non resectable primary tumor or with metastatic disease is challenging. Medical therapy to reduce cortisol may not normalize the cortisol or resolve symptoms. RFA of the metastasis, even if the primary tumor is not treated, may result in control of the serum cortisol and resolution of Cushing’s syndrome. This may be a reasonable alternative to bilateral adrenalectomy.

Abstract #105

ABSTRACT WITHDRAWN
METASTATIC PHEOCHROMOCYTOMAS: THE IMPORTANCE OF SURVEILLANCE

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Objective: The objective of this presentation is to identify clinical predictors of metastatic pheochromocytomas and to emphasize the importance of surveillance in high risk individuals.

Case Presentation: A 60-year old man presented to the endocrine clinic for follow-up visit. He had a history of right adrenalectomy dating back to nine years secondary to pheochromocytoma. His original tumor measured 9 cm in greatest dimension. One year later he underwent left adrenalectomy and partial hepatectomy after metastatic disease was discovered. He remained stable until seven months prior to visit when he presented with symptoms of palpitations, night sweats, and panic attacks. A CT scan of the abdomen and pelvis showed two sub centimeter hypoattenuating foci within the dome of the liver that were too small to characterize, and two additional small soft tissue densities along the inferior and superior margin of the spleen. Fractionated 24 hour urine normetanephrine was slightly elevated at 663 μg/d (50-650 μg/d), metanephrine level was normal at 298 μg/d. Subsequent; Octreoscan described a diffuse heterogeneous radiotracer uptake throughout the liver concerning for metastatic recurrence. The patient elected to proceed with medical management and to undergo genetic testing to inform his children of their potential risk, currently results are pending.

Discussion: Pheochromocytomas are rare neuroendocrine tumors. Approximately 10% of these tumors are malignant, but because histopathology features of benign and malignant tumors are similar, the diagnosis is often delayed. Patients presenting with benign tumors (tumor localized to adrenal) may later develop metastatic disease. Most patients with evidence of metastasis have not had adequate follow-up and as a result may have unresectable disease by the time the malignancy is recognized. Currently, only three clinical predictors of metastasis in patients with pheochromocytomas are well recognized: primary tumor size, primary tumor location and germline mutation of the succinate dehydrogenase B (SDHβ) gene.

Conclusion: It is important to identify clinical predictors of metastasis to determine need of long-term careful surveillance in efforts to detect and treat disease recurrence early.

PRIMARY PREVENTION OF ADRENAL INSUFFICIENCY IN PATIENTS ON CHRONIC ORAL BUDESONIDE THERAPY.

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Objective: To describe a case with hypothalamic-pituitary-adrenal axis (HPA axis) suppression from oral budesonide therapy.

Case Presentation: A 84-year-old woman with hypothyroidism and hypertension underwent evaluation for diarrhea and weight loss. She was started on oral budesonide (9 mg/day) after diagnosed with collagenous colitis. The patient reported improvement in diarrhea and weight loss. During evaluation, she was noted to have low morning serum cortisol 1.3 μg/dl while taking budesonide. Similarly, evening cortisol level was low at 1.3 μg/dl. She was referred to endocrinology clinic by her gastroenterologist, for evaluation of adrenal insufficiency. She was asked to hold budesonide for three days before scheduled adrenocorticotropic hormone (ACTH) stimulation test. On the day of test, her baseline morning serum was ACTH 11pg/ml and cortisol was 18 μg/dl. On ACTH (0.250mg) stimulation, cortisol increased from 18 to 25ug/dl in 30 minutes and 31ug/dl in 60 minutes. The patient resumed budesonide. Serum glucocorticoid screen performed on budesonide (9 mg/day) showed positive blood levels of budesonide 0.20 (cut off 0.10 mcg/dl). Her serum biochemical abnormalities were attributed due to systemic budesonide absorption that lead to suppression of HPA axis. Budesonide dose was lowered to 6mg daily and repeat serum glucocorticoid screen was negative for budesonide in the blood.

Discussion: Budesonide is a commonly prescribed topical synthetic glucocorticoid that has minimal systemic absorption due to high topical affinity for glucocorticoid receptors, its extensive first pass metabolism in the liver, and its formulation that targets its release into the intestine. Despite these properties, budesonide can cause adrenal insufficiency. Two cases of severe adrenal insufficiency from budesonide have been reported in literature. In a review of eleven budesonide studies for maintenance of remission in crohn’s disease, abnormal ACTH stimulation test was three times more frequent in the budesonide vs. placebo group. Adrenal insufficiency can be prevented by preemptively screening these patients with morning serum cortisol levels, and/or serum glucocorticoid screen. In patients with low blood cortisol level or elevated serum budesonide levels, lowering of budesonide dose may be considered.
**Conclusion:** We report a case with HPA axis suppression from budesonide therapy. Budesonide dose was lowered before patient could have developed adrenal insufficiency from prolonged HPA axis suppression. In patients on chronic budesonide therapy, proactive approach of ruling out HPA axis suppression could prevent untoward consequences from excess glucocorticoid exposure.

**Abstract #108**

RECURRENCE CUSHING’S SYNDROME AFTER BILATERAL TOTAL ADRENALECTOMY

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**Objective:** Endogenous Cushing’s syndrome is a debilitating endocrine disorder which results from excess circulating cortisol. Bilateral adrenalectomy is an effective therapeutic option for non-localised adrenocorticotropic hormone (ACTH) dependent Cushing’s syndrome. The incidence of residual, functioning adrenal tissue in patients treated by total bilateral adrenalectomy is not known. We report a case of recurrent Cushing’s syndrome after bilateral adrenalectomy due to enlargement of residual adrenal tissue causing hypercortisolism.

**Case Presentation:** A 54 y.o woman presented to the clinic with increasing weight and newly diagnosed diabetes. She had elevated 24 hour urinary cortisol (158 mcg/24 hr), elevated ACTH (133 pg/ml) and inadequate suppression with 1 mg dexamethasone (27 mcg/dL). She had MRI of brain done which was unremarkable. Inferior petrosal sinus sampling showed elevated ACTH bilaterally and was non lateralising suggestive of a potential ectopic source of ACTH. She had extensive work up including octreotide scan but the source of ACTH was not localised. Due to the severity of her symptoms, patient underwent laparoscopic bilateral adrenalectomy revealing enlarged adrenal glands.

Few months after the surgery, patient developed severe symptoms of hypercortisolism including weight gain, worsening diabetes and hypertension. She had CT scan of the abdomen done which showed interval development and enlargement of a mass in the area of left adrenal gland bed which may represent some residual adrenocortical tissue or ectopic rest of adrenal tissue. The recurrent adrenal mass was surgically removed and patient had improvement in her symptoms. She had residual adrenocortical tissue which underwent subsequent hypertrophy under continued adrenocorticotropic hormone stimulation.

**Discussion:** Bilateral adrenalectomy is a useful treatment modality in patients who have recurrence following pituitary tumor excision and in patients where the source of ACTH hypersecretion is not identifiable. However, because of technical surgical problems or the presence of ectopic adrenal tissue, this procedure does not guarantee total remission. Any residual adrenal tissue would be exposed to continued stimulation by adrenocorticotropic hormone resulting in recurrence.

**Conclusion:** As there is a possibility of residual, functioning adrenal tissue after total bilateral adrenalectomy for ectopic ACTH dependent Cushing’s syndrome, continuous surveillance for hypercortisolism is important.

**Abstract #109**

FATAL CUSHINGS

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**Objective:** To present the extreme vulnerability of patients with ectopic Cushing’s syndrome and discuss the importance of early aggressive care and need for updated management guidelines.

**Case Presentation:** A 63 year old Hispanic female presented with acute onset low back pain. She had been living independently approximately 6 weeks prior to presentation. At that time, she had developed left leg pain and weakness. She was given PO steroids by her PCP but subsequently noted to have a potassium of 1.5 mmol/L (3.3 – 5.1 mmol/L) and admitted to an outside hospital. There she had mild hypertension and persistent hypokalemia. The aldosterone/renin activity ratio was suppressed but ACTH was 562.8 pg/mL (7.7 – 63.3 pg/mL) and 8 am cortisol was > 50 mcg/dL (nl 5-25 mcg/dL). A CT abdomen was negative for adrenal mass but CT chest revealed a 16 x 8 x 10 mm density in right middle lobe. She was diagnosed with Cushing’s syndrome. Her potassium stabilized on amiloride, KCl, spironolactone and ketoconazole and she was discharged for further outpatient follow up. Two weeks after discharge, she presented to our institution with severe low back pain and progressive weakness. She also reported 20 lb. weight loss over the past month. She had a 43 pack year history of smoking but otherwise had an unremarkable PMH. Her vital signs were stable but she exhibited a depressed affect, rounded face with mild plethora as well as diffuse hyperpigmentation without areas of bruising or striae. Potassium was stable on recently prescribed medications, repeat aldosterone/renin activity was suppressed and random cortisol level was 175 mcg/dL. After 8mg dexamethasone, the am cortisol was 238 mcg/dL. 24 hr urine free cortisol was 14,186 mcg/24 hr. The octreoscan revealed an area of increased uptake near the lower pole of right kidney though this did not correlate with any masses on the CT scan. A spinal MRI
revealed multilevel compression fractures and pituitary MRI was negative for any mass. On hospital day 3, patient underwent bronchoscopy, complicated by pneumothorax requiring chest tube placement. Patient’s respiratory status deteriorated requiring intubation. Bronchoscopy results were positive for pneumocystis, CMV and parainfluenza. In addition to bactrim and ganciclovir, etomidate drip was started on hospital day 7. Despite cortisol levels declining, reaching a nadir of 26 mcg/dL, patient died of overwhelming respiratory infection.

**Conclusion:** Ectopic Cushing’s is a rare disease and localizing the focus of cortisol production can be challenging. Urgent control of hypercortisolism with early bilateral adrenalectomy should be instituted in such cases.

**Abstract #110**

**HEMMORRHAGIC SUBDIAPHRAGMATIC BRONCHOCGENIC CYST MIMICKING AN ADRENAL TUMOR: A RARE CASE**

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**Objective:** We report a rare case of hemorrhagic subdiaphragmatic bronchogenic cyst (sBC) and discuss the clinical presentation, radiographic and pathologic findings.

**Case Presentation:** A 38 year-old Japanese woman presented with left upper quadrant abdominal pain. A non-contrast CT scan demonstrated a left 8cm cystic adrenal mass with possible hemorrhage. Her CBC and chemistry panel were normal. There was no clinical or biochemical evidence of pheochromocytoma, Cushing’s syndrome, or hyperaldosteronism. MRI of the adrenals without contrast demonstrated a left 8cm cystic adrenal mass involving the left adrenal gland. There was no loss of signal on fat saturation to reveal a lipid-rich lesion. The radiographic differential diagnosis of a cystic mass within the left adrenal gland was not suggestive of a definitive neoplastic or aggressive infectious process but still suspicious for hemorrhage within an adrenal cyst or an occult metastatic lesion. She underwent laparoscopic left adrenalectomy. Pathology revealed a benign adrenal gland and an adjacent, unilocular, thin walled cyst lined with ciliated columnar epithelium. The cyst also contained cartilage, bronchial mucous glands, and smooth muscle. Associated with the cyst were inflammatory cells, focal hemorrhage, necrosis, and evidence of prior hemorrhage. This constellation of histologic findings was most consistent with a hemorrhagic subdiaphragmatic bronchogenic cyst.

**Discussion:** Bronchogenic cysts arise as developmental abnormalities of the primitive foregut during the third to seventh week of gestation, resulting from aberrant budding from the ventral diverticulum or tracheobronchial tree. They usually occur in the chest and seldom inhabit subdiaphragmatic or retroperitoneal locations. They may present with abdominal pain or be found incidentally. These cysts are composed of ciliated pseudostratified columnar epithelium, cartilage, smooth muscle, and bronchial mucus glands. As a diagnostic dilemma, surgical excision is often required to confirm the diagnosis. Although hemorrhagic esophageal bronchogenic cysts have been described, very few hemorrhagic sBCs have been reported.

**Conclusion:** Subdiaphragmatic bronchogenic cysts, although rare, may hemorrhage, enlarge and become symptomatic. SBCs are scarcely described but should be kept in the differential diagnosis of a suspicious adrenal lesion.

**Abstract #111**

**CUSHING’S SYNDROME DUE TO OCCULT ECTOPIC ACTH SYNDROME: CASE REPORT AND REVIEW OF THE LITERATURE**

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**Case Presentation:** A 75-year-old male was referred for evaluation of fatigue, unintentional weight gain, hypertension, and severe hypokalemia (potassium 1.8 mM, 3.6-5.1). The patient was not receiving exogenous glucocorticoids or diuretics. Examination was notable for moon facies, proximal muscle weakness, and scattered bruises. Twenty-four hour urine free cortisol (3,675 μg, ≤ 60) and midnight salivary cortisol (2.770 μg/dL, < 0.112) were markedly elevated, and morning ACTH level (136 pg/mL, 7-69) indicated ACTH-dependent Cushing’s syndrome. Cortisol and ACTH levels fell more than 50% from baseline after 8 mg of dexamethasone, and magnetic resonance imaging (MRI) demonstrated a 6 mm mass of the mid-to-posterior pituitary. However, there was no central-to-peripheral ACTH gradient on inferior petrosal sinus sampling (IPSS). Computed tomography (CT), positron emission tomography (PET), and octreoscan failed to identify potential sources of ectopic ACTH secretion, and measurements of serum chromagranin A and 24 hr urine 5-hydroxyindolacetic acid were unremarkable. Serum cortisol remained > 20 μg/dL despite maximum dose ketoconazole. Following recovery from diverticulitis complicated by pericolic abscess, laparoscopic bilateral adrenalectomy was performed for definitive management of hypercortisolemia. Cushing’s syndrome resolved after surgery.
Discussion: Approximately 15% of corticotropin-dependent Cushing’s syndrome cases are due to ectopic secretion of ACTH by non-pituitary tumors. Small cell lung cancers, bronchial carcinoids, islet cell tumors, and thymic carcinoids account for approximately 75% of ectopic ACTH syndrome (EAS) cases, with nearly half of tumors occurring in the lungs. Despite advances in imaging, the source of ectopic ACTH may remain elusive. Four patient series published in the past decade document a 10-20% rate of occult EAS, and in a fifth series from Japan the rate was much higher (37.5%). CT and MRI appear to be superior to PET and octreoscans for localizing tumors. When indicated and available, IPSS has high diagnostic accuracy for distinguish pituitary and peripheral ACTH secretion. Patients with occult EAS have a better prognosis for survival than patients with detectable tumors, though, as in our patient’s case, they are just as likely to experience florid Cushing’s syndrome.

Conclusion: Occult EAS presents significant diagnostic and management challenges. When the source of ACTH cannot be localized, management with agents that reduce cortisol production, such as ketoconazole or metyrapone, is indicated. When hypercortisolemia is refractory to medical management, laparoscopic adrenalectomy is preferred to resolve severe Cushing’s syndrome.

Abstract #112
A CASE OF UNEXPLAINED ISOLATED TERTIARY ADRENAL INSUFFICIENCY PRESENTING WITH HYPOGLYCEMIA
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Objective: Corticotropin releasing hormone (CRH) is mainly produced in the hypothalamic at the level of periventricular nucleus to regulate pituitary Adrenocorticotropic hormone (ACTH). Isolated CRH deficiency is a rare disorder, characterized by tertiary adrenal insufficiency with low or absent cortisol production, normal secretion of all pituitary hormones other than ACTH and the absence of structural pituitary defects. We report a case of patient with hypoglycemia secondary to isolated tertiary adrenal insufficiency.

Case Presentation: A 44 year old African American male presented for evaluation of hypoglycemic episode that happened randomly throughout the day. It was first noted in February of 2011 with a blood sugar of 44 and without symptoms. He was noted to have 10 pounds weight loss in a 3-month period. On further evaluation, he admitted to having concussions while he was on military duty in 1990. His hypoglycemia medication panels were all negative. His mixed meal test showed that his lowest blood sugar at 60 minutes was 58 with an insulin level of 34.5 and C-peptide at 4.55.

The suspicion of counter regulatory hormone defect was added to our differential diagnosis since his morning ACTH was < 1.1; cortisol was 0.7; 24 hours urinary cortisol was 1. The decision was to further investigate adrenal insufficiency by performing an ACTH stimulation test. The test showed a baseline cortisol of 3.8 with 30 and 60-minute levels at 9.6 and 12.4 respectively. The baseline ACTH of 9.0 at 30 minutes post ACTH injection was 14.6. A test for secondary adrenal insufficiency with insulin stimulation was also performed. The results were as follows: blood sugar dropped to 36; ACTH 1.8; cortisol 0.6; Growth hormone < 0.1; Somatomedin 122. The magnetic resonance imaging of his pituitary was within normal limit.

A further investigation was then pursued to rule out possible tertiary adrenal insufficiency with CRH stimulation test. At the end of 60 minutes his baseline ACTH of 5.4 increased to 25.3 after the CRH ovine injection and his baseline cortisol of 0.9 increased to 3.2. Currently the patient is on steroid replacement treatment.

Discussion: Isolated tertiary adrenal insufficiency as an etiology for hypoglycemia is an unusual condition and should be considered as one of the possible causes. The pathogenesis is still not completely understood yet. A CRH stimulation test has been used to diagnose and localize adrenal insufficiency. The result of ACTH response to CRH provides distinction between primary, secondary and tertiary adrenal insufficiency.

Conclusion: A way to diagnose adrenal deficiency at the level of the hypothalamus has not been sufficiently developed. Further investigation is warranted.

Abstract #113
ABSTRACT WITHDRAWN

Abstract #114
LOW SURVIVAL RATE IN PATIENTS WITH METASTATIC ADRENAL CORTICAL CARCINOMA
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Objective: Adrenal cortical carcinoma (ACC) is an aggressive lethal disease of adrenal cortex. The incidence is 1-2 cases per million. We conducted a retrospective chart review to investigate the outcomes of metastatic adrenal carcinoma in patients admitted for a surgical excision of
Methods: Two cases of metastatic ACC were identified among patients hospitalized in Methodist University Hospital, Memphis, TN between 2003 and 2008. Demographics, tumor size, morphologic, immunohistobiochemical markers, post-surgical treatment, prognosis were analyzed.

Case Presentation: Case 1: A 65-year old white male with past history of prostate cancer status post prostatectomy, diabetes mellitus and resection of a 4-cm right adrenal cortisol secreting adenoma 1 year prior and extensive family history of cancer including breast, prostate, stomach and liver cancer of first degree relatives was found a recurrent 8.3 cm cortisol secreting right adrenal carcinoma metastatic to liver and omentum and underwent adrenalectomy, partial hepatectomy and partial omentectomy in 2008. Mitotane and decador were started before surgery. Immunohistochemical stains were positive for inhibin, melan-A, synaptophysin and BCL-2. Metastasis extended to bilateral lung and breast despite radiation and chemotherapy with Afinitor. He died from acute respiratory failure four and half years after diagnosis.

Case 2: A 37-year old hypertensive and diabetic black female with no family history of cancer was found a cortisol and DHEA-S secreting 9-cm right adrenal mass metastatic to liver during the work up of a right scapular pain in 2004. She underwent right adrenalectomy and partial hepatectomy. Pathology revealed multiple necrosis and high Weiss score. Immunohistochemical stain were positive for vimentin, synaptophysin and placental alkaline phosphatase. Mitotane therapy was started. She died two years after diagnosis.

Discussion: Following radical resection of the tumor, mitotane plays an important role in treating cortisol-secreting stage IV ACC. The response rates to mitotane ranges from 13% to 31%. Low dose hydrocortisone should be empirically started to avoid adrenal crisis while on mitotane. Recent trials revealed that patients who received the combination of mitotane with etoposide, doxorubicin and cisplatin achieved better outcomes. Therapies targeting multiple molecular pathways in ACC are still under development.

Conclusion: Stage IV ACC 5-year survival remains very low. Cytotoxic chemotherapy and mitotane may have limited impact on the survival in patients with metastatic ACC.
Abstract #116

AN UNLIKELY BUT NOT UNUSUAL PRESENTATION OF CUSHING’S SYNDROME

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Objective: To describe a case of Cushing’s Syndrome caused by Adrenocortical carcinoma

Methods: We present a 34 year old lady with Cushing’s syndrome diagnosed during pregnancy. She had excessive weight gain over a period of a few months. She developed a dorscervical fat pad deposit and a round face. She had numerous striae on her abdomen and torso. Her biochemical profile suggested ACTH independent Cushing’s syndrome. Other work up for phaeochromocytoma, hyperaldosteronism and androgen excess were negative.

A dedicated Adrenal Computed tomography (CAT) scan showed a 5.1 cm left adrenal mass which was well circumscribed without evidence of local invasion. A Positron emission tomography scan showed avid uptake only in the left adrenal mass. She delivered a normal infant. The patient was consented post delivery for surgery.

Case Presentation: The patient underwent laparascopic left adrenalectomy. There was no localized invasion visualized. The histology confirmed adrenocortical carcinoma pathological stage pT2N0M0. Patient had a complication free surgery and recovery. She was commenced on hydrocortisone 20 mg orally once daily and mitotane 1500 mg orally once daily with planned dosage adjustments as needed. Serial CAT scans have not revealed metastatic disease. All of her symptoms have resolved since surgery.

Discussion: Adrenocortical Carcinomas are a rare though recognized cause of ACTH independent Cushing’s syndrome. Of note, this patient’s presentation may have been delayed because some of the features of Cushing’s i.e weight gain and abdominal striae are often features of pregnancy. A high degree of clinical suspicion led to doing the relevant diagnostic work up. Adrenocortical cancers can arise either sporadically or be familiar.

Patients will have relief of their symptoms once the source of cortisol excess is removed.

If these malignancies are caught at an earlier stage then the prognosis is more favorable.

Conclusion: Adrenocortical carcinomas are a rare though recognized cause of ACTH independent cushing’s syndrome. It is not clear if there is a temporal relationship between pregnancy and onset of a Cushings presentation like this. At this time, our patient demonstrates no evidence of residual disease. Her presenting symptoms have resolved.

Abstract #117

METASTATIC PHEOCHROMOCYTOMA MASQUERADING AS “RENAL MASS”

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Objective: Pheochromocytomas are rarely diagnosed during work-up of incidentally discovered renal masses upon imaging. It would be unexpected to diagnose pheochromocytoma retrospectively following surgery. We present a case of asymptomatic, but metastatic, pheochromocytoma diagnosed after resection of what appeared to be a renal mass upon pathology report.

Case Presentation: 63 year old asymptomatic female with a history of mild and controlled hypertension was referred to urology after ultrasound identified a left renal mass during work-up of acute kidney injury. MRI described it as Bosniak type IV renal mass, arising from the upper pole of the left kidney. Her only medications at the time were simvastatin and atenolol 50mg which she had been on for 5 years. She underwent laparoscopic resection of the mass without complications and was taken off atenolol due to low blood pressure in the weeks following surgery. She was referred to endocrinology after pathology of the mass was consistent with pheochromocytoma.

She remained asymptomatic and denied ever having headaches, palpitations, or increased sweating.

Labs following endocrinology appointment:
- Plasma normetanephrine 627 pg/mL (0-145)
- Plasma Metanephrine 12 pg/mL (0-62)
- 24 hour urine normetanephrine 2,736 mcg/24hr (82-500)
- 24 hour urine metanephrines 113 mcg/24hr (43-290)

Imaging following labs:
- MIBG avid lesion in the left posterior parietal calvarium correlating with hypodense lesions on CT images consistent with metastatic disease
- MRI: 1.2cm avidly enhancing lesion in the left high posterior parietal calvarium

She was started on phenoxybenzamine followed by beta-blockade prior to surgical resection of her skull which was an uncomplicated procedure and pathology was consistent
Abstract #118

CUSHING’S SYNDROME INITIALLY PRESENTING AS PULMONARY EMBOLISM

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Case Presentation: A 65-year old female presented with acute onset shortness of breath. Patient had decreased mobility for one week after sustaining a right foot fragility fracture. Medical history include uncontrolled diabetes, hypertension, hyperlipidemia, obesity, subclinical hypothyroidism, osteopenia with vertebral compression fracture, and meningioma s/p resection. Examination showed Cushingoid features of facial plethora, “moon facies”, central obesity, thin extremities. She had tachypnea, tachycardia, proximal muscle weakness, bipedal edema, and right calf tenderness on palpation. Chest CT revealed a pulmonary embolism in the right main pulmonary artery. Lower extremity ultrasound showed no deep venous thrombosis. Labs: elevated 24-hour urinary free cortisol 456 (n 4-50 mcg) and random cortisol 43 (n 4-22 mcg/dL), undetectable ACTH < 5 (6-50 pg/mL), normal plasma metanephrines/aldosterone/plasma renin activity. CT adrenal: 3.5 x 4 cm right adrenal mass with enhancement and washout pattern compatible with benign adrenal adenoma. Hypercoagulable work-up was negative for Factor V Leiden, Protein C/S deficiency, and antinuclear/anticardiolipin antibody. Patient was started on heparin drip bridged with warfarin, then switched to rivaroxaban (which was later stopped due to development of hematuria requiring blood transfusion). Patient eventually underwent right laparoscopic adrenalectomy without complications.

Discussion: Patients with untreated CS have a more than 10-fold increased risk of developing VTE. VTE not related to surgery occurs in 1.9-2.5% of patients with CS. Hypercoagulability in CS is due to both increased production of procoagulant factors (Fibrinogen, Factor VIII, Von Willebrand Factor), and impaired fibrinolytic capacity, resulting in a shortened activated partial thromboplatin time and an increased clot lysis time, respectively. In our patient, immobility and her CS were thought to be the etiologic factors for her VTE/PE.

Conclusion: It is important for physicians to suspect and recognize the high risk for VTE/PE in patients with CS for appropriate work-up and management. There are no guidelines on the type, dosage and duration of thromboprophylaxis for patients with CS. It should be considered in patients with active CS from the time of diagnosis, while awaiting surgery, until at least 4 weeks postoperatively. The benefit of prophylaxis should be weighed against the risk of bleeding.

Abstract #119

EVALUATION OF HYPERCORTISOLISM IN A PATIENT WITHOUT CUSHING’S SYNDROME

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Case Presentation: Cushing’s syndrome is characterized by many signs and symptoms but many are nonspecific. Diagnosis is confirmed through biochemical testing. However, there are several conditions in which there may be elevated cortisol levels that mimic Cushing’s syndrome such as obesity and untreated obstructive sleep apnea. We present a case in which diet and intense exercise caused hypercortisolism.

A 31 year old white male was initially evaluated by his primary care physician for isolated episode of erectile dysfunction. Patient denied low libido, decreased strength, or recurrent sexual dysfunction and had no complaints. He had no significant past medical history and was taking only a multivitamin and glucosamine. He was normotensive with normal BMI. He reported that several years ago he lost about 40lbs and now maintains it by exercising twice a day and eating 2500kcal a day. Exam showed no moon facies, facial plethora, dorsocervical fat padding, supraclavicular fullness, striae, or truncal obesity. He was found to have morning total testosterone of 163ng/dL (normal 250-1100ng/dL) and free testosterone of 24pg/mL (35-155pg/mL) with normal FSH and LH. Pituitary imaging was normal and pituitary labs were significant for a morning cortisol of 24.9mcg/dL (6.2-19.4mcg/dL) with an associated ACTH of 24pg/mL (6-50pg/dL). He was referred to endocrinology for further evaluation. Repeat testosterone panel was normal. A 24
hour urine free cortisol was 113 mcg/dL (5-50 mcg/dL) with 2.9L collection. Cortisol was 7.3 mcg/dL after 1 mg dexamethasone suppression, but dexamethasone level was only 133 ng/dL (180-550 ng/dL). Cortisol suppressed to 8 ng/dL with 2 mg dexamethasone but dexamethasone level was 169 ng/dL. With 4 mg dexamethasone and his cortisol suppressed to 3.8 ng/dL and dexamethasone level was 457 ng/dL. Late night salivary free cortisol was within normal. He was admitted for late night plasma cortisol levels and they were elevated at 6.9 ng/dL and 6.0 ng/dL. Cortisol binding globulin was 3.2 mg/dL (1.7-3.1 mg/dL). Patient was instructed to take in more calories and he gained approximately 5 lbs. Repeat 24 hour urine free cortisol was 23 mcg/dL and late night salivary cortisol was normal.

**Conclusion:** This case illustrates several points when evaluating for Cushing’s syndrome. A morning cortisol and ACTH is not part of screening for Cushing’s syndrome. A history and physical is important because although our patient’s labs can be interpreted as having Cushing’s syndrome, he never manifested any signs or symptoms nor did he have any cause that can explain Cushing’s. This patient appeared to have pseudo-Cushing’s secondary to his diet and intense exercise.

**Abstract #120**

**CASE REPORT: MITOTANE INDUCED SECONDARY HYPOTHYROIDISM IN A PATIENT WITH ADRENOCORTICAL CARCINOMA**

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UCLA

**Objective:** To report a case of secondary hypothyroidism associated with the initiation of Mitotane in a patient with metastatic adrenocortical carcinoma (ACC).

**Case Presentation:** A 64 year old female with a past history of Cushing’s Syndrome and left adrenal mass found on computed tomography. The 8.5 cm adrenal mass was found to be ACC after left adrenalectomy. Three months later, the patient was found to have metastatic ACC to the lungs. The patient then presented to our hospital for treatment with doxorubicin, etoposide, cisplatin and adjuvant Mitotane. Eight weeks after the initiation of Mitotane, she presents with fatigue and cold intolerance. Exam noted supraclavicular fat pad, moon facies, and wide abdominal striae, central obesity, and ecchymoses. Thyroid labs done prior to treatment were normal. With eight weeks of mitotane treatment, TSH was 0.60 mIU/mL (0.4-4.7), Free T4 was 0.6 ng/dL (0.8-1.6), and free T3 was 90 pg/dL (222-383). After the initiation of thyroxine replacement, labs returned to the normal range.

**Discussion:** Mitotane is an isomer of the insecticide p,p’-DDD and a chemical congener of the insecticide DDT. Mitotane is an adrenolytic agent that acts by inhibiting 11-beta hydroxylase and cholesterol side-chain cleavage enzymes. This drug also leads to mitochondrial destruction and necrosis of adrenocortical cells in the zona fasciculata and reticularis. The toxicity of adjuvant mitotane treatment is poorly known in part because ACC is a relatively rare malignancy with an incidence of 2 per 1 million population. Mitotane exerts a complex effect on the endocrine system that may require hormone replacement therapy. Newer studies indicate a direct inhibitory effect of mitotane on TSH secretion. We describe a case of secondary hypothyroidism after initiation of Mitotane, highlighting the important evaluation of thyroid function tests in cancer patients on this oral chemotherapeutic agent.

**Conclusion:** This case illustrates the potential for secondary hypothyroidism with the use of Mitotane and the importance of diagnosis and subsequent management. Mitotane is used in completely resected ACC due to a 50-70% recurrence rate after radical surgery, and careful monitoring and treatment of potential adverse events are critical. Thyroid dysfunction may not be recognized in cancer patients due to complexity of the clinical picture and symptoms of hypothyroidism may be incorrectly attributed to the primary cancer. Current literature describes the need for thyroid hormone replacement for management of clinical symptoms of hypothyroidism in Mitotane induced hypothyroidism. This case emphasizes the need for early recognition of secondary hypothyroidism associated with use of Mitotane.

**Abstract #121**

**HYPERANDROGENISM AND MASCULINIZATION AFTER BILATERAL ADRENALECTOMY – A CASE OF SUSPECTED OART**

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**Objective:** Testicular adrenal rest tumors are a relatively common development in male patients with Congenital Adrenal Hyperplasia (CAH). There are few reported cases of ovarian adrenal rest tumors (OART). In this case report we present a suspected case of OART in a female with CAH after bilateral adrenalectomy with worsening hyperandrogenism and masculinization.

**Methods:** Review of medical and surgical records along with new lab data and imaging studies are discussed. A review of pertinent case reports is included.

**Case Presentation:** A 43 year-old female with documented CAH due to 21-hydroxylase deficiency is discussed. The
patient was born with ambiguous genitalia and had clitoral surgery and correction for right renal malformation at 8 months of age. As a neonate, the patient was started on hydrocortisone and fludrocortisone replacement therapy. At 8 years of age the patient started to undergo changes associated with precocious puberty. After years of suboptimal medical management, the patient elected for bilateral adrenalectomy on October 2007. The patient had return of menses and improvement in pigmentation, however, these changes were not long lasting. Laboratory data demonstrates a persistently increasing ACTH and testosterone levels with clinical masculinization. MRI of the brain was performed to exclude Nelson’s syndrome along with serial pelvic ultra sounds failing to demonstrate any ovarian abnormality.

**Discussion:** Review of case reports of ovarian adrenal rest tumors shows a similar biochemical and phenotypical pattern. This report demonstrates the complexity and difficulty with diagnosis of OARTs and the lack of concise guidelines/diagnostic approach recommendations. The patient is currently awaiting approval from pelvic MRI to further explore the possibility of OART.

**Conclusion:** OARTs can present as a complex constellation of signs and symptoms. Clear and concise diagnostic recommendations for OART are needed. Although these cases are seemingly rare, they pose a challenge to clinicians in practice. Awareness of clinical and biochemical presentation of these cases may disclose further case reports as this condition may be more common than currently appreciated.

**Abstract #122**

3β-HYDROXOSTEROID DEHYDROGENASE DEFICIENCY IS COMMONLY MISDIAGNOSED AS POLYCYSTIC OVARY SYNDROME

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**Objective:** Clinical hyperandrogenism (HA) is defined by hirsutism, acne, and alopecia. The majority of women with HA have polycystic ovary syndrome (PCOS), the most common HA disorder affecting 10% of women. However, it is important to exclude similar disorders. We describe 2 patients initially diagnosed with PCOS who were subsequently diagnosed with non-classic congenital adrenal hyperplasia (NC-CAH) due to 3β-hydroxysteroid dehydrogenase (3βHSDII) deficiency.

**Case Presentation:** Case 1: 31 yo woman was referred for PCOS with hirsutism, oligomenorrhea, and obesity. PE was notable for BP 143/83, HR 98, BMI 35, no significant facial hair due to waxing and shaving around the umbilicus. Labs notable for normal LH 1.1 mIU/mL, FSH 3.8 mIU/mL, total testosterone (TT) 29 ng/dL (ref 2-45), and 17OH-progesterone (17OHP) 133 ng/dL (ref <200), and UFC 36.9 mcg/24h (ref 4-50), but elevated DHEAS 705 mcg/dl (ref 55-430) and 17OHPregnenolone (17OHpreg) 467 ng/dL (ref <200) consistent with 3βHSDII deficiency. Adrenal CT showed normal adrenal glands.

Case 2: 21 yo woman referred for PCOS with hirsutism, oligomenorrhea, and obesity. PE notable for BP 132/83, HR 77, BMI 38, facial and abdominal hirsutism, facial and back acne. Labs notable for normal LH 2.6 mIU/mL, FSH 5.6 mIU/mL, 17OHP 72 ng/dL (ref <200) and 17OHpreg 109 ng/dL (ref <200) but mildly elevated (TT) 47 ng/dL (ref 2-45) and markedly elevated DHEAS 732, 944, 988 mcg/dL (ref 55-430). Adrenal CT and pelvic ultrasound were normal. Cortrosyn stimulation testing (baseline=>60 mins) showed a normal cortisol 13=>29 ug/dL (x2) and 17OHP 15=>45 ng/dl (x3) response with a disproportionate elevation in 17OHPreg 146=>947 ng/dL (x6.5) consistent with partial 3βHSDII deficiency.

**Results:** We report two patients with HA and oligomenorrhea diagnosed with PCOS who upon additional evaluation of adrenal steroids had elevated DHEAS and 17OHpreg in the absence of adrenal/ovarian tumors consistent with 3BHSDII deficiency.

**Discussion:** PCOS and NC-CAH share many clinical features including HA symptoms and oligomenorrhea, the presence of which meets NIH or Rotterdam criteria for PCOS. However, both diagnostic criteria require exclusion of other disorders with similar presentations. NC-CAH is the cause of hirsutism in 8-10% of women. Although less common, 3βHSDII deficiency should be considered in the differential of these symptoms. Patients should be carefully evaluated with 17OHP, 17OHpreg and potentially cortrosyn stimulation testing in unclear cases.

**Conclusion:** PCOS is the underlying cause of HA and oligomenorrhea in most women but clinicians should be aware that NC-CAH 3BHSDII deficiency can easily be misdiagnosed as PCOS.
Abstract #123

PREIMPLANTATION GENETIC DIAGNOSIS FOR A SINGLE GENE MUTATION FOR SUCCINATE DEHYDROGENASE SUBUNIT B (THE GENETIC BASIS FOR MALIGNANT PARAGANGLIOMA) WITH SUCCESSFUL PREGNANCY

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Objective: To report the first successful case of the birth of normal baby using preimplantation diagnosis for hereditary paraganglioma followed by embryo transfer and to emphasize the importance of using mild follicle stimulating hormone (FSH) stimulation for IVF in women with diminished oocyte reserve.

Methods: The female partner had a baseline serum FSH of 16.5 mIU/mL and the male partner had the malignant hereditary form of the paraganglioma—pheochromocytoma (PGL/PCC) syndrome related to a mutation of the nuclear mitochondrial enzyme, succinate-dehydrogease enzyme (specifically the B subunit) (SDHB). He was suffering from the malignant transformation of these neuroendocrine tumors. Before his death, he wanted to enjoy for a short time a baby with his own genes but feared passing the SDHB autosomal gene mutation to their child.

Case Presentation: Eight blastomeres from 8 embryos biopsied on day 3 were tested for SDHB gene by polymerase chain reaction. These 8 metaphase II oocytes were obtained following mild FSH stimulation (150 units from day 3). Intracytoplasmic sperm injection (ICSI) was performed using the frozen/thawed sperm of this 35 year old male suffering from a malignant pheochromocytoma. Five of the 8 embryos were found to have mutations of the SDHB gene. Two embryos with normal SDHB were transferred and one resulted in a healthy baby. Genetic testing of the baby confirmed the absence of the SDHB mutation.

Discussion: Donor sperm was not a personal option for this couple. The success supports, but does not prove, the importance of using mild FSH stimulation in the presence of diminished oocyte reserve to inhibit the iatrogenic development of a much higher percentage of embryos with aneuploidy. There are data suggesting that the reason for some centers reporting poor pregnancy rates following conventional or high dose FSH stimulation in the presence of low egg reserve is down regulation of certain FSH receptors producing factors necessary for proper events of meiosis especially meiosis II. Precedents are sometimes important in helping other patients/physicians choosing the best personal option for them – IVF with genetic probes vs. donor sperm for the SDHB mutation.

Conclusion: This seems to be the first reported case of successful pregnancy for the SDHB type of hereditary PGL/PCC syndrome following transfer of embryos determined by pre-implantation genetic diagnosis to be devoid of the SDHB mutation despite the presence of the autosomal dominant gene in a parent.

Abstract #124

CORRELATION BETWEEN THE VALUE OF METANEPHRINES AND NORMETANEPHRINES AND THE PRESENCE OF IMPARED GLUCOSE TOLERANCE IN PATIENTS WITH PHEOCHROMOCYTOMAS

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Objective: Our objective was to see if there is any correlation between the plasma and urinary metanephrines and normetanephrines and the presence of impaired glucose tolerance in patients with pheochromocytomas.

Methods: This is a retrospective study which included 35 patients with pheochromocytomas diagnosed between 1990-2012 in National Institute C.I.Parhon Bucharest. We calculated the value of plasma and urinary metanephrines and normetanephrines in patients with impaired glucose tolerance and patients without this disorder in pheochromocytomas.

Results: In our lot of study 13 patients representing 37.1% of the total patients had impaired glucose tolerance. Mean values of plasma and urinary metanephrines and normetanephrines for these patients were: 515.692±126.374 pg/mL and 736.308 ±55.615 pg/mL for plasma metanephrines and normetanephrines and respectively 1179.154±178.949 μg/24h and 845.538 ±60.983 μg/24h for urinary metanephrines and normetanephrines. Mean values of plasma and urinary metanephrines and normetanephrines for patients with pheochromocytomas but without impaired glucose tolerance were: 425.546±119.106 pg/mL and 663.818±103.796 pg/mL for plasma metanephrines and normetanephrines and respectively 1179.154±178.949 μg/24h and 845.538 ±60.983 μg/24h for urinary metanephrines and normetanephrines. Patients with impaired glucose tolerance and pheochromocytomas had bigger values of plasma and urinary metanephrines and normetanephrines and the differences were statistically
significant: p=0.045 for plasma metanephrines, p=0.032 for plasma normetanephrines, p<0.001 for urinary metanephrines and p=0.031 for urinary normetanephrine.

**Discussion:** Hyperglycemia is caused in part by the alpha adrenergic inhibition of insulin release. Improvement in glucose tolerance was noticed after the resection of pheochromocytomas or by blocking the α receptors without blocking β receptors. Compared to patients without impaired glucose tolerance, patients with impaired glucose tolerance have higher tumors and a higher level of catecholamines.

**Conclusion:** In our lot of study the value of plasma and urinary metanephrines and normetanephrines was correlated with the association of impaired glucose tolerance in patients with pheochromocytomas.

Abstract #125

**ONCOCYTIC ADRENAL TUMOR PRESENTING AS CUSHING’S SYNDROME-RARE PRESENTATION OF A RARE TUMOR**

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**Objective:** Oncocytic adrenocortical neoplasms are rare. A majority of them have a benign clinical course. To date, around 20 oncocytic adrenocortical neoplasms have been described. We present the clinical, histological and immunohistochemical features of oncocytic adrenocortical carcinoma presented as Cushing syndrome.

**Case Presentation:** A 52-year-old lady presented with polyuria, generalized weakness, proximal muscle weakness, recurrent boils, weight gain, hirsutism and constipation. She is diabetic and hypertensive for 12 years. On examination, she had mooning of face, pelvic girdle weakness, BP-150/100 mmHg, Other systemic examination-normal. CBC-normal, FBS-217 mg/dl, PPBS-310 mg/dl, HbA1c-6.1%, S.creatinine-1.2 mg/dl, S.Na-137 mEq/l, S.K-3.69 mEq/l, total Cholestrol-145 mg/dl, S.Tg-81 mg/dl, LFT-normal, LVH on ECG and X-ray Chest, S.T3-0.54 ng/ml, S.T4-7.01 µg/dl, TSH-1.23 mIU/ml, S.cortisol- 8 a.m-41.79 µg/dl, after overnight 1 mg dexamethasone suppression-24.75 µg/dl, after overnight 8 mg dexamethasone suppression-26.90 µg/dl, DHEAS-45, ACTH-<5.00 pg/ml and total testosterone-0.01 ng/dl. USG abdomen showed hypoechoic lesion in the right adrenal gland. MRI abdomen showed heterogeneously hyperintense soft tissue lesion over the right adrenal gland without perilesional stranding or intrallesional haemorrhage measuring 3.2 × 2.6 × 2.5 cm. Pituitary was normal on MRL.Laparoscopic excision of adrenal tumor was done. On histopathology, trabecular architecture with broad fibrous bands were seen. The neoplastic cells had pink granular cytoplasm with some showing empty cytoplasmic appearance with brown pigmentation and fibrovascular septae, suggestive of adrenocortical neoplasm. Immunohistochemical examination revealed it to be immunoreactive for cytokeratins (AE1/AE3 and CAM5.2). Inhibin was focally positive and final diagnosis of an adrenocortical oncocytoma was made.

**Discussion:** An adrenocortical localization of oncocytoma is diagnosed rarely. These are mostly nonfunctioning and benign and detected incidentally. In our case, the tumor was found during workup of Cushing syndrome. Pathological examination of this tumor was based on the Weiss scale. As per this scale, our patient was diagnosed to have an oncocytic neoplasm with malignant potential. Post surgery, the patient was regularly followed for 2 years, she lost 10 kg weight, diabetes and BP remained under control with minimal medications. There is no evidence of any recurrence or metastasis either on physical examinations or imaging.

**Conclusion:** Adrenocortical oncocytoma, although extremely rare, should be considered as a possible diagnosis in adrenal tumors. Although most of these tumors are nonfunctioning but they can also be hyper secreting.

Abstract #126

**COMPLETE QUICK RESOLUTION OF CHRONIC GASTROPARESIS IN A MALE WITH MILD ADRENAL INSUFFICIENCY HETEROZYGOUS POSITIVE FOR THE CYP2D6*41 REDUCED ACTIVITY VARIANT BY TREATING WITH AN EXTREMELY LOW DOSAGE OF DEXTROAMPHETAMINE SULFATE AND LOW DOSAGE HYDROCORTISONE**

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**Objective:** To determine if chronic gastroparesis showing only a fair response to domperidone plus significant side effects could respond to treatment with dextroamphetamine sulfate. In this instance the case was complicated by being positive for the heterogygous CYP2D6*41 reduced activity variant which is associated with diminished drug metabolism including amphetamines related to decreased debrisoquine hydroxylase.

**Methods:** A 53 year old male was diagnosed several years before with gastroparesis. He was unable to tolerate
various medications including metoclopramide which caused burning throughout his body, associated with erythema of the neck and chest and severe headache (nor did it relieve his gastrointestinal symptoms). He was tried on domperidone and he showed some relief initially but this worsened over time. The patient sought an opinion from our endocrine group. Mild adrenal insufficiency was detected based on serial random a.m. cortisols ranging from 1.8-4.1 ug/dL. Hydrocortisone was started. Subsequently he was started on 5mg dextroamphetamine extended release capsules.

**Case Presentation:** Hydrocortisone 10mg twice daily relieved his exercise intolerance including flushing of his neck and chest and palpitations but did not relieve his gastroparesis symptoms. The dextroamphetamine sulfate 5mg extended release capsule completely relieved his symptoms within one day of taking the amphetamine. However, because of chest pain and hypertension he stopped the medication (he had a history of coronary artery disease). He was treated with 500mg of ranolazine for his coronary artery disease and his dosage of dextroamphetamine sulfate was reduced to 2.5mg tablets daily which completely eradicated symptoms of gastroparesis without raising his blood pressure (118/78) or giving him any chest pain.

**Discussion:** There have been other anecdotal reports of using dextroamphetamine for gastroparesis and other gastrointestinal motility disorders. The hypothesized mechanism is that the abnormality is related to an intrinsic defect in permeability of the stomach smooth musculature complicated by sympathetic nervous system hypofunction. The sympathetic nervous system controls cellular permeability. Dextroamphetamine sulfate may stimulate dopamine which acts as a neurotransmitter for the sympathetic nervous system, restores sympathetic tone and consequently diminishes cellular permeability.

**Conclusion:** Dextroamphetamine sulfate can be used to successfully treat gastroparesis even in the presence of decreased debrisoquine hydroxylase as long as the dosage is markedly reduced.

**Abstract #127**

**AYOUNG GIRL WITH PREMATURE ADRENARCHE SECONDARY TO A NON-CLASSICAL 3 BETA-HYDROXYSTEROID DEHYDROGENASE DEFICIENCY WHOSE SEVERE VULVOVAGINITIS WAS CAUSED BY SYMPATHETIC NEURAL SYSTEM HYPOFUNCTION**

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**Objective:** To demonstrate that premature production of increased Δ5 androgens causing premature adrenarche in a young girl due to a non-classical form of congenital adrenal hyperplasia (CAH) related to deficiency of the 3-β hydroxysteroid dehydrogenase enzyme was not the cause of a very unusual severe vulvovaginitis.

**Methods:** An 8 year old girl started to develop axillary and pubic hair development at age 4 ½ accompanied by adult body odor. At age 6 she developed a severe puzzling vulvovaginitis. To exclude precious puberty serum LH, FSH, and E2 were measured. To exclude the 21 hydroxylase deficient type of CAH a serum 17-hydroxyprogesterone level was repeated as were serum testosterone, androstenedione and DHEA sulfate and 8:00a.m. serum cortisol. Her vulvovaginitis was empirically treated with amphetamine salts extended release capsule 15mg in view of its known benefit in treating various aspects of pelvic pain including vulvovaginitis.

**Case Presentation:** The serum DHEA sulfate was 115 mcg/dl which was increased for her age (normal <34 mcg/dL, serum T was slightly increased for her age at 8 ng/dL, and the 8:00 a.m. serum cortisol was a little low at 7.8 mcg/dL (nl 9-22 mcg/dL). The serum estradiol was <20pg/mL and the LH and FSH were <1 mIU/mL. Her vulvovaginitis completely resolved after 1 month of dextroamphetamine sulfate (and has remained so over 4 years of treatment).

**Discussion:** A chronic yeast infection as the cause of the vulvovaginitis was deemed unlikely in view of the estrogen deficiency state and with the positive response to dextroamphetamine sulfate after having failed to improve in the past two years over several courses of anti-fungal medication. True precocious puberty was excluded by low gonadotropins and estrogen. The 21 hydroxylase deficiency type of CAH was excluded by normal serum 17-OH progesterone levels. The non-classical type of CAH related to a 3-β hydroxyl steroid dehydrogenase deficiency was not only established by an increase in the Δ5 androgens it was further established by her younger brother’s development of premature adrenarche without the demonstration of premature puberty. Besides a slight increase in DHEA
sulfate he also had a mild increase in the Δ5 steroid 17-hydroxyprogrenalone at 247 mcg/dL (normals <209 mcg/dL) with normal 17-OH progesterone levels.

**Conclusion:** Premature adrenarche is uncommon as is vulvovaginitis in the pediatric population so it is natural to think that the two must be connected in some way. However, the quick response to sympathomimetic amine therapy suggests just a fortuitous co-existence of an unusual presentation of the common condition known as the sympathetic neural hyperalgesia edema syndrome.

**Abstract #128**

**CA-125 GLYCOPROTEIN SECRETION BY AN ANDROGEN-SECRETING ADRENAL ADENOMA IN AN ADULT FEMALE PATIENT.**

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**Objective:** CA-125 is a glycoprotein encoded by MUC16 gene. It is most frequently used tumor marker for ovarian cancer. We present a female pt. w/ androgen-secreting adrenal tumor (AST) that co-secreted CA125.

**Methods:** Clinical, hormonal, imaging, histopathological, & short term FU data.

**Case Presentation:** A 21-yr. old pt. presented w/ 2-yr. hx. of irregular menses, hirsutism & acne. Investigations showed AST that was resected.

Hormonal & tumor marker data: serum testosterone (T) 7.73 nmol/l (female RR: 0.2-2.9), DHEAS 25.7 umol/l (R: 4.29-11.2), DHEA 89 ng/ml (R: <13), androstenedione 4.7 nm/l (R 1-12.2), Estradiol 228 pmol/l (R:46-1800), Free androgen index 41.8 % (R:<8.5), SHBG18.9 nmol/l (R:20-113), 17-OHP <0.4 nmol/l (R:0.6-12 ), 24 hr UF cortisol 112 nmol/D (R: 50-150), AM ACTH 6 ng/l (R: 5-60), AM cortisol AM 104 nmol/l (R:170-536), CA 12-5 850 u/ml(R: 0-35).

Imaging data: CT & MRI abdomen/Pelvis: 6 cm well demarcated hypervascular lt. adrenal mass rest exam nl.

A decline in following hormones was noted within 2 wks post op : T 0.39, DHEAS 5, DHEA 2.1. CA 12-5 declined rapidly to 85.

Histopath data: Tumor measured 5.5 cm, weighed 72 g, w/out vascular/soft tissue invasion, necrosis or mitotic activity, margins free of tumor. Ki-67 index focally positive (5%). Immunostains positive for CA 12-5, & inhibin.

**Discussion:** CA 125 is the largest membrane- associated protein containing about 22,000 amino acids. It may be elevated in sera of pts. w/ different neoplasia, including, lung, breast, fallopian tube, & GI cancer. Our pt. had a large but benign tumor w/ unique feature co-secreting T & CA-125, a finding not reported previously. The exact pathogenesis of AST is unclear. It is believed that Leydig cells are present in adrenal gland & may have an active role in AST. Histologic exam can confirm presence of crystalloids of Reinke specific for Leydig cells. They have been identified in only 3 cases, their absence, as in our patient, does not exclude a Leydig cell character.

Most ASTs are usually malignant, are larger, have serum T level > x2 higher than benign ones. The distinction between benign versus malignant adrenal tumor is generally based on tumor size & imaging phenotype or presence of invasion/metastases. Most adenomas are <4 cm in diameter & have lower HU. Surgical resection provides effective treatment when metastases are not present. Our pt. had a large tumor but a low HU, & needs close FU.

**Conclusion:** Herein we describe a large but benign testosterone & CA 125-producing adrenal tumor in a female w/ a prompt decline of these tumor markers following resection. Adrenal neoplasm can now be added to a large list of conditions associated w/ abnormal circulating CA 125.

**Abstract #129**

**NEW ONSET SIADH S/P BILATERAL VP SHUNT WITH PRE-EXISTING PRIMARY ADRENAL INSUFFICIENCY**

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**Objective:** Primary AI has a prevalence of 40-60 cases per 1 million in the US and the incidence of SIADH in Neurosurgical patients is almost 50%. This case describes severe hyponatremia due to primary AI and SIADH from repeated CNS disturbances. Literature search for these diagnoses yielded few findings despite each commonly causing hyponatremia. This case illustrates the need for early recognition of SIADH in a chronic AI patient as a means of mitigation of morbidity by highlighting comorbidities of excessive steroid administration.

**Case Presentation:** 38 year old incarcerated male with PMH of primary AI from prior fluconazole treatment, was admitted 3/2014 to ICU after 7 days of headache, weakness & vomiting. Appropriate treatment for AI was initiated; subsequently diagnosed with Normal Pressure Hydrocephalus (NPH) and VP shunt was placed. After procedure, patient became hypotensive and hyponatremic necessitating stress dose steroid replacement to normalize blood pressure. After 2 weeks of steroids, patient developed Cryptococcal meningitis.A month of antifungals were administered as steroid dosage was tapered.
Patient returned to facility on 5/2014 after recurrence of severe vomiting and headache, also found hypotensive and hyponatremic. Treatment initiated for AI and an additional VP shunt was placed to treat residual NPH. Post-op patient became hypotensive and hyponatremic; managed with stress dose steroids for several weeks. Cryptococcal meningitis recurred and another course of antifungals ensued.

A week into treatment, patient was lethargic and hypotensive. Pressors were started and workup found Klebsiella bacteremia. Patient had profound muscle wasting with consistently elevated serum glucose. Despite Cushing’s Syndrome related comorbidities, stress dose steroids were continued for 2 more weeks. Ongoing profound hyponatremia was associated with elevated ADH of 36.2 and increased Urine Na. Tolvaptan ordered for SIADH and serum Na improved. Due to funding concerns Tolvaptan was discontinued; Demeclocycline was ineffective. Eunatremia achieved after titrating NaCl to 9 grams QDay. Steroids were tapered; upon D/C the patient still required NaCl 2 grams TID.

**Conclusion:** Over zealous steroid treatment to correct AI increases vulnerability to opportunistic infections by a factor of 1.5, promotes muscle wasting, and hyperglycemia. Immunosuppressed patients, who have risk factors of recent neurosurgery, meningitis, or severe hyponatremia with resistance to stress dose steroid replacement, should have prompt workup for SIADH. Early diagnosis and treatment (V2 receptor blockade or NaCl supplementation) can spare patients from morbidity of excessive steroid administration and improve recovery time.

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**Abstract #130**

**ADRENAL FUNCTIONING CARCINOMA IN A WOMAN WITH HISTORY OF ADRENAL TUMOR OF OVER 40 YEARS OF EVOLUTION**

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**Objective:** To report a case of functioning adrenocortical carcinoma (ACC).

**Methods:** We report the clinical and paraclinical characteristics of patient with a functioning ACC.

**Case Presentation:** Women, 64 yo; absent pubertal development and primary amenorrhea, menarche at age 22 with OCP use and prednisone, no children, was subjected to clitoroplasty, states that the diagnosis was informed of the existence of “adrenal tumor” unknown origin, without subsequent monitoring and irregular hormonal treatment. 2 years of difficult control hypertension and subsequent diagnosis of T2DM in January this year that requires insulin; 04 mo begins with progressive lower limb edema, subjective dizziness and headache without flushing associated with marked increases in PA, progressive dyspnea added to medium efforts, palpitations, decreased muscle strength. In ER: hypertensive, BMI: 23.8kg/m2, skin atrophy, edema of the extremities to distal third of the thigh, multiple bruises on the trunk and extremities, moderate hirsutism and alopecia androgenous; impressive mass in the right upper quadrant tenderness, decreased muscle strength. Analyses: FSH: 0.37mIU/ml, LH: 0.32mIU/ml, androstenedione: >10ng/ml, DHEAS: 895ug/dl, F 8a.m: >50ug/dl, aldosterone>500, free Testo: 3.08pg/ml, UFC1: 1141ug/d, UFC2: >1911ug/day, PFT: normal, CT: heterogeneous mass with lobulated contours in adrenal right of 12x10cm, contacts without infiltrating the liver, adrenal left of 5.5x6cm with fat density. She underwent right adrenalectomy, Pathology: adrenal carcinoma, Fuhrman histological grade III with focal areas of necrosis in 15% of tumor, oxyphilic 5% to 2% of pleomorphic nuclei, measuring 110x90x55mm, encapsulated, solid histological pattern, trabecular, sinusoidal, areas and microacinar infiltrating tumor capsule and extending focally to periadrenal fatty tissue. Venous and lymphatic tumor microemboli. IHC: Ki-67: 10%, S100(-), CD34 (+). Analysis 21 α OH no available.

**Discussion:** ACC is a rare, aggressive neoplasm with poor prognosis; represents <0.2% of all malignant tumors with a poor prognosis and a median survival of <30 mo. An overall incidence is estimated 0.5-2 per 1 million cases reported annually worldwide. The disease shows a slight female preference and bimodal age distribution, with the first peak in children <5 years of age and the second peak in the fourth to fifth decade of life. The ACC derived from the cells of the adrenal cortex in tumorigenesis can lead to overproduction of hormonal up to 79%, have poor prognosis and have few treatment options based on the staging of the disease.

**Conclusion:** Could be a malignancy that occurs in an existing adrenal tumor from many years of evolution producing multiple hormones.
Abstract #131

RESISTANT METABOLIC ABNORMALITIES PROMPTING CUSHING’S SYNDROME WORK-UP AND TREATMENT WITH MIFEPRISTONE

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1. Douglas C Beatty MD Internal Medicines, 2. Corcept Therapeutics

Objective: Hypertension (HTN) and metabolic abnormalities [diabetes (DM), obesity, and weight gain] are predominant in Cushing’s syndrome (CS) patients resulting in an increased cardiovascular risk (e.g. atherosclerosis, coronary artery disease, heart failure, and stroke). Yet, CS is not well recognized and often goes undiagnosed due to pervasiveness of metabolic syndrome in the general population. Herein we detail a morbidly obese patient with uncontrolled HTN and DM, prompting a CS workup revealing bilateral adrenal adenomas secreting autonomous cortisol.

Case Presentation: A 61y/o male presented 14 years ago with multiple co-morbidities: uncontrolled HTN, DM, hyperlipidemia (Fredrickson Type IV), morbid obesity, degenerative joint disease requiring multiple hip replacements, atherosclerosis and peripheral arterial disease. Years of medical interventions and diets were unsuccessful in controlling weight and worsening co-morbidities. Indeed, the patient’s weight increased 25lbs in the past year (peak weight 315lbs, BMI 45). Attempts to control hyperglycemia were unsuccessful even with Lantus (70U/d) and multiple anti-diabetic medications [A1c and fasting blood glucose (FBG) remained elevated at 9.1% and 197mg/dL, respectively]. He exhibited classic cushingoid features and failed to adequately suppress cortisol (5mcg/dl) on a 1mg dexamethasone suppression test. A CT scan revealed bilateral adrenal adenomas (18x13mm right, 26x11mm left). Unbeknownst to the clinician, a chest CT performed 6 years earlier had detected the adenomas but was never flagged by the radiologist for further work up. The size of the adenoma remained unchanged since the first scan. Refusing surgical treatment, he elected medical therapy with mifepristone (MIFE, Korlym®, Corcept Therapeutics), a selective glucocorticoid receptor antagonist. MIFE therapy was initiated and titrated to 600mg/d within 4 months, adjusting to QOD based on patient’s tolerability.

After 4 months, MIFE decreased A1c to 8.0% and FBG to 109 mg/dL, resulting in insulin discontinuation. BP decreased to 118/80 mmHg. Weight decreased by 25lbs, resulting in improvements to the patient’s cushingoid appearance (predominately facial).

Conclusion: CS can be difficult to diagnose in the presence of concomitant obesity, HTN, DM and metabolic syndrome. CS should be suspected when HTN and DM are poorly controlled, and rapid weight gain occurs. Interdisciplinary collaboration between primary care professionals, radiologists, and endocrinologists are necessary to identify patients with the potential for hypercortisolism to reduce the time to diagnosis of CS and appropriate care, which may include non-surgical alternatives.

Abstract #132

HYpercortisolism without clinical stigmata of Cushing’s syndrome: a possible variant of glucocorticoid resistance syndrome

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Objective: Primary glucocorticoid resistance is a rare familial or sporadic condition characterized by increased plasma and urinary free cortisol levels, inadequate adrenal suppression in response to dexamethasone without the clinical stigmata of Cushing’s syndrome. We present a case, a possible variant of cortisol resistance syndrome.

Case Presentation: A 41 year old woman was referred in 2008 for elevated 24 hour urinary free cortisol level of 317 mcg (3.5-45mcg/24 hour). She had normal body mass index (21.1 kg/m2) and normal blood pressures in the range of 122/70 to 130/80 mmHg. She had history of irregular menstrual cycles and hirsutism for over 20 years, depression and hypothyroidism. Potassium level was 4.3 mEq/L (3.5-4.9 mEq/L). Dehydroepiandrosterone sulfate level was 278 mcg/dl (35-430 mcg/dl) with an elevated testosterone level of 136 ng/dl (<20-80 ng/dl, ovulatory women). TSH levels ranged from 0.28 to 2.47 µIU/ml (0.35-5.5 µIU/ml) while receiving exogenous levothyroxine. Pelvic ultrasound revealed a single cyst in the left ovary measuring 1.1cm representing a follicle. Overnight and low dose dexamethasone (0.5mg every 6 hours for two days) failed to suppress cortisol levels which were 20.6 mcg/dl and 26.1 mcg/dl respectively. Repeated dexamethasone suppression tests and 24 hr. urinary free cortisol confirmed persistent hypercortisolism. ACTH levels ranged from 53-60 pg./ml (10-60 pg./ml) confirming inappropriately high levels. Magnetic resonance imaging of the adrenal gland and the pituitary gland were normal. The causes of pseudo Cushing’s were excluded and she was assured that she did not have clinical Cushing’s. In the interim, she saw another endocrinologist and inferior petrosal sinus sampling was done which suggested
pituatary source of ACTH. Plasma cortisol levels in her mother and two daughters were normal. When last seen in October 2014 she continued to have hypercortisolism with no clinical stigmata for Cushing’s syndrome and without any endogenous effects of steroids such as obesity, hypertension, osteoporosis and impaired glucose tolerance. The coding regions of the human glucocorticoid receptor gene (hGR, NR3C1) were sequenced and showed no mutation. (Courtesy of Dr. Sertedaki, Athens Greece)

Discussion: Cortisol resistance syndrome results from mutations in the hGR gene, which decrease tissue sensitivity to glucocorticoids through a decrease in the number or affinity of the encoded glucocorticoid receptors.

Conclusion: Although our patient has typical clinical and laboratory features of glucocorticoid resistance syndrome, the molecular mechanism for this variant is not clear.

Abstract #133

UNMASKING OF CUSHING SYNDROME BY TREATMENT OF PHEOCHROMOCYTOMA

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Objective: The simultaneous occurrence of pheochromocytoma and Cushing syndrome from ACTH secreting neuroendocrine tumors is extremely rare. The occurrence of subclinical Cushing syndrome from a cortisol secreting adenoma in the contralateral adrenal to an active pheo does not appear to have been previously reported.

Case Presentation: A 44 year old Caucasian lady presented with severe headaches, excessive perspiration and malignant hypertension. (BP 230/145) She had previously been in excellent health with no known personal or family history hypertension, MEN, or familial pheo syndromes. Genetic testing for all known mutations at the time was negative. Other than her severe hypertension examination was unremarkable. Lab revealed normal routine chemistry/cbc. Serum and urine catecholamines were 10-15x upper limit of normal as were serum and urine metanephrine. Urine free cortisol was mildly elevated at 64 ug/24 hours. CT imaging revealed a 3.5cm high HU left adrenal mass, and a 0.5cm low attenuation right adrenal mass. MIBG scan was strongly positive in the large left adrenal mass with no uptake on the left. She was treated with methyltyrosine, labetalol and dibenzyline with good effect and underwent successful laparoscopic adrenalecmy with removal of a 4 cm pheo, relief of hypertension and symptoms without meds. One month follow up revealed weight gain, appearance of centripetal obesity, striae, facial broadening and plethora. Additional evaluation showed urine free cortisol 70, ACTH levels low, and non-suppression of serum and urine cortisol by high dose dexamethasone. The patient declined additional invasive testing and surgery and was treated for eight years with ketoconazole . She had resolution of all Cushing symptoms, no drug toxicity, and no change in the CT appearance of her small right adrenal adenoma. She eventually underwent right adrenal laparoscopic adenomectomy with preservation of remaining normal adrenal tissue. She has done well for three years post operatively with no additional medication.

Discussion: This appears to be the first reported case of subclinical ACTH independent Cushing syndrome from an adrenal adenoma unmasked by treatment of excessive catecholamines from a contralateral pheochromocytoma.

Conclusion: Serious illness caused by apparently incidental benign imaging findings can be obscured by severe unrelated presenting pathology. Careful clinical follow up is necessary to determine long term best treatment outcomes.

Abstract #134

STERIOD ABUSE - WRONG WAY TO MAKE A RIGHT: A CASE REPORT

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Objective: To present a case of a patient with steroid abuse for weight gain presenting with adrenal crisis.

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

Case Presentation: In January 2012, 30 years old male bus supervisor admitted to BIRDEM with gastrointestinal upset, fever with altered level consciousness. Patient later stated that he used to take mixture of multiple drugs consists of Dexamethasone, Vitamin B complex, Diazepam and Ranitidine for weight gain for last two and half years by advice of another bus supervisor. Examination revealed patient was confused, GCS- 12, pulse - 104 beats/min, BP- 90/60 mm Hg, skin is thin with multiple striae in the lower chest and abdomen. Investigation revealed TC of WBC- 17,800/cu mm, Poly- 84%, ESR- 54 mm in 1st hour, RBS- 18 mmol/L, HbA1C-14.5%, S. Electolodies-Na+-132.3, K--4.3, Cl--103.5, HCO3--22.6 mmol/L, Serum cortisol(basal)-36 nmol/l. Patient was immediately treated with IV Hydrocortison, IV fluid and diabetes was managed with insulin split mixed regimen. When the patient became stable steroid dosage was gradually taper to maintenance dose during discharge. Patient was
counseled regarding steroid misuse and our plan of steroid withdrawal protocol and necessity of frequent follow up.

**Discussion:** This case report highlights complications of chronic steroid abuse. Management of these complications overburdens an already overstretched health care system.Judiciously used, steroids are invaluable in the management of several inflammatory diseases but becomes dangerous when available over-the-counter and used in an unregulated manner.

**Conclusion:** Increasing trends of steroid abuse have been reported in developing countries due to loosely audited health care systems. It is important that appropriate regulatory measures are put in place to control over-the-counter access of steroids and mass awareness regarding effects of steroid abuse.

**Abstract #135**

**UNDIAGNOSED ENDOGENOUS CUSHING’S SYNDROME WITH FLORID FEATURES PRECIPITATED BY POSSIBLE CHRONIC EXOGENOUS GLUCOCORTICOID INJECTIONS**

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**Objective:** Cushing’s syndrome (CS) results from sustained exposure of the body tissues to high levels of exogenous or endogenous glucocorticoids. Hypercortisolism, the hallmark may be ACTH dependent from pituitary adenoma or ectopic tumor; or non-ACTH dependent adrenal secretion.

The classical features of centripetal obesity, plethoric moon face, buffalo hump and hirsutism are seen only in florid CS requiring a high index of suspicion for diagnosis of less obvious cases.

**Case Presentation:** A 45-year-old male patient reported to the medical out-patient clinic of the University of Nigeria Teaching Hospital complaining of worsening breathlessness, fatigue, and abdominal distension in the past 4 months. He had a history of stroke with right-sided hemiparesis, 4 years previously, when he was found to be hypertensive at a private hospital. He also had recurrent leg ulcers and a history of treatment for bleeding peptic ulcer disease within this period. He had noticed a more protuberant abdomen and a more robust face but thought nothing of it initially. However, he later noticed accelerated abdominal distension with fuller cheeks, after receiving several daily doses of an unknown intramuscular medication for 4 weeks from an unorthodox medical practitioner.

Examination revealed a plethoric ‘moon face’, wasting of the temporalis muscles, facial deviation to the right, thinning of scalp hair, acne on face and trunk, marked abdominal obesity, wide spread purplish abdominal striae, thinning of skin with bruising, proximal myopathy of limb muscles and chronic ulcers in the distal lower limbs.

His BP = 170/110mmHg, apex beat displaced, 24-Hour urinary free cortisol value = 210µg; overnight dexamethasone suppression test value= 89nmol/L. He had hypokalemia & impaired fasting glucose.

A diagnosis of florid Cushing’s syndrome was made and he was unable to do other requested investigations opting to be discharged against medical advice due to financial constraints.

**Discussion:** Heightened suspicion is required for early diagnosis of CS using discriminatory features which also distinguish true CS from pseudo cushinoid states. Exogenous CS should be excluded appropriately. With endogenous CS, ACTH- dependent & non-ACTH dependent should be differentiated using 9 am serum ACTH levels with further differentiation done between pituitary and ectopic ACTH dependent CS.

Treatment modalities include medical, surgical or radiotherapy depending on the cause and prognosis.

**Conclusion:** Early diagnosis of CS is imperative as it confers better prognosis. Prompt referral of suspected cases ensures better utility of patient’s resources as investigations and treatment are not easily affordable.

**Abstract #136**

**BILATERAL ADRENAL NON-HODGKIN’S B-CELL LYMPHOMA WITH CALCITRIOL MEDIATED HYPERCALCEMIA AND INCREASED ANGIOTENSIN CONVERTING ENZYME: CASE REPORT**

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**Case Presentation:** A 81 year old male with previous history of hypertension and chronic back pain presented with weight loss and abdominal pain. Laboratory results reported new hypercalcemia with corrected values between 11.8 and 14 mg/dl (range 8.5-10.5). The initial workup showed increase creatinine 2.41 mg/dl (baseline 1.8-2.2), normal phosphorus, normal PTH 34 pg/ml (range 15-88), normal PTH-RP 0.7 pmol/Lt (range <2), normal 25-hydroxyvitamin D 34 ng/ml (range 25-80) and high 1,25 Dihydroxyvitamin D 90 pg/ml (range 18-78) with high Angiotensin Converting Enzyme (ACE)100 U/L (range 8-53). CT of the brain and chest was normal. CT abdomen reported a 1.5 x 4 cm right adrenal mass and a 10 x 8.4 x 7.4 cm heterogeneous left adrenal mass with
negative findings in pelvis. Bone Nuclear Medicine Scan was negative and the rest of the endocrine workup was normal including Cortisol, ACTH, DHEA-S, Metanephrine and Testosterone. Left adrenal mass core biopsy reported a large B-cell lymphoma with non-germinal center and reactivity for CD20 and for CD43. Hypercalcemia was treated with IV fluids and pamidronate with good response and chemotherapy was started, unfortunately patient died 3 months later.

**Discussion:** Primary Adrenal Lymphoma (PAL) represents less than 1% of all Non-Hodgkin’s lymphomas, among other extranodal lymphomas like primary bone or breast lymphoma. Approximately 100 cases have been reported in the literature with case series or case reports. The initial clinical presentation can be just an incidentaloma, or range between unspecific symptoms like abdominal/back pain or fever to more specific symptoms like adrenal insufficiency. Only 4 previous cases of adrenal lymphoma with hypercalcemia have been reported, and only one was worked up showing increase PTH-RP. In our patient the hypercalcemia was calcitriol mediated with increase ACE. Hypercalcemia is often noticed in patients with hematological malignancies and this is usually caused by calcitriol increase, but there are only a few reports with increase ACE suggesting a possible similar mechanism as presented in sarcoidosis, like in our patient. In 70% of the PAL cases the adrenal involvement is bilateral and the most common histologic finding is Diffuse Non-Hodgkin’s B-cell lymphoma. Usually the prognosis is poor however recently reports show a better outcome when Rituximab is added to regular CHOP treatment.

**Conclusion:** Patients with primary adrenal lymphoma can be asymptomatic for long periods of time and sometimes only found in autopsies, but with the increase use of imaging, bilateral adrenal incidentalomas should be work up for all different causes including lymphoma because early diagnose will definitely impact the prognosis.
DIABETES MELLITUS/PREDIABETES

Abstract #200

THE RELATIONSHIP BETWEEN ALBUMIN EXCRETION RATE AND ESTIMATED GLOMERULAR FILTRATION RATE IN NIGERIAN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Objective: The prevalence of type 2 Diabetes mellitus (DM) and its complications is increasing in developing countries. Diabetic nephropathy, a complication of DM, can be determined using the urine albumin excretion rate or the glomerular filtration rate. In Nigeria, there are few studies on the correlates of albumin excretion rate (AER) including its relationship with glomerular filtration rate in patients with type 2 Diabetes Mellitus. This study was carried out to determine the correlates of the albumin excretion rate in patients with type 2 DM and its relationship with estimated glomerular filtration rate (eGFR).

Methods: The study was carried out at the Diabetes Screening Centre in Jos, Plateau state. Three hundred and forty four participants were examined. Early morning urine samples were obtained from each participant, for the estimation of urine albumin and creatinine using the DCA 2000 autoanlyser. The AER was calculated as a ratio of the urine albumin to creatinine. Blood samples were also obtained for the estimation of serum creatinine and glycosylated haemoglobin (Hba1c). The eGFR was calculated using the Modification of Diet in renal Disease (MDRD) study formula. Data analysis was done using IBM SPSS 20.0.

Results: The mean age of the study population was 55.4±9.4 years. There were more males than females (males 66.6%, females 33.4%) in this study. The median duration since diagnosis of DM was 5 years (interquartile range 8 years). Glycaemic control (HbA1c <6.5%) was present in 10.2% of participants and 68% had hypertension. The median values for eGFR and AER were 93.9ml/min and 8.7mg/mmol respectively. Normoalbuminuria and microalbuminuria was present in 23.8% and 56.4% of participants respectively. There were no significant differences in these values between the sexes (p>0.05). There were no significant correlations between duration since diagnosis of DM, sex, cholesterol levels and AER, after controlling for age. However, there was a significant correlation between AER and eGFR (r = -0.28, p=0.00). After adjusting for blood pressure, duration since diagnosis of DM, glycaemic control and sex, AER still had some influence on eGFR (OR=5.48, 95% CI= 1.64 -18.4).

Discussion: In this study, males did not have significantly higher AER as seen in some studies. In patients with type 2 DM, microalbuminuria was not significantly associated with declining eGFR. Contrary to most studies, there was no relationship between duration of DM, age and glycaemic control with AER in this study. Conclusion: Glycaemic control, hypertension and duration since diagnosis of DM are not associated with AER. There is a significant relationship between AER and eGFR in Nigerian Patients with type 2 DM.

Abstract #201

HEALTH RELATED QUALITY OF LIFE OF ADULTS WITH DIABETES MELLITUS IN JOS

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Objective: The prevalence of diabetes mellitus (DM) is increasing in developing countries such as Nigeria. The complications of DM and its management have an impact on the quality of life (QoL) of patients with the disease. Management DM requires the participation of the patient. Self-management of this disease is dependent on the patient’s perception of their QoL. This index of treatment outcome is often neglected. This study was carried out to evaluate the health related quality of life of adults with diabetes mellitus in Jos, Plateau State.

Methods: Sixty six adult persons with DM, who visited the Diabetes Screening Centre, Jos, were recruited into the study. A self-administered structured questionnaire, WHOQOL-BREF, was used to obtain socio-demographic characteristics and QoL. Duration since diagnosis of DM was noted and fasting plasma glucose was measured. Data analysis was done using IBM SPSS 20.0.

Results: The mean age of the study participants was 55.5±11.8 years. Of those studied 65.2% were women and the median duration since diagnosis of DM was 7 years. Out of a possible score of 20, the WHOQOL-BREF scores ranged from 11.5±3.7 in the social relationships domain, to 12.8±3.3 overall. Overall health related QoL scores were significantly higher in men than in women (t=2.62, p=0.01). Married participants had higher scores than the widowed (t=2.73, p=0.01). There was a significant correlation between level of education and QoL. This index of treatment outcome is often neglected.

Discussion: DM has an impact on the health related QoL of adults in this study as seen in similar studies around the
Abstract #202

INDEPENDENT AND ADDITIVE PROGNOSTIC VALUE OF PRETRANSPLANT DIABETES MELLITUS FOR EARLY CARDIOVASCULAR COMPLICATIONS AFTER ORTHOTOPIC LIVER TRANSPLANTATION

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Objective: Evidence of increased risk for cardiovascular outcomes associated with pretransplant diabetes mellitus (DM) in liver transplantation is lacking. The objective of this study was to assess the risk of cardiovascular complications associated with DM in patients undergoing orthotropic liver transplantation (OLT).

Methods: Consecutive isolated OLT recipients were retrospectively reviewed. The cohort was categorized into 2 groups according to history of DM and followed up for early cardiovascular complications after liver transplantation (a composite of elevated troponin, significant arrhythmia, and significant hypotension).

Results: The cohort comprised of 164 recipients with mean age of 55±9 years old and 62% were male. Median MELD score was 24 (13-32). Prevalence of DM, hypertension and smoking were 52%, 40% and 48%, respectively. The DM group was more likely to be hypertensive (66% vs 42%; p=0.003). Overall, the cohort exhibited 34% (n=56) incidence of cardiovascular complications post-OLT. These comprised of 38 significant hypotension, 13 elevated troponin and 19 significant arrhythmia. In multivariate analysis adjusted for MELD and alcohol use, DM was independently associated with post-OLT cardiovascular events (HR 2.87; 95%CI 1.41-5.82; p=0.003). Adding DM to the predictive model with MELD, alcohol use significantly increased predictive performance for the events (p=0.003).

Conclusion: In patients undergoing OLT, pretransplant DM was independently and incrementally associated with increased early post-OLT cardiovascular complications.

Abstract #203

DIABETIC KETOACIDOSIS FOLLOWING SGLT2 INHIBITOR THERAPY IN DM2

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Objective: To describe two cases of diabetic ketoacidosis developing after utilization of SGLT2 inhibitor therapy in patients with pre-existing DM2.

Case Presentation: An 18 year old female, with history of DM2 and no previous DKA episodes, presented with persistent vomiting and abdominal pain occurring within the preceding 24 hrs. She had DM2 since age 8 with negative antibodies and had never been on insulin. She was taking metformin 1g BID and canagliflozin was initiated three weeks earlier. She was advised by her PCP to increase the dose from 100mg to 300mg one week prior. She had recently been treated for vaginitis and had completed a course of flagyl. She was afebrile, tachypneic and tachycardic. BMI was 31 kg/m2. She appeared lethargic with dry mucous membranes, had mild abdominal tenderness and normal pelvic exam. Labs notable for A1c of 12.9%, glucose 300 mg/dL, positive ketones, leukocytosis, serum bicarbonate 5 mmol/L (22-30 mmol/L) and ABG pH 6.95. She was felt to be significantly volume depleted and was treated for DKA with insulin drip and aggressive IVF; no focus of infection was found. She was discharged on basal bolus insulin regimen and advised to continue metformin.

A 55 year old male diagnosed with DM2 at age 49 with most recent A1c of 12.1% presented with dizziness and near syncope while working in his yard. He had been taking metformin 1g bid and glipizide XR 5mg daily for the past 3 months and dapagliflozin 5mg daily was added one month earlier. He was afebrile with BP 102/66 and HR 102. His BMI was 21.7 kg/m2 and physical exam was notable for dry mucous membranes, mild abdominal tenderness and normal pelvic exam. She had also recently been treated for vaginitis and had completed a course of flagyl. She was afebrile, tachypneic and tachycardic. BMI was 31 kg/m2. She appeared lethargic with dry mucous membranes, had mild abdominal tenderness and normal pelvic exam. Labs notable for A1c of 12.9%, glucose 300 mg/dL, positive ketones, leukocytosis, serum bicarbonate 5 mmol/L (22-30 mmol/L) and ABG pH 6.95. She was felt to be significantly volume depleted and was treated for DKA with insulin drip and aggressive IVF; no focus of infection was found. She was discharged on basal bolus insulin regimen and advised to continue metformin.

Conclusion: SGLT2 inhibitors are a new class of diabetes medications affecting the renal handling of glucose and approved for use in DM2. Beneficial effects include A1C lowering as well as modest weight loss and improvement in BP via the glycosuric affect. In the cases presented, given the degree of poor baseline glycemic control, it is concerning if these agents propagated the state of dehydration thus accelerating the development of DKA. As such, it is suggested that more specific counselling be given to patients regarding hydration status when being started on this class of medications. Furthermore, safety of re-initiating SGLT2 therapy after an episode of DKA warrants further study.
Abstract #204

THE MANAGEMENT OF DIABETES MELLITUS IN NEW IRELAND PAPUA NEW GUINEA

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Objective: The goal of this study was to determine the percentage of patients with diabetes mellitus who had their fasting blood glucose (FBG), total cholesterol (TC) and blood pressure (BP) treated to national targets.

Methods: A retrospective chart review was carried out of all patients who attended the outpatient Diabetes Clinic in Kavieng Hospital, New Ireland, Papua New Guinea (PNG) from May 2013 to May 2014. Data collected included sex, age, body mass index (BMI), BP, FBG, TC, smoking status, medications and diabetes complications. Data is reported as mean ± SD.

Results: There were 190 patients (91M:99F) with diabetes mellitus type 2 (DM2) and none with type 1 seen at the clinic. Age was 58±9 years, BMI 26.8±5.6 kg/m2, BP 131/78±23/16 mmHg, FBG 10.45±4.87 mmol/L and TC 4.54±1.12 mmol/L. Active smokers were 17.4%. We identified foot ulcers in 13.2% of patients, neuropathy in 25.3% and diabetic retinopathy in 25.3%. With regard to DM2 therapy, there were 22% of patients diet controlled, 47% on single oral hypoglycemic agent (OHG), and 31% on dual OHG; insulin was not used in the outpatient setting. With regard to antihypertensive therapy, 72% of patients were not on any agent, 21% were on a single agent, 6% on dual agent and 1% on triple agent.

Discussion: DM2 is a significant global health problem due mainly to rising obesity rates secondary to a more westernized lifestyle (increased calorie consumption, reduced physical activity). It is optimally managed in conjunction with its co-morbidities of hypertension and hyperlipidemia to prevent micro and macrovascular complications of the metabolic syndrome. In response to this health burden, in July 2012, PNG Department of Health released its first national DM2 clinical practice guidelines with targets of FBG (< 6 mmol/L), BP (≤ 130/80 mmHg), BMI (< 25 kg/m2) and TC (< 5 mmol/L). We found that 84% of patients had a FBG above target, 43% had BP > 130/80 mmHg, 67% had a BMI ≥ 25 kg/m2, and 36% had a TC above target. This data suggests underutilization of medical therapy.

Conclusion: There is a paucity of academic literature on DM2 management in PNG, which like other developing countries has a dual burden of infectious and lifestyle related non communicable disease. Clinicians face numerous challenges including an under resourced healthcare setting and a local population with poor health seeking behavior and poverty. Our data suggests that while promising work is been done (e.g. healthy dietary advice 90%, diabetes education 94% of clinic attendees), a large proportion of patients with DM2 remain above national targets. Therefore, there is scope to optimize patients’ health with increased use of DM2, antihypertensive and lipid-lowering medications.

Abstract #205

ORAL HYPOGLYCEMICS: ARE THEY ENOUGH?

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Objective: The rate of new onset type 2 diabetes mellitus in America is steadily rising. The AACE/ACE guidelines state that insulin should be started in symptomatic patients if the HbA1C is above 9. While insulin is an effective hypoglycemic, it has several adverse effects, such as, weight gain, which severely limits its effectiveness. In addition, patient resistance in initiating insulin and non-compliance with insulin therapy are major setbacks in glucose control.

On the other hand, there are several oral medications that are extremely effective in glucose control without the added adverse effects that insulin provides. These medications sensitize insulin without promoting weight gain, and in some cases, actually promote weight loss. Given these advantages, we evaluated the effectiveness of using oral medications alone to control diabetic patients with a HbA1c of 9 or greater to a goal HbA1c of 7 or less.

Methods: We present a case series of 18 patients who were diagnosed with type 2 diabetes mellitus and had a HbA1c of 9 or greater at diagnosis. All 18 patients were treated with either oral medications exclusively or were started on oral hypoglycemics after less than three months of insulin therapy.

Case Presentation: All 18 patients were able to achieve adequate glycemic control with a HbA1c of 7 or less within six months on oral agents alone. 6 patients had a HbA1c of 12 or higher at diagnosis. 15 patients were treated with only 1-2 medications, with only 3 patients requiring 3 medications. Follow up revealed that 17/18 patients were still successfully controlled on oral agents alone after 15 months.

Discussion: This case series is just the beginning of exploring a better algorithm for the management of patients with type 2 diabetes mellitus. In general practice, oral medications are the initial treatments of choice for patients with lower HbA1cs at the time of diagnosis.
However, given the results of our case series, it seems that patients with higher HbA1cs should also be considered on oral therapy instead of insulin. We are aware of the limitations to this case series. Since this was a retrospective review, we do not have data on the importance of lifestyle changes. Therefore, in the future, we hope to validate our conclusions with a double blinded placebo controlled trial and subsequent meta analysis, which will be the first of its kind.

**Conclusion:** Practitioners can effectively treat type 2 diabetic patients that have an HbA1C above 9 with oral medications alone, which has several advantages, including weight loss and better glycemic control, not seen in insulin-based regimens.

**Abstract #206**

**GUIDELINES TO IMPROVE PERIOPERATIVE MANAGEMENT OF DIABETES MELLITUS: ASSESSMENT OF THE IMPACT OF CHANGE ACROSS TIME**

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**Objective:** Assess impact of perioperative guidelines on care of diabetes patients undergoing elective surgical procedures.

**Methods:** Perioperative guidelines were developed and implemented by a team with representatives from surgery, anesthesiology, and endocrinology. Overall changes in key measures were evaluated over the course of 12 months after guidelines were introduced and compared with a previously published 4 month historical cohort.

**Results:** There were 254 surgical procedures in the historical and 1,387 in the post-guideline implementation cohort. Preoperative medical evaluations occurred in 85% of cases post-guideline implementation compared to 80% in the historical cohort (P=.045). Hemoglobin A1c measurements were obtained in 72% vs. 47% (P<.01). Glucose monitoring was performed in the preoperative area in 93% of cases after the guidelines were implemented vs. 88% in the historical cohort (P<.01) but the frequency of measurements declined over the course of the 12 months (from 95% to 91%, P=.044). Intraoperative glucose monitoring occurred in 67% of cases after guidelines were implemented vs. 29% historically (P<.01), but frequency decreased over the course of the year (from 67% to 55%, P<.01). No change in glucose monitoring in the postanesthesia care unit (PACU) was found between the two cohorts (86% vs. 87%, P=.57), but the frequency of monitoring did decline in a pattern similar to that seen in the preoperative and intraoperative areas (91% to 87%, P<.01). After introduction of the guidelines, insulin use increased in the preoperative, intraoperative, and PACU areas (all P<.01), but insulin was given in fewer cases by the end of 12 months than the time immediately following introduction of guidelines (all P<.01). Mean preoperative glucose was 128 mg/dL in the post-guideline implementation cohort vs. 141 mg/dL in the historical cohort (P<.01). In the PACU, mean values were 149 mg/dL in the post-guidelines implementation group vs. 162 mg/dL in the historical group (P<.01).

**Discussion:** Implementation of multidisciplinary diabetes management guidelines for patients undergoing surgery can improve performance in key measures of care. Although adherence to key measures remained higher as compared to the historical period, improvement was not sustained, and began to decay over time.

**Conclusion:** Implementing standards of care improved preoperative assessment of diabetes patients, perioperative glucose monitoring, insulin use, and glucose control. The improvement decreased as time from intervention passes, but the rates did not fall below the historical period. Further research needs to be conducted on how to sustain adherence to guidelines.

**Abstract #207**

**THE IMPACT OF DIABETES MELLITUS AND FASTING GLUCOSE LEVELS ON CLINICAL OUTCOMES IN COLORECTAL CANCER.**

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**Objective:** There is evidence of an emerging etiologic link between diabetes mellitus (DM) and several gastrointestinal malignancies. However, the mechanisms underlying the correlation are still under investigation. The role of insulin and the insulin-like growth factor-I have been implicated in carcinogenesis and tumor growth via their regulation of cell growth and proliferation. The aim of this study was to investigate the influence of DM and glucose levels on clinical outcomes and treatment of patients with colorectal cancer (CRC).

**Methods:** We conducted a retrospective review of all patients diagnosed with CRC at our institution between 2011 and 2013. Demographics, tumor characteristics, DM diagnosis data and fasting glucose levels at diagnosis and before chemotherapy were abstracted. Pearson chi-square test was used to compare variables. Kaplan-Meier and Cox regression were used for survival and multivariate analysis.
Results: We identified 376 patients, among whom 28% (104) had DM. The CRC patients with diabetes were older with a mean age of 69 years vs. 65 years of patients without DM, but had similar tumor characteristics including stage and grade. Adenocarcinoma was the most common histologic subtype representing 87% of all cases. The mean HbA1C among diabetic patients was 6.7 (range 5.6-12.2). The average fasting glucose at diagnosis was 156 (79-399) and before chemotherapy it was 134 (56-340). Diabetic patients were less likely to receive adjuvant chemotherapy or second surgical interventions (51% vs. 65%, p<0.04 and 9% vs. 24%, p<0.004, respectively). Patients with DM had shorter overall median survival when compared to patients without DM, 17.4 months (95%CI: 14.7-20.1) vs. 27 months (95%CI: 25.1-28.2) (p<0.03). After adjusting for several comorbidities including obesity, DM was an independent and significant predictor of survival (OR: 1.41, p<0.02). Fasting glucose levels were not predictors of survival by univariate or univariate analysis.

Discussion: Our CRC patients with DM had a decreased overall survival of approximately 10 months compared to those without DM. Despite having similar tumor characteristics, diabetic patients were less likely to receive adjuvant chemotherapy or second surgical interventions, which could be partially explained by the lack of comorbidities and a younger age in the non-diabetic patients.

Conclusion: Our findings represent a clear example of the role of comorbidities in the treatment of cancer patients. Patients should be seen in a holistic manner where each co-morbidity can affect outcomes. Further investigation is needed, as this could potentially change the way we treat cancer patients with DM.

Abstract #208

DELAYED-ONSET INSULIN ALLERGY IN A PATIENT WITH DIABETES MELLITUS TYPE II

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Case Presentation: Rapid and long acting insulin are rare causes of an allergic reaction in diabetic patients with a prevalence of 0.1 to 3%. The most common type of insulin allergy occurs through a Type I IgE mediated allergic response, which typically manifests within minutes to an hour with local symptoms, such as burning at the site, rash, and itching. However, there are rare instances where the timing of the onset of the reaction to insulin is more consistent with a delayed hypersensitivity reaction (Type IV). Severe reactions of either type can result in anaphylactic shock. Several cases of allergic reactions have been attributed to impurities and additive components of insulin, such as zinc, protamine, and metacresol. Oral anti-diabetic agents or insulin immunotherapy are current treatment recommendations for patients with an insulin allergy.

A 60-year-old Hispanic female with a past medical history of Diabetes Mellitus Type II, hypertension, and hyperlipidemia presented with dysuria and hyperglycemia. She had hypersensitivity reactions in the past to multiple medications such as metformin, pioglitazone, metformin/saxagliptin, and glargine insulin, regular insulin, and aspart insulin. Her symptoms included rashes, blisters, pruritus, swelling of her lips, upper respiratory symptoms, and bone pain. She also reported a delayed allergic reaction to lispro insulin in which she developed a rash and lip swelling 2-3 days after exposure. Hemoglobin A1C was 13.4% on admission. She was given a lispro insulin challenge and developed lip swelling and itching more than 24 hours after administration. All insulin preparations were discontinued. She was started on oral anti-diabetic medications using a step-wise approach with the initiation of acarbose and sitagliptin and the addition of repaglinide several days later. Lab work was notable for eosinophilia, significantly elevated IgE of 3071, elevated IgM of 330, negative insulin antibody, negative latex IgE, negative anti-mitochondrial antibody, and negative C1 esterase inhibitor. The patient tolerated acarbose, repaglinide, and sitagliptin without any further hypersensitivity reactions.

Conclusion: Current literature emphasizes the importance of early detection and prompt initiation of allergic/immunological work-up to prevent potentially fatal complications, such as anaphylactic shock. Although true insulin allergy is very rare, angioedema occurs in 0.3% of diabetic patients taking insulin who have a delayed hypersensitivity reaction (Type IV), and this should be one of the differential diagnoses for a diabetic patient presenting with hypersensitivity or intolerance to insulin therapy.

Abstract #209

ABSTRACT WITHDRAWN

Abstract #210

ABSTRACT WITHDRAWN
Abstract #211

NECK CIRCUMFERENCE AS AN INDICATOR OF METABOLIC SYNDROME

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Objective: To evaluate the utility of neck circumference as a marker of metabolic syndrome.

Methods: A descriptive cross-sectional study of adults with hypertension and or diabetes. Metabolic syndrome was defined as the presence of insulin resistance (type 2 diabetes mellitus, impaired fasting glycaemia or impaired glucose tolerance) and 2 of antihypertensive medication use and/or high blood pressure (≥140 mm Hg systolic or ≥90 mm Hg diastolic), Plasma triglycerides ≥150 mg/dL (≥1.7 mmol/L), HDL cholesterol <35 mg/dL (<0.9 mmol/L) in men or <39 mg/dL (<1.0 mmol/L) in women, body mass index (BMI) >30 kg/m2 and/or waist: hip ratio (WHR) >0.85 in women. Neck circumference (NC) was measured with head erect and eyes facing forward, horizontally at the upper margin of the laryngeal prominence.

Results: There were 43 patients, females 27(62.8%), mean age 55.02±11.91 years. Mean age female 55.8±11.47 years, males 53.63±12.89 years,(p=0.56). Mean BMI 28.63±5.74, mean BMI males 25.48±4.35, females 30.49±5.71, (p=0.004). 29.6% females vs 25% males were overweight. Obese 40.7% females vs 25% males. Morbidly obese 7.4% of females. Mean WHR 0.92±0.07; mean WHR females 0.90±0.07, males 0.96±0.06, (p=0.01). Elevated WHR in 33(76.7%) patients, 20(60.6%) were female. 96.3% of females had waist circumference >80cm, while 50% of males had waist circumference >94cm, (p=0.01). Metabolic syndrome was diagnosed in 29(67.4%) using World Health Organization criteria, with 58.6% being female, 22(75.9%) were previously undiagnosed, (p=0.045).

Mean neck circumference was 34.57±2.90cm, utilizing receiver operator curve to determine the cut off value of neck circumference that correctly identified the presence of metabolic syndrome; the area under the curve was 0.61. A cut off of 34.5cm for neck circumference had a sensitivity of 65.5% and a specificity of 57.1% for correctly detecting metabolic syndrome, irrespective of gender.

Discussion: Metabolic syndrome is a constellation of cardio-metabolic risk factors. The presence of one risk factor should prompt a search for the others. Females were more likely to be overweight or obese and only females were morbidly obese. Waist circumference and WHR were higher in females. 51.2% of the patients had not been previously diagnosed as having metabolic syndrome. Neck circumference of 34.5cm had a sensitivity of 65.5% and a specificity of 57.1% for diagnosis of metabolic syndrome, irrespective of gender. Gender specific neck size cut off values could not be determined due to the small sample size.

Conclusion: Neck circumference appears to be a simple and useful screening tool for metabolic syndrome. Gender specific reference values are recommended.

Abstract #212

EFFECT OF OUTPATIENT DIABETES EDUCATION ON CLINICAL OUTCOMES

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Objective: To determine the effectiveness of employing diabetes education to assist pre-diabetic and diabetic patients with lowering hemoglobin A1c (HbA1c) levels and body mass index (BMI). Diabetes education is a program accredited by the American Association of Diabetes Educators that offers regular one-on-one and group classes for patients with diabetes mellitus (DM), pre-diabetes, and metabolic syndrome. Through this program, patients are taught ways to modify their behavior through diet, exercise, medication, and medication compliance in order to prevent or to manage diabetes. Lifestyle intervention has been shown to significantly reduce the incidence of Type 2 DM and reduce mortality in those with diabetes.

Methods: The study involved a retrospective chart review of 63 pre-diabetic and type 1 and type 2 diabetic patients 18 years of age or older who participated in at least one diabetes education class. Data was collected for one year prior to starting diabetes education and one year after. These subjects were then compared to 62 age and gender matched controls on whom data was also collected during a two year time period. Mean BMI and HbA1c were compared using Student’s T test for mean comparison assuming equal variance.

Results: Mean BMI fell by 0.85 kg/m2 in the intervention group compared to an average gain of 0.62 kg/m2 for the control group (p = 0.0114). The intervention group also had an average HbA1c reduction of 0.35% while the control group (p = 0.0114). The intervention group also had a significantly positive effect on BMI but not on HbA1c.

Conclusion: In this population, attending diabetes education class did not appear to have a greater effect on BMI or HbA1c.
Abstract #213

A CASE OF MULTIPLE PRESENTATIONS OF METFORMIN-INDUCED LACTIC ACIDOSIS OCCURING IN A SINGLE PATIENT

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Objective: Metformin-induced lactic acidosis is a rare but potentially fatal adverse event. Here we discuss a patient who developed Metformin-induced lactic acidosis three times in the course of several months.

Case Presentation: A 55 year old woman with DM2 and ESRD was sent to the ED from dialysis for hypoglycemia and hypotension. She reported experiencing generalized weakness for the past couple of days. This was accompanied by dizziness and feeling off balance. Review of systems was otherwise negative. Upon arrival to the ED, her hypotension and hypoglycemia resolved with normal saline and dextrose. On exam, she appeared lethargic but was easily aroused. The rest of the exam was unremarkable. Admission labs uncovered severe acidosis with a PH of 6.99, bicarbonate of three, anion gap of 45, and a lactic acid of 17. Upon medication reconciliation, it was revealed that the patient had been taking 850mg of Metformin twice a day although she had been told to discontinue its use in the past. Review of the patients chart revealed two similar presentations in the past several months. At those times she required multiple dialysis sessions to correct the metabolic acidosis. She was emergently dialyzed in the ED. Her metabolic acidosis improved after several dialysis sessions. She was counseled at length by multiple physicians about discontinuing the Metformin for good and she expressed understanding. She was discharged home on insulin therapy for her diabetes.

Discussion: Metformin, a biguanide, is considered the first line drug for patients with DM2. The FDA prescribing guidelines contraindicate its use in men and women with creatinine concentrations $\geq 1.5$mg/dl and $\geq 1.4$mg/dL because of the increased risk of lactic acidosis given the drugs renal clearance, although the frequency in general is rare. However, studies have shown that the incidence of lactic acidosis is similar in patients on metformin versus other oral antidiabetic agents. Other studies showed no incidence of lactic acidosis among patients taking Metformin even with creatinine levels of 1.5 mg/dl to 2.5mg/dl. In fact, many countries allow Metformin to be used in patients with GFR’s as low as 30mL/min/1.7m2 and many physicians feel the current contraindication to metformin in CKD needs to be updated. Nevertheless, although this is an extreme case, it demonstrates that Metformin-induced lactic acidosis does occur in patients with CKD, and is associated with significant mortality.

Conclusion: Although Metformin-associated lactic acidosis is extremely rare and there is extensive evidence that it is often is used without adverse effects in patients with reduced renal function, it still does occur and is potentially fatal.

Abstract #214

GESTATIONAL DIABETES IN A TERTIARY HEALTHCARE CENTRE IN ABEOKUTA: A FIVE YEAR RETROSPECTIVE REVIEW

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Objective: In the recent years, there has been a rapid rise in the incidence of diabetes in pregnancy. This is due to the increasing number of women in the reproductive age population with pre-gestational diabetes (type 2 DM) and the number of women being diagnosed with gestational diabetes mellitus(GDM).

This study sought to determine the incidence of gestational diabetes at Federal Medical Centre, Abeokuta and to evaluate the feto-maternal outcome of their pregnancies.

Methods: This study is a 5 year retrospective review of gestational diabetes mellitus cases at the Federal Medical Centre Abeokuta (between 2009 to 2013) as well as the outcomes of these pregnancies. A proforma was used to collect data from case notes of all gestational diabetes mellitus cases diagnosed within the stated period. All pregnant women in 24 weeks of gestation and above who are considered to be at risk after undergoing preliminary clinical examination were given a 75 goral glucose load, using the WHO standardized oral glucose tolerance test. Gestational diabetes mellitus was diagnosed if 2 hour plasma glucose was $\geq 140$mg/dl.

Case Presentation: The number of expectant mothers discovered to have GDM were 41 out of 3624 pregnancies giving an incidence rate of 1.13%. The majority of mothers with GDM in this study, had maternal age $\geq 31$yrs (78.1%), parity of 2-3 (48.78%), increased body mass index $\geq 25$ (82.93.0%) . Most of the GDM mothers had previous intrauterine fetal death (28.3%), spontaneous miscarriage (20.8%) and fetal macrosomia (20.8%). Caesarean section as the mode of delivery was significantly high at 61%.

Discussion: The incidence of GDM in our current study...
is similar to that of 1.1% by Chen et al at Brooklyn, New York, US, although less than that of Kuti et al in Ibadan who quoted an incidence rate of 13.9%. This difference may be related to the screening methods, diagnostic criteria used or population studied. Most of the mothers (43.9%) were diagnosed at an earlier gestational age of ≤ 20 weeks. This is because many high risk women may have booked on our facility due to their previous bad obstetric outcomes. The previous bad obstetric outcomes of intrauterine fetal death (28.3%), spontaneous termination of pregnancy (20.8%) and fetal macrosomia (20.8%), were mainly due to previous undiagnosed hyperglycaemia in pregnancy which adversely affected those gestations.

**Conclusion:** The morbidities associated with gestational diabetes are still enormous and timely screening of mothers could be beneficial in reducing the complications seen in gestational diabetes mellitus mothers.

**Abstract #215**

**TREATMENT GOALS ATTAINMENT IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AT THE OBAFEMI AWOLOWO UNIVERSITY TEACHING HOSPITAL, ILE-IFE SOUTH WEST NIGERIA**

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**Objective:** Many studies and treatment guidelines have emphasized that the treatment of diabetes mellitus extends beyond glycaemic control, and include lowering lipids and blood pressure. This study determined the proportion of Type 2 DM patients reaching the combined triple goals of HbA1c, blood pressure and lipid between January to December 2013.

**Methods:** This cross-sectional descriptive study involved three hundred (300) consecutive Type 2 diabetic patients presenting at OAUTHC, Ile-Ife Nigeria. Relevant clinical information and physical examination were carried out. Venous blood was collected to determine HbA1c, total cholesterol, LDL, HDL and triglycerides. Treatment goals were based on HbA1c < 7%, blood pressure <130/80mmHg, total cholesterol < 200mg/dl, triglycerides < 150mg/dl, LDL <100mg/dl and HDL <40mg/dl in males and < 50mg/dl in females.

**Results:** One hundred and six (35.3%) were males and one hundred and ninety four (64.7%) female. The mean age was 61.17 ± 10.5 years (62.0± 10.9 years for males and 60.7±10.3years females). Of the 300 participants, 8.3% achieved the combined treatment goals for HbA1c, blood pressure and lipids. 23.3% achieved HbA1c of <7.0%, 45.5 % attained the ADA blood pressure goal of <130/80mmHg and 37.0% achieved lipid goals. Logistic regression analysis showed that patients with short duration of DM and good compliance with medication were more likely to attain HbA1c goal.

**Discussion:** The majority of study participants did not achieve HbA1c of less than 7%. It is known that lack of funds account for poor glycaemic control among our diabetic patients as most patients have to pay out of pocket for their drugs and tests. This is closely associated with poor adherence with medications another strong predictor of glycaemic control as shown by our data. High frequency of lipid abnormalities was also observed in study participants. 63% of the study subjects did not achieve the ADA target for lipid profiles. Dyslipidaemia has been shown to be strongly related to increased CVD risks and the report of the NCEP III advised physicians on intensive treatment of this to reduce CVD risks.

**Conclusion:** The proportion of patients not attaining treatment goals was high. Adherence with medication, as well as adequate management of blood glucose, hypertension and dyslipidaemia should be paramount in the management of patients with type 2 diabetes.

**Abstract #216**

**KNOWLEDGE ABOUT INPATIENT DIABETES MANAGEMENT: IMPACT OF AN EDUCATIONAL INTERVENTION IN NURSES AT THE UNIVERSITY HOSPITAL OF PUERTO RICO**

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**Objective:** To evaluate the knowledge about inpatient management of Diabetes Mellitus in registered nurses, and to determine the efficacy of an educational intervention to improve disease knowledge.

**Methods:** This is a prospective cohort study of Registered Nurses (RN) at the University Hospital of Puerto Rico. A questionnaire (pre-test) consisting of 15 questions based on general information about DM was administered. The instruments were developed by endocrinology fellows and revised and approved by endocrinology faculty. Themes tested in the questionnaire included: diabetes diagnosis and management, target glucose levels, insulin mechanism of action, and outcomes of uncontrolled diabetes in hospitalized patients. Based on the pretest evaluation, a conference regarding current guidelines
about inpatient management of hyperglycemia was given to RN participants. The questionnaire was repeated 6 months after the conference (post-test) to assess the efficacy of the educational intervention. Pre- and post-test scores were compared using paired t-tests.

**Results:** The study population consisted of 119 RN. The mean age for RN was 43.9 ± 11.01 years. Ten percent of subjects were males. The overall score for the pre-test and post-test for RN was 48.90% ± 14.81% and 55.35% ± 15.97%, respectively, showing a significant improvement in knowledge among RN (p < 0.001). Specifically questions testing insulin mechanism of action showed a significant increase in correct items in the pre and post-tests from 37.8% to 46.2% (p=0.005). Also questions about diabetic management and glucose targets resulted in a significant increase in correct items from 47.4% to 54.9%, in the pre and post-tests (p<0.001).

**Discussion:** The data of this study demonstrates a positive and significant impact in knowledge about inpatient DM therapy, with the educational strategies employed, in nursing staff at our institution. Areas that require special attention and improvement include the diagnosis of diabetes disease and outcomes of uncontrolled diabetes in hospitalized non-critically ill patients. These topics are essential in order to understand the importance of attaining adequate inpatient glycemic control and avoid complications.

**Conclusion:** An improvement in knowledge about DM management among RN at the University Hospital of Puerto Rico was achieved with the current educational intervention. Further strategies need to be established in order to reinforce knowledge in hospital staff, and deliver optimal care to patients with diabetes.

**Abstract #217**

**COMBINED PREDICTABILITY OF PHYSICAL ACTIVITY AND BODYWEIGHT ON HEALTH-RELATED QUALITY OF LIFE AMONG NIGERIAN TYPE 2 DIABETES MELLITUS**

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**Objective:** Physical inactivity and adiposity had been shown to increase the risk and progression of diabetes mellitus but its combine effect on Health-Related Quality of Life (HRQoL) among Type 2 Diabetes Mellitus (T2DM) is not well understood. This study examines the impact of physical activity (PA) and body weight on HRQoL among T2DM.

**Methods:** A cross-section of 119 participants’ PA was assessed using long form of International Physical Activity Questionnaire and was categorized as physically active or inactive. Their quality of life was assessed with Short Form-36 questionnaire. Their body weight and height were assessed. The t-test, Pearson’s correlation and regression analyses were performed.

**Results:** About 69% of the participants were physically active and 61.8% were overweight or obese. Role limitation due to physical health (RP) and role limitation due to emotional problems (RE) were the worst affected domains of HRQoL. The HRQoL decreases in all domains with increasing bodyweight. The HRQoL of physically active participants were better than physically inactive in all domains of HRQoL scale. The effects of PA persisted on HRQoL when the bodyweight was adjusted for. The HRQoL scores were better among physically active participants in all domains of normal weight and overweight/obese group. PA showed significant correlation with HRQoL in all domains with exception RE, emotional well-being and pain domains. Regression models showed that Physical activity remains a significant predictor of HRQoL.

**Conclusion:** This study confirms that physically active participants have better HRQoL than inactive patients, regardless of their bodyweight.

**Abstract #218**

**IS IT GOUT, CELLULITIS OR CHARCOT NEUROPATHIC OSTEOARTHRPATHY?**

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**Objective:** The prevalence of diabetes mellitus and its associated complications is growing. Charcot Neuropathic Osteoarthropathy is a relatively painless, progressive, and degenerative arthropathy of a single or multiple joints caused by underlying neurologic deficits. However it can sometimes present acutely and this can be a diagnostic challenge. We present a case of Acute Charcot Neuropathic Osteoarthropathy of the foot diagnosed after lack of response to treatment for cellulitis and/or Gout.

**Case Presentation:** A 61 year old woman with Type 2 Diabetes mellitus who presented to our clinic with a two week history of left foot swelling associated with erythema of her left great toe for one week. She also developed few blisters around her left toe. No complaints of pain. She denied any history of trauma or surgery on her feet. She had a past medical history of Gout, Diabetic Neuropathy, hypertension and stage 3 chronic kidney disease. Given her past history of gout with the possibility of associated
cellulitis she was placed on Colchicine and antibiotics, however her symptoms did not improve.

On physical examination, her left foot was diffusely edematous on the dorsum with erythema and blisters around the base of the great toe. Peripheral pulses were normal and neurologic examination using a 10g monofilament revealed loss of neuroprotective sensation bilaterally. Skin was intact with no signs of infection. Cardiovascular, respiratory and abdominal examination revealed no significant abnormalities.

Magnetic resonance imaging of her left foot showed severe destructive changes at the Lisfranc joint consistent with Charcot changes. She was referred to Podiatry where she was treated with rest, analgesics and a short fracture brace for her left foot.

**Discussion:** Diabetes is the leading cause of Charcot foot and presents a diagnostic and therapeutic challenge. The syndrome is characterized by bone and joint destruction leading to deformities. It usually presents with swelling, warmth and erythema that can be difficult to distinguish from infection and other causes of arthropathy like gout as seen in our patient. This can result in injudicious use of antibiotics and delayed treatment. A high index of suspicion is key to early diagnosis in a diabetic with peripheral neuropathy who presents with new-onset swelling, erythema, and increased warmth of the foot and ankle.

**Conclusion:** Suspicion of Charcot joint and early recognition are of utmost importance, since early treatment may prevent progressive deformity and secondary ulceration that may lead to abscess, osteomyelitis and amputation.

### Abstract #219

**PERITONSILLAR ABSCESS LEADING TO HYPEROSMOLAR HYPERGLYCEMIC STATE IN NON-DIABETIC PATIENT**

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**Case Presentation:** Hyperosmolar hyperglycemic state (HHS) is a relatively common endocrine emergency occurring as complication of DM, which can present as profound dehydration with marked hyperglycemia and neurologic impairment. While infection precipitating HHS is common in previously known diabetics, overwhelming infections can itself cause a rise in the blood sugars in patients with no known previous diabetes.

We report a case of 48 year old male without significant past medical history who presented in hyperosmolar hyperglycemic state from overwhelming sepsis due to tonsillar abscess. He presented to the hospital with worsening right sided face pain after failing outpatient antibiotic treatment. On examination he was found to have dry mucous membranes with exudates noted on the right tonsil and tender lymphadenopathy on the right side. On lab investigations he was found to have normal CBC with blood sugars of 1893 mg/dL, Serum Osmolality of 386, BHB was 3.52 with anion gap of 18 and normal bicarbonate level. His HbA1c was 17.2. The patient was treated with insulin drip and was taken off insulin after a few weeks once his infection cleared and his blood sugars normalized. Within a month his HbA1c normalized to 5.7.

His initial hospital stay was complicated by hypotension requiring vasopressor support and development of bilateral arterial emboli in lower extremities ultimately requiring below knee amputation of the right leg.

**Conclusion:** Hyperglycemia in critically ill patients is thought to be at least in part due to stress leading to release of counter regulatory hormones and increased insulin resistance. This condition has been shown to have increased mortality. It is also necessary to understand that hyperglycemia can present even in non-diabetic patients requiring insulin therapy as seen in the above mentioned case. Hence it is important that the blood sugars be frequently monitored in critically ill patients and be adequately controlled.

### Abstract #220

**SIMULATION USING STANDARDIZED PATIENTS FOR FOOT EXAMINATION IN DIABETES**

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**Objective:** Clinical simulation is a technique that enables training through the re-creation of some aspects of a real life clinical situation. It provides the opportunity for a hands-on experience in a supportive environment using standardized patients (SPs). SPs are trained to present a medical history and mimic physical signs in a standardized manner. In this project, we utilized SPs to teach healthcare providers the best practices for conducting foot care examinations on patients with diabetes. The ADA recommends that all patients with diabetes should have an annual comprehensive foot examination to identify the risk factors predictive of ulcers.

**Methods:** The 4 objectives of the Diabetes Foot examination workshop included: 1) identifying strategies for preventing foot problems in patients with diabetes, 2) recognizing appropriate diagnoses, 3) recommending suitable treatment in problems of the feet and 4) discussing methods for patient education to promote proper care of the feet. The learner completed a survey that assessed their
self-reported competency using measures established by NDEP and the self-assessment of comfort level and frequency with conducting foot exams and providing patient education. There was a brief didactic lecture followed by a hands-on experience with foot examination which was supervised by podiatrist. There were four SPs who had various grades of moulaged foot ulcerations. The learners completed a guided foot examination session with an SP and received handouts to reinforce the concepts covered. There was debriefing at the end which included facilitated discussion promoting reflection upon foot examination procedure and the learning experience.

**Results:** Fifty people attended the workshop and more than 90% reported that they gained knowledge which will help in the clinical practice and 94% reported that their competencies in foot examination improved

**Discussion:** Simulation education can help fill the gap in education and can be a useful tool in training healthcare teams. Evidence indicates that clinical skills acquired in simulation session translate into improved patient care practices and outcomes. The lifetime risk of a person with diabetes developing a foot ulcer may be as high as 25% and a comprehensive foot exam can identify high risk patients with diabetic neuropathy

**Conclusion:** Virtual case based simulated diabetes education intervention has been shown to improve diabetes management skills. Adding a new dimension of using SPs to reinforce the importance of foot care could improve examination skills in healthcare professionals and ultimately reduce foot problems and diminish the subsequent risk of diabetes-related lower-extremity amputations in patients with diabetes.

**Abstract #221**

**EMPHYSEMATOUS PYELONEPHRITIS IN A PATIENT WITH TYPE 2 DIABETES**

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Rutgers Robert Wood Johnson

**Objective:** To report a poorly controlled diabetic patient with multidrug resistant E.coli emphysematous pyelonephritis (EPN)

**Case Presentation:** A 44-year-old female with history of poorly controlled type 2 diabetes (T2DM) and previous E.coli pyelonephritis complicated by bacteremia presented with fatigue and abdominal pain. On the day before admission, she developed subjective fevers and chills. The patient denied dysuria, hematuria, and urinary frequency. Lab data on admission was significant for the following: positive urinalysis (nitrites +, leukocyte esterase +1, glucose 4+, protein +1, ketones +1), serum glucose 461 mg/dL, CO2 15.5 mEq/L, anion gap 28 mEq/L, lactate 8.6 mmol/L, hemoglobin A1C 14.4%, and WBC 7.8 thousand/ul. Patient had a temperature of 104 F, HR 150, BP 109/68. While in the ED, the patient’s blood pressure decreased to 86/58, requiring norepinephrine and vasopressin infusion. She was empirically started on Vancomycin, Zosyn, and Levaquin, of which Vancomycin and Zosyn were continued. The patient was also placed on an insulin infusion for concurrent mild DKA. Soon after admission to the ICU, the patient was noted to have increasing abdominal distention. A CT scan of the abdomen and pelvis was significant for emphysematous pyelonephritis and hydronephrosis of the left kidney. Urology services were consulted and the patient was managed with stent placement. Infectious disease was also consulted, as cultures demonstrated panresistant E. coli, and antibiotics were switched to ceftriaxone based on sensitivities. The DKA resolved and she was bridged to combination insulin therapy and transferred out of the ICU. The patient was later discharged home to complete 2 weeks of IV ceftriaxone infusions.

**Discussion:** EPN is a severe, gas-producing infection involving the renal parenchyma. E.coli accounts for the majority of infections, however Klebsiella,Proteus, Pseudomonas, and Streptococcus species have also been identified. Renal stones and diabetes are predisposing factors for EPN. Diagnosis is typically made by plain films of the abdomen and/or CT. The latter may be more useful as it can characterize any obstructing lesions and illustrate the extent of gas formation. Treatment includes aggressive fluid resuscitation and systemic antibiotics, as well as prompt surgical therapy to relieve obstruction.

**Conclusion:** Emphysematous pyelonephritis is a rare but potentially fatal disease and must be considered in the differential diagnosis of diabetics with infected urine, fever, and abdominal symptoms. This case emphasizes the need for early recognition and aggressive management, especially in patients with poorly controlled diabetes.
Abstract #222

DYSGLYCAEMIA AMONG HIV PATIENTS ON HIGHLY ACTIVE ANTIRETROVIRAL THERAPY IN KANO, NORTH WESTERN NIGERIA

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Objective: To determine the prevalence and factors associated with dysglycaemia among HIV patients treated on Highly active antiretroviral therapy (HAART) in Aminu Kano Teaching Hospital (AKTH), Kano, North western, Nigeria.

Methods: In a cross sectional study of 300 HIV patients at the AKTH Kano, we assessed the glycaemic parameters of study participants. The patients were evaluated as per HAART-treated and HAART-naïve groups and the results compared for the two groups. Fasting plasma glucose (FPG) was determined using glucose oxidase method after an overnight fast and WHO criteria was used to classify FPG < 6.0mmol/L (Normal), 6.0 - 6.9 mmol/L Impaired Fasting Glucose (IFG) and ≥ 7.0mmol/L as Diabetes Mellitus (DM).

Results: The prevalence of hyperglycaemia among HAART-exposed and HAART-naïve participants was 22% and 5.3% respectively, (p=0.001). DM was found among 12.7% HAART exposed participants vs 2.7% among HAART naïve, while IFG was found among 10.0% HAART exposed vs 4.7% among HAART naïve. Increased BMI (overweight and obesity), advanced age, prolonged duration of HIV diagnosis and HAART, hypertension, increased waist circumference and waist-hip ratio, increased CD4 cell counts, and elevated total cholesterol and triglyceride were found to be significantly associated with hyperglycaemia among HAART exposed participants (p<0.05). However only increased CD4 cells count was found to be independently associated with hyperglycaemia (OR 1.0, 95% CI 1.000-1.005, p=0.027).

Discussion: Hyperglycaemia (IFG and DM) was found to be more common among participants that were HAART exposed compared to HAART naïve. This could be due to the effect of the drugs that cause insulin resistance particularly Protease inhibitors in addition to the HIV inflammation which also alters glucose metabolism. It could also be indirectly related to obesity and increased waist circumference which are associated with insulin resistance. Raised CD4 cell count was found to be an independent predictor for the development of hyperglycaemia among participants exposed to HAART.

Conclusion: The use of HAART causes disturbances of glucose metabolism among HIV patients, the severity of which varies with prolonged therapy. Routine evaluation of glucose parameters among HIV patients on HAART is advised.

Abstract #223

DIABETES MEDICATIONS IN PATIENTS WITH LEFT VENTRICULAR ASSIST DEVICES: SAFETY AND EFFICACY

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Objective: Type 2 diabetes mellitus (DM) and congestive heart failure (CHF) are frequent co-morbidities. Among recent advances for patients who progress to end-stage left heart failure are left ventricular assist devices (LVAD). The safest and most efficacious method of blood glucose control in diabetics with LVADs is unclear, and data are now accruing regarding unforeseen negative cardiovascular effects related to the popular dipeptidyl peptidase-4 (DPP-4) inhibitors. Additionally, metformin seems to offer the most cardiovascular benefit of all diabetes medications yet is contraindicated in many patients with CHF.

Methods: We performed a retrospective chart review utilizing the Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) and our hospital’s electronic medical record. Patients were included if they had type 2 DM and underwent HeartMate II LVAD placement between 1/1/2008 and 12/31/2012. Data were collected at discrete time frames. Variables considered included survival, death from all causes, death from cardiovascular causes, re-hospitalization for any reason, severe hypoglycemia, length of stay, hemoglobin A1c, and six-minute walk time. Diabetes medications were grouped for analysis. Statistical analysis was performed using ANOVA and paired T-test. Statistical significance is determined at an alpha of 0.05.

Results: 56 patients were included in the study. Patients taking metformin prior to admission (N = 10) demonstrated 100% survival at 6 months compared with 92% of patients not taking metformin prior to admission (P value = 0.04). Re-hospitalizations were more prevalent among patients taking insulin alone or incretin-related agents alone compared with patients taking no medications (P value = 0.04). There was no difference in re-hospitalizations.
Abstract #224

A RANDOMIZED CONTROLLED TRIAL OF MOBILE PHONE INTERVENTION TO IMPROVE DIABETES CARE IN RURAL AREAS

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Objective: To determine the effect of mobile phone intervention on glycosylated haemoglobin (HbA1c) in type 2 DM patients living in rural areas of a low income country.

Methods: This randomized controlled trial was conducted in the Endocrinology Clinic from December 2013 to June 2014. A total of 440 patients in intervention and control groups were enrolled. Patients between 18-70 years of age, residing in rural areas, HbA1c ≥ 8.0% and having mobile phone were included. Intervention group patients were called on mobile phone after every 15 days for a period of 4 months. They were asked about the self-monitoring blood glucose, intake of medications, physical activity, healthy eating and were physically examined after 4 months. Control group was examined initially and after 4 months physically in the clinic without mobile phone contact. Data was analyzed using SPSS version 19. Baseline socio-demographic and clinical characteristics were compared using independent T-Test for quantitative variables, Chi-Square Test for categorical variables and Fischer exact test was applied to compare categorical variables. Baseline and endline clinical outcomes at the end of 4 months follow up were compared using paired T-Test for quantitative variables and Mcnemar Test for categorical variables.

Results: Patients in intervention group showed improvement (<0.001) in following diet plan from 17.3% at baseline to 43.6% at endline however the control group showed insignificant increase (p=0.522) from 13.6% at baseline to 15.9% at baseline. Multivariate analysis showed that intervention group (RR=3.09, 95% CI 1.33-7.33) and dietary restriction (RR=6.53, 95% CI 1.80-23.63) remained significant. Patient with Low Density Lipoprotein (LDL) levels of >100 mg/dl had significantly less chance of good HbA1C control (RR=0.20, 95% CI=0.04-0.87). Other variables (age, gender, socioeconomic status, region, education, hypertension, body mass index (BMI), taking medications and physical activity) remained insignificant.

Discussion: Strength of the study was that the communication with the patients was done by a Physician which provided confidence to the patients in sharing their problems. Intervention group had shown improvement in HbA1C and dietary restriction was significant. Patients with LDL levels of <100 mg/dl had significantly good chance of good HbA1C control. BMI and physical activity did not show any significant association.

Conclusion: Mobile phone technology in rural areas of a low income country was helpful in lowering HbA1C levels in intervention group through direct communication with the diabetic patients. Lowering LDL and following diabetic diet plan can reduce HbA1C in these patients and help in preventing future complications.

Abstract #225

THE EFFECTIVENESS OF AN INPATIENT HYPERGLYCEMIA MANAGEMENT EDUCATIONAL PROGRAM AMONG INTERNAL MEDICINE RESIDENTS

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Objective: The purpose of this study is to identify knowledge gaps in the management of inpatient hyperglycemia and diabetes mellitus among the internal medicine (IM) residents at the University Hospital of Puerto Rico. We also want to explore the effectiveness of this residents’ oriented educational program in their knowledge.

Methods: This is a prospective study of IM residents attending the University Hospital of Puerto Rico. A questionnaire (pre-test) consisting of 19 questions based on current inpatient management of hyperglycemia guidelines was administered to IM residents. The questionnaire was developed by the endocrinology fellows and revised and approved by an endocrinology
facilitate. The instrument included questions regarding inpatient management and glycemic targets, insulin mechanism of actions and management of acute glycemic complications. All residents were invited to participate in three subsequent lectures regarding current guidelines of inpatient management of hyperglycemia. Six months after the educational intervention, the residents were asked to take the same baseline questionnaire (post-test) to assess the efficacy of the educational intervention. Pre- and post-test scores were compared using paired t-tests.

**Results:** A total of 45 internal medicine residents participated in this study, of which 33.3% were male and the mean age was 27.8±2.0 years. The overall average score for the pre and post-questionnaires were 59.1% and 70.1% (p<0.01), respectively. Regarding the general management and glycemic target during hospitalization, the average scores for the pre and post-test were 55.9% and 68.2% (p<0.01). An improvement in scores was also seen between the pre and post questions regarding their knowledge of insulin mechanism of actions (71.7% vs. 81.7%, p=0.025).

**Discussion:** Although no significant improvement was observed on residents’ knowledge of acute diabetes complications, the number of items with correct answers on the inpatient management, glycemic targets and insulin mechanism of action categories increased significantly among residents, after their participation in the educational program. Whether still uncertain if these interventions may or may not have direct effect on clinical outcomes, efforts focusing on improving medical knowledge among residents must be encouraged.

**Conclusion:** Educational programs targeted to IM residents are effective in improving overall knowledge on inpatient hyperglycemia management. However additional interventions and strategies must be developed among trainees to encourage and promote their learning to ultimately impact the management of our patients.

**Abstract #226**

**BARIATRIC SURGERY RESTORES SOMATIC AND AUTONOMIC NERVE FUNCTION TOWARDS NORMAL IN OBESE PATIENTS WITH AND WITHOUT DIABETES**

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**Objective:** Somatic and autonomic nerve dysfunction are significant predictors of mortality in diabetes (DM). Reversal of nerve dysfunction is rare in DM. Bariatric surgery induces marked weight loss and ameliorates DM and related comorbidities. Cardiac and sudomotor autonomic dysfunction occur early in DM and prediabetes. Sweat glands are innervated by sympathetic C-fibers whose function is measurable through electrochemical activation in a process of reverse iontophoresis applied to hands and feet. Cardiac autonomic dysfunction is measureable using indices of heart rate variability. The aim of this study was to evaluate the impact of bariatric surgery on cardiac autonomic and sudomotor peripheral C-fiber function in obese subjects with and without Type 2 diabetes (T2DM), using sudorimetry, heart rate variability and other validated measures of nerve function.

**Methods:** Patients were evaluated at baseline, 4, 12 and 24 weeks after vertical sleeve gastrectomy (VSG) (24 subjects) or Roux-en-Y gastric bypass (RYGB) (11 subjects). All subjects were assessed using SudoscanTM of hands and feet, Neurologic Impairment Scores of lower legs (NIS-LL), time and frequency dependent cardiac autonomic function tests (QAFT), quantitative sensory tests (QST) for pressure, cold and warm perception thresholds and sural nerve conduction studies (NC-STAT).

**Results:** Thirty five patients completed 12 and 24-weeks follow-up. ESC of feet improved significantly (MANOVA) by 12 and 24 weeks (Baseline=61.73±2.55 vs 12-weeks=67.01±2.77 vs 24-weeks=70.76±2.71, p<0.0001) ESC of hands improved significantly by 24 weeks (Baseline=56.38±2.80 vs 24-weeks=62.01±2.71, p<0.05). NIS-LL scores and QAFTs improved significantly by weeks 12 and 24, but other measures of somatic nerve function did not. Weight, body mass index, and percent body fat also improved significantly. T2DM patients had abnormal ESC at baseline and showed greater improvement of feet ESC (mean difference of +17.67 ESC units at week 24) when compared to non-T2DM patients (mean difference of +4.9 ESC units at week 24). No differences were observed in the rate of improvement of sudomotor or cardiac autonomic function when comparing the 2 types of surgeries. On linear regression analysis ESC of feet correlated significantly with % body fat but not with other measures of metabolic function.

**Discussion:** This study shows that bariatric surgery can potentially restore towards normal both cardiac autonomic and peripheral C-fiber dysfunction in DM, thereby impacting morbidity and mortality.

**Conclusion:** This is the first demonstration of rapid improvement of autonomic and somatic C-fiber dysfunction after bariatric surgery.
Abstract #227

THE EFFECT OF INNER SEED PADDLE OF WALNUT ON BLOOD GLUCOSE

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Objective: The effect of aqueous alcoholic extract of inner seed paddle of walnut on blood glucose level of mice was assessed in this study.

Methods: Hydro-alcoholic extract of inner seed paddle of walnut was obtained by mixing dried and powdered inner seed paddle of walnut with 96% ethanol over a week. The solution was filtered and evaporated under vacuum. The residue was then kept in the fridge to be used in the experiment. The study was conducted using mice. The mice were divided into 5 groups.
1. Healthy (control) given dose of saline water
2. Diabetic (control) given dose of saline water
3. Diabetic given dose of 1000 mg/Kg of extract
4. Diabetic given dose of 2000 mg/Kg of extract
5. Diabetic (treatment control) given dose of 10 mg/Kg of Glibenclamide Diabetes mellitus was induced by single administration of Streptozotocin (STZ) 200 mg/Kg, IP. After daily administration of single dose, the blood glucose level was measured at 0, 1, 3, 5 and 24 hours. Blood glucose level was measured by extracting 0.25 to 2.0 mL of blood and analyzing using the BIonime Right TS GM300 instrument. The data obtained was evaluated and analyzed statistically by variance and using ANOVA.

Results: Administration of a single dose 1000mg/Kg of extract revealed significant reduction of blood glucose level after 1, 3, and 5 hours. Comparatively, the glibenclamide treated group showed significant reduction of glucose level only at 1 and 3 hours.

Discussion: The hydro-alcoholic extract of inner seed paddle of walnut has shown a significant decrease in diabetic mice. The effect was seen even after 1 hour after administration of the extract. The effect of this naturally and plant-based product is comparable to the drug Glibenclamide.

Conclusion: This study supports the claims from traditional medicine about the usefulness of inner seed paddle of walnut on blood glucose reduction. Identification of the mechanism of the action of the extract on reduction of blood glucose requires more focused experiments such as measurement of blood insulin content, glucose content in urine, and comparison of the extract with other available drugs on the market. Furthermore, it is important to set up further experiments in order to identify the active Ingredient(s), chemical nature of the extract as well understanding its effect on the pancreatic islets.

Abstract #228

FOOT CARE IN DIABETES: KNOWLEDGE & PRACTICE PATTERN AMONG URBAN & SUBURBAN BANGLADESHI TYPE 2 DIABETIC SUBJECTS.

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Objective: To evaluate and compare knowledge & practice pattern on foot care among urban and suburban Bangladeshi T2DM subjects.

Methods: Cross-section observational study (Jan- June 2014). 148 Bangladeshi T2DM subjects [men 48.6%, women 51.4%, aged >18 yrs, duration of DM>5yrs,] were selected randomly from OPD in United Hospital Ltd, MARKS Medical College & Hospital (urban) and primary care centre in Gazipur (suburban). With consent, set-written questions were asked by investigator by face-to-face interview. Statistical analysis was done with IBM SPSS ver 20. Outcome: evaluate and compare knowledge & practice pattern on foot care in urban and suburban diabetic subjects.

Results: 78(52.7%; men=58.9%, women=41.1%) and 70(47.3%; men=37%, women=63%) lived in urban & suburban respectively. Urban versus suburban subjects had age (yrs):50.06±10.90 vs 51.78±10.06, p 0.32; diabetes duration (yrs):8.95±4.08 vs 8.43±3.59, p 0.41; BMI (kg/m2):25.81±3.64 vs 25.54±3.60, p 0.64; HbA1c%:8.23±1.42 vs 8.53±1.52, p 0.23; diabetic foot 57.7% & 52.86% [p 0.55] [onychomycosis(25.6%), paronychia(20.7%)]; Smoking [p0.23], monthly expenditure [0.15] & educational status [0.34] were not different.

Knowledge & practice pattern on foot care (urban vs suburban): Good glycemic control:know=93.6% vs 91.42%(p0.61), practice=79.5% vs 70%(p0.18); avoid smoking :know=100% vs 98.6%(p0.3), practice=79.5% vs 78.5%(p0.89); observe daily: know=79.5% vs 78.6%(p0.89), practice=35.9% vs 25.7%(p0.18); clean warm water-soap:know=69.2% vs 41.4%(p0.001), practice=17.9% vs 4.2%(p0.009); dry gently after clean:know=74.4% vs 51.4%(p0.004), practice=58.9% vs 37.1%(p0.008); skin soft:know=87.2% vs 72.8%(p0.03), practice=52.6% vs 48.6%(p0.63); toe cleft dry:know=35.9% vs 38.6%(p0.74), practice=26.9% vs 21.4%(p0.48); nail cut after bath:know=26.9% vs 31.4%(p0.55), practice=12.8% vs 20%(p0.24); cut nail straight:know=34.6% vs 42.8%(p0.30), practice=29.5% vs 40%(p0.18); avoid walk barefoot:know=56.4% vs 47.1%(p0.26), practice=38.5% vs 21.4%(p0.03); well fit shoe:know=87.2% vs 81.4%(p0.34), practice=80.7%
Discussion: Knowledge & practice about foot care were not satisfactory and did not differ significantly between urban & suburban diabetic subjects except for cleaning-gently drying.

Conclusion: Foot care knowledge & practice pattern of urban and suburban Bangladeshi diabetic subjects were not much different and satisfactory.

Abstract #229

AN INTEGRATIVE REVIEW OF LITERATURE OF REGULAR R U-500 INSULIN IN CONTINUOUS SUBCUTANEOUS INSULIN INFUSION

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Objective: To conduct an integrated review of the literature on best practice approaches for patients with type 2 diabetes and severe insulin resistance who require insulin R U-500 in a continuous subcutaneous insulin infusion (CSII).

Methods: The research questions is: Is the use of insulin R U-500 safe and helpful in reaching optimal glycemic control in patients diagnosed with type 2 diabetes and severe insulin resistance? The second step included searching for the clinical evidence in various databases. The author searched for articles published from the early 2000s until 2014 to allow for a broad depth of information, since the literature amount in this subject is limited. The third step included the analysis, synthesis and evaluation process of the literature.

Results: The results showed that multiple studies have been published in regards to the use insulin R U-500. The initial search found approximately 6,000 studies about diabetes management and the use of insulin R U-100 and insulin R U-500. A subset search showed 120 articles that mentioned insulin R U-100 and insulin R U-500 in a CSII in patients diagnosed with diabetes type 1 or type 2. After reading titles and abstracts, 89 studies were eliminated due to not meeting the inclusion criteria for this project. The articles found in the literature addressing the use of insulin R U-500 in CSII included 31 studies, 18 of which were review studies. The sample population in all the studies was patients diagnosed with type 2 diabetes and severe insulin resistance, injecting more than 200 units of insulin R U-100 daily via MDIs or through a CSII.

Discussion: The application of insulin R U-500 via a CSII has been implemented by endocrinologists, and supported by published studies, conferences, and experts’ opinions, but this innovation continuous to be unfamiliar to other healthcare providers. All the studies in this literature review were from different points of view and levels of evidence. The studies reported that implementing insulin R U-500 in a CSII improves the discomfort associated with the MDIs and increases adherence to treatment. In all the studies the patients decreased the volume of insulin infused daily. Patients improved their glycemic control as demonstrated by a decrease in their HbA1c. The side effects associated were weight gain and mild hypoglycemia.

Conclusion: Using insulin R U-500 in a CSII is clinically practical with minimal side effects. Hypoglycemia and weight gain can happen with any insulin. The use of insulin R U-500 in a CSII must be managed by healthcare providers at the endocrine setting, but primary care providers must be aware of its clinical value.

Abstract #230

BULLOUS PEMPHIGOID-ADVERSE REACTION TO LINAGLIPTIN (TRADJENTA): A CASE REPORT

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Icahn School of Medicine at Mount Sinai

Objective: To report a patient with Diabetes Mellitus (DM) type 2 who developed Bullous Pemphigoid (BP) as an adverse drug reaction to Linagliptin.

Case Presentation: An 82-year old male with type 2 DM for 3 years was treated with glimepiride 1 mg/day. Linagliptin 5mg/day was prescribed while his HbA1C was 7.6. His other medications were Crestor and vitamin D supplements. Four weeks later he was admitted to the hospital for 4 days with generalized erythematous vesicular bullous eruption with ulceration. On admission, the patient had no fever, no mucosal involvement, no adenopathies or increased eosinophil level. On examination, Nikolsky’s sign was not present and the skin eruption was located on the trunk, upper and lower extremities with ulcerations which suggested BP. This was confirmed by skin biopsy which shows sub epidermal bullous dermatosis and ulceration. Positive direct immunofluorescence study shows 2+ linear C3 and 1+ linear IgG at the basement membrane zone (BMZ). Results of full blood cell count, liver and renal function studies were unremarkable. His condition was improved after withdrawal of Linagliptin and topical treatment with clobetasol. There was complete resolution of symptoms after 3 weeks, and follow up 6
months post discharge shows no recurrence of symptoms. **Discussion:** Dipeptidyl peptidase IV inhibitors have been known to cause adverse skin reactions and there are case reports of Vidaagliptin and Sitagliptin induced BP. Linagliptin, which is frequently prescribed is relatively safe and cutaneous adverse reactions are uncommon. BP is the most common sub-epidermal autoimmune bullous disease which is characterized by development of auto antibodies directed against the cutaneous BMZ. BP mainly affects elderly patients and can cause considerable morbidity. Several mechanisms have been postulated for the development of gliptins-induced BP. (a) Inhibition of DPP-IV was shown to enhance the CCL11/Eotaxin-mediated recruitment of eosinophils into the dermis and increased the homing of skin-targeting Sezary syndrome lymphocytes. (b) Gliptins have pluripotent biological action and can modify the immune response or alter the antigenic properties of the epidermal BMZ. According to the Naranjo ADR probability scale, this patient has a score of 5 which suggests “probable” reaction. The temporal relationship between the initiation of Linagliptin and the development of BP and the prompt resolution of bullae after drug discontinuation suggest that the BP was drug induced. **Conclusion:** To the best of our knowledge this is the first case report of BP induced by Linagliptin. Physicians should be aware of possibility of this adverse effect of Linagliptin.

**Abstract #231**

**PUMP THERAPY SUPERIOR TO FURTHER INTENSIFICATION OF MULTIPLE DAILY INJECTION THERAPY IN TYPE 2 DIABETES**

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1. Medtronic, Inc., 2. SUNY Upstate Medical University, 3. University of Caen Côte de Nacre Regional Hospital Center

**Objective:** Therapy intensification in poorly-controlled type 2 diabetes often involves insulin. A randomized controlled trial, OpT2mise (NCT01182493), was conducted to compare pump therapy (CSII) with multiple daily injections (MDI).

**Methods:** Subjects with poor glycemic control (N=495) on MDI were enrolled into a run-in period for dose optimization, after which those with A1Cs of 8-12% (N=331) either continued MDI (n=163) or switched to CSII (n=168) for 6 mo. Glycemia was evaluated with 2 blinded continuous glucose monitoring (CGM) studies and with periodic A1C measurements. Treatment satisfaction was assessed via questionnaires. Response dependence on autoimmune status and endogenous insulin were evaluated by stratification according to pre-randomization anti-GAD Ab concentrations (<1 or ≥1 U/mL) and C-peptide concentration quartiles (using cutoff values of 156, 310, and 569 pmol/L).

**Results:** At baseline, mean A1C was 9% in both groups. By 6 mo, the change in A1C (ΔA1C) was -1.1±1.2% (CSII) and -0.4±1.1% (MDI), for a between-group difference of -0.7% in favor of CSII (95% CI, -0.9 to -0.4%, p<0.001). Patients in the CSII group were 1.9-fold more likely to achieve a 6-mo A1C <8% than those in the MDI group (p<0.001). Six-month total daily insulin doses were 97±56 U (CSII) and 122±68 U (MDI), p<0.0001. Compared to the first (pre-randomization) CGM study, 24-hour sensor glucose (SG) values at 6 months were significantly lower in CSII group than in the MDI group (between-group difference of -17.1 mg/dL, p<0.05); the CSII group also spent 169 fewer minutes per day in hyperglycemia >180 mg/dL (p<0.001) with no difference in exposure to SG <70 mg/dL. Greater A1C decreases at 6 months were significantly associated with improved treatment satisfaction in the CSII group (p<0.05) but not in the MDI group. There was no significant difference in ΔA1C between patients with (n=27) or without (n=135) anti-GAD antibodies in either group, and no association between ΔA1C and C-peptide concentration quartile in either group (p>0.1 for each).

**Discussion:** For the ~30% of patients with type 2 diabetes who are unable to reach A1C targets with MDI, CSII offers significant glycemic and treatment satisfaction benefits while allowing for decreased insulin use. **Conclusion:** OpT2mise has demonstrated that switching to CSII from optimized MDI therapy allows many patients with poorly-controlled type 2 diabetes to decrease their A1C values and reach A1C goals. The benefits were achieved with no increased exposure to hypoglycemia, 20% less insulin usage, and improved treatment satisfaction. Benefits were independent of baseline C-peptide and anti-GAD antibody concentrations.

**Abstract #232**

**EFFECT OF LIRAGLUTIDE ON POST PRANDIAL GLUCAGON, CARBOHYDRATE INTAKE AND ON INFLAMMATION IN PATIENTS WITH TYPE 1 DIABETES**

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**Objective:** We have recently shown that liraglutide, a GLP-1 receptor agonist, improves diabetic control in patients with type 1 diabetes through reduction in glycemic levels...
Abstract #233

PRE-IMPAIRED GLUCOSE TOLERANCE, A RISK FACTOR FOR DIABETES PROGRESSION IN ASIAN INDIANS

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Objective: The aim of this study is to evaluate the risk of pre-impaired glucose tolerance (pre-IGT) in the progression of diabetes in Asian Indians.

Methods: Thirty two patients were randomized into two groups, one of whom was treated with liraglutide 1.8 mg daily and the other with placebo for 12 weeks.

Results: HbA1c fell by 0.43% in the liraglutide group with a reduction in the insulin dose by 20% while it was reduced by 0.3% in the placebo group without any change in insulin dose. C-peptide concentrations were non-detectable both at the beginning and at the end. There was no significant change in fasting levels of glucagon following 12 weeks of treatment while there was a significant increase in fasting GLP-1 and GIP concentrations in the liraglutide group by 19±6% and 15±6% (P<0.05). Before start of interventions, the consumption of a high fat and high carbohydrates (HFHC) meal, induced a significant increase in plasma glucagon levels in both study groups. At the end of 12 weeks, there was in increase by 35±7% (P=0.018) in the liraglutide group compared to baseline. This was associated with lower glucose excursion by 21±8% (P=0.017) at 12 weeks while there was no significant change in glucose excursions in the placebo group. In addition, carbohydrate intake fell, both as total quantity by 30±5% (from 153±18 grams to 107±15 grams, p<0.05) and as the number of daily helpings (from 3.5 to 3 / day). Liraglutide treatment for 12 weeks induced a significant reduction in basal plasma concentration of CRP, FFA and endotoxin by 19±8%, 21±5% and 24±6%, respectively (P<0.05) and in basal mRNA expression of IL-1β, JNK-1, and SOCS-3 in peripheral blood mononuclear cells (MNC) by 22±7%, 19±6% and 23±6%, respectively (p<0.05) as reported. There was no change in these parameters in the placebo group.

Conclusion: We conclude that the beneficial effects of liraglutide on glycemia in patients with type 1 diabetes are due to marked reductions in post prandial concentrations of glucagon and carbohydrate intake. In addition, the anti-inflammatory actions may also contribute to insulin sensitivity and glucose disposal.

Abstract #234

SIMULTANEOUS REDUCTION IN BOTH A1C AND BODY WEIGHT WITH CANAGLIFLOZIN VERSUS GLIMEPIRIDE IN METFORMIN-TREATED PATIENTS WITH TYPE 2 DIABETES OVER 104 WEEKS

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Objective: Canagliflozin (CANA), a sodium glucose co-transporter 2 (SGLT2) inhibitor developed to treat type 2 diabetes mellitus (T2DM), lowers the renal threshold for
glucose and increases urinary glucose excretion, leading to decreased plasma glucose levels and a net caloric loss. Glimepiride (GLIM) is a sulfonylurea that stimulates insulin secretion. In patients with T2DM on background metformin (MET), CANA showed durable glycemic improvement and body weight (BW) reduction versus GLIM over 104 weeks; this post hoc analysis evaluated the proportion of patients who had decreases in both A1C and BW with CANA versus GLIM.

Methods: In this randomized, double-blind study, patients with T2DM (N=1,450; mean baseline A1C, 7.8%; BW, 86.6 kg) received CANA 100 or 300 mg or GLIM as add-on to MET over a 52-week core period, followed by a 52-week extension (n=1,050). Using individual patient data, the proportion of patients achieving both change from baseline in A1C <0% and BW <0 kg was assessed at Weeks 52 and 104.

Results: At Week 52, least squares (LS) mean changes from baseline in A1C were –0.82%, –0.93%, and –0.81% with CANA 100 and 300 mg and GLIM, respectively; LS mean percent changes in BW were –4.2%, –4.7%, and 1.0%. At Week 104, LS mean changes from baseline in A1C were –0.65%, –0.74%, and –0.55% with CANA 100 and 300 mg and GLIM, respectively; LS mean percent changes in BW were –4.1%, –4.2%, and 0.9%. The proportion of patients with A1C reductions at Week 52 was 83.9%, 86.9%, and 81.9% with CANA 100 and 300 mg and GLIM, respectively; 84.1%, 87.3%, and 32.3% had reductions in BW. A greater proportion of patients had reductions in both A1C and BW at Week 52 with CANA 100 and 300 mg versus GLIM (72.4%, 78.5%, and 26.8%, respectively; differences [95% confidence interval (CI)] of 45.6% [39.7, 51.5] and 51.7% [46.0, 57.3]). The proportion of patients with A1C reductions at Week 104 was 75.7%, 79.7%, and 72.6% with CANA 100 and 300 mg and GLIM, respectively; 83.1%, 85.2%, and 34.6% had reductions in BW. A greater proportion of patients at Week 104 had reductions in both A1C and BW with CANA 100 and 300 mg versus GLIM (65.5%, 71.1%, and 26.8%, respectively; differences [95% CI] of 38.7% [32.6, 44.7] and 44.3% [38.4, 50.2]). At Week 104, the overall incidence of adverse events was 73%, 78%, and 78% with CANA 100 and 300 mg and GLIM, respectively. The incidence of documented hypoglycemia (<70 mg/dL) at Week 104 was lower with CANA 100 and 300 mg versus GLIM (7% and 8% vs 41%).

Conclusion: CANA provided greater attainment of reduction in both A1C and BW compared with GLIM at 52 and 104 weeks and was generally well tolerated in patients with T2DM as add-on to MET.

Abstract #235
LONG-TERM SAFETY AND EFFICACY OF REPEATED APPLICATIONS OF CAPSAICIN 8% PATCH (QUTENZATM) IN PAINFUL DIABETIC PERIPHERAL NEUROPATHY: PACE STUDY

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Objective: PACE assessed the safety and efficacy of repeated capsaicin 8% patch applications plus standard of care (SOC) versus SOC alone over 52 weeks in painful diabetic peripheral neuropathy (PDPN). The Norfolk QOL-DN scale was utilised to assess any adverse functional consequences of repeat capsaicin 8% patch applications reflected in reduced quality of life and sensory testing, including the Utah Early Neuropathy Scale (UENS), was performed to identify changes in sensory function or symptoms of early neuropathy that may be associated with such treatment.

Methods: This open-label, 52-week study randomised patients with painful, distal, symmetrical, sensorimotor polyneuropathy due to diabetes, glycosylated haemoglobin ≤9%, and numeric pain rating scale ≥4, to capsaicin 8% patch 30 min plus SOC, capsaicin 60 min plus SOC or SOC alone. Patients received up to seven applications. The primary endpoint was change from baseline to end of study (EoS) in Norfolk QOL DN total score. Secondary endpoints were UENS score, sensory perception testing, Brief Pain Inventory-Diabetic Neuropathy (BPI-DN) 24 hr average pain, ≥30% reduction in BPI-DN average pain, BPI-DN pain severity and interference indices.

Results: In total, 468 patients with mean pain 5.6 and mean Norfolk QOL-DN score 41.4 were randomised to capsaicin patch 30 min plus SOC (n=156), capsaicin 60 min plus SOC (n=157) or SOC alone (n=155). The incidence of adverse events was 73%, 78%, and 78% with CANA 100 and 300 mg and GLIM, respectively. The incidence of documented hypoglycemia (<70 mg/dL) at Week 104 was lower with CANA 100 and 300 mg versus GLIM (7% and 8% vs 41%).

Conclusion: CANA provided greater attainment of reduction in both A1C and BW compared with GLIM at 52 and 104 weeks and was generally well tolerated in patients with T2DM as add-on to MET.
Objective: 1. SAIMS Medical College, 2. MGM Medical College
Subodh Banzal, MD, DM, FRCP, Sonal Banzal, MBBS

**DRUGS IN A 24 WEEK RANDOMIZED STUDY CONTROLLED ON ORAL HYPOGLYCEMIC WITH TYPE 2 DIABETES INADEQUATELY HUMAN PREMIX INSULIN IN PATIENTS COMPARISON OF INSULIN GLARGINE WITH**

Abstract #236

Substantial safety issues. The capsaicin 8% patch in PDPN relieved pain without any functional deterioration in quality of life and improved pain relief versus SOC in PDPN.

**Discussion: Repeated application of the capsaicin 8% patch over 52 weeks was well tolerated with no loss of sensation, no functional deterioration in quality of life and improved pain relief versus SOC in PDPN.**

**Conclusion: PACE showed that long-term treatment with the capsaicin 8% patch in PDPN relieved pain without any substantial safety issues.**

Abstract #236

**COMPARISON OF INSULIN GLARGINE WITH HUMAN PREMIX INSULIN IN PATIENTS WITH TYPE 2 DIABETES INADEQUATELY CONTROLLED ON ORAL HYPOGLYCEMIC DRUGS IN A 24 WEEK RANDOMIZED STUDY**

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1. SAIMS Medical College, 2. MGM Medical College

**Objective:** Type 2 diabetes is a progressive disorder of β-cell dysfunction. A majority of patients with a longer duration of diabetes remain poorly controlled with oral agents, and use of insulin, which could improve glycemic control, is often long delayed and is not aggressive enough. Glargine is a long acting insulin analogue with a more favorable 24-hr time action profile than long or intermediate acting insulin preparations, can be especially suited in this condition. With this study our aim was to compare the safety and efficacy of the long acting analog insulin glargine and human premix insulin in patients with type 2 diabetes who were previously treated with oral hypoglycemic drugs alone but were inadequately controlled.

**Methods:** A total of 750 subjects with type 2 diabetes who were receiving oral hypoglycemic drugs for diabetes control were randomized to receive insulin glargine once daily (n=370) or human premix insulin twice daily (n=380) for 24 weeks in an open label study, tertiary centre study. Doses were adjusted systematically to obtain target fasting glucose <100 mg/dl. Outcomes included fasting blood sugar, HbA1C levels, and change in weight and insulin dose from study start to end. The variables were tested using Chi square test and p values were calculated between the two groups.

**Results:** At the start of the study, age range was 30-70 years, BMI was 26.48 ± 6.3 kg/m and HbA1C was 11.9 +/- 3.1% for both groups. The mean change in HbA1C from baseline to endpoint was similar in the insulin glargine group (-3.0 ± 1.68%) and the human premix insulin group (-2.89 ± 1.79%) P value = 0.3861. The symptomatic hypoglycemic episodes were greater with human premix insulin than with glargine (significant level = 0.00002). Subjects in the insulin glargine group experienced less weight gain than those in the premix human insulin group (0.4 v/s 1.4 kg, P<0.0001).

**Conclusion:** In patients with type 2 diabetes, once daily bed time insulin glargine is as effective as twice daily human premix insulin in improving and maintaining glycemic control. In addition, insulin glargine provides a lower risk of symptomatic hypoglycemia and less weight gain compared with human premix insulin. The treatments were associated with similar reductions in fasting glucose and HbA1C levels.

Abstract #237

**TYPE 2 DIABETES AND CARDIOVASCULAR DISEASE RISK: AN AGE CUTOFF TO INITIATE STATINS WITHOUT A BASELINE LIPOID PROFILE**

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Colombo South Teaching Hospital

**Objective:** Type 2 Diabetes is associated with 2-4 fold increased cardiovascular disease (CVD) risk. Intensive multiple risk factor control approach has shown to be beneficial in preventing cardiovascular disease in patients with Type 2 Diabetes. The aim of this study was to determine an age cut-off for initiation of statins in patients with Type 2 Diabetes who do not have baseline CVD.

**Methods:** A descriptive cross sectional study conducted in a tertiary care hospital in Sri Lanka. Sixty one males and sixty one females with newly diagnosed diabetes, aged between 30 to 74 years, who did not have prior cardiovascular disease and were not on any lipid lowering agents, were recruited to the study. Sample size was calculated using PS software for power and sample size calculation with: a value = 0.05, power = 0.9, regression slope = 0.388, SD of the dependent variable = 12, SD of independent variable = 12. Ten year CVD risk was calculated using Framingham’s cardiovascular risk score. Transition from low to moderate risk was set at ten year CVD risk of 10% and from moderate to high risk at 20%.

**Results:** Mean age of the study population was 50.6 ± 11.5 years. This was 51.8 ±12 years for males and 49.4 ±10.6 years for females. The mean 10-year CVD risk for the total population was 15%, and this was 16.4% and 13.6% for
males and females respectively. Both males and females showed CVD risk variation with age, which was stronger in females than males (i.e. 74% in females 51% in males). The age transition from a low to moderate CVD risk at age 47 in males and 46 in females. Use of an age cut off of 47 for males had a sensitivity of 78% and a specificity of 62%. In females an age cut off of 46 had a sensitivity of 97% and a specificity of 62%. Similarly age transition from moderate to high risk occurred at 55 years for both sexes. This showed sensitivity and a specificity of 82% and 79% in males and 78% and 90% in females respectively.

**Discussion:** Use of a risk cutoff of 10% ten year CVD showed a higher sensitivity in females than in males. When a cutoff of 20% used it increases specificity in both sexes but decreases sensitivity for females than using a cutoff of 10%. However, we recommend using the lower cut off of 10% ten year CVD to initiate statins since it allow preventing more CVD events in Type 2 Diabetes.

**Conclusion:** In patients with Type 2 diabetes who do not have baseline CVD, initiation of lipid lowering therapy irrespective of lipid profile can be considered at 47 years for males and 46 years for females in the studied population, where the transition from low to moderate risk occurs (i.e. > 10% CVD risk).

**Abstract #238**

ABSTRACT WITHDRAWN

**Abstract #239**

**EFFECTIVENESS OF ONLINE MEDICAL EDUCATION AT IMPROVING TYPE 2 DIABETES MANAGEMENT**

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1. Medscape Education, 2. Mount Sinai School of Medicine

**Objective:** The standards of care for type 2 diabetes (T2D) management are continuously evolving to reflect new clinical data. Published in 2013, the AACE Comprehensive Diabetes Management Algorithm Consensus Statement provided an updated framework for the comprehensive management of patients with T2D. We sought to determine if an online educational intervention could improve the knowledge and understanding of internists about the place of modern oral antihyperglycemic agents in T2D management, according to recent guideline updates.

**Methods:** The continuing medical education (CME) activity was developed as an online video-based activity with leading experts in T2D. The educational effect was assessed using a linked pre/post-assessment study design that separated learners into 3 categories: improved, reinforced, and unaffected. For all questions combined, the McNemar’s chi-squared test was used to assess the difference between the pre- and post-assessment score. P values <.05 are statistically significant. Cramer’s V was used to calculate the effect size. The activity launched online on January 21, 2014 and data were collected for 64 days.

**Results:** A total of 427 internists completed all pre- and post-assessment questions during the study period and were included in the analysis. Comparison of individually linked pre-assessment question responses to the respective post-assessment question responses demonstrated improvement (n = 427; P<.05). Correct responses on post-assessment questions were up to 101% higher after CME, with an overall large effect size of 0.89. While only 129 (30%) learners answered all 4 questions correctly on the pre-assessment, 278 (65%) answered them all correctly on the post-assessment.

**Discussion:** For internists who participated in the CME activity, improved understanding of the most current recommendations and strategies involving oral antihyperglycemic agents in patients with T2D demonstrates the impact of the intervention. These results could be applied to future educational activities to help guide strategies for designing education in the area of T2D and to determine future educational needs related to T2D management.

**Conclusion:** This study demonstrates the success of a targeted educational intervention and access to the right physician audience (those at the forefront of diabetes care) on improving the knowledge and understanding of internists on the place in therapy of modern oral agents to treat T2D according to recent guideline updates. The large sample size of physicians included in this study and the statistically significant improvements demonstrate the benefits of educating a large audience base with aptly designed educational activities using adult-learning principles.

**Abstract #240**

**IMPROVED GLYCEMIC CONTROL UTILIZING BASAL BOLUS INSULIN DELIVERY WITH THE V-GO® DISPOSABLE INSULIN DELIVERY DEVICE IN THE LONG-TERM CARE SETTING**

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**Objective:** Various diabetes therapies and insulin delivery systems are being used to improve glycemic control and satisfaction in patients with type 2 diabetes (T2DM). Glycemic variability and adequate mealtime dosing still
present a significant challenge to both patients and staff in the long-term care (LTC) setting. V-Go provides insulin via a continuous pre-set basal rate and on-demand bolus dosing that simplifies the administration and management of insulin therapy. To assess whether introducing V-Go in patients requiring basal bolus insulin therapy in the LTC setting can improve glycemic control and reduce glycemic fluctuations. 

**Methods:** A retrospective chart review evaluated the effect of introducing V-Go in 4 patients in the LTC setting. Daily blood glucose (BG) readings were obtained by nursing staff at up to 4 time points (8 AM, 11 AM, 4 PM, and 9 PM) at the same time each day for 31 days pre- and 31 days post- V-Go initiation. Efficacy variables included proportion of time in euglycemia (100 mg/dl - 200 mg/dl), change in daily BG, and change in basal bolus insulin delivery.

**Results:** Patients had a mean age of 79 years and were on existing insulin therapy regimens. Among all patients, the percentage of time spent in euglycemia pre-V-Go was 45.1% (range 36.1% - 50.5%) and during V-Go was 56.2% (range 39.5% - 76.6%). Initiation of V-Go also resulted in a reduction of high blood glucose readings. Pre-V-Go mean BG (SD) was 198 mg/dL (10.54) and Post-V-Go was 176 mg/dL (34.91), corresponding to a calculated A1C change from 8.53% to 7.76%. The mean time spent above 200 mg/dl was 47.4% (range 41.5% - 60.7%) pre-V-Go versus 29.7% (range 2.4% - 51.6%) with V-Go. No patient in either cohort had a BG measurement below 50 mg/dl. Mean BG at 8 AM changed from 134.7 to 147.6 mg/dl, 11 AM from 235.6 to 214.4 mg/dl, 4 PM from 194 to 165.6 mg/dl, and 9 PM from 215.6 to 176.3 mg/dl. There was a 7 unit/day (or 9%) reduction in total daily insulin dose. The basal: bolus insulin ratio was 64:36 pre-V-Go and changed to 46:54 with V-Go, more closing aligning with an appropriate distribution of basal bolus insulin therapy.

**Discussion:** Use of V-Go in the LTC setting in patients with type 2 diabetes requiring insulin therapy demonstrated favorable changes in glycemic control and time in the target euglycemic range.

**Conclusion:** Given these findings additional studies are needed to evaluate V-Go in patients receiving insulin in the LTC setting.

**Abstract #241**

**TECHNICAL PITFALLS OF INSULIN PUMPS INTERNAL CLOCKS: AN EXAMPLE OF AN AM-PM GLITCH**

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**Objective:** The internal clocks of commercially available insulin pumps do not adjust time automatically, nor are they wireless connected to enable GPS synchronization. For correct insulin delivery per an insulin pump, the pump’s time settings must always be current. Otherwise, potential dosing errors may arise if the pump’s time setting is not correct. We report a case of a patient with type 1 diabetes (T1DM) who incorrectly set up the pump’s time, switching the AM-PM formats. Fortunately, no harm resulted from this potentially serious glitch.

**Case Presentation:** A 28-year-old female with T1DM recently started on an insulin pump was seen for a routine follow up visit. When the nursing staff attempted to download her pump to the clinic’s computer, synchronization failed, despite changing the pump’s battery. It was then noted that the pump’s time was 4:42 AM, which the actual time was (obviously) 4:42 PM. It was then speculated that this glitch could be due to the incorrect pump’s time setting. After correcting the setting, by flipping the AM-PM modes, synchronization occurred. The patient then admitted having had incorrectly set up the AM-PM format, by mistake. Being a new pump-user, the patient was using just one basal rate, and one insulin:carb ratio, and therefore no basal or bolus dosing errors occurred.

**Discussion:** Recent literature has pointed out the potential for insulin dosing errors in patients using insulin pumps, resulting from incorrect time settings. Our group has recently reported representative examples of these technical glitches in recent publications, media stories and online postings and blogs, underscoring the potential risk that may result from incorrect settings related to DST change as well as AM-PM format. We suggested that because insulin pumps clocks do not automatically adjust, it is prudent that patients manually make the DST change. As well, depending on the pump’s brand, time settings must be checked upon changing batteries or after a pump’s electronic dysfunction. It is very prudent that the AM-PM format is set up correctly at all times. Incorrect time settings may result in non-synchronization with clinics’ computers, and may cause insulin dosing errors in patients using multiple basal rates or insulin:carb ratios.

**Conclusion:** This case report emphasizes the importance of correct time settings of insulin pumps, which should be routinely checked by clinicians and educators during visits. Patients should be educated to verify the pumps’ time settings at all times, and to check the time settings after changing batteries. Patients should be constantly educated about the DST change which occurs twice annually, and as important, to ensure correct AM-PM settings.
Abstract #242

THE PREVALENCE OF DIABETIC RETINOPATHY IN PREGNANT HISPANIC WOMEN WITH PRE-EXISTING DIABETES MELLITUS OR GESTATIONAL DIABETES MELLITUS

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1. University of California, San Francisco, Fresno Medical Education Program 2. Community Diabetes Care Center

Objective: To assess the prevalence of diabetic retinopathy (DR) in a cohort of pregnant Hispanic women with pre-existing Diabetes Mellitus (DM) or Gestational Diabetes Mellitus (GDM).

Methods: This is a retrospective, cross-sectional study conducted at a community diabetes care center. The center offers the retinal screening to all pregnant women with pre-existing DM or GDM who have not had the retinal examination during the current pregnancy. We reviewed the reports of the retinal examination, age, duration of DM, HbA1c and gestational age of 674 consecutive pregnant Hispanic women who were referred for the management of pre-existing DM or GDM over a 6-year period between 2006 and 2011. The data of the Hispanic patients with and without DR were compared. During the same period, 206 non-Hispanic pregnant patients had retinal examination. Data of the patients with DR in both Hispanic and non-Hispanic groups were also compared. The retinal screening was performed by using a Canon DGi digital fundus camera. The high-resolution digital retinal pictures were then transmitted to the University of California Berkeley School of Optometry for interpretation.

Results: Of the 674 Hispanic patients screened, 52.6% (21/40) of those with DM type 1, 25.06% (96/383) with DM type 2 and 3.59% (9/251) with GDM were found to have various degrees of DR. In pregnant Hispanic women, mean duration of DM and A1c level were significantly greater in patients with pre-existing DM (DM type 1 and DM type 2) with DR compared to those without. 3.59% of pregnant Hispanic women with GDM were found to have DR at retinal screening and the differences in the mean age, gestational age and A1c level between those with and without DR were not significant. In those with DM type 2, rate of DR was significantly higher in Hispanics than in non-Hispanic patients with DM2 and GDM. Those with DR had a longer duration of DM and higher A1c than those without. In addition, our study has shown that DR may develop in pregnant Hispanic patients with GDM. Further studies are needed to determine if the screening for DR in this group of patients is warranted.

Conclusion: Retinopathy is a common finding in pregnant Hispanic women with pre-existing DM. The rate of DR was significantly higher in Hispanics than in non-Hispanic patients with DM2 and GDM. Those with DR had a longer duration of DM and higher A1c than those without. In addition, our study has shown that DR may develop in pregnant Hispanic patients with GDM. Further studies are needed to determine if the screening for DR in this group of patients is warranted.

Abstract #243

REGIMEN ADHERENCE, GLYCEMIC CONTROL AND PARENTING KNOWLEDGE IN PATIENT WITH TYPE 1 DIABETES IN BANGLADESH

Fazlarabbi Khan, MD

DWF

Objective: Non-adherence to prescribed treatment regimen among diabetes patients with type 1 is common and making optimal glycemic control, difficult to achieve. This study aimed to examine relationship among regimen adherence, glycemic control and parenting knowledge in Bangladeshi type 1 diabetes.

Methods: Under a cross-sectional design all patients with type 1 diabetes who attended the diabetes care unit at Segunbagicha, Dhaka, Bangladesh were included in the study. Parents of 48 children completed regimen adherence and parenting knowledge questionnaire. Glycemic results were collected from their medical records. Independent t-test was using for group differences. Chi-square test along with descriptive statistics was used to assess the association between regimen adherence and parenting knowledge.

Results: Among the study patients, 53.2% were girls and mean ±SD age was 18.57 (±4.55) years. More than half (53.2%) of the patients were adherent to their prescribed insulin regimen, though the glycemic status of the patient was (FBG, mmol/L, 7.5± 1.9 vs 6.5± 0.72, p=0.04; RBG, mmol/L, 11.16± 4.3 vs 8.18± 0.77, p=0.01) significantly higher in non-adherence group. About 66.7% patients whose parents had good knowledge regarding diabetes were non-adherence to insulin regimen.

Conclusion: In this study, parenting knowledge is associated with non-adherence to regimen. Efforts must be given to authoritative parenting, characterized by support and affection may be advantageous for the regimen adherence and glycemic control of the patient with type 1 diabetes.
**Abstract #244**

**PREVALENCE OF GROWTH HORMONE DEFICIENCY IN TYPE1 DM PATIENTS AT A TERTIARY CARE CENTRE IN INDIA**

Banshi Saboo, MD, Shashank Joshi, MD, Sudhir Bhandari, MD

**Diacare**

**Objective:** To find the prevalence of growth hormone deficiency in type 1 DM patients at a tertiary care centre in India.

Type 1 DM is associated with various hormonal disturbances and autoimmune conditions like hypothyroidism, celiac disease and growth hormone deficiency. Both growth hormone deficiency and type 1 DM are associated with low IGF-1 levels (insulin dependent growth factor 1). IGF1 levels are independent of glycemic status of the type 1 patients.

**Methods:** We screened 100 (68 males, 32 females) patients with type 1 DM of the duration of more than 5 years between the age of 8 to 14, for their Growth hormone levels. Also IGF-1, HbA1c and TSH were assessed. Their anthropometric data was collected and growth charts were plotted for height and weight individually corresponding to their age.

**Case Presentation:** It was found that in 35% (n=35) patients had growth hormone deficiency and their IGF-1 levels were found to be very low. Their HbA1c varied from 7.5-8.5%. The growth chart showed stunted growth these kids.

The rest 65% (n=65) patients showed normal growth hormone levels.

58% (n=58) of patients showed hypothyroidism with high TSH levels.

**Conclusion:** The prevalence of growth hormone deficiency at a tertiary care centre in India is 35%.

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**Abstract #245**

**TWICE-DAILY INSULIN GLARGINE FOR GLUCOSE CONTROL IN ENTERAL NUTRITION THERAPY**

Mohsen Eledrisi, MD, FACE, FACP, Noor Suleiman, MD

Hamad Medical Corporation

**Objective:** Hyperglycemia is a common complication of enteral nutrition therapy. We present a case of a patient with uncontrolled type 2 diabetes who was on enteral nutrition that significantly improved after changing insulin Glargine to twice-daily regimen.

**Case Presentation:** A 76-year-old woman was admitted to the hospital with a history of type 2 diabetes, stroke, and Hepatitis C virus. She was started on enteral nutrition therapy. During hospitalization blood glucose levels were persistently elevated with increasing doses of insulin which consists initially of 34 units of insulin Glargine at bedtime and 18 units of Aspart three times daily. Because blood glucose levels remained elevated particularly before lunch and dinner, insulin Glargine was changed to 20 units twice-daily. Capillary blood glucose levels were measured 4 times daily and readings were noted two weeks on once-daily Glargine and 4 weeks after the change to twice-daily Glargine. Capillary glucose levels were reported as mean (±SD) and results from the once-daily and twice-daily insulin Glargine regimens were compared using ANOVA and the paired Student’s t test. On once-daily Glargine, the mean blood glucose readings were as follows: fasting: (300 ± 12 mg/dl), 11 AM: (262 ± 15 mg/dL), 6 PM: (287 ± 16 mg/dl) and 9 PM: (309 ± 18 mg/dl). Two weeks following the initiation of twice-daily insulin Glargine, the mean blood glucose values were as follows: fasting: (171 ± 14 mg/dl), 11 AM: (150 ± 16 mg/dL), 6 PM: (173 ± 13 mg/dl) and 9 PM: (193 ± 11 mg/dl). All these values were statistically significant (p value of < 0.001). HbA1c decreased from 7.9 on admission to 6.9 after 6 weeks (p value < 0.01). Doses of insulin Aspart remained stable during the period of twice-daily insulin Glargine.

**Discussion:** Data are limited on the most appropriate insulin regimen for patients with diabetes who are on enteral nutrition therapy. Control of glucose in these patients remains a challenge to clinicians. Intravenous insulin infusion has been used in these patients particularly in the critical care setting. Basal-meal insulin regimen is commonly used in hospital wards usually with once-daily Glargine with meal insulin three times daily and has been shown to improve glucose better than sliding-scale insulin. Insulin Glargine is regarded as a 24-hour basal insulin that is commonly used in the inpatient setting to control hyperglycemia. In our patient, once-daily insulin Glargine failed to achieve acceptable glucose control. Switching to twice-daily Glargine resulted in significant improvement in glucose values.

**Conclusion:** Twice-daily insulin Glargine should be considered in patients who are on enteral nutrition therapy and have uncontrolled glucose levels.
Abstract #246

INTERMEDIATE METABOLIC STATES AND DIABETES MELLITUS IN AN URBAN NIGERIAN POPULATION

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1. University of Calabar, 2. University of Lagos

Objective: Although the transition from Intermediate metabolic states including impaired glucose tolerance (IGT) and impaired fasting glucose (IFG) that precede diabetes may take many years; current estimates indicate that many individuals with these intermediate states eventually develop diabetes. Since both categories identify individuals at risk for diabetes, the identification of individuals at risk for diabetes represents a strategic tool to prevent diabetes since the magnitude of the epidemic, coupled with the complex treatment requirements are difficult and costly to implement in both developing and developed countries.

Methods: The study was a cross sectional survey of a representative sample of Calabar metropolis comprising 645 males (56.9%) and 489 females (43.1%) aged between 15 and 79 years. A multistage sampling method was applied to select participants for the study. Anthropometric data was obtained and an oral glucose tolerance test (OGTT) was performed on all participants following which participants were categorized as normal glucose tolerance (NGT), IFG, IGT and diabetes mellitus (DM). Anthropometric indices were expressed as mean (standard deviation). The categorisation was done using American Diabetes Association (ADA) classification (2003) and the result in percentages.

Results: The prevalence of IFG was 8.8% (male 9.3%, female 8.2%), IGT 19.6% (male 21.1%, female 17.6%), isolated IFG 19% (male 17.2%, female 21.5%), isolated IGT 8.5% (male 9.8%, female 6.7%), combined IFG/IGT 4.5% (male 4.2%, female 4.9%), DM 6.5% (male 7.9%, female 4.7%).

Discussion: A number of studies have recently tried to determine whether IGT or IFG is a better predictor of future diabetes. Although there are some differences between the studies, the following general conclusions may be drawn. The incidence of subsequent diabetes is highest in individuals with combined IGT and IFG. It tends to be similar in those with isolated IFG (I-IFG) and I-IGT, although there may be differences in some populations suggesting a higher incidence in those with I-IFG. However, because in most populations I-IGT is much commoner than I-IFG, it identifies a greater proportion of those who will develop diabetes. A substantial minority, well over a third, of individuals who develop diabetes have normal glucose tolerance at baseline.

Conclusion: Identification of individuals with intermediate metabolic states is a necessary strategy for the prevention of diabetes mellitus given the high prevalence of individuals with IGT.

Abstract #247

VITAMIN D DEFICIENCY IN PATIENTS WITH TYPE 2 DIABETES IN NORTH INDIAN POPULATION

Brij Makkar, MD, FRCP, Namrata Harichandan, Pratima Sharma

Diabetes and Obesity Centre

Objective: To study Vitamin D levels and its deficiency in Type 2 Diabetes patients in urban population in north India

Methods: This a retrospective study carried out at Diabetes and Obesity Centre in New Delhi, India. A total of 203 adult Type 2 Diabetes(T2D) patients who had data available for comprehensive health and metabolic status evaluation including serum 25-hydroxy vitamin D3(25(OH)D3 (Vit D)) levels were included in the study. Serum 25(OH)D3 level(ng/ml) of more than 30ng/ml was defined as Vit D sufficiency; between 21-30 as insufficiency; 10-20 as deficiency; and <10 as severe deficiency. Comparison was also made for Vit D levels between patients with recent onset diabetes(<6months duration) and those with diabetes duration of more than 1 year to study the impact of duration of diabetes on Vit D levels.

Results: The study population of 203 type 2 diabetes patients included 114 males and 89 females with a mean age of 50years (+9.79years, age group 26-74 years). Mean Body Mass Index(BMI) was 29.97kg/m2(+8.76) and average duration of diabetes was 14.72years(+6.53yrs). Of these 42 patients had recently diagnosed (<6months) T2D. Mean serum 25(OH)D3(Vit D) level was 13.59(+11.77) ng/ml , with only 19/203 patients(9.36%) {(5/114(4.39%) males and 9/89(10.11%) females)} having Vit D levels more than 30ng/ml. Mean Vit D level was 12.98ng/ml in males and 14.37ng/ml in female T2D patients. Vit D deficiency was present in 168/203(82.76%) patients {97/114(85.09%) of males, 71/89(67.88%) of females} and of these 44.33%(90/203) had severe Vit D deficiency. Mean Vit D levels in patients with recent onset diabetes (<6months duration) and those with diabetes duration of more than 1 year to study the impact of duration of diabetes on Vit D levels.

Discussion: A number of studies have recently tried to determine whether IGT or IFG is a better predictor of future diabetes. Although there are some differences between the studies, the following general conclusions may be drawn. The incidence of subsequent diabetes is highest in individuals with combined IGT and IFG. It tends to be similar in those with isolated IFG (I-IFG) and I-IGT, although there may be differences in some populations suggesting a higher incidence in those with I-IFG. However, because in most populations I-IGT is much commoner than I-IFG, it identifies a greater proportion of those who will develop diabetes. A substantial minority, well over a third, of individuals who develop diabetes have normal glucose tolerance at baseline.

Conclusion: Identification of individuals with intermediate metabolic states is a necessary strategy for the prevention of diabetes mellitus given the high prevalence of individuals with IGT.
**Abraham, MD**

**Objective:** Type 2 diabetes is widely prevalent across India. Vit D deficiency has also been documented in all age groups and both sexes from all across India. A number of studies have linked Vit D deficiency to T2D and metabolic syndrome. However, there is very limited data on Vit D deficiency in T2D patients in North India. Recently one study reported a very low levels of Vit D (11.0±7.5 ng/ml) in T2D patients in North India. Our study also shows a very high prevalence Vit D deficiency {Mean serum Vit D level 13.59(+11.77)ng/ml} in north Indian T2D patients, affecting more than 80% T2D patients.

**Conclusion:** Our study clearly shows a very high prevalence of Vit D deficiency in adult type 2 diabetes patients, affecting men and women from all age groups. Also, Vit D deficiency did not show correlation with age, duration of diabetes, BMI or A1c levels in our study population.

**Abstract #248**

**UTILIZATION OF REGULAR INSULIN IN V-GO® FOR PATIENTS UNCONTROLLED WITH TYPE 2 DIABETES MELLITUS (T2DM): A CASE SERIES**

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**Objective:** The cost of diabetes continues to rise. Patients age 65 and older can be faced with a substantial cost burden when they reach a coverage gap. Less expensive treatment options are needed. Data is limited on the administration of regular insulin by the V-Go Disposable Insulin Delivery Device (V-Go). We report 2 cases where utilizing regular insulin in V-Go led to improved glycemic control in patients with T2DM.

**Case Presentation:** Case 1: A 65 year old male with T2DM of 10 years, poorly controlled, HbA1c 12.3%, with stage 3 kidney disease presented to our endocrine clinic for initial evaluation and management of diabetes. His diabetic regimen upon presentation was 30-35 U BID of NPH insulin and a sodium glucose cotransporter 2 (SGLT2) inhibitor. Upon the initial visit, patient was switched to regular insulin delivered using V-Go and a sulfonylurea (SU). The SGLT2 was discontinued due to renal insufficiency. Following 3 months of V-Go therapy with regular insulin and SU, HbA1c was reduced to 8.8% and the total daily insulin dose decreased to 45 units. Patient reported occasional mild to moderate hypoglycemia when meals were missed.

Case 2: A 66 year old male was evaluated for uncontrolled T2DM, HbA1c 9.6%, without mention of complication in our endocrine clinic. The patient’s insulin requirement had progressively increased and prandial insulin was added at preceding visit. Prior to being switched to V-Go, his insulin delivery regimen consisted of 25 U BID of insulin detemir and 14 U/ day of insulin aspart. Patient reported history of moderate to severe hypoglycemia with increased activity. V-Go was initiated with rapid acting insulin (RAI) to simplify insulin delivery and provide continuous infusion of basal insulin with flexible meal time dosing. After 3 months of using RAI in V-Go his HbA1c decreased to 8.3%. The RAI was substituted with regular insulin to decrease cost to patient. Following 6 months administering 30-36 U of regular insulin by V-Go the HbA1c was further reduced to 8.0%. The patient reported occasional hypoglycemia in the morning on V-Go.

**Discussion:** Patients are forced to make decisions between medical care and living expenditures when a coverage gap is reached. Many discontinue taking necessary medications or skip doses to save money. Utilization of regular insulin can result in significant cost savings for those where cost is a barrier. Controlled studies are needed to fully evaluate the safety and efficacy of using regular insulin in V-Go.

**Conclusion:** Regular insulin is a less expensive option compared to many therapeutic regimens and when administered by V-Go resulted in improved glycemic control.

**Abstract #249**

**EFFECTIVENESS OF A MULTIDISCIPLINARY TEAM FOR DIABETES MANAGEMENT IN A RURAL PRIMARY CARE OFFICE**

**Rashi Agarwal, MD, FACP, Julie Vines, RRT, Girish Mour, MD**

1. St. Catherine Hospital, 2. Univ of Pittsburgh

**Objective:** Diabetes is a complex chronic medical condition with a prevalence of 9.3%nationally. The numbers are comparable to those in Kansas with an estimated prevalence of 8.5%. Although a covered Medicare benefit, medical nutritional therapy(MNT), certified diabetes educator(CDE) services, were not accessed by several patients in the region. A multidisciplinary diabetes clinic was set up to meet the standards of care for diabetes management to achieve optimal clinical outcomes, minimize the complications and delay the progression of the disease.

**Methods:** A weekly “one stop shop” multidisciplinary clinic at the primary care physician(PCP) office with a CDE, nutritionist, physical therapist(PT), a sleep lab person and a clinic navigator(CN) was set up. The patients met with the services individually in an extended clinic appointment following the PCP evaluation.

**Results:** 62 patients rotated through the clinic in 4 months. Hemoglobin A1C was checked as per the guidelines. Patients were encouraged to bring in finger stick logs frequently for real time interventions. CDE and
MNT identified the needs of the individual patients and scheduled follow up visits to address their needs further. PT tried to address the barriers for moderate intensity physical activity. Patients were enrolled in active therapy if indicated. 32% were enrolled to a supervised exercise program at YMCA. Sleep lab personnel screened all patients for obstructive sleep apnea (OSA) without a prior diagnosis. 40% were referred for further formal testing. Patients with prior history of OSA were sent for follow up. CN visited with each patient to identify their individual needs. She helped them with their dental, eye, podiatry and mental health referrals. She followed up with the patients if they failed to show up for any referrals and helped them reschedule. She assisted the patients with Diabetes Self-Management Education and other diabetic education classes enrollment which were either free or a covered insurance benefit. Other factors evaluated: urine albumin excretion (45% did not have a prior evaluation), lipid therapy, ASA therapy, vaccinations, etc.

Conclusion: Despite the lack of an endocrinologist (the nearest being 200 miles away) or any formal diabetes center in the region, with this multidisciplinary clinic in one place, we hope to bring top of the line standard of care to our diabetic patients in rural Southwest Kansas. The easy access to these services through the PCP’s office provides the patients an opportunity towards better understanding of the importance of comprehensive management of diabetes and its impact on day to day and long term outcomes. Outcomes data is not available at this time due to short follow up period.

Abstract #250
DIABETIC PERIPHERAL NEUROPATHY AMONG SAUDI PATIENTS WITH NEWLY DIAGNOSED TYPE 2 DIABETES MELLITUS.

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1. Diabetes Care Center, Prince Salman Hospital, 2. King Saud Medical City

Objective: To study the rate of painful diabetic neuropathy (PDN), diabetic peripheral neuropathy (DPN) and the risk of foot ulceration (RFU) among Saudi patients with newly diagnosed type 2 diabetes mellitus (T2DM).

Methods: A cross-sectional study was conducted on 366 out of 544 Saudi patients with T2DM, referred from primary health care centers according to inclusion-exclusion criteria. 125 Patients with newly diagnosed T2DM (< 6 months) were identified. Informed consent obtained. Painful neuropathic symptoms (PNS) were assessed using neuropathy symptom-score (NSS). Severity of PNS was defined as: none (0-2), mild (3-4), moderate (5-6), severe (7-9). DPN was determined using neuropathy disability-scores (NDS). DPN present if NDS ≥ 3. RFU present if NDS ≥ 6. Clinically significant PDN was defined as: moderate (NSS ≥ 5) and mild (NDS ≥ 3). SPSS-17 was used for statistical analysis.

Results: Mean age of newly diagnosed T2DM patients: 45.4 ± 10.3 years. Male to female ratio: 1.4. BMI: 31.6 ± 6.9 kg/m². History of foot ulceration was present in 0.8%. Hypertension and dyslipidemia were present in 31.2%, 48.8% respectively. PNS was present in 35.2%. 12.0% of them had PNS of moderate severity and 23.2% had severe PNS. Clinically significant PDN was present in 8.0%. DPN defined as NDS ≥ 3 was present in 8.8% and RFU in 4.0%.

Discussion: We demonstrated that about one third of Saudi patients with newly diagnosed T2DM have PNS, and 8.8% have DPN. Results are not lower but comparable to international reported rates.

Conclusion: As a considerable percentage of T2DM patients have PNS and DPN at diagnosis of T2DM, which predisposes them to increased RFU; it is important to intensify strategies for early detection of T2DM among high risk Saudi individuals.

Abstract #251
CORRELATION OF LEFT VENTRICULAR HYPERTROPHY & LEFT VENTRICULAR DIASTOLIC DYSFUNCTION WITH HBA1C IN NEWLY DIAGNOSED TYPE 2 DIABETICS

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LLRM Medical College

Objective: To study the frequency of left ventricular hypertrophy (LVH) and left ventricular diastolic dysfunction (LVDD) in normotensive newly diagnosed type 2 diabetic patients by using 2D echocardiography and correlation with HbA1C.

Methods: The present study is an observational cross sectional study in which 100 newly diagnosed normotensive type 2 diabetes mellitus patients between 30 - 60 year of age were enrolled from endocrine OPD of a tertiary care center during a period of 1 year. All cases were subjected to thorough clinical history, examination and 2D echocardiography along with HbA1C.

Results: Out of 100 patients of newly diagnosed normotensive type 2 DM; 41 % patients had LVH and 37 % patients had LVDD. The mean HbA1C of population with LVDD was 7.67 ± 0.90 % and that with LVH was 7.74 ± 0.91 %. The LVDD and LVH were positively
correlated with HbA1C (p value = 0.0057 & p value = 0.0011) respectively.

**Discussion:** Diabetes is associated with dysfunction, and failure of different organs, especially the eyes, kidneys, nerves, heart, and blood vessels. Diabetic macrovascular complications are the leading cause of deaths in diabetics. The correlation between LVH & LVDD with HbA1C is not clear in newly diagnosed T2DM Indian diabetics.

**Conclusion:** Left ventricular diastolic dysfunction & left ventricular hypertrophy were positively correlated with HbA1C in newly diagnosed T2DM population.

**Abstract #252**

**ONCE WEEKLY DULAGLUTIDE MAY BE CO-ADMINISTERED WITH WARFARIN WITHOUT DOSE ADJUSTMENT**

Amparo de la Pena, PhD, Corina Loghin, MD, Xuewei Cui, PhD

Eli Lilly and Company

**Objective:** Dulaglutide slows gastric emptying and thus has the potential to reduce the rate of absorption of concomitantly administered oral medications. This study evaluated the effects of dulaglutide on the pharmacokinetics (PK) of both enantiomers of warfarin, S-warfarin (SW) and R-warfarin (RW), and on the pharmacodynamics (PD) of warfarin in healthy subjects.

**Methods:** This was an open-label, randomized, 2-period, 2-sequence crossover study conducted in 28 healthy subjects. Subjects received a 10 mg warfarin tablet on Day 1 of one of the periods. In a different period, subjects received a single dose of dulaglutide 1.5 mg on Day 1, followed by a 10 mg warfarin tablet on Day 3. During both periods, serial blood samples were collected up to 1 week post dose to evaluate the plasma PK of SW and RW and to assess warfarin PD. There was a washout period of at least 24 days between treatment periods. PK parameters were calculated by noncompartmental methods. Warfarin PD measures were derived from the international normalized ratio (INR). The ratios of geometric least squares means (geoLSM) and their respective 90% confidence interval (CI), were calculated for PK and PD parameters.

**Results:** The ratio of geoLSM (90% CI) for area under the curve from time zero to infinity [AUC(0-∞)] were 0.986 (0.959, 1.01) for SW and 0.989 (0.958, 1.02) for RW, and 0.857 (0.817, 0.900) for RW maximum concentration (Cmax). The SW Cmax decreased approximately 22% (0.783 [0.737, 0.833]), and the time to maximum concentration (tmax) was delayed for both SW (4 hours [hr]) and RW (5.5 hr). The ratio (90% CI) of the maximum INR response (INRmax) was 1.02 (0.977, 1.07). The median delay in the time to maximum INR (tINRmax) was 6 hr, consistent with the tmax delays for both warfarin enantiomers. In total there were 23 treatment-related adverse events (21 mild, 2 moderate), the most common of which were nausea, vomiting and paraesthesia.

**Discussion:** Dulaglutide coadministration did not affect the overall exposure to SW or RW or the RW Cmax, as the 90% CI of the ratios for all measures were within (0.80, 1.25). The decrease in SW Cmax was not reflected as a change in INRmax. Time parameter delays are not expected to affect the efficacy or safety of warfarin. Drug levels of oral medications with narrow therapeutic indices should be monitored when coadministered with dulaglutide. The coadministration of both drugs was well tolerated.

**Conclusion:** Based on the PK, PD and safety data, no dose adjustment is needed when warfarin is coadministered with once weekly dulaglutide.

**Abstract #253**

**INSULIN USE AMONG PATIENTS WITH DIABETES MELLITUS, CHALLENGES WITH ADMINISTRATION AND STORAGE: A NARRATIVE FROM UMUAHIA**

Ignatius Ezeani, MD, Abali Chuku, MD

Federal Medical Center, Umuaiahia

**Objective:** To document the pattern of insulin prescription, regimen, and attendant problems associated with its use.

**Methods:** This was a prospective descriptive study were 381 consecutive diabetic patients who were only on insulin or in combination with oral glucose lowering agents seen at the medical out-patient clinic and medical wards and who fulfilled the criteria for inclusion were recruited over a one year period. Information on their demographic characteristics, diabetes history, management, type of insulin in use, the number of daily injections, method of insulin administration and problems associated with insulin use were extracted. Long term and short term glycaemic control was evaluated using glycosylated haemoglobin and fasting plasma glucose respectively. Data was analyzed using the statistical software: Statistical package for social sciences (SPSS) version 17. Test statistics used were chi-squared test and binary logistic regression. The level of significance was set at a p-value of less than or equal to 0.05.

**Results:** The mean (SD) age and BMI of the study population was 54±13.2 years and 27.3±5.8 respectively. Majority of patients (46.3%) were on premixed insulin. Majority of patients (63%) were on at least twice daily dose of insulin. Hypoglycemia was the commonest (59%) challenge encountered by patients. The mean glycated hemoglobin and fasting blood glucose was significantly
higher (p<0.01) in patients who did not adhere than those who adhered to prescribed insulin regimens. Duration of DM was the only factor that predicted insulin adherence.

**Discussion:** The importance of insulin in the management of DM cannot be overemphasized and patients use combinations of different types of insulin to achieve glycemic control. In this study, we note that the majority of persons with type 2 DM who are on insulin therapy use Premix insulin and they are on twice daily insulin regimen. Reason for this trend is not clear although Premix insulin is relatively commoner in this locale. Hypoglycemia was the commonest problem noted in our study.

**Conclusion:** Duration of DM and insulin associated side effects are some of the factors implicated in adherence to insulin prescription.

Abstract #254

**INDEPENDENT PREDICTORS OF ERECTILE DYSFUNCTION (ED) IN TYPE - 2 DIABETES MELLITUS**

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1. SMS Medical College & Hospital, 2. Lilavati Hospital, 3. Dia Care, 4. Consultant Physician

**Objective:** The aim of the study was to evaluate the independent predictors of erectile dysfunction (ED) in Type 2 diabetes mellitus (T2DM).

**Methods:** We have recruited 357 T2DM male patients referred to our hospital between February 2013 to August 2014. All the patients were scored with International Index of Erectile Function (IIEF)-5 Questionnaires. Contribution of age, Body Mass Index (BMI), Smoking, Blood Pressure, Lipid Profile, Fasting Plasma Glucose (FPG), Glycosylated Hemoglobin (HbA1C), Free testosterone concentration, and duration of diabetes to risk of ED were evaluated.

**Results:** Of 357 men T2DM, 59.5% (212 patients) had ED (95% CI : 52% - 62%). A negative significant correlation was found between potency score and HbA1c (r : 0.20, p : 0.01), FPG (r : 0.17, p : 0.03) and SBP (r : 0.18, p : 0.02). A positive significant correlation was found in between potency score and serum testosterone level (r : 0.23, p : 0.02), but no correlation between other risk factor such as lipid profile & BMI. By using multivariate logistic regression analysis we found that the only two independent predictor of Erectile Dysfunction (ED) in these group of patients are age (OR : 2.8, p : 0.01) and serum testosterone (OR : 3.8, p : 0.02).

**Discussion:** We found that age and testosterone level in T2DM men were the only independent predictors and other previously published risk factors including BMI, SBP, DBP, HbA1c, impaired lipid profile, high creatinine, testosterone level, and even history of smoking did not have predictive value for ED risk in T2DM patients. Endothelial dysfunction, diabetic vasculopathy & neuropathy, dyslipidemia, hypogonadism and psychological disorders that were commonly found in diabetics have been suggested as pathophysiology of ED in diabetic patients.

**Conclusion:** In conclusion, we found that ED prevalence is high in men with T2DM and is associated with some variables notably with age and testosterone level.

Abstract #255

**COMPARATIVE STUDY BETWEEN THE EFFECTS OF SITAGLIPTIN AND VILDAGLIPTIN AS ORAL HYPOGLYCEMIC DRUGS IN UNCONTROLLED TYPE II DIABETES MELLITUS**

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**Objective:** This study was carried out over a period of four months. It involved 189 type II DM patients, in two groups, received Sitagliptin (Group 1) and vildagliptin (Group 2), who both groups were receiving Sulphonylurea and Metformin prior to the study.

**Methods:** Group 1: 158 patients (89 male & 69 female), with mean age of 51.12 ±12.21 years. Group 2: 31 patients (14 male & 17 female), with mean age of 44.6 +13.2 years

**Case Presentation:** Group 1: HbA1c dropped from 8.8%+2.1% to 7.9%+1.9%. Fasting Blood Sugar (FBG), decreased from 9.93+3.8mmol/L to 8.53+3.3 mmol/L. Total Cholesterol decreased from 4.9±1.4mmol/L to 4.5±1.1mmol/L, LDL-C decreased from 2.9±1.0mmol/L to 2.7± 0.9mmol/L, HDL-C increased from 1.1±0.3mmol/L to 1.3±1.1mmol/L and Triglyceride decreased from 2.3±3.7mmol/L to 1.8±1.0mmol/L. Group 2: HbA1c decreased from 8.9%+1.71% to 7.8%+1.7%, FBG decreased from 10.91+3 mmol/L to 9.47+3.5mmol/L, Total Cholesterol decreased from 5.3±0.7mmol/L to 4.6±1.6mmol/L, LDL-C decreased from 3.5±0.6mmol/L to 2.7±0.9mmol/L, HDL-C increased from 1.05±0.18mmol/L to 1.09±0.24mmol/L and Triglyceride increased from 2.65±2.2mmol/L to 2.71±3.2 mg/d.

**Discussion:** Student T test was applied and was highly significant in both groups, before and after results but insignificant between two groups. However Blood Urea Nitrogen, Serum Creatinine, Uric acid level and urine albumin/creatinine ratio statistically insignificantly before and after and between both groups. The percent decrease of LDL was 22.8% for Vildagliptin (Group2), while it was...
7.6 for Sitagliptin (Group 1), and there was a statistically significant difference between the decrease of them in LDL (p-value = 0.027).

**Conclusion:** Addition of Sitagliptin or Vildagliptin improves equally DM control and lipid profile in previously uncontrolled DM; Except Vildagliptin is more superior in lowering LDL-C. Both drugs are safe on kidney.

Abstract #256

**COMPARISON OF ACID FAST BACILLI SMEAR MICROSCOPY EXAMINATION AND XPERT MTB/RIF IN DIAGNOSIS PULMONARY TUBERCULOSIS IN TYPE 2 DIABETES**

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**Objective:** Traditionally, tuberculosis is mostly being diagnosed by combination of chest X-rays, the staining of sputum, the growth of Mycobacterium tuberculosis in culture, and the Mantoux test. The main objective of this study was to determine the sensitivity and specificity of Acid Fast Bacilli (AFB) smear and Xpert MTB/RIF for diagnosis of TB in DM.

**Methods:** This study was a cross-sectional descriptive analytic study in patients with DM group were still underwent treatment at Persahabatan General Hospital from May 2014. Patients with DM who have TB complaints that have not been taken either TB drug or with a history of treatment and supported from chest X-ray shows the suspicion of TB will require the microbiological diagnosis of AFB smear and Xpert MTB/RIF.

**Results:** Seventy subjects were screening and only 55 subjects met the inclusion criteria. There were 32 males (58.2%) and 23 females (41.8%). Age between 25-72 years old. Body mass index were less 11(20%), normal 31(56.4%) and over 13(23.6%). The blood sugar between 110-481 g/dl. The length of suffer DM <5 years were 40(72.7%), 5-10 years were 7(12.7%), 10-15 years were 6(10.9%) and >15 years were 2(3.6%). The controlled HbA1c 11(20%) and uncontrolled 44(80%). By history of TB has never suffered 41(74.5%), treatment cured 9(16.4%) and failure or withdrawal 5(9.1%). Smear of AFB positive in 29 pts(52.7%) and Xpert MTB/RIF positive in 36 pts(65.5%).

**Discussion:** Some concerns have been raised about the Xpert MTB/RIF, including minor operational issues and cost. A review to assess the diagnostic accuracy when Xpert TB was used as an add-on for cases of negative smear microscopy the sensitivity was only 67% and specificity 98%. In this study we found sensitivity 77.8%, and specificity was 94.7%.

**Conclusion:** The Xpert MTB/RIF has a higher value of positivity that detect M.Tb than AFB smear. There is no difference in the sensitivity and specificity of AFB smear and Xpert MTB/RIF for TB diagnosis in patients with DM.

Abstract #257

**CELIAC CRISIS: A RARE COMPLICATION IN AN ADULT PATIENT WITH TYPE 1 DIABETES**

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**Objective:** The prevalence of celiac disease (CD) in type 1 Diabetes Mellitus (DM) is as high as 10%. Celiac crisis is a life-threatening syndrome in which patients with celiac disease have profuse diarrhea and severe metabolic disturbances. Celiac crisis is rare in adults.

**Case Presentation:** A 68 year old female with Type I diabetes was admitted from the Nursing Home (NH) after a fall during which she scraped her arm, she was also noted to be severely dehydrated in the Emergency Department. Her past medical history was significant for brittle type 1 DM of 40 year duration, recurrent DKA, hypoglycemia, HTN, hypothyroidism, depression and celiac disease. She was noted to have hyperglycemia and metabolic acidosis with a blood sugar of 592 mg/dl, HCO3 of 8 mmol/L, Anion Gap of 19 mmol/L, and pH of 7.11. Her potassium level was 2.8. The patient was treated with IV fluids and insulin infusion, which led to resolution of hyperglycemia and normalization of anion gap but she had persistent non gap acidosis which required IV bicarbonate infusion for several days. Her Non Gap Metabolic Acidosis (NGMA) was thought to be related to ongoing diarrhea. Workup for infectious causes including C Diff was negative. The eight am cortisol level of 18.3 ruled out adrenal insufficiency. A small bowel biopsy obtained showed severe villous atrophy consistent with CD. Patient was started on IV methylprednisolone for her severe CD and showed improvement in diarrhea, hyperglycemia and metabolic acidosis. The patient was eventually discharged to a long-term acute care facility for further management with a plan for 2 weeks of steroids.

**Conclusion:** Adult celiac disease, in contrast to its
Objective: Currently available insulin pumps are neither GPS-enabled, nor automatically time-adjusting. Insulin delivery per an insulin pump is time-sensitive and potential dosing errors may arise if the pump’s internal clock is not set up correctly. We report a case of a patient with type 1 diabetes (T1DM) who forgot to change his insulin pump’s time setting during the daylight saving time (DST) change, fortunately without harm resulting from this trivial dosing errors.

Case Presentation: A 30-year-old male with T1DM was seen in the endocrinology clinic for a routine follow up visit 11 days after the DST change in November, 2014. The nursing staff attempted to download his pump to the clinic’s computer, via the downloading interphase software. Synchronization failed, and the staff noticed a low battery alarm sign, and changed batteries, without success of synchronization. As the provider was evaluating the pump, it was noted that the pump’s time was one hour ahead. Since the our practice is familiar with such glitches, it was speculated that the glitch was due to incorrect pump’s time setting, and when the time was updated, synchronization occurred. The patient then realized that he forgot to make the DST change. The patient was not using the pump’s bolus calculator, and therefore no bolus dosing errors occurred. Although the patient used 4 basal rates, ranging from 1.0 to 1.65 U/H, no harm resulted from the dosing errors caused by the DST-related one-hour difference.

Discussion: Recently emerging literature has cautioned the medical community about the potential for insulin dosing errors in patients using insulin pumps, resulting from incorrect time settings. We have encountered examples of these glitches and published few representative cases demonstrating problems related to DST change as well as AM-PM format. Because insulin pumps do not automatically adjust (nor GPS-enabled), it is prudent that patients manually make the DST change. As well, depending on the brand, time should be set up or checked upon changing batteries or after a pump’s electronic dysfunction. It is prudent that the AM-PM format is set up correctly. Otherwise, synchronization with computers for data downloading will fail, but more importantly may cause insulin dosing errors.

Conclusion: Diabetes clinicians and educators should always check the time settings of insulin pumps during patients’ visits. They should also educate patients about the importance of verifying the insulin pump time settings at all times, and to check the pump’s time settings after changing batteries, and to be aware of the DST change which occurs in the fall and spring. As important is to educate patients to ensure correct AM-PM settings.

Abstract #259

SELF GLUCOSE MONITORING PRACTICES, ITS IMPACT ON GLYCEMIC CONTROL AND PRESENCE OF CHRONIC COMPLICATIONS IN TYPE 2 DIABETIC PATIENTS.

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Objective: Self-monitoring of blood glucose (SMBG) has been recommended by various regulatory bodies to monitor and achieve glycemic control. There is however no consensus regarding the overall benefits of SMBG in patients with type 2 diabetes. We aimed to assess self glucose monitoring practices and its impact on glycemic control and presence of chronic complications in type 2 diabetic patients attending a tertiary referral center in the South-Western part of Nigeria.

Methods: Cross-sectional study carried out at the Lagos State University Teaching Hospital, Ikeja Lagos. 249 who gave consent were randomly recruited. Clinical parameters sought include, age, level of education, duration of DM, treatment, SMBG, duration and frequency of SMBG. Co-morbidities such as hypertension and dyslipidemia, anthropometric indices taken, presence of complications assessed, retinopathy with direct fundoscopy, neuropathy assessed with biothesiometry, nephropathy assessed with...
ABSTRACTS – Diabetes Mellitus/Prediabetes

urine albumin/creatinine ratio, fasting lipid profiles, fasting blood glucose, and glycated hemoglobin assessed with boronate affinity method. Parameters of Subjects who practice SMBG were compared with those who do not. Data analysis done with SPSS version 20. Independent T-test and chi-square, p-value of <0.05 is statistically significant.

Results: Mean age (SD) 62(11) years. 77(31%) were males, 172(69%) females. Mean BMI 27.84(7.3) kg/m2, 159(64%) practice SMBG, comparison of those who do SMBG (group A) and those who do not (group B) are as follows: age and duration of DM similar in both groups p-value 0.149, more male patients practice SMBG- p> 0.05, more educated patients did SMBG- p <0.01, Mean HbA1c of group A and B is 7.43(1.86) and 8.24(2.28) respectively p = 0.004, mean FPG of both groups p value = 0.003, Mean PPG of both groups p value =0.013, mean lipid values p>0.05, Hypertension p= 0.78 ,presence of Retinopathy p= 0.49, Neuropathy p = 0.52, more frequent SMBG and presence of complications p= 0.92.

Discussion: In this study, more than 50% of study subjects do SMBG, being educated correlated positively with practice of SMBG, as well as short and long term glycemic control. There was however no positive impact of SMBG on presence of complications or comorbidities.

Conclusion: SMBG improves both short and long term glycemic control, however impact of SMBG on presence of DM complications is not significant. A longitudinal study of newly diagnosed patients who practice SMBG would be necessary to elucidate impact of SMBG on chronic complications.

Abstract #260

TARGETING SGLT2 INHIBITION IN T2D MANAGEMENT: EFFECT OF ONLINE CME AND CONTINUED EDUCATIONAL GAPS

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Objective: Successful implementation of new standards of care begins with a thorough understanding of the mechanisms of action of newer agents and where they fit into modern T2D treatment algorithms. We sought to determine if online continuing medical education (CME) could improve the clinical performance of primary care physicians (PCPs) regarding use of SGLT2 inhibitors in T2D management and assess continued educational gaps.

Methods: The CME activity consisted of an online video lecture with a leading expert on the role of the kidney and SGLT2 in the treatment of T2D. The effects of education were assessed using a case-based linked pre-/post-assessment. In addition, a smaller sample was analyzed for follow-up (30-60 days post-education). For all questions combined, the McNemar’s chi-squared test was used to assess differences from pre- to post-assessment. P values are shown as a measure of significance; P values <.05 are statistically significant. Cramer’s V was used to calculate the effect size. The activity launched online on August 27, 2014 and data were collected for 3 months.

Results: Overall, the analysis demonstrated significant improvement for PCPs (n = 316; P <.001) related to integration of SGLT2 inhibitors into clinical practice. The effect of the education immediately after participation (pre-/post-assessment) was moderate (V = 0.484): 26% answered all questions correctly on the pre-assessment compared with 41% on the post-assessment. Follow-up analysis showed retention, as well as a progression of the educational impact, with increases in correct responses from pre- to post- to follow-up ranging from 5-16% pre to post and an additional 4-18% post to follow-up. Data indicate future educational need concerning the rationale for targeting SGLT2 to improve glycemic control, A1c, and other important endpoints in T2D.

Discussion: For participating PCPs, the moderate effect observed indicates an increase in evidence-based practice choices, demonstrating the impact of the intervention. The continued improvement in clinical decision-making seen from post to follow-up could be a result of subsequent education on this topic that was part of a series of 5 activities, demonstrating the positive impact of serial learning. Further, additional education on the rationale for targeting SGLT2 to improve glycemic control and other endpoints in T2D is needed.

Conclusion: This study demonstrates the success of a targeted educational intervention with access to the right physician audience (PCPs at the forefront of diabetes care) on improving clinical performance regarding the use of SGLT2 inhibitors for the treatment of T2D. The additive effect of serial learning was also demonstrated.

Abstract #261

ABSTRACT WITHDRAWN
Abstract #262

CLINICAL PROFILE AND OUTCOME OF DIABETIC KETOACIDOSIS AMONG SAUDI ADOLESCENT DIABETIC PATIENTS IN A SAUDI TERTIARY CENTER

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Objective: To study the clinical profile of adolescent type 1 diabetic patients presenting with diabetic ketoacidosis (DKA) and their outcome.

Methods: This was a prospective study of all cases of diabetic ketoacidosis (DKA) admitted to the adolescent care unit in security forces hospital, Riyadh, Saudi Arabia during the period 1 May, 2014 till 30 October, 2014. Criteria for defining DKA were: serum glucose of more than 250 mg/dl, arterial PH of 7.25 or below, serum bicarbonate of 15 mmol/l or less and evidence of ketonemia or ketonuria. The clinical characteristics, possible precipitating cause, clinical outcome and mortality rate were recorded.

Case Presentation: 32 patients were diagnosed to have DKA. There were 21 females and 11 males. Their mean age was 16.41 ± 3.77 years. There were 5 newly diagnosed cases of type 1 diabetes mellitus. All other patients were known and previously followed up in the adolescent diabetes clinic and who have received adequate diabetic education program. The mean duration of diabetes in this group was 7.1 ± 2.3 years. They were all on basal/bolus insulin program. In 19 patients, the precipitating cause was stopping the insulin injections (in 14 of the, the insulin glargine). In 4 patients, infection was responsible for precipitating DKA. Of these, 3 had upper respiratory tract infection and 2 had urinary tract infection. In 4 patients, there was no obvious cause for the DKA. 8 patients had recurrent admissions with DKA during the study period (average of 2), both related to missing insulin injections. Polydipsia, polyuria and abdominal pain were seen in all cases. Altered sensorium was seen in 13 patients. The mean presenting PH was 7.21 ± 0.23. There were no cases of cerebral edema or mortality recorded at presentation or during treatment.

Discussion: The study reveals that most patients were females. Non-compliance was the predominant cause despite adequate education. Recurrence of admissions was seen frequently. This emphasizes the importance of continuous diabetic education especially in the difficult adolescent age group particularly in female patients. Repeated education sessions may be necessary including group interaction, social and family support. The favourable outcome in this study suggests that as missed dose of insulin and infections were found to be the most frequent precipitating factors in our population, favourable outcome in DKA can be achieved by improved access to medical care.

Conclusion: Diabetic ketoacidosis occurs frequently among type 1 Saudi diabetic adolescents. The high recurrence admission rate underscores the importance of repeated diabetic education, social and family support in this difficult age group.

Abstract #263

IRISIN IN THE GLUCOSE CONTINUUM – FROM NORMAL GLUCOSE TOLERANCE THROUGH PREDIABETES TO TYPE 2 DIABETES MELLITUS

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Objective: Skeletal muscle can produce substances such as cytokines or other peptides that can modulate metabolic processes. These cytokines, called “myokines” act as hormones either locally or by targeting distant organs. One such myokine is irisin. It has been identified as a promoter of “browning” of white adipose tissue and a possible marker reflecting the metabolic status. The aim of this study was to evaluate the serum levels of irisin in individuals with normal glucose tolerance, prediabetes and type 2 diabetes mellitus (T2DM) and to observe its relations to the traditional metabolic parameters.

Methods: A total of 160 subjects recruited from 2013-2014 in an University Hospital setting participated in the study. The subjects were divided into three groups – 50 with normal glucose tolerance (NGT); 60 with prediabetes (PreDM); 50 with T2DM. PreDM and T2DM were established based on the ADA criteria. Anthropometric measures included waist circumference, weight, height. Biochemical measurements included HbA1c, liver enzymes, uric acid (UA), lipids. Standart OGTts with Immunoreactive Insulins(IRI) were performed where Type 2 Diabetes Mellitus (T2DM) was not already diagnosed. FINDRISC questionnaire was performed. Circulating serum irisin was quantified by ELISA and its association with markers of metabolic phenotype was analyzed by Pearson bivariate correlation. Receiver operating characteristic and non-parametric tests were employed where applicable.

Results: Median Age of the study participants was 49 yrs (IQR=13), median BMI was 34.6 kg/m2 (IQR=7.34).
60 (37.5%) of the study participants were male. The three groups – NGT, preDM and T2DM did not differ statistically by BMI, age and gender. Irisin progressively decreased from NGT (median = 619 ng/ml), preDM (median = 314 ng/ml) to T2DM (median = 228 ng/ml) and the observed differences were statistically significant between all groups (p<0.005). Irisin correlated positively with BMI (r=0.387), and negatively with FPG (r=0.358), triglycerides (r=-0.204), ALT (r=-0.202), UA (r=-0.241), FINDRISC score (r=-0.191). Adjusting for age and BMI the observed correlations persisted statistically significant. Employing ROC curve analyses we determined that irisinemia was a good predictor for T2DM (r=0.705).

Discussion: Irisin appeared to be associated with important metabolic factors and might prove to be of value when evaluating patients with increased metabolic risk.

Conclusion: Circulating irisin levels progressively decrease with the worsening of the glucose tolerance. Its role in the pathogenesis of T2DM is yet to be elucidated.

Abstract #264

IMPACT OF CANAGLIFLOZIN IN TYPE 2 DIABETIC PATIENTS IN A REAL WORLD SETTING

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Objective: To evaluate the effect of adding canagliflozin to complex regimens in patients with type 2 diabetes in a private practice setting.

Methods: Charts were reviewed on 41 patients started on canagliflozin. Indications for starting it were glycemic control, weight reduction, reduction in insulin/SU dose or avoidance of hypoglycemia. For HbA1c below 8%, SU was reduced 50-100%, basal insulin was reduced 20% and prandial insulin was reduced 50% or stopped if the dose was less than 8 units per meal. In the registration trials investigators adjusted the blood pressure medications as needed. Reductions in systolic blood pressure (SBP) were noted, with no mention of how the medications were adjusted. In our practice, blood pressure medication was reduced before starting canagliflozin if SBP was below 120 mm Hg or if there was an orthostatic drop of more than 10 mm Hg, and further reduced if needed.

Results: Seven of the 41 patients stopped canagliflozin (2 for lack of benefit, 2 for genital mycotic infection, 1 for frequent urination with persistent hyperglycemia, 1 for hypoglycemia on metformin and liraglutide, and 1 for body rash). Results on the remaining 34 patients were analyzed. Duration of therapy was 4 to 30 weeks (average 19 weeks). Average age was 66 years. Other medications were metformin (47%), insulin (32.4%), GLP-1 agonists (32.3%), SU (32%), TZD (11.8%), and DPP-4 Inhibitors (5.9%). Starting HbA1c was 7.3% and final HbA1c was 6.7%, a decrease of 0.6% (range -2.3% to +0.5%). HbA1c decreased in 26, was unchanged in 1, and increased in 7 patients, despite reductions in insulin dose in 70% of patients on insulin and reductions in SU dose. Starting weight was 213 lbs, and decreased by 9.6 lbs (4.5%). 29 patients lost weight, two stayed the same, and 3 gained an average of 1.2 lbs. Less weight loss was noted in the group taking GLP-1 agonists vs. those not on GLP-1 agonists (6.6 lb vs 11 lb). Baseline SBP was 125 mm Hg, and decreased overall by an average of 7.8 mm Hg, (range -40 to +10). However, 8 patients had reductions in blood pressure medication and excluding them the average reduction was 11.3 mm Hg. Potassium rose by 0.11 mEq/L.

Discussion: Addition of canagliflozin to heavily treated T2 diabetic patients resulted in a 0.6% drop in HbA1c starting from 7.3%. Weight reduction of 9.6 lbs (-4.5%) was seen, and was less in the group on GLP-1 agonist therapy. SBP dropped 11.3 mm Hg when blood pressure medications were not reduced. Blood pressure medication had to be reduced in 23.5% of patients.

Conclusion: Addition of canagliflozin was strongly beneficial when added to patients on comprehensive regimens for T2DM. Reductions in blood pressure medication were often required to avoid hypotension.

Abstract #265

TRENDS OF INCIDENT AND PREVALENT USE OF HUMAN REGULAR U-500 INSULIN OVER A 9-YEAR PERIOD IN THE UNITED STATES

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Eli Lilly and Company

Objective: With the growing prevalence of obesity, more patients with diabetes are becoming severely insulin-resistant, requiring total daily doses of insulin >200 Units (U) or >2 U/kg. Insulin-resistant patients may need >4 daily injections of regular U-100 insulin in large volumes to get their required dose. Concentrated human regular U-500 insulin (U-500R, 500 U/ml) allows for subcutaneous injection of large insulin doses in a reasonable volume. While U-500R has been available in the US since 1997, the patterns of its use have not been evaluated. This retrospective analysis captured the trends of incidence and prevalence per year of U-500R use from 2005 to 2013 using the Truven MarketScan® database of medical and pharmacy claims for >20 million US residents.
Methods: Patients with type 1 diabetes (T1D) were identified using the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes 250.x1 or 250.x3. Patients with type 2 diabetes (T2D) were identified by excluding patients with T1D from all patients with diabetes (code 250.xx). Incidence was defined as the number of new patients initiating U-500R for the first time within each year. Prevalence was defined as the number of patients using U-500R within a 1-year period. While the incidence and prevalence of patients using U-500R were determined for each year, we report data from 2005, 2009, and 2013 to represent the beginning, middle, and end of this 9-year period.

Results: There were 475 incident cases (T1D 28, T2D 447) of patients using U-500R in 2005, which increased to 1415 cases (T1D 65, T2D 1350) in 2009, and 1903 cases (T1D 96, T2D 1807) in 2013. The prevalence of patients using U-500R in 2005, 2009, and 2013 was 30, 140, and 245, respectively for T1D, and 470, 2562, and 5144 for T2D. The overall age (mean ± standard deviation) among prevalent users was consistent between 2005 (55.6 ± 10.2 yr) and 2013 (56.4 ± 10.1 yr). Prevalent users with T1D were slightly younger (45.6 ± 15.1 yr) than patients with T2D (55.4 ± 9.8 yr) in 2009, and for all other years. Between 55% (2005) and 61% (2013) of prevalent users were male and about 5% had T1D. Among incident users, similar trends in age and gender were observed during this time.

Discussion: Between 2005 and 2013, the total number of prevalent U-500R users increased 9.8-fold, while the incidence of new users grew 3.0-fold. Patients using U-500R were mostly male with an average age of about 55 yr, and around 95% had T2D. The number of incident users of U-500R increased from 2007 to 2010 and remained steady from 2010 to 2013.

Conclusion: There is a trend for escalated use of U-500R among patients with T2D.

Abstract #266

PREVALENCE AND PATTERN OF CHRONIC COMPLICATIONS OF TYPE 2 DIABETES AMONG BANGLADESHI POPULATION

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Objective: The aims of this study were to describe the prevalence of chronic complications among Bangladeshi type 2 diabetes patients; and to analyze the associations between chronic complications and patients’ demographics.

Methods: This cross-sectional study was conducted in the out-patient departments (OPDs) of hospitals of Bangladesh Diabetes Association (BADAS) in Dhaka, during the period of July 2012 to June 2013. They were interviewed face to face by trained interviewers using a semi-structured questionnaire.

Results: Among 2,598 type 2 diabetic patients, 1,398 (53.81%) of them had one or more diabetes related complications. The mean duration of diabetes was 7.9 years. The prevalence of cardiovascular complications, neuropathy, renal complications, ocular lesions, diabetic foot disease and other complications such as erectile dysfunction were 27.44%, 11.2%, 14.97%, 12.63%, 2.50% and 10.32%, respectively. About 14.97% patients had diabetic nephropathy, 12.63% ocular and 2.50% ha foot complications.

The average level of HbA1c of patients with chronic complications was 8.9% (ranging from 5.7% to 15.8%).

Discussion: The study found that complications are highly prevalent among urban Bangladeshi type 2 diabetes patients. M than half of the patients of this study suffered from at least one chronic complication of diabetes. Thus, chronic complications of type 2 diabetes exert a huge burden on Bangladesh’s health care system. The overall prevalence of macrovascular complications (29.94%) noted in the present study is somewhat lower than the corresponding rates reported from Oklahoma, Warsaw, Havana, Berlin and Australia, but is higher than the rates reported in previous studies conducted in China. This study also found a predominance of cardiovascular complications (27.44%) among diabetic patients in Bangladesh over other morbidities. Neuropathy, with a prevalence of 11.2%, was somewhat less common in this study than in studies carried out in Canada, the United States and Sweden. The most surprising finding was the low prevalence of foot diseases at 2.5%, much lower than the 8.0% reported for Asian-Americans. In Bangladesh, even low prevalence translates into substantial absolute disease burden figures due to the high number of diabetic patients. The incidence of chronic complications in type 2 diabetes patients was significantly associated with the degree of hyperglycemia, as measured by the HbA1c level.

Conclusion: A high prevalence of chronic complications was found among outpatients with type 2 diabetes, with a predominance of cardiovascular and renal complications. The patients with diabetes-related complications having a poor glycemic control.
Abstract #267

INCIDENCE OF GENITAL MYCOTIC INFECTIONS DECLINES OVER TIME IN PATIENTS WITH TYPE 2 DIABETES MELLITUS TREATED WITH CANAGLIFLOZIN OVER 2 YEARS

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Objective: Sodium glucose co-transporter 2 inhibitors, such as canagliflozin (CANA), improve glycemic control by lowering the renal threshold for glucose reabsorption and increasing urinary glucose excretion; a mechanism of action associated with increased incidence of genital mycotic infections (GMIs). The incidence of GMIs was evaluated over a 2-y period in patients with type 2 diabetes mellitus (T2DM) treated with CANA.

Methods: In this active-controlled Phase 3 study, patients aged 18–80 y with T2DM (mean baseline A1C 7.8%) received CANA 100 mg (n = 483) or 300 mg (n = 485), or glimepiride (GLIM; n = 482) up-titrated to 6 mg or 8 mg per day. Blinded therapy was administered once daily on a background of metformin for 52 wks, followed by a 52-wk extension. Incidence of GMIs was evaluated overall and at 3-mo intervals.

Results: The cumulative incidence of GMIs over 2 y was higher for CANA 100 mg and 300 mg than GLIM in females (13.9% and 15.6% vs 2.7%) and males (9.5% and 9.1% vs 1.9%). In patients treated with CANA, the highest incidence of GMIs occurred at Months 0–3 (CANA 100 mg and 300 mg: females, 7.4% and 7.8%; males, 3.6% and 3.3%) after which the incidence of GMIs decreased. In females, incidence of GMIs decreased during Months >3–6 to 3.3% and 4.5% for CANA 100 mg and 300 mg, then stabilized through Months >9–12, before decreasing further (Months >12–15: 2.2% and 2.6%); it then remained low until study completion (Months >21–24). In males, incidence of GMIs decreased slightly between Months >3–6 (CANA 100 mg and 300 mg: 2.9% and 3.1%), decreased to 0.4% and 1.9% between Months >6–9, and then remained low until study completion (Months >21–24: 0.5% and 0.6%). GMIs were generally mild to moderate in intensity, and few led to study discontinuation. Risk factors for GMI were a history of GMIs in females and being uncircumcised in males.

Discussion: In this 2 y study of patients with T2DM, CANA was associated with a higher incidence of GMIs than GLIM. The highest incidence of GMIs with CANA occurred during the first 3 mo of treatment and then decreased over time. GMIs were generally mild to moderate in intensity and few led to study discontinuation. These data suggest that the risk of GMIs with CANA use is mostly increased early after treatment initiation.

Conclusion: The incidence of GMIs associated with CANA occurred primarily during the first 3 mo of treatment and decreased over time in patients with T2DM.

Abstract #268

INCREASED SERUM FETUIN-A IS AN IMPORTANT ADVERSE PREDICTOR OF GLYCEMIC OUTCOMES IN PREDIABETES: A 4 YEAR PROSPECTIVE STUDY FROM INDIA

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Objective: Fetuin-A worsens insulin resistance. This study evaluated its role in predicting progression to diabetes or reversal to normoglycemia in individuals with prediabetes (IPD).

Methods: 2119 individuals were screened using glucometer at health camps conducted from 2010-2014 from which 144 IPD, 50 normal individuals and 66 newly diagnosed diabetes were included after confirming diagnosis using 2 consecutive OGTT done within a week. Study participants underwent estimation of fasting insulin, fetuin-A, IL6, IL1β, TNFa, lipids, 25-hydroxyvitamin-D (25OHD), non-alcoholic fatty liver disease (NAFLD) assessment using ultrasonography and fatty liver index (FLI). All included individuals were advised therapeutic lifestyle interventions whose compliance was ensured using text messages weekly, monthly telephone calls and sessions with dietician 3 monthly. IPD were followed 3 monthly, when fasting and 2-hour post meal glucose levels were checked using glucometer and confirmed using OGTT. IPD with at least 12 months of follow-up were analyzed according to quartiles of fetuin-A and glycemic outcomes.

Results: Fetuin-A, IL1β, IL6, TNFa, lipids, 25-hydroxyvitamin-D (25OHD), non-alcoholic fatty liver disease (NAFLD) assessment using ultrasonography and fatty liver index (FLI). All included individuals were advised therapeutic lifestyle interventions whose compliance was ensured using text messages weekly, monthly telephone calls and sessions with dietician 3 monthly. IPD were followed 3 monthly, when fasting and 2-hour post meal glucose levels were checked using glucometer and confirmed using OGTT. IPD with at least 12 months of follow-up were analyzed according to quartiles of fetuin-A and glycemic outcomes.

Discussion: In this 2 y study of patients with T2DM, CANA was associated with a higher incidence of GMIs than GLIM. The highest incidence of GMIs with CANA occurred during the first 3 mo of treatment and then decreased over time. GMIs were generally mild to moderate in intensity and few led to study discontinuation. These data suggest that the risk of GMIs with CANA use is mostly increased early after treatment initiation.

Conclusion: The incidence of GMIs associated with CANA occurred primarily during the first 3 mo of treatment and decreased over time in patients with T2DM.
ml), IL1β (6.36±1.97pg/ml), FLI (60.02±29.77), NAFLD and lower 25OHD (45.33±22.56nmol/L). IPD in highest fetuin-A quartile [median: 549.5mcg/ml, range: 509.5-774.85mcg/ml] had highest progression to diabetes [Relative risk (RR): 2.68; 95% Confidence Interval (CI): 0.95–7.55; P=0.06] and lowest reversal to normoglycemia (RR: 0.27; 95% CI: 0.08–0.85; P=0.03). Fetuin-A levels correlated with IL1β (r=0.420; P<0.001), IL6 (r=0.231; P=0.022) and FLI (r=0.319; P<0.001). Cox regression revealed baseline fetuin-A (P=0.022), 25OHD (P=0.057) and BMI (P=0.073) to be predictive of reversal to normoglycemia. Every unit increase in fetuin-A, 25OHD and BMI were associated with 8.8% decreased, 6.5% increased and 19.7% decreased reversal to normoglycemia respectively. Age (P=0.02), triglycerides (P=0.024), IL6 (P=0.026), and IL1β (P=0.066) were predictive of progression to diabetes. Every unit increase in age, triglycerides, IL6 and IL1β were associated with 17.4% decreased, 2% increased, 15.7% increased and 17.1% increased progression to diabetes respectively.

Conclusion: Increased fetuin-A in prediabetes is associated with increased progression to diabetes and decreased reversal to normoglycemia through increased insulin resistance and systemic inflammation.

Abstract #269

PHARMACOKINETIC BIOEQUIVALENT AND NON-BIOEQUIVALENT CONCENTRATED INSULIN FORMULATIONS: IMPLICATIONS FOR CLINICAL USE AND DOSING

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Eli Lilly and Company

Objective: To provide practical clinical insights for use/potential use and dosing of 2 concentrated insulin formulations, we reviewed 2 separate pharmacokinetic (PK) studies of clinically relevant doses of human regular U-500 insulin (500 units [U]/mL; U-500R) and insulin lispro 200 U/mL (IL U-200) versus respective U-100 formulations. U-500R was approved in the US in 1994 allowing administration of large doses at one-fifth the volume of U-100 insulins to severely insulin-resistant patients with diabetes. IL U-200, recently approved in the EU as bioequivalent to insulin lispro 100 U/mL, provides the same dose in half the volume. To be bioequivalent per the FDA, 90% confidence intervals (CIs) for the ratio of PK parameters (generally area under the curve [AUC] and peak concentration [Cmax]) should be within [0.80,1.25] (FDA Industry Guidance: Bioavailability and Bioequivalence Studies Dec 2013-Mar 2014).

Methods: Insulin was dosed as single subcutaneous bolus injections in single-site, randomized, crossover, euglycemic clamp studies. U-500R and human regular U-100 insulin (U-100R) were administered as 50- and 100-U doses to 24 healthy obese subjects (de la Peña. Diabetes Care. 2011;34:2496-2501). IL U-200 and IL U-100 were given as 20-U doses to 38 healthy subjects (NCT01133392).

Results: U-500R overall exposure (AUC from zero to return to baseline) was similar to that of U-100R for both the 50- and 100-U doses, with 90% CIs of ratios within [0.80, 1.25]. However, for U-500R compared to U-100R, Cmax was lower for both doses (50-U: 548 vs 809 ρmol/L; 100-U: 1020 vs 1400 ρmol/L; p<.001) and time to maximum insulin concentration was longer for the 100-U dose (8 vs 3 hrs, p<.001). IL U-200 demonstrated a similar PK profile relative to IL U-100, with 90% CIs for the ratios of AUC from zero to last measurable concentration and Cmax within [0.80, 1.25].

Conclusion: U-500R, with its lower Cmax and prolonged exposure, is not bioequivalent to standard U-100R. Thus, U-500R is dosed differently and may be used as insulin monotherapy without concomitant U-100 basal insulin to meet prandial/basal needs. Accordingly, U-500R requires a transition formula and different dosing proportions when switching from U-100 insulins and unique dosing algorithms relative to conventional U-100 insulins. In contrast, IL U 200 is bioequivalent to IL U-100, so dosing by 1-U increments (half the volume with IL U 200) should be identical for both. PK profiles of concentrated insulin formulations may be similar to or different from their U-100 counterparts, which will determine how these agents may be used/dosed in clinical practice.

Abstract #270

OUTCOMES OF A STANDARDIZED PROTOCOL FOR DIABETES MANAGEMENT IN SURGICAL INPATIENTS

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Objective: The aim of the study is to evaluate the outcomes of a standardized protocol for preoperative management of diabetes mellitus (DM) on the rates of hypoglycemia and hyperglycemia in patients undergoing surgical procedures.

Methods: Eligible patients were 18 years or older diabetics on hypoglycemic medications, undergoing surgical procedures, and kept NPO >8 hours prior to the procedure.
The investigators developed a protocol for the preoperative medical management of DM, implemented as an order set for patients undergoing surgical procedures. In the order set, hypoglycemia was defined as a blood glucose (BG) <=70mg/dl, and hyperglycemia as BG >=300mg/dl. Retrospective data were collected from the electronic medical record of patients placed in two cohorts, pre- and post- protocol use. Pre- protocol data included: type of DM, DM medications, and type of surgical procedure. Post- protocol data additionally included pre-operative orders for NPO status and IV fluids, pre-operative BG measurement and incidence of hypo- or hyperglycemia while NPO, as well as time of dietary resumption. Chi-square tests were used to compare the percent (%) of appropriate orders written, % BG values in target 140-180mg/dl, and episodes of hypo- and hyperglycemia pre- and post- protocol. The mean pre-surgical BG value was compared using an independent t-test.

**Results:** Study entailed n=117 subjects, n=48 in pre- and n=69 in post-protocol groups. The majority of subjects in each group were Type 2 DM on oral hypoglycemic medications: pre- 18/48, (41%) and post- 21/69, (32%). Using the protocol led to identification of significantly fewer subjects with hypoglycemia (pre- 21%, post- 4%, p=0.012) while NPO. However, there was a significantly higher number of subjects with hyperglycemia in the post-protocol group (pre- 4%, post- 17%, p=0.041) and higher pre-surgical BG values as well (pre- 140.9±45, post- 167.9±62, p=0.007). There was no significant difference between groups for the % BG in target range, written orders for IV fluids or NPO status.

**Discussion:** Patients with DM are at a greater risk for perioperative complications from poor glycemic control. Hypo and hyperglycemia contribute to poor outcomes. Medication and IV fluid modifications should be made pre and post operatively, taking into consideration the patient’s oral intake. The American Association of Clinical Endocrinologists recommends developing and implementing protocols to improve standardized care of diabetes patients.

**Conclusion:** Our study demonstrated that a standardized approach to perioperative DM management may be beneficial in reducing hypoglycemia. Further work is needed to identify strategies that do not concurrently increase the risk of hyperglycemia.

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**Abstract #271**

**IMPACT OF PREGABALIN ON SIGNS AND SYMPTOMS OF GASTROPARESIS**

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**Objective:** Evaluate our anecdotal experience of dramatic improvement in signs and symptoms of intractable gastroparesis following treatment with pregabalin in patients with long-standing poorly controlled diabetes.

**Methods:** We conducted a two-center randomized, double-blind, placebo controlled cross-over study to assess the impact of pregabalin on patients with diabetes and documented (by gastric emptying study or GES), symptomatic gastroparesis. Enrolled subjects were started on pregabalin or placebo and doses titrated up to either symptom resolution or a maximum of 300 mg daily over a period of 8 weeks. Following a 1-week washout subjects underwent treatment cross-over and an additional 8 weeks of treatment. Gastroparesis Cardinal Symptom Index (GCSI) score and GES were measured at baseline and at the end of each treatment period. We consented 24 subjects with symptoms suspicious for gastroparesis as per GCSI; 12 subjects had a normal GES.

**Results:** Twenty patients with data (70% women, 25% type 1 diabetes, 80% on insulin) had the following means (±SD): age 49±10 years, weight 84.3±21.0 kg, BMI 31.6±6.4 kg/m2, A1C 8.3±1.6%. Baseline GCSI (27.7±10.2) improved in both treatment groups with mean change in the pregabalin group of -10.5 (95% CI: -18.56, -2.44) and placebo of -11.33 (95% CI: -21.44, -1.23). Gastric emptying was measured as % of retained Tc-99; mean baseline retention at 1 and 4 hours were 82.7±12.9% and 20.2±20.1%, respectively. The mean change in % retained at 1 and 4 hours was -13.7±15.7% and -14.3±28.5%, respectively, in the pregabalin group, and -10.7±20.6% and -4.3±28.6%, respectively, in the placebo group, at the end of the treatment period. Pearson’s correlation coefficients were used to explore the relationship between GCSI and GES. Results revealed no significant relationship between GCSI and any of the GES results (All p>0.05).

**Discussion:** Despite compelling anecdotal observation, the use of pregabalin in patients with documented symptomatic gastroparesis did not appear to provide additional benefits over placebo. Many of the subjects with suspicious symptomatology on GCSI actually had normal GES.
Conclusion: There was poor correlation between GES results and symptomatology as per GCSC, calling into question the reliability of either assessment in the diagnosis, or management, of gastroparesis in clinical practice. While at this time there is no strong evidence for a beneficial effect of pregabalin on gastroparetic symptomatology, this pilot study might inform additional investigations on a larger sample of affected subjects, or encourage further studies on appropriate diagnostic tools for this condition.

Abstract #272

EXPERIENCE USING V-GO® IN PATIENTS WITH LATENT AUTOIMMUNE DIABETES OF THE ADULT (LADA) AND TYPE 1 DIABETES

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Objective: To date, no data has been published regarding the specific use of V-Go Disposable Insulin Delivery Device (V-Go) in patients diagnosed with LADA or with type 1 diabetes (T1DM). The objective of this study was to assess the efficacy and safety of patients with these forms of diabetes suboptimally controlled with multiple daily injections (MDI) switched to V-Go.

Methods: A subanalysis of patients with LADA or T1DM was conducted from a larger study evaluating patients poorly controlled on previous therapies switched to V-Go. Data was collected using an electronic medical records database. Change from baseline was examined for HbA1c, fasting plasma glucose (FPG), weight, insulin dosing and reported hypoglycemia. Evaluation criteria included patients ≥21 years of age and previously using insulin with an HbA1c >7.0%.

Results: Twenty one patients with LADA or T1DM with elevated blood glucose were switched to V-Go therapy. Mean baseline characteristics were: age 44 yrs, weight 88 kg (193 lbs), duration of diabetes 19 yrs, HbA1c 9.6%, FPG 245 mg/dl, basal insulin dose 38 U/day, and total daily insulin dose (TDD) 66 U/day. Mean exposure to V-Go therapy was 103 days at the time of this analysis. Twenty one patients with LADA or T1DM with elevated blood glucose were switched to V-Go therapy. Mean baseline characteristics were: age 44 yrs, weight 88 kg (193 lbs), duration of diabetes 19 yrs, HbA1c 9.6%, FPG 245 mg/dl, basal insulin dose 38 U/day, and total daily insulin dose (TDD) 66 U/day. Mean exposure to V-Go therapy was 103 days at the time of this analysis.

Discussion: Many patients with diabetes are unsuccessful at reaching and maintaining therapeutic goals. Multiple daily injections can be a burden for those with LADA or T1DM and data is limited in this patient type using V-Go therapy. Our data suggests that V-Go offers an efficacious approach to deliver basal-bolus therapy and reduce the burden of glucose management through simplified delivery. Larger controlled studies are needed to fully evaluate the use of V-Go in this patient population.

Conclusion: Switching to V-Go resulted in significant HbA1c reductions, decreased insulin requirements, and no increase in reported hypoglycemia for patients uncontrolled with LADA or T1DM.

Abstract #273

EVALUATING THE EFFECT OF V-GO® THERAPY IN SUB-OPTIMALLY CONTROLLED PATIENTS WITH DIABETES – A RETROSPECTIVE COHORT ANALYSIS IN A LARGE SPECIALIZED DIABETES SYSTEM

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Objective: The purpose of this retrospective analysis was to evaluate the effect of switching to the V-Go Disposable Insulin Delivery Device (V-Go) in patients with Diabetes Mellitus (DM) sub-optimally controlled on previous therapeutic regimens.

Methods: An electronic medical records database from a large specialized diabetes system was queried to identify patients exceeding glycemic targets (HbA1c > 7.0) on multiple daily insulin injections (MDI), basal insulin therapy (Basal), or naïve to insulin (Naïve) at baseline, changed to V-Go between April 2013 and May 2014. HbA1c, weight, insulin dosing, and reported hypoglycemia were collected at baseline and at each follow-up office visit with an HbA1c result.

Results: One-hundred fifty three patients had a follow-up visit (FV1) with a documented HbA1c, and to date, 102 patients had a second HbA1c result (FV2) at the time of these analyses. The mean age was 52 yrs, weight 96 kg (212 lbs), and duration of DM 14 yrs. Eighty six patients were on MDI, 45 on Basal and 22 were Naïve at baseline. Mean exposure to V-Go therapy was 98 days for FV1 and 180 days for FV2. Mean baseline HbA1c levels were 9.7% for the total population and 9.4%, 9.6%, and 11.2% for the MDI, Basal and Naïve cohorts, respectively. Significant HbA1c reductions at both FV1 and FV2 were observed for all patients and all cohorts (p<0.0001). Mean changes [95% CI] from baseline for FV1 and FV2 were as follows: total population (-1.7 [-2.0, -1.4] , -1.8 [-2.1, -1.5]), MDI cohort (-1.2 [-1.5, -0.89], -1.2 [-1.6, -0.86]), Basal cohort (-1.9 [-2.4, -1.5] -2.3 [-2.8, -1.7]), and Naïve cohort (-3.1 [-4.0, -2.3], -3.3 [-4.2, -2.4]), respectively. Patients previously on
MDI therapy experienced a 31% reduction (88 to 61 U/day) in mean total daily insulin from baseline while on V-Go. A reduction in fasting plasma glucose (192 to 146 mg/dl) was observed in the Basal cohort despite a 33% reduction (51 to 34 U/day) in the mean daily basal insulin dose. The total population experienced a median increase in weight of 1.5 – 2 kg (p<0.0001). Despite robust improvements in glucose control the overall incidence of reported hypoglycemia was similar to baseline at both visits.

Discussion: Patients with suboptimal DM control switched to V-Go achieved significant HbA1c improvements with reductions in total daily insulin requirements by most. Patients on previous Basal insulin regimens and Naïve to insulin experienced the greatest reductions in HbA1c.

Conclusion: V-Go is both safe and effective in patients with uncontrolled DM requiring insulin therapy. V-Go was efficacious in patients with marked hyperglycemia and previously naïve to insulin therapy.

Abstract #274

ELEVATED AST AND ALT RESULTS AND AN AST/ALT RATIO BETWEEN 0.7 AND 1.0 LINKED TO AN INCREASED RISK OF NASH IN PATIENTS WITH DIABETES

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Objective: Nonalcoholic steatohepatitis (NASH) is thought to affect 5% of Americans, with even higher prevalence in those with diabetes (DM). There is no known lab test to screen for NASH. We studied a national lab test database (Medivo Inc., NY, NY) to search for lab tests that may be used to screen.

Methods: We conducted 3 analyses on database lab tests conducted July 2013 - June 2014. We looked at 145,059 patients with DM who had lab tests including AST, ALT and AST/ALT ratio, ALK Phos, and creatinine. Second, we looked at 1,500 patients with DM and 71 patients with NASH who had results of all tests available. Logistic regression was used to determine what test results have significant association with NASH. Finally, we studied patients with these test results (N = 225,444) and compared the risk of NASH in patients with DM (N = 109,594) vs. those without DM (N = 115,850). We defined an AST/ALT ratio between 0.7 - 1.0 and an abnormal AST of >40 U/L as indicating NASH risk.

Results: In the first analysis, 126 patients (0.087%) had an ICD-9 code for NASH; 125 had ICD-9 codes for cirrhosis/other liver diseases (0.086%); 5 had an ICD-9 code for alcoholism (0.003%); 8,794 (6.06%) had an abnormal AST; 15,759 (10.86%) had an abnormal ALT; 8,927 (6.15%) had an abnormal ALK Phos; and 23,112 (15.93%) had an abnormal creatinine. In the second analysis, we found that AST and ALT were significant predictors of NASH in patients with DM. We found that patients with DM with elevated AST and/or ALT were 2.5 - 3 times more likely to have NASH (OR (AST)=3.004, OR(ALT)=2.586, p<0.01) than patients with abnormal results on other tests. In the third analysis, we found that 5,072 (4.63%) of patients with DM were at elevated risk for NASH with an AST/ALT ratio between 0.7 - 1.0, and AST > 40; 2,547 (2.20%) of patients without DM also met the criteria. Moreover, we found that DM has a significant association with NASH. DM patients were 116% more likely to have NASH than patients without DM (OR=2.16, p<0.001).

Discussion: Our analyses suggest that elevated AST and ALT lab test results, and an AST/ALT ratio between 0.7 - 1.0 are associated with NASH/ risk for NASH. Further, we found a significantly higher risk of NASH in patients with DM compared to those without DM.

Conclusion: Patients with DM are at higher risk for NASH compared to those without DM. We also found that the results of AST, ALT, AST/ALT ratio lab tests may be associated with NASH in patients with and without DM. More study is needed to confirm these results, to compare them with histological findings, and to study patient demographics to identify populations that will benefit from screening for NASH.

Abstract #275

THE CDE-AMBASSADOR: A NOVEL APPROACH TO CONTROL DIABETES AT THE PRIMARY CARE LEVEL LEADS TO SIGNIFICANT IMPROVEMENT IN GLYCEMIC CONTROL AND CARDIOVASCULAR RISK FACTORS

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Objective: Since the incidence of diabetes is increasing and the number of endocrinologists is limited, we hypothesized that certified diabetic educators (CDE) trained and continuously guided by endocrinologists, called CDE-Ambassadors (CDE-A) could be used to instruct and guide patients’ treatment at the primary care level to induce significant improvements in glycemia (A1c), body weight, blood pressure, lipid concentrations and albuminuria.
Methods: We conducted a retrospective review of one hundred type 2 diabetic patients managed by their primary care provider (PCP) and compared those referred by their PCP to consult with CDE-A with those who were not. The start date was the first visit with the CDE-A. The follow up visit date was the scheduled visit with their PCP following the intervention. Most patients met with the educator twice during that period and no patient consulted an endocrinologist.

Results: Over a mean duration of follow up of 4.6 months, the mean A1c dropped from 8.4 ±2 % to 6.8 ±1%; weight by 2.8 Kg from 102 ± 22 to 99 ± 22 Kg; and BMI by 0.96 (p <0.0001 for all). Systolic blood pressure decreased from 134 ±17mm Hg to 128 ±13 mm Hg and the diastolic blood pressure dropped from 80±10 mm Hg to 77±9 mm Hg (p< 0.005 for both). LDL fell from 108±36 to 96± 36 mg/dl and triglycerides fell from 189 ±121 to 162±90 mg/ dl (p< 0.005). The urine microalbumin/creatinine ratio also dropped from 64±536 to 27± 153 mg/g (p=0.33). In contrast, in another group of forty five patients with diabetes from the same practice not referred to the CDE-A during the same timeframe, there was no significant change in any of the indices.

Discussion: Our data show clearly that the participation of the CDE-A, under the guidance of an endocrinologist at the primary care level led to a marked reduction in HbA1c, LDLc, triglycerides, blood pressure and body weight within 5 months. These changes were dependent on changes in dietary habits and drug therapy including the addition or optimization in the doses of anti-diabetic drugs and insulin doses. It is of interest that the changes in lipids occurred without any change in statin therapy, probably due to increased compliance.

Conclusion: The changes in glycemia, blood pressure, lipids and body weight would potentially result in a significant reduction in microvascular and macrovascular complications and improvement in the quality of life of these patients. In addition, it will reduce the magnitude of expenditure which currently occurs in the management of these complications. We are now contemplating prospectively randomized studies comparing centers which are supported with CDE-A with those that are not and to study the durability of and cost saving related to these effects.

Abstract #276
INSULIN PUMP THERAPY USE DURING SURGERY: AN UPDATE ON A QUALITY INITIATIVE

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Objective: Little data is available on insulin pump therapy use in the perioperative period, and few recommendations exist on how to manage patients on insulin pumps during the surgical episode of care. In 2012 an institutional care process model (CPM) was implemented to provide guidance to surgical and anesthesiology staff on how to care for such patients. The objective of this analysis was to review the effectiveness of the CPM for patients on insulin pump therapy undergoing elective surgical procedures.

Methods: Electronic medical records were reviewed to assess the impact of the CPM on documentation of insulin pump status, glucose monitoring, and safety during the perioperative phase of care. Post-CPM care was compared with management provided before CPM implementation.

Results: We reviewed 45 cases on insulin pump therapy in the pre-CPM cohort and 75 in the post-CPM cohort. Demographic characteristics, categories of surgery, and perioperative times were not significantly different between the 2 groups. The frequency of recommended hemoglobin A1c testing increased from 58% in the pre-CPM cohort to 92% in the post-CPM group (P<.001). Staff documentation of the insulin pump for the pre-CPM and post-CPM cohorts improved during the intraoperative (14% vs 62%; P<.001) and in the postanesthesia care unit (59% vs 80%; P=.02) segments of care but not in the preoperative segment (80% vs 90%; P=.14). Glucose monitoring improved only during the intraoperative segment of care (57% vs 77%; P=.04). In the pre-CPM and post-CPM cohorts, respective mean (SD) point of care blood glucose (POC-BG) values were 171 (66) and 171 (74) mg/dL during the preoperative segment of care and 179 (53) and 179 (52) mg/dL in the PACU (P=.99 for both). For patients who had surgical procedures lasting ≥60 minutes, mean intraoperative POC-BG was 172 (54) mg/dL and 183 (58) mg/dL in the pre-CPM and post-CPM groups, respectively (P=.46). Hypoglycemic events were rare in both groups. There were no adverse events associated with perioperative insulin pump use such as devices becoming inadvertently disconnected, catheters being kinked, or pump malfunctions.

Discussion: This report adds to previous data and represents an analysis of the largest sample of perioperative insulin pump use to date. Patients on insulin pump therapy who
undergo elective surgical procedures do not necessarily have to disconnect from their devices.

**Conclusion:** Some aspects of care require additional attention, but data continue to indicate that a standardized approach to care can lead to a successful and safe transition of insulin pump therapy throughout the perioperative period.

**Abstract #277**

**SELECTIVE BIOMARKERS OF ISOLATED IFG (IIFG) AND ISOLATED IGT (IIGT)**

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**Objective:** IFG and IGT are distinct prediabetic states which may be characterized by different metabolite profiles. This work focused on identifying metabolites selective for the non-overlapping conditions of iIFG and iIGT.

**Methods:** A targeted metabolomic analysis of fasting plasma samples taken at time=0 of an OGTT was performed. Quantitative measurements for a panel of 23 metabolites previously associated with prediabetes and type 2 diabetes were made using the isotope dilution method. The initial samples came from subjects at risk for diabetes (IFG, IGT, of FINDRISC score >12) in the DMVHI study (part of the DEXLIFE project). The data was rank normalized using the GenAbel package. Disease states were classified as normal (normal glucose tolerance & fasting glucose, n=485), iIFG (n=104), or iIGT (n=31). The associations of metabolites for normal vs iIFG or iIGT were made using logistic regressions controlling for age, sex, and BMI. Odds ratios for a one SD change in the metabolite level, 95% confidence intervals and p values were calculated for each metabolite. P values were adjusted with a false discovery rate of 0.1.

**Results:** Two metabolites associated with iIFG, 2-oxoaloeine (1.65 (1.3-2.2), 0.001) and 2-oxovaline (1.58 (1.2-2.0), 0.001) had no significant association with iIGT. α-Hydroxybutyrate (α-HB) was associated with iIGT (2.54 (1.9-3.5) 5E-9) and had no significant association with iIFG. In both cohorts, all three metabolites are associated with combined IFG and IGT.

**Discussion:** IIFG and iIGT have different metabolite profiles as is befitting two distinct physiological states characterized by different perturbations in glucose metabolism. Two branched-chain amino acid metabolites, 2-oxoaloeine and 2-oxovaline, were linked to elevated fasting glucose. The small organic acid, α-HB, in contrast, was linked to impaired glucose tolerance. These compounds represent different biochemical pathways and may reflect different pathophysiological aspects of prediabetes.

**Abstract #278**

**INSULIN PUMPS FOR “LIFE” VS INSULIN PUMPS FOR “LUXURY”-THE INDIAN EXPERIENCE IN TYPE 2 DIABETES**

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**Objective:** Insulin Pumps started getting popular in India since 2004. Unlike in the West, 80% of the pump users in India are type 2 diabetes (T2DM) subjects. With increasing longevity, majority of subjects with T2DM will ultimately require multiple doses of insulin to sustain life. Pumps have gained popularity with evidence & experience as an advanced insulin delivery device, superior to conventional syringes and pens. Studies have proven this to be a mechanism, offering profound improvement in QOL, alleviation of neuropathic pain and flexibility in lifestyles. In India, pumps and accessories are out of the pocket expenses and hence affordability could be one criteria while choosing pumps. In this study, we look into evidence and possibilities of misuse of pump and need to limit the sessions on advanced pump functions.

**Methods:** In our center, usual initial pump training provided is on basic functions like basal, bolus & suspend. Advanced functions like insulin sensitivity factor, insulin carb ratio, bolus wizard, temporary basal & dual/square wave bolus are taught only after 1-2 months when they are more comfortable and less confused. We identified 2 groups of pump users with T2DM from our electronic medical records – Group A (n = 63) who used pumps for life and Group B (n=31) who used pumps for luxury.
Group A used new knowledge judiciously and intelligently whereas group B misused it for eating and bolusing more. Average baseline A1c in both groups was 7.7%.

**Results:** Six months after advanced training. ‘A’ had mean A1c 6.9% and ‘B’ had 7.6%. In ‘A’, weight reduction was around 2.5%(p<0.001, CI 1.6) compared to ‘B’ with a weight gain of 3.0%(p=0.12) from the baseline. ‘A’ had a reduction in total daily dose of insulin (TDD) by 6-8 IU compared to increase in ‘B’ by 8-10 IU. Thus, ‘A’ had significant reduction in weight, TDD, and A1c compared to ‘B’.

**Discussion:** ‘A’ had followed the instructions on diet, exercise, telemedicine follow up and along with it utilised the extra pump functions judiciously for sustaining life ("Pumps for Life") whereas B exploited the features like bolus wizard, temporary basal, extended bolus etc for extra doses of insulin in accordance with food intake ("Pumps for Luxury").

**Conclusion:** We recommend identifying patient specific characteristics and modulating initial and advanced insulin pump training sessions accordingly with help of dietician, diabetic educator, psychologist etc., customizing their sessions to meet individual challenges so as to prevent inadvertent misuse of an advanced gadget for insulin infusion. Affordability should never be the criterion for selecting the candidate whereas the eligible candidate for pump should be selected as per published guidelines.

**Abstract #279**

**LIVER DISEASE CONTRIBUTES TO COGNITIVE IMPAIRMENT ASSOCIATED WITH INADEQUATE GLYCEMIC CONTROL IN PATIENTS WITH MULTIPLE ENDOCRINE AND METABOLIC ABNORMALITIES**

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**Objective:** Report cognitive impairment associated with liver disease among endocrine and metabolic patients and its dependence on glycemic control.

**Methods:** Patients had cognition monitored with the Montreal Cognitive Assessment (MoCA), liver disease determined by liver enzymes, ultrasound, CT, liver spleen scans with modified fractal analysis of liver SPECT (to determine a parameter, Sn from log-log plots of Isocontours and their average activity) and liver biopsy. Fibrosis was monitored with a NAFLD fibrosis calculator. Routine endocrine tests included blood sugars, HbA1c, serum and salivary cortisol, NMR lipid analysis, Free T4, Total T3, reverse T3 and TSH. Statistical analysis of nonparametric t tests and correlation analysis used Excel 2013.

**Results:** Among 420 patients with liver-spleen scans, 29 were near normal with Sn 0.81+0.13, 253 had fatty liver and normal liver enzymes with Sn 2.09+0.77; 46 had hepatic steatosis, usually with abnormal liver enzymes, with Sn 2.67+0.94 and 35 had fibrosis, with Sn 3.1+1.5. MoCA scores were 26.6+2.1 for near normals, and less, 24.4+3.56 for 391 patients with any liver disease (p<0.001); including 24.2+3.9 for 39 with insulin resistance (p<0.02) and HbA1c > 5.6%, 24.6+3.2 for 74 with thyroid disease (p<0.03), 24.0+3.7 for 46 with hepatic steatosis (p<0.006) and 22.3+3.4 for 29 with hepatic fibrosis (p<0.001). Among 20 patients with HbA1c 10+1.4 who had Sn 3.2+2.5, MoCA was 21.81+3.8 (p<0.01). HbA1c correlated with MoCA for 39 liver disease patients with insulin resistance and HbA1c > 5.6% (r=0.56), for 56 with psychiatric depression (r=0.61) for 46 with hepatic steatosis (R=0.77) and for 25 with hypercorticolism (r=0.67), although hypercorticolism patients had insignificantly decreased MoCA 25.9+3.3 (p=0.44).

**Discussion:** Cognitive impairment has multiple causes. A single major factor can cause marked cognitive impairment, such as hepatic encephalopathy. Less often appreciated is that even minor metabolic abnormalities, particularly if coexisting, can result in significant cognitive impairment. Moreover, in a population context, minor metabolic abnormalities, such as obesity and the metabolic syndrome, with nearly invariant fatty liver, reach epidemic proportions; hence, their contribution to cognitive impairment is remarkable. Reversibility of much liver disease and increasingly achievable glycemic control offer potential for significant improvements in cognitive impairment.

**Conclusion:** Liver disease, particularly mild disease detected by sensitive liver-spleen scans, is at least as epidemic as insulin resistance and contributes significantly, along with inadequate glycemic control, to widespread cognitive impairment.

**Abstract #280**

**A PREVALENCE SURVEY OF PEDIATRIC TYPE 2 DIABETES MELLITUS AMONG PATIENTS OF FILIPINO PHYSICIANS**

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**Objective:** To determine the prevalence of pediatric type 2 diabetes mellitus among patients of Filipino physicians.

**Methods:** A cross-sectional survey conducted from January to March 2014 among physician-members of
the American Association of Clinical Endocrinologists-Philippine Chapter, Diabetes Philippines, Philippine Society of Endocrinology and Metabolism and Philippine Society of Pediatric Metabolism & Endocrinology.

**Results:** The prevalence of pediatric type 2 diabetes mellitus aged 10 to 18 years of age, among patients of Diabetes specialists in the Philippines was 0.091%. More than half were symptomatic and most of them were managed by adult endocrinologists and adult diabetologists. Metformin was the most commonly used oral agent for diabetes.

**Discussion:** The prevalence of pediatric type 2 diabetes mellitus among Filipino patients of physician-respondents was 0.091% or 0.91 per 1000 patients of the physician-respondents. This is a higher prevalence rate compared to the total prevalence rate in SEARCH study which was 0.22 per 1000.

**Conclusion:** Our data show that there is a low prevalence of pediatric type 2 diabetes mellitus among patients of Filipino physicians.

**Abstract #281**

ABSTRACT WITHDRAWN

**Abstract #282**

**EFFICACY AND SAFETY OF NEW INSULIN GLARGINE 300 U/ML IN BASAL INSULIN-TREATED PATIENTS WITH TYPE 2 DIABETES MELLITUS USING SELECTED COMPREHENSIVE DIABETES CARE HEDIS MEASURES**

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**Objective:** EDITION 2 was a 6-month efficacy and safety study comparing the new insulin glargine 300 U/mL (Gla-300) with insulin glargine 100 U/mL (Gla-100) in patients (pts) with uncontrolled (A1C >7.0%) T2DM treated with ≥42 units of basal insulin plus oral antidiabetes drugs. Real-world diabetes performance measures based on American Diabetes Association guidelines and US National Committee for Quality Assurance Healthcare Effectiveness Data and Information Set (HEDIS) 2014, which measures and documents health plan performance in diabetes care, were applied to the EDITION 2 dataset to assess glycemic control and incidence of hypoglycemia in a population at high risk of hypoglycemia.

**Methods:** Pts were randomized to once-daily Gla-300 or Gla-100 in the evening, and discontinued sulfonylurea treatment. Doses were switched unit-for-unit for prior once-daily dosing or reduced by 20% for prior twice-daily NPH dosing. Insulin was titrated weekly to a fasting plasma glucose target of 80–100 mg/dL, based on the median of 3 fasting self-monitored plasma glucose readings. High-risk pts were selected by age (≥65 years) or presence of HEDIS-defined comorbidities. Comorbidities included coronary disease, kidney failure, dementia, blindness, and lower extremity amputation. The percentage of pts achieving A1C <8.0% without confirmed (blood glucose <54 mg/dL) or severe hypoglycemia from baseline to 6 months was analyzed.

**Results:** At baseline, 199 high-risk pts were included: mean age 68.8±5.4 y, T2DM duration 15.1±8.4 y, and A1C 8.11%±0.77. At 6 months follow-up, comparable percentages of Gla-300 and Gla-100 treated pts achieved A1C <8.0% (63.7% vs 65.7%, respectively; P=0.768). Numerically higher proportions of Gla-300 treated pts, compared with Gla-100 pts, did not experience confirmed (<54 mg/dL) or severe hypoglycemia (70.3% vs 61.1%, respectively; P=0.173) or A1C <8.0% without confirmed or severe hypoglycemia at any time (24h) (47.3% vs 38.9%; P=0.235).

**Discussion:** Performance on diabetes measures in real-world patients are an important consideration for health care decision-makers in diabetes management. This study examined the performance of pts at high risk of hypoglycemia transitioning to Gla-300. Although statistical analysis was limited by the number of pts who met the study criteria, more pts were likely to achieve target A1C without confirmed (<54 mg/dL) or severe hypoglycemia when treated with Gla-300 compared with Gla-100.

**Conclusion:** More pts randomized to Gla-300 tended to achieve target A1C without confirmed (<54 mg/dL) or severe hypoglycemia compared with Gla-100 in a high risk (aged ≥65 y or with comorbidities) T2DM population, although the differences did not reach statistical significance.
EFFECT OF TEAM-BASED CLINICAL INTERVENTION ON GLYCAEMIC CONTROL AND VARIABILITY IN TYPE 2 DIABETIC CHRONIC HAEMODIALYSIS PATIENTS: REPORT OF 2 CASES

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Objective: Diabetic chronic haemodialysis (HD) patients are at high risk of nocturnal hypoglycaemia and prandial hyperglycaemia. We compared glycaemic control and variability in two DM2 patients on insulin and chronic HD, at baseline and after team-based intervention to avoid the above, using Continuous Glucose Monitoring (CGM) and HbA1c

Methods: The patients were instructed to perform fingerprick glucose premeal and at bedtime, and food chart during CGM (Medtronic iPro). Changes to diet and insulin therapy based on baseline data were made by a team of endocrinologist, dietitian and nurse clinician. Repeat CGM was performed within 3 months, after an interim assessment at 1 month. HbA1c, serum fructosamine, and CGM glucose parameters were compared before and after intervention.

Case Presentation: 57-year-old Chinese female, HD thrice weekly for 12 months; sc Recornom 4000U 3x/week. Baseline Rx sc glulisine 8U premeal, insulinatard 6U on; 30.6.14 HbA1c 7.9%, Hb 12.7 g/dl, % reticulocytes 2.8% (0.5-2.3), serum fructosamine 525 uM (205-285); CGM 14-20.10.14 : (1664 sensor values, 27 valid calibrations) glucose average 12.4 mM, highest 22.2 mM, lowest 4.5 mM, SD 4.4 mM, MAD% 8.8%. Post-intervention Rx sc glulisine 6-10U premeal, glargine 6U on, 2-4U for carbohydrate snacks; 8.12.14 HbA1c 5.8%, Hb 9.4 g/dl, % reticulocytes 2.6%, fructosamine 397 uM;CGM 01-06.12.14 : (1849 sensor values, 27 valid calibrations) glucose average 9.9 mM, highest 17.7 mM, lowest 4.6 mM, SD 2.9 mM, MAD 8.6%. 35-yr-old Malay male, HD thrice weekly for 36 months; sc Recornom 4000U 3x/week. Baseline (01.02.13) Rx sc insulatard bid 30U, 28U; actrapid 20U premeal, HbA1c 10%, Hb 13.2 g/dl; CGM 22-26.3.14 : (1232 sensor values,15 valid calibrations) glucose average 10.4 mM, highest 22.2 mM, lowest 3.1 mM, SD 4.3 mM, MAD% 9.1%. Post-intervention Rx sc glargine 22U om, glulisine 20-24U premeal; 5.6.14 HbA1c 6.4%, Hb 11.6 g/dl; CGM 02-06.6.14 : (821 sensor values, 13 valid calibrations) glucose average 8.0 mM, highest 13.1 mM, lowest 3.9 mM, SD 2.2 mM, MAD% 12.2%.

Discussion: High glucose variability has been shown to increase risk of all-cause and hypoglycaemia-related hospitalization in diabetic chronic HD patients. We found that intensified team-based diabetes education and care involving diet advice, use of insulin analogues, flexible premeal glulisine dosing (depending on carbohydrate content) and avoidance of high carbo snacks improves glycaemic control and variability.

Conclusion: Rational use of basal and prandial insulin analogues in relation to diet and HD requirements may help improve overall glycaemic control and variability whilst minimizing hypoglycaemia, in patients with type 2 diabetes on insulin and chronic HD.

WOLFRAM SYNDROME : CLINICAL AND GENETIC DATA OF SIX PATIENTS FROM NON CONSANGUINEOUS FAMILIES

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Objective: Wolfram Syndrome(WS) is a very rare, neurodegenerative disorder characterized by juvenile onset insulin requiring diabetes, bilateral progressive optic atrophy ,sensorineural deafness and diabetes insipidus,also known as DIDMOAD (Diabetes Insipidus,Diabetes Mellitus,Optic Atrophy,and Deafness) syndrome. There is very scanty data on WS from this part of the world. Our objective was to study the clinical characteristics and mutations in WS and to determine the genotype of WS patients to establish a genotype/phenotype correlation.

Methods: Six suspected cases of WS underwent neuropsychiatric evaluation, audiometry, biochemical tests, confirmed for WS by clinical phenotype and genetic testing. WFS1 gene exon 2 to 8 were amplified by the polymerase chain reaction using the patient’s genomic DNA as template followed by automated DNA sequencing to generate nucleotide sequences of entire coding region and intron-exon boundaries of the WFS1 gene.

Case Presentation: There were 3 males and 3 female confirmed cases. Diabetes related symptoms were first detected. Then bilateral primary optic atrophy was followed by bilateral sensorineural deafness in all. Diabetes insipidus developed in 3/6 ,neuropsychiatric complications(seizures, tremors, mental retardation, gait ataxia) were present in 5/6 and Chronic kidney disease in 3/6. There was no consanguinity in any family. Family history of diabetes was present in 4/6.Six cases were confirmed in five families for WS by presence of WFS1 gene mutations. Our study increases the spectrum of WFS1 mutations with two novel variants. In three patients
polymorphic variants associated with suicidal tendency were detected. Mean age of detection of diabetes and optic atrophy was 5 and 11 years respectively. Sensorineural deafness and neuropsychiatric symptoms appeared later. Bladder atony, delayed puberty, hypogonadism, mental retardation, seizures were also observed.

**Discussion:** This data resembles the previous case series on WS. A unique feature here is absence of consanguinity in all families. Insulin dependent diabetes and optic atrophy in a child should always be thoroughly investigated for possibility of WS. In addition to known disease causing mutations found in WS, we have also shown some novel mutations which may help in detecting these patients early.

Detection of genetic variants associated with suicidal tendency can forewarn and prompt these families to seek psychological support.

**Conclusion:** WS is a very rare genetic syndrome, early suspicion in diabetic children can help in proper management and prognostication. Our study increases the spectrum of WFS1 mutations with novel variants in six patients.

**Abstract #285**

**LINAGLIPTIN: A POTENT ANTI-INFLAMMATORY AGENT**

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**Objective:** Diabetes mellitus is associated with low-grade inflammation which persists even after glycemic control. Linagliptin, known to effect wound epithellization and exert anti-inflammatory effect in diabetic mice. Anti-inflammatory effect of linagliptin in type 2 diabetic patients besides its ability to regulate blood glucose may contribute to its potentially beneficial effect on chronic complications of the disease. The present study was designed to evaluate the effects of dipeptidyl peptidase-IV (DPP-4) inhibitor, Linagliptin on systemic inflammatory markers in treatment naive type 2 diabetes patients.

**Methods:** A prospective, randomized, open-label study was performed in 30 newly detected type 2 diabetes patients after initial run in period of 4 weeks on diet and metformin. Those with glucose level above the target were randomly assigned to receive linagliptin 5mg once daily along with Metformin and to receive other oral antidiabetic drug with Metformin for 24 weeks. Assessment of systemic inflammatory markers like hs-CRP and TNF-α was performed at baseline and after 12 and 24 weeks in all patients.

**Results:** Fifteen patients were in linagliptin and same number of patients were in metformin and sulfonylurea group. The fasting and postprandial glucose, HbA1c, and inflammatory markers were similar between the groups at baseline. After treatment, both groups achieved a similar degree of glycemic control (p = NS). Linagliptin treatment was associated with greater decrease in hs-CRP and TNF-α more so after 24 weeks (p value 0.001) than at 12 weeks.

**Discussion:** Linagliptin, like others in class of DPP-IV inhibitors, has glucose lowering effect by improving insulin secretion through endogenous GLP-1. It differs from other DPP-IV in its pharmacokinetics and metabolism. Some of its class effect in addition to DPP-IV inhibition may be more pronounced. Anti-inflammatory effect of linagliptin was reported on ob mice earlier. We tested it in patient with diabetes by estimation of inflammatory markers like hs-CRP and cytokines TNF-α . In a short duration of 24 weeks of treatment, glucose lowering effect was similar to sulfonylurea but anti-inflammatory effect was remarkable.

**Conclusion:** Linagliptin treatment is associated with reduction of systemic inflammatory markers in type 2 diabetic patients independent of glycemic control. The class effect or specific action of the drug needs to be studied. However, potential role for cardiovascular protection and anti-atherosclerotic action of linagliptin in diabetes is suggested for immediate future clinical trial.

**Abstract #286**

**VANISHING HEMICHOREA-HEMIBALLISMUS DUE TO NONKETOTIC HYPERGLYCEMIA: AN UNUSUAL PRESENTATION**

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**Objective:** Hyperglycemia is an unusual and rare cause of hemicoreha-hemiballismus. Rapid correction of the hyperglycemia usually results in prompt and total resolution of the signs and symptoms. Knowledge of this disorder is paramount so as to rule out other causes of intracranial pathology.

**Case Presentation:** A 66 year old Bengali female came to the ER with steadily worsening purposeless involuntary movements of the upper and lower right extremities over the last two weeks. Two days prior to the onset of symptoms, patient visited the ER with a glucose of >600 and no ketonemia. She briefly received insulin and fluids but was sent home on metformin and sitagliptin when she declined to use insulin at home. On exam, patient was awake, alert,
and well oriented. Choreiform movements of the right upper and lower extremities were noted. Power was 3/5 on the right side and 4/5 on the left. CT and MRI with DWI MRA all showed high density in the left basal ganglia suggesting possible hyperglycemia related hemichorea-hemiballismus syndrome. Movements did not lessen with sleep. Basal ganglia stroke was also in the differential. Insulin was used aggressively to lessen the hyperglycemia. Over the next few days, the purposeless movements started to lessen. However, patient required almost a month before all the abnormal movements disappeared.

Discussion: Nonketotic hyperglycemia is a rare cause of hemichorea-hemiballismus. This disorder is characterized by involuntary unilateral purposeless movements that develop over several hours. Women are affected more than men with mean onset at age 72. This may be the first sign of decompensated diabetes but can also occur after a few years of poor glycemic control. Our patient’s slower onset and delayed resolution of symptoms raise questions as to the veracity of our original diagnosis.

Conclusion: Since timely glucose control can result in rapid complete resolution of symptoms, one must quickly distinguish this disorder from other intracranial pathology such as stroke. When hyperglycemia is present, a low threshold for consideration of this syndrome is in order.

Abstract #287

CORRELATES OF SECONDARY FAILURE TO ORAL HYPOGLYCEMIC AGENTS AMONG TYPE TWO DIABETIC PATIENTS IN ZARIA, NORTHERN NIGERIA

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Objective: To determine the characteristics and risk factors associated with the development of secondary failure of oral hypoglycemic agents (OHA) among type 2 DM subjects living in northern Nigeria.

Methods: A total of 200 consecutive type 2 diabetic (T2DM) patients (females 120, males 80) were studied over a period of one year. T2DM was defined according to American Diabetes Association criteria while secondary failure to OHA was defined as persistence of hyperglycemia despite maximal dosages of combined oral agents (metformin and glibenclamide) in the absence of known secondary causes of glucose intolerance. Parameters studied included age, gender, age at onset of T2DM, duration of diabetes, body mass index (BMI), waist circumference (WC), serum glucose and lipids profile and glutamic acid decarboxylase antibody positivity. The relative risk for secondary failure to OHA was estimated by calculating the odds ratio (OR).

Results: The mean (±SD) age of the subjects was 53.2 ± 8.9 years (range 34-75). THE MEAN DURATION OF DM AMONG THE SUBJECTS WAS 6.9 ±(5.5) YEARS. The prevalence of secondary failure of OHA among the 200 subjects was 36% (72 subjects) with a female preponderance of 46 and males 26. The mean BMI 22.9 ± 5.4 kg/m2 and mean WC for both males (87.7 ± 11.3 cm) and females (90.3 ± 7.9 cm) were significantly lower in subjects with OHA failure than those without OHA failure (mean BMI 27.2 ± 4.8 kg/m2; male WC 93.5 ± 10 cm; female WC 95.7 ± 6.8 cm; p <0.05). The mean A1c of the study population is 7.45%(1.85)[3.8-14.1].The mean HbA1c (8.3 ± 1.42%) of those with OHA failure was significantly higher than those without OHA failure (7.0 ± 2.07%). The mean total cholesterol, LDL-C and TG (4.89 ± 0.90 mmol/L; 3.8 ± 0.9 mmol/L; 0.95 ± 0.34 mmol/L) in subjects with OHA failure were lower than in subjects without OHA failureTC, LDL, TG are 5.12(0.9)[2.2-7.1], 4.1(1.0)[1.3-6.3] and 1.1(0.3)[0.6-2.0] mmol/L. (p > 0.05). Presence of anti-GAD antibodies was significantly higher (31.4%) among those with OHA failure than in those without (3.1%).

Discussion: Secondary OHA failure is associated with the earlier development of complications of diabetes. The burden of the morbidity and mortality from these complications is enormous particularly in a developing country like Nigeria. In this study patients with lower BMI and waist circumference, lower lipid concentrations and higher prevalence of anti-GAD antibodies were more likely to fail therapy with OHA. One-third of those that failed therapy 72,had detectable anti-GAD antibodies, while the percentage of GAD antibody in the study population is (13%). Considering the age of the study population and the duration of the diabetes means that this subset of the subjects are likely to be LADA . This group though a T1DM because of the presence of the antibody behaves differently this may explain the absence of DKA.

Conclusion: The prevalence of secondary OHA failure is high among T2DM patients in northern Nigeria, and notably increased in women and in those with a lower BMI. The high presence of anti-GAD antibodies suggests that many of these patients may have autoimmune diabetes, and clinicians need to consider this when treating patients as they may require early therapy with insulin for success.
Abstract #288

ALTERNATE DAY DOSING OF LINAGLIPTIN 5MG IN PATIENTS CONTROLLED ON ONCE DAILY DOSE: A CASE SERIES

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**Objective:** Linagliptin has the longest terminal half-life among the available DPP4 inhibitors and it has been shown that, at steady state, the DPP4 enzyme is significantly inhibited by linagliptin up to 48 hours after the last dose. The effect of alternate day dosing has not been evaluated on glucose control. Here we present our experience with 8 patients who were switched to alternate day dosing of linagliptin from once daily (OD) dosing.

**Case Presentation:** Eight patients maintaining stable HbA1c with acceptable FPG and PPG levels, and receiving linagliptin 5 mg OD for at least 6 weeks (median of 19 weeks; range 6 to 71 weeks) with stable dose of concomitant anti-diabetic medications, were switched to receive 5 mg of linagliptin every alternate day. Consent was obtained after explaining the potential risks. The median age of the patients was 56 (42-75) years and the median duration of diabetes was 7 years (range, 0.75 -16 years). The median HbA1c while on the OD regimen was 6.4% (range, 5.8 - 8.1%). After switching over to the alternate day regimen, patients were closely monitored through telephonic calls and clinic visit at least once in 12 weeks. Patients were followed up for a median period of 17.5 weeks (range, 12 – 25 weeks). Patients were followed up for a median period of 17.5 weeks (range, 12 – 25 weeks). The glycemic status was similar to the baseline values (median HbA1c = 6%, range, 5.1 – 7.4%). Concomitant anti-diabetic medications used were metformin in five patients and metformin and glimepiride, NPH, and premix insulin in one patient each. Interestingly the patient receiving NPH insulin required only metformin 500 mg OD later in the course of linagliptin alternate day therapy. The dose and frequency of concomitant medications in other patients were not altered.

**Discussion:** Linagliptin inhibits DPP4 for prolonged time due to its unique slow-off enzyme kinetics. Our experience shows that glycemic control with alternate day linagliptin was similar to OD dose of linagliptin in a carefully selected group of patients on stable concomitant anti-diabetic medication. The findings can be extrapolated to the clinical scenario of poor compliance to medications, where missing a dose of linagliptin may affect the glycemic control minimally. Paradoxically alternate day dosing may affect compliance if the patient forgets when they took the last dose.

**Conclusion:** Linagliptin 5 mg on alternate days can be considered in patients who are controlled on linagliptin 5 mg OD, as missing a dose may not alter the glycemic status adversely. Further studies are needed to validate this finding and identify patients who can benefit from the alternate day regimen.

Abstract #289

ANALYSIS OF FACTORS ASSOCIATED WITH THE OCCURRENCE OF PULMONARY TUBERCULOSIS IN PATIENTS WITH TYPE 2 DIABETES

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**Objective:** To determine the prevalence of pulmonary tuberculosis and the factors that affect the appearance of pulmonary tuberculosis in patients with type 2 DM at Persahabatan General Hospital, Jakarta, Indonesia.

**Methods:** This study was a cross sectional study. Subjects was 174 type 2 DM patients taken by consecutive sampling. Data were performed bivariate and multivariate analyzes between independent and dependent variables.

**Results:** 174 subjects consisted of male 40.8%, and female 59.2%. Prevalence of pulmonary TB in patients with type 2 DM are 49 peoples (28.2%). The radiologic presentation of TB was : minimal lesion(12.1%),extensive lesion(17.2%),cavities(9.2%),pleural effusion in 0.6% subject. Factors that have a correlation with development of pulmonary TB in diabetic patients were patients with a history of close contact with TB patients (adjusted OR 3.2.15,p=0.003), under weight (aOR 10.15, p=0.001), duration of diabetes less than 1 year (adjusted OR 23.136, p <0.001) , and HbA1c levels > 8 (adjusted OR 17.475,p=0.001).

**Discussion:** Our data suggest that history of close contact with TB patients, underweight, and poor glycemic control is a risk factors for tuberculosis. It is interesting that majority of TB developing in naive diabetic patients, who recognized diabetes less than 1 year.

**Conclusion:** The prevalence of pulmonary tuberculosis in patients with type 2 DM was 28.2%. There were correlation between sex,age,smoking habits, contact with TB patients, underweight, and poor glycemic control is a risk factors for tuberculosis. It is interesting that majority of TB developing in naive diabetic patients, who recognized diabetes less than 1 year.
Abstract #290

THE CHALLENGES OF RAMADAN & DIABETES IN THE WESTERN HEMISPHERES: THE ROLE OF PRE-RAMADAN DIABETES CLINICS IN PATIENTS’ CARE & SAFETY

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Objectives: To assess the usefulness of pre-Ramadan diabetes education.

Methods: A specialised ‘Ramadan Diabetes Clinic’ was set up to achieve the goal of safe fasting for those who are keen to observe this religious obligation. In that clinic a total of 16 patients were seen (10 males), mean age 57 years, mean BMI 29.5 and mean pre-Ramadan HBA1c of 9.1% (76 mmol/mol). All patients had Type-2 diabetes with the exception of one patient who had Type 1 diabetes and was on Novomix 30. Advice and counselling on issues relevant to diabetes and Ramadan fasting were provided to these patients together with written instructions on issues such as avoiding hypos, glucose monitoring and when to break their fast. Individualised management was provided to each patient with change in dose, timing and type of diabetes medication as felt appropriate. All patients were then provided with a structured questionnaire asking them about their experience during Ramadan fasting and if they had any hypos as well as their views about the clinic. Results: A reduction of HbA1c of 0.4% was achieved when checked post Ramadan without any excess hypos and the service was well received and highly appreciated by the patients as shown by the results of the questionnaire. Moreover it was felt that the clinic improved engagement of these patients with the diabetes team.

Discussion: Some preliminary small studies had shown the value of pre-Ramadan advice and counselling of patients. Our study has confirmed that structured and tailored advice given to diabetic patients where adjustment of dosing and timing of diabetes medications were coupled with advice regarding self-care, avoidance of hypos and self-blood glucose monitoring has resulted in a safe fasting for their patient with no detrimental effects on their wellbeing.

Conclusion: Pre-Ramadan structured education to patients can enable many patients to observe this religious ritual without complications and untoward impact on health.

Abstract #291

REGISTRY STUDY FOR TYPE II DIABETES MELLITUS PATIENTS IN DIABETIC CENTER WITH COMPARATIVE ANALYSIS FOR CONTROLLED VERSUS UNCONTROLLED CASES

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Objective: Our objective is to see the outcome for different treatment methods in type II DM as well as comparative analysis of controlled 109 cases versus uncontrolled 120 Cases. The mean ± SD duration of DM in years 6±7.4 & 11±7.8 respectively.

Methods: Study was conducted in Diabetic Center, included 229 Type II Diabetic Patients with mean age of 49.6 ± 12.6 years. 1.7% of patients were on diet only, 69% on Oral hypoglycemic drugs (OHD), 4.8% on Insulin and 24.5% on combined insulin & OHD.

Case Presentation: FBS dropped by “-3.1%, -15.9%, -12.7%, & 20.2% and HbA1c by “-6.3%, -10.7%, -7.4% & -10.7% respectively after management in the different treatment groups. A comparative analysis was carried out between controlled & uncontrolled cases. Vitamin D deficiency was present in 65.8% & 57.8%, Dyslipidemia 38.3%, 53.6%, HTN 28.3% & 37.6% and Hypothyroid 16.7% & 7.3% in controlled and uncontrolled patients respectively at start of registry.

Discussion: Vitamin D Level increased from 31.3 to 70.3ng/ml and 31.4 to 69.6ng/ml in controlled & uncontrolled patients between beginning & end of the study. Total cholesterol, HDL-C, LDL-C & TG improved by -11.2% & -4.8%, +19.8% & +3.1%, -11.1% & 0.8% and -30.4% & -3.4% in controlled & uncontrolled patients.

Conclusion: The duration of DM affect negatively more the uncontroled DM. Vitamin D deficiency and lipid profile improved significantly with DM control.
HYPOGLYCEMIA

Abstract #300

DOEGE-POTTER SYNDROME AND PAPILLARY THYROID CANCER: COINCIDENCE OR CAUSE AND EFFECT?

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Unity Health System

Objective: Doege-Potter syndrome is a rare paraneoplastic syndrome characterized by hypoglycemia caused by a non-islet cell tumor, usually a solitary fibrous tumor of the pleura (SFTP) or a retroperitoneal tumor. These tumors cause hypoglycemia through secretion of a prohormone form of insulin-like growth factor-2 (IGF-2).

Case Presentation: A 74-year-old male of Asian descent presented for evaluation of a multinodular goiter. A chest X-ray disclosed a lung nodule. Biopsy of a thyroid nodule was reported as an atypical follicular lesion. The patient declined any further evaluation of the thyroid or lung nodules. A year later he returned with recurrent hypoglycemia associated with mental status changes that resolved after administration of intravenous dextrose. Laboratory tests at the time of presentation were as follows: blood glucose 42 mg/dl, serum insulin < 1 uIU/ml (3-25 uIU/ml), C-peptide < 0.1 ng/ml (0.8-3.9 ng/ml), insulin-like growth factor-1 (IGF-1) 66 ng/ml (34-245 ng/ml), IGF-2 1348 ng/ml (411-1248 ng/ml), and IGF binding protein-2 (IGF BP-2) 382 ng/ml (47-350 ng/ml). A chest CT revealed a large right pleural-based mass. Surgical resection disclosed an 18x15x4 cm mass which was well circumscribed and grossly encapsulated. Ki-67 staining showed no increase in mitotic activity. The mass was reported to be morphologically consistent with a benign solitary fibrous tumor. The patient’s hypoglycemic symptoms completely resolved with resection of the tumor. The patient subsequently underwent a total thyroidectomy, which disclosed multifocal papillary thyroid carcinoma.

Discussion: SFTP is a non-islet cell mesenchymal tumor of the pleura which is usually benign. It can present with hypoglycemia as a paraneoplastic syndrome caused by hypersecretion of “big IGF-2”, a partially processed precursor of IGF-2. Big IGF-2 activates insulin receptors, increases peripheral glucose uptake, especially by skeletal muscle, and inhibits hepatic glycogenolysis and gluconeogenesis, thereby resulting in hypoglycemia. Hypoglycemic symptoms and elevated levels of serum big IGF-2, in combination with increased levels of IGF BP-2, are highly suggestive of the diagnosis. A definitive diagnosis is made by pathology and by resolution of hypoglycemia after complete resection of the tumor, as was demonstrated in this case.

Conclusion: We postulate that elevated IGF-2 levels produced by this type of tumor may be a factor in the growth of secondary tumors, in this case a papillary thyroid cancer, possibly by activating IGF-2 receptors.

Abstract #301

INSULINOMA DIAGNOSED IN A PATIENT WITH RENAL INSUFFICIENCY AND MANAGED WITH ENDOSCOPIC ETHANOL ABLATION AND DEXAMETHASONE

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Objective: We present a case of an insulinoma in an elderly patient with multiple co-morbidities including renal insufficiency. The hypoglycemia was managed successfully with endoscopic ultrasound(EUS) and ethanol ablation of the pancreatic mass and low dose dexamethasone.

Case Presentation: An 86-year-old man with coronary artery disease, atrial fibrillation, acute on chronic kidney injury due to obstructive uropathy, requiring hemodialysis, presented with hypoglycemia. Eight months prior to admission the patient was found agitated and confused with a blood glucose of 40 mg/dL with mental status improvement after dextrose administration. Since then the patient has found it necessary to eat mixed meals of carbohydrates and protein every four hours to maintain euglycemia. Upon arrival to our hospital, dextrose10% intravenous fluids were used to maintain euglycemia overnight while the patient was fasting. Two hours after discontinuing the dextrose solution, the patient became hypoglycemic, with a glucose of 43 mg/dL. Concomitant labs showed elevated C-peptide 18.5 ng/mL, elevated pro-insulin 103pmol/L, low beta-hydroxybutyrate 0.6mmol/L, negative insulin antibodies and negative sulfonylurea screening. CT scan with intravenous contrast revealed a 1.9x2.1 cm arterially enhancing mass in the uncinate process of the pancreas. The patient was started on dexamethasone 2.5 mg intravenously twice daily, which normalized his blood glucose. He underwent EUS with ethanol ablation of the pancreatic lesion. Months later, he remains euglycemic on low dose dexamethasone 0.5 mg daily.

Discussion: Published guidelines for the evaluation of adult hypoglycemia may be difficult to apply to patients with renal failure since insulin and C-peptide are renally cleared and may be elevated in these patients. The patient’s profound episodes of hypoglycemia coupled with very high C-peptide and a pancreatic lesion on CT scan, strongly corroborated the diagnosis of insulinoma. Due to the patient’s co-morbidities, advanced age, and preference he did not proceed with usual standard of care: surgical removal of the insulinoma.

Conclusion: To the best of our knowledge this is first case of a patient requiring hemodialysis presenting with an insulinoma whose hypoglycemia was successfully managed with
endoscopic directed ethanol ablation and dexamethasone. The first line treatment of insulinoma, surgical resection of the pancreatic tumor, poses greater immediate risk of morbidity and death and longer recovery time for the patient. Less invasive techniques including endoscopic ethanol ablation and steroids should be considered as primary modalities to manage medically ill patients with hypoglycemia due to insulinoma.

**Abstract #302**

**HYPOGLYCEMIA AFTER PANCREATIC TRANSPLANT**

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**Case Presentation:** A 49 year-old Caucasian male was electively admitted for work-up of his hypoglycemia five years after undergoing cadaveric kidney-pancreatic transplant. He is known to have Type 1 Diabetes Mellitus (DM) since age 13, with microvascular complications. He had been off insulin since the surgery. His post-transplant course was complicated by Cytomegalovirus and BK virus infection that was appropriately treated. He began having recurring episodes of hypoglycemia for the past six to seven months with episodes of syncope. He was hooked to a continuous glucose monitoring machine that confirmed hypoglycemia with levels below 50 mg/dL occurring between nine to 10 o’clock at night and three to four o’clock in the morning. His dinner and bedtime snack are usually 2-3 hours before the hypoglycemic episodes. His hypoglycemia followed a pattern that was dependent on his meal times.

During his stay in the hospital, he was placed on a 72-hour fast and a mixed meal tolerance test was also performed. He did not have any hypoglycemic episode at any point. His lab work-up revealed no insulin antibody, negative sulfonylurea screen, no evidence of exogenous insulin or presence of insulinoma. It was later determined that he likely had reactive hypoglycemia, stemming from his consumption of high carbohydrate meals due to his fear of hypoglycemia. His years of living with DM had developed a habit of consuming regular and frequent meals in order to prevent hypoglycemia that the older forms of insulin usually caused.

**Discussion:** Hypoglycemia has been described in about 30-50% of post-pancreatic and kidney-pancreatic transplant patients. Causes of hypoglycemia in this group of patients is usually due to exogenous insulin administration, pancreatic adenoma, and nesidioblastosis. Profound hypoglycemia in patients with pancreatic pathology have required partial allograft pancreatectomy in some patients. Pharmaceutical interventions for this type of hypoglycemia includes acarbose, diazoxide, and octreotide, with the intention of reducing carbohydrate absorption and inhibition of insulin release that would cause a surge in insulin. The mechanism of hypoglycemia is poorly understood, with proposed mechanisms of circulating autoantibodies, postprandial hyperinsulinemic surge from the systemic drainage of the draft, and persistence of metabolic abnormalities in type 1 DM post-pancreatic transplantation.

**Conclusion:** Pancreatic transplantation has proven to be of durable therapy for patient with type 1 DM. Hypoglycemia is a known and common complication of this surgery. It is imperative to recognize the cause of hypoglycemia in these subset of patients as to prevent detrimental outcomes, including mortality.

**Abstract #303**

**HYPERINSULINEMIC HYPOGLYCEMIA IN A PATIENT WITH CARCINOID TUMOR-CHALLENGES IN DIAGNOSIS AND MANAGEMENT**

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Marshall University

**Case Presentation:** 38-year old patient with no significant medical history who was admitted to the hospital with abdominal discomfort and SOB. During the admission, patient was referred to Endocrinology service for hypoglycemia. Patient had no significant surgical or family history. He was on Prevacid for GERD.

On examination, patient had stable vitals. The most significant finding on abdominal examination was hepatomegaly. For the abdominal discomfort, patient had a CT scan of the abdomen which had shown metastatic lesions in the liver. Hypoglycemia was thought to be due to impaired gluconeogenesis from metastatic disease. Patient was started on dextrose fluids. He had recurrent hypoglycemia with reduction in the rate of fluids especially in the mornings.

Detailed work up with plasma glucose 46mg/ml showed elevated proinsulin of 134.8pmol, insulin 16.5IU/ml and betahydroxybutyrate of 2.7m/dl. C-peptide was 10.5ng/ml. Findings were consistent with hyperinsulinemic hypoglycemia.

Pathologic analysis of the liver biopsy was significant for carcinoid tumor. Stains were strong and diffuse for CAM 5.2, synaptophysin and chromgranin. Negative for VIP, gastrin and Insulin. He had EGD which was not negative for any pathology.

Patient was started on diazoxide. IV fluids were weaned.
off within 24 hours after commencing medication and patient was discharged home with it.

Discussion: Hyperinsulinemia from pancreatic tumor is the commonest cause of endogenous hypoglycemia. Hypoglycemia here is caused by excessive insulin secretion. Hypoglycemia can be mediated by a lot of different mechanisms amongst which include insulin, IGF, impaired release or decreased secretion of glucagon and impaired gluconeogenesis. Hyperinsulinemia is mainly secondary to insulinoma and there are very few cases where it could be secondary to ectopic secretion.

Patient had a biopsy of the liver that showed neuroendocrine tumor for which staining was consistent with carcinoid tumor. Patient was seen by oncology with follow up on outpatient basis and started on temozolomide. Carcinoid tumors affect a lot of organs in the body but they are commonly seen in the GI and respiratory systems. Hepatic metastasis of carcinoid tumor is common. These patients can present with diarrhea and flushing but of note this patient had none of those symptoms.

Conclusion: Hyperinsulinemic hypoglycemia in the presence of carcinoid tumor is a rare finding. Exact source of the hyperinsulinemia is difficult to determine. Our patient had good resolution of hypoglycemia after commencing diazoxide. Diazoxide can be of benefit as evidence in our patient in the management of hypoglycemia in these patients.

Abstract #304

RATES OF INPATIENT HYPOGLYCEMIA SIX MONTHS BEFORE AND AFTER THE IMPLEMENTATION OF A RESTRICTIVE SULFONYLUREA USE POLICY

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Objective: North Shore University Hospital is an 803 bed quaternary care center with Joint Commission Certification in Inpatient Diabetes. We have devised several initiatives to decrease the rates of hypoglycemia, including the restriction of sulfonylurea use in patients over the age of 70, with a creatinine greater than or equal to 1.5 mg/dL or with a creatinine clearance less than 30 mL/min, or with serum glucose less than 100 mg/dL on two episodes.

Methods: 9,838 patients with diabetes were admitted six months before and after the creation of the sulfonylurea restrictive policy. In all patients, we collected the number of hypoglycemic events, inpatient sulfonylurea use, and hypoglycemic events secondary to inpatient sulfonylurea use. We compared the frequency of these events six months before and six months after the policy was enforced. We used the Wilcoxon signed-rank test for this analysis to compare the percentage difference in these events.

Results: Comparing the time periods six months before and after implementation of the protocol, 18.5% of patients with diabetes had hypoglycemic episodes before and 15.5% afterwards (z-score -3.064, 2 tailed p-value 0.002). In the six months prior, 5.8% of patients with diabetes were administered sulfonylurea agents during their admission, compared with 2% after the protocol (z-score -2.201, 2-tailed p-value 0.028). Hypoglycemic episodes secondary to sulfonylurea use averaged 21% before implementation of the protocol and 25.3% afterwards (z-score -3.061, 2 tailed p-value 0.002).

Discussion: Administering a sulfonylurea agent to patients with diabetes in the hospital carries a risk of hypoglycemia, as they often have changes in enteral intake or renal function. It has been shown this adverse event can lead to an increase in patient morbidity and mortality, as well as an increase in patient length of stay. Advanced age, renal insufficiency, and low serum glucose have been identified as further increasing the risk of hypoglycemia in this setting. Hypoglycemic events secondary to sulfonylurea use increased even after restricting use in this high risk population.

Conclusion: Patients with diabetes administered sulfonylurea agents while admitted to the hospital are at risk for hypoglycemia. Restricting use does not reduce this risk. This suggests a benefit to removing sulfonylurea agents from inpatient formularies.

Abstract #305

HYPOGLYCEMIA: A COMPLICATION OF POST-BARIATRIC SURGERY

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Case Presentation: A 39 year-old African-American male presented to the emergency department with complaints of confusion, weakness, and diaphoresis and was found to have profound hypoglycemia with a serum glucose level of 35 mg/dL. Two hours prior to his hypoglycemic state, he ate chicken salad sandwich, a bowl of dry cereal, and eight ounces of sweet tea. The type and amount of food he eats at home is typical of this meal. He required intravenous administration of 25 grams of dextrose 50% which promptly relieved his symptoms. During his hospital course, he was placed on a regular diet and showed no recurrence of hypoglycemia. His fasting C-peptide was relatively low with a high normal
C-peptide during the period of hypoglycemia. He had negative sulfonylurea screen, normal morning cortisol, and glycosylated hemoglobin was consistent with pre-diabetes. A computed tomography scan of the abdomen and pelvis showed no distinct pancreatic mass. He was discharged with recommendations of consuming frequent, low carbohydrate meals, and frequent glucose monitoring. If he was to have repeated episodes of hypoglycemia as an outpatient, the plan was to employ continuous glucose monitoring and perform an oral glucose tolerance test or a mixed meal tolerance test.

The patient is known to have pre-diabetes and morbid obesity for several years prior to undergoing Roux-en-Y bariatric bypass surgery which occurred three years prior to his most recent hospitalization. As an outpatient, he described symptoms of palpitations and dizziness upon standing approximately seven times a year. There are no documented glucose levels during these episodes. These symptoms are not related nor relieved with food intake.

Discussion: The patient fulfills the criteria of Whipple’s triad - neuroglycopenic symptoms, plasma glucose level <55 mg/dL, and alleviation of symptoms with administration of glucose. Hyperinsulinemic hypoglycemia after bariatric surgery was originally published in a case series Mayo Clinic in 2005. It is estimated that this particular complication after gastric bypass is less than 1% and may occur months to years following surgery. Mechanisms thought to be involved to this process include altered beta cell function, including beta cell proliferation, as well as non-beta cell factors.

Conclusion: Bariatric surgery is among the most durable agents for effective weight loss, after lifestyle modifications and pharmaceutical interventions have failed. With the pandemic of obesity, it is paramount that we gain better understanding of its effects and complications. Understanding the mechanisms behind such complications will help prevent the detrimental effects of profound hypoglycemia, including mortality.

Abstract #306

A HYPOGLYCEMIC CONUNDRUM

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Baystate Medical Center

Objective: Recognition and discernment of possible causes of abnormal glycaemia in a woman with genetic, metabolic, and anatomic predispositions.

Case Presentation: 59-year-old woman with MEN1 presented to clinic for evaluation of hyperglycaemia and sporadic post-prandial hypoglycaemia with neuroglycopenic symptoms relieved by oral intake. MEN1 was diagnosed in 2002 when a CT abdomen, performed in evaluation of nephrolithiasis, revealed asymptomatic 7cm and 3cm pancreatic head and tail masses. Immunohistochemistry confirmed neuroendocrine tumors staining positive for keratin, insulin, VIP, and somatostatin; 2 of 12 lymph nodes had metastatic foci. A Whipple procedure was performed along with 3.5-gland parathyroidectomy. Mild fasting hyperglycaemia developed 10 years later, and a recent hemoglobin A1c was 6.3%. Two years ago she began having acute episodes of overwhelming fatigue, diaphoresis and weakness, occasionally associated with slurred speech, that occurred twice per month approximately 2 hours post-prandial with concomitant glucometer readings ranging 38-60. There was no associated abdominal cramping, pain, diarrhea or identifiable meal culprits. Yearly screening contrasted abdominal CT scans have been negative for mass or lymphadenopathy. Lab evaluation of 2 separate episodes revealed the following respective levels: serum glucose 57 and 66mg/dL; insulin 6.7 and 2.8IU/mL; pro-insulin of 24 and 24pmol/L. Insulin antibodies and sulfonylurea screen both negative. 72-hour inpatient fast failed to reproduce symptoms or hypoglycaemia but confirmed fasting hyperglycaemia. 7-day continuous glucose monitor revealed frequent hyperglycaemia and 1 symptomatic “hypoglycemic” episode with a glucose of 55 occurring 100 minutes after a small mixed-meal and 45 minutes after a glucose of 140.

Discussion: Neuroglycopenic symptoms in a patient with known MEN1 warrant careful evaluation for possible insulinoma. However, biochemical confirmation prior to more invasive evaluation is critical, and other etiologies of hypoglycemic symptoms still need to be considered. Our patient’s Whipple procedure altered her GI and pancreatic anatomy and hormone profiles, which in turn altered her glycemic homeostasis.

Conclusion: Our patient’s diagnosis remains inconclusive but is unlikely to be an insulinoma given the lack of true venous hypoglycemia on multiple symptomatic occassions. Her hyperglycaemia is likely due to incretin/ beta cell loss and to hepatic insulin resistance from pancreatic polypeptide loss. Neuroglycopenic symptoms are likely multifactorial in nature and in part related to rapid glycemic decline rather than absolute hypoglycemia. Acarbose and dietary manipulation are likely the best symptomatic treatment options.
Abstract #307

DETECTION OF AN INSULIN ANALOG USING LIQUID CHROMATOGRAPHY COUPLED TO ION MOBILITY MASS SPECTROMETRY (LC-IM-MS) IN A PATIENT WITH FACTITIOUS HYPOGLYCEMIA

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**Objective:** Factitious hypoglycemia should be considered in every patient evaluated for a hypoglycemic disorder. In the case of exogenous insulin injection, detection of the type of injected insulin has been a challenge. We present a case of a non-diabetic woman who presented with hypoglycemia. Her laboratory data suggested the exogenous use of insulin. Additional testing revealed the type of injected insulin, which confirmed the diagnosis of factitious hypoglycemia.

**Case Presentation:** A 41-year-old non-diabetic woman was admitted to the hospital after being found unresponsive. Her fingerstick blood glucose was <20 mg/dL. She was treated with IV D50 and immediately regained consciousness. She denied any history of similar episodes, use of insulin or her husband’s oral hypoglycemic medications, or intention of self-harm. She had normal vital signs and physical exam. Laboratory results were as follows: blood glucose 38 mg/dL, insulin 3904 uIU/mL (3-25 uIU/ml), C-peptide <0.1 ng/mL (0.8-3.9 ng/ml), and beta-hydroxybutyrate <0.1 mmol/L (<0.4mmol/L). These results were suggestive of exogenous hyperinsulinemic hypoglycemia. A sulfonylurea panel was negative, and a CT scan of the abdomen was normal. On day 2, her blood glucose was 31 mg/dL, insulin 231.6 uIU/mL, C-peptide <0.1 ng/mL, and pro-insulin <5 pmol/L (≤ 18.8 pmol/L). On day 3, her hypoglycemia resolved. Insulin levels were measured in blood samples from days 1 and 2 using liquid chromatography-mass spectrometry (LC-MS, Quest Diagnostics), which specifically tests for human insulin, and were found to be 4.7 uIU/mL and <6 uIU/ml respectively. To confirm the type of synthetic insulin used, a liquid chromatography coupled to ion mobility-mass spectrometry LC-IM-MS assay was done, and insulin aspart was detected. Later it was discovered that the patient’s husband was on insulin aspart in addition to oral agents.

**Discussion:** Insulin is commonly measured using immunochemiluminometric assays (ICMA) which show variability between different platforms. The Siemens Advia Centaur platform used in our laboratory measures both human and analog insulin. While these immunoassays lack specificity for the type of insulin, LC-MS based approaches can provide a highly specific alternative. LC-IM-MS is a new technique which can determine the type of insulin analog used, as was demonstrated in this case.

**Conclusion:** Factitious use of insulin is a rarely detected but dangerous cause of hypoglycemia in non-diabetic patients. Understanding the specific detection capabilities of each assay is essential to the evaluation of factitious insulin-induced hypoglycemia.

Abstract #308

MEDICAL THERAPY OF SEVERE HYPERINSULINEMIC POST-GASTRIC BYPASS HYPOGLYCEMIA

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**Objective:** To describe the evaluation and medical treatment of severe hyperinsulinemic hypoglycemia in adults who had undergone gastric bypass surgery.

**Methods:** We report the demographics, diagnostic results, response to medical therapy, and subsequent course of six referral patients with documented post-Roux-en-Y hypoglycemia.

**Case Presentation:** Clinical and metabolic parameters consistent with hyperinsulinemic hypoglycemia were identified. In the context of exclusively post-prandial symptoms, simultaneous glucose ≤55 mg/dL, insulin ≥17 µU/ml, c-peptide ≥3.0 ng/ml, and an insulin:glucose ratio >0.3 were associated with Roux-en-Y gastric bypass hyperinsulinemic hypoglycemia. Five of six patients improved on therapy consisting of dietary modification plus either calcium channel blockade, acarbose, or both. Two have remained on therapy for 15 to 18 months. The non-responder had had hypoglycemic events for several decades. Subsequent to medication failure, she was given a continuous glucose monitor with substantial reduction in symptomatic hypoglycemic events and improvement in quality of life. Three medically treated patients were subsequently observed to undergo partial or complete remission from hypoglycemic episodes after 2 to 37 months of therapy. Duration of remission has ranged from 13 to 31 months. No case has undergone pancreatectomy or had evidence of insulinoma. Invasive diagnostic procedures were of limited utility.

**Discussion:** Hyperinsulinemic hypoglycemia following gastric bypass surgery can be diagnosed on the basis of a history of exclusively post-prandial symptoms of hypoglycemia with no vasomotor or bowel symptoms.
suggestive of dumping. The diagnosis can be confirmed with simultaneous measurement of serum glucose, insulin, c-peptide, and negative sulfonylurea testing during hypoglycemia. Invasive testing is not required. We show that some cases can be controlled without pancreatectomy, secondary gastric restrictive surgery, or gastrostomy. Successful medical intervention included a low carbohydrate, frequent feeding diet supplemented with one or two medications independently targeting insulin secretion or intestinal carbohydrate absorption. In our single case of hypoglycemia refractory to medical intervention, continuous glucose monitoring provided significant benefit. Finally we observed that medical therapy could be associated with complete or partial remission of symptoms over time.

**Conclusion:** In a subset of patients with post-Roux-en-Y hyperinsulinemic hypoglycemia, medical management can be efficacious and an alternative to partial pancreatectomy.

**Abstract #309**

**DOEGER-POTTER SYNDROME: AN UNUSUAL CASE OF RECURRENT HYPOGLYCEMIA**

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Hospital Edgardo Rebagliati/ Universidad Nacional Mayor De San Marcos

**Objective:** To report a case of recurrent paraneoplastic hypoglycemia.

**Methods:** We present the clinical and paraclinical characteristics of a patient with recurrent hypoglycemia (Doege-Potter syndrome) as a manifestation of a solitary fibrous tumor of the pleura (SFTP) recurrent.

**Case Presentation:** Male, 66 y.o.; history of left pneumonectomy for giant solitary fibrous tumor in another center in 2006. He reports that 10 months before admission presents oppressive pain in left upper quadrant and flank associated with increased volume in these regions, dyspnea effort and feeling of fullness associated with early weight loss of 5 kg in 6 mo; further directed episodes of profuse sweating, followed by confusion and abnormal behavior, presented at dawn and improve the intake of sugary drinks or food. He was admitted to the emergency department with consciousness disorder associated with blood glucose of 31 mg%. On examination in hospital he was lucid, alert, tachypnea, Weight: 60kg, BMI: 22kg/m2, PA: 110/60mmHg, FC: 82x ’, FR 28x’, left thoracotomy scar, absent in left chest; palpable mass in the left upper quadrant and flank reaching mesogastro, lower limb edema. Analytical Fasting: Glucose: 31-60mg/dl, Insulinemia: <2.00ulU/ml; Peptide C: <0.10ng/mL. IGF-1: 100ng/ml (VN: 69-200); IGF-2: 398ng/ml (VN: 50-250). Counter-regulatory hormones: normal. CT: large solid mass of contours defined heterogeneous aspect sarcomatous occupying the left hemithorax and hypochondria and the same side of 19x18x32cm AP diameter, DT, DL and then moves to the spleen and bowel loops laterally likewise exerts crowding the pancreas and left kidney.

**Discussion:** Tumor-induced hypoglycemia is a rare entity that can occur in patients with different tumor types and can be caused by different mechanisms: insulin secretion by pancreatic islets (insulinoma), ectopic secretion of insulin by NETs and GISTs. In addition, there are cases of tumor-induced hypoglycemia no insulinoma, where main etiology of hypoglycemia is IGF2 production or high molecular weight precursor (big-IGF2). Other mechanisms include secretion of IGF-1, production of autoantibodies against insulin or receptor, or more rarely, the secretion of GLP-1. It has been postulated that the DPS factors responsible for hypoglycemia may include: excessive secretion of IGF-2, failure compensatory mechanisms to prevent hypoglycemia and accelerated glucose consumption by large tumors.

**Conclusion:** Given the occurrence of recurrent symptomatic hypoglycemia (no relation to causes such as DM or other endocrinopathies) should be ruled a paraneoplastic syndrome type DPS. The SFTP may manifest as symptomatic hypoglycemia and surgical resection is the treatment of choice in these cases.

**Abstract #310**

**CHARACTERIZING HYPOGLYCEMIC EVENTS AMONG HOSPITALIZED PATIENTS WITH DIABETES**

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**Objective:** To determine factors associated with hypoglycemic events in patients with diabetes mellitus (DM) on a designated medical unit.

**Methods:** A retrospective analysis was performed identifying hypoglycemic events among hospitalized patients with DM on a specified medical ward, over a 10.5 month period (n=118). Data was obtained from RALS-Web3, a database which syncs and uploads point-of-care glucose results. The electronic medical record (EMR) was then reviewed for further information. Events were
included if the point-of-care finger stick (POCT FSG) was <70 mg/dl and the patient was documented as having DM in the EMR. Data recorded included: POCT FSG values, time and date of event, timing and type of last insulin administration, patient age, gender, weight, height, creatinine, dialysis status, type 1 or 2 DM status, outpatient DM regimen, length of stay (LOS), NPO status, expiration status, provider notification, medication adjustments, and intervention type. A standard regression model for the rate of hypoglycemic events was used to compare dialysis and non-dialysis patients.

**Results:** Among the cohort of patients identified with at least one episode of hypoglycemia (n=118), the mean hypoglycemia rate was 0.30 events/days hospitalized (mean number of events 2.08, mean LOS 9.8 days). The following additional mean values were determined: POCT FSG value at the time of hypoglycemia 55 mg/dl, age 64, creatinine 2.5 mg/dl, GFR 55 ml/min/m², and BMI 27 kg/m². In addition, 56% were female, 14% were Type 1, 63% had a GFR of ≤ 60 ml/min/m², 20% were on dialysis, 15% were NPO, 47% had recurrent events, and 3.4% (n=4) expired during the hospitalization. Events were more frequent in the morning hours, with most occurring between the hour of 7 and 8 am (24%). The average rates of hypoglycemia in dialysis (n=23) and non-dialysis (n=95) patients were 0.25 and 0.31 events/days hospitalized respectively (P=0.27).

**Discussion:** Hypoglycemic events were found to occur more frequently in the morning hours, which may be a consequence of the normal fasting effect, insulin dosing, or simply the routine time blood sugars are checked at our institution. Hypoglycemia was also commonly seen among patients with renal dysfunction and among patients with prior hypoglycemic events.

**Conclusion:** To further improve diabetes care at our hospital, interventions to decrease hypoglycemia will be developed targeting our high risk patients (renal dysfunction, recurrent hypoglycemia), especially during the early morning hours.

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**Abstract #311**

**NON-ISLET-CELL TUMOR HYPOGLYCEMIA (NICHT) IN A PATIENT WITH RETROPERITONEAL TUMOR**

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**Case Presentation:** A 56 years old male with no previous medical history and whose father had T2D was aware of abdominal distension and pain for 3 months. He was admitted to another hospital for neurosurgery in the morning because of loss of consciousness after having no dinner the day before. Though brain MRI showed no abnormal findings, his plasma glucose concentration (PG) was 20mg/dl. His consciousness was improved after glucose infusion. An abdominal CT showed a large abdominal tumor. He was transferred to our hospital to investigate the relationship between hypoglycemia and the tumor. His body weight had decreased 8kg in the prior 6 months, and an elastic soft tumor was palpable in his abdomen. Laboratory findings under continuous glucose infusion were HbA1c 5.4%, fasting PG 76mg/dl, serum insulin <1.0μU/ml and C-peptide levels <0.1ng/ml. IGF-I 64.4ng/ml and GH 0.066ng/ml were low, and IGF-II was 660.9ng/ml (normal:294-1492). IGF-II/IGF-I ratio 10.26 was relatively high. Counter regulatory hormone levels were considered to respond normally against hypoglycemia. Insulin autoantibody was negative. Continuous glucose monitoring (CGM) revealed hypoglycemia in the early morning even under continuous glucose infusion. An abdominal CT showed retroperitoneal tumor (approx. 20cm) in multiple lobes, with necrosis in the center of the tumor. He underwent resection of the tumor. Histopathological findings suggested hemangiopericytoma/solitary fibrous tumor that was positive for CD34, bcl-2, CD99 and partially epithelial membrane antigen. Immunoblot studies from the patient’s serum detected the high molecular weight of IGF-II (“big”-IGF-II). Glucose levels measured by CGM after operation improved even without continuous glucose infusion, and there was no recurrence of hypoglycemia. On the other hand, he was diagnosed with impaired glucose tolerance (IGT) by OGTT at 3 months and 1 year after the operation.

**Conclusion:** NICHT is very rare, but presents severe hypoglycemia. It is usually seen in large mesenchymal and epithelial tumors. IGF-II usually forms ternary complex with IGFBP-3 and ALS (acid labile subunit), but the “big”-IGF-II secreted by the tumors forms soluble type or binary complex. This can easily pass through the capillary wall and increase IGF bioavailability, causing hypoglycemia. The “big”-IGF-
II is suggested to induce hypoglycemia through binding insulin receptors. It is useful for diagnosis of NICTH to show the low GH, IGF-I and insulin levels, and to detect the “big”-IGF-II by immunoblotting. He had a family history of T2D from his father and showed IGT after resection of the tumor. Before the operation, his IGT might not be apparent because of “big”-IGF-II from the NICTH.

Abstract #312

DETECTION OF LIVER CIRRHOSIS (LC) IN PATIENTS WITH TYPE 2 DIABETES (T2D) WHILE PRESENTING AS SEVERE HYPOGLYCEMIA

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Objective: To detect liver cirrhosis in T2D with CAD, hospitalised with hypoglycemia.

Methods: This study was conducted on 26 consecutive patients (age group 56–92yrs) in 2012 admitted with severe hypoglycemia (random plasma glucose<54 mg/dl). All of them had T2D & CAD and with normal LVEF. They were subjected to ultrasound scan for elastography of liver. Their liver echotexture & shear velocity measurements at 4 different sites were carried out by acoustic radiation force imaging (AFRI) sonoelastography. Their clinical history, diabetes duration, antidiabetic & cardiac drugs intake, alcohol, hepatitis, BMI, systemic examinations were recorded. Lab tests including LFTs, CBC, coagulogram, lipids, Hepatitis B&C markers, troponin, ferritin, duration & status of diabetes complications, random, fasting, post prandial plasma glucose & HbA1c, thyroid function & cortisol were done. Regular follow ups & telephonic calls were done for 2 yrs. Their cardiac evaluation & upper GI endoscopy to detect oesophageal varices in patients with liver fibrosis were also done. Stages of liver Fibrosis: F1-1.185 to 1.215; F2-1.215 to 1.54; F3-1.54 to 1.94; F4-1.94 & beyond.

Results: 4 out of 26 patients detected LC(15.38%). Age of patients having LC were 62-83 years. Duration of diabetes in LC group was 8-21 years. All 4 of them had oesophageal varices. These patients had normal transaminases (SGPT & SGOT) however serum albumin levels were low (2.6, 1.9, 2.8, 2.5 gm/dl). One case required ventilatory support. All patients had preexisting CAD (coronary angioplasty, CABG or MI). 1 out of 4 patients had a sudden death at home, 8 months after discharge from hospital.

Discussion: NAFLD is a common association in patients with obesity & diabetes, however CLD prevalence has not been studied in patients with diabetes with CAD. All three are associated with obesity & insulin resistance linking atherosclerosis & progressive liver damage. Management of diabetes needs to be changed in the presence of LC. Few antidiabetic drugs are hepatotoxic & antiplatlets are relatively contraindicated in LC. In our study, patients presenting with severe hypoglycemia had high incidence of liver cirrhosis which needed significant change in management of all 3 diseases. LFT in diabetics is not a good test to detect liver cirrhosis whereas Elastography/Fibroscan of the liver are good tests, as shown in our study. Old age and prolonged duration of T2D are more commonly associated with LC.

Conclusion: 1) Our study suggests that work up for LC is recommended, especially in diabetic patients presenting as severe hypoglycemia. 2) Normal transaminases does not always rule out CLD & LC. 3) Long duration of diabetes, preexisting CAD & old age are co-morbid factors for hypoglycemia & LC.

Abstract #313

INSULIN AUTOIMMUNE SYNDROME AND HYPOGLYCEMIA: INSULIN IMMUNOASSAY VARIABILITIES, CONTINUOUS GLUCOSE MONITORING, GLUCOSE INTOLERANCE AND GLUCOCORTICOID IMMUNOTHERAPY


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Objective: To describe diagnostic and therapeutic challenges in insulin autoimmune syndrome [hypoglycemia – hyperglycemia].

Case Presentation: A 80 year non-diabetic female [hypertension and joint pains; medications: homeopathy, enalapril, amlodipine, clopidogrel and levocetirizine], developed over 2 weeks, repeated fasting / premeal spontaneous hypoglycemia [weakness and tiredness, sweating, and slurring of speech; serum glucose 32 - 50 mg/dl], with post prandial hyperglycemia [serum glucose 255 - 323 mg/dl]. There was no evidence of surreptitious exogenous insulin, sulfonylurea or meglitinide use. Her fasting[F] and post prandial[PP] serum [undiluted] insulin levels were found to be repeatedly very grossly [F and PP > 1000 uU/ml] and disproportionately [in relation to simultaneous normal serum C peptide: F= 3.99, PP=]
ABSTRACTS – Hypoglycemia

11.9 ng/ml] elevated in one assay system (#1). However, in another assay system (#2), parallel measured insulin levels were within normal range if assayed with undiluted serum [F= 14 – 18, PP= 24 uU/ml], but grossly elevated [F > 1000 uU/ml] when the same serum was diluted [“hook effect”]. In 2 other assay systems (#3, 4), undiluted serum insulin levels were in the intermediate range [F= 60, 96 uU/ml]. Serum protein and 24 urine immunofixation electrophoresis were normal. Extended 75 G OGTT: [0, 3, 8 and 9 hours] Baseline versus 24 hour post Prednisolone 20 mg bid: 65, 90, 206, 180 versus 58, 152, 314, 266 [mg/dl]. Serum insulin autoantibody: Baseline= Significant elevation. Continuous glucose monitoring – CGM: enabled better: (a) analysis of blood glucose profiles and prompt correction of significant hypoglycemic episodes; (b) understanding of glucose and insulin dynamics in response to oral glucose and mixed meal challenge; (c) analysis of 24 hour glycemic profiles during therapeutic 6 and 11 meals per day plans; and (d) monitoring the initial responses to longer term immunotherapy. Glucocorticoid immunotherapy: Prednisolone 20 mg bid resulted in parallel and progressive immunologic and endocrine remission [normalization of serum insulin autoantibodies, glucose and insulin] over one year, with simultaneous tapering of glucocorticoid dose. 3 year follow up= normal.

Discussion: Diagnosis of spontaneous insulin autoimmune syndrome [hypoglycemia – hyperglycemia], is confounded by specific immune assay systems. CGM facilitates rational nutrition and immunotherapy.

Conclusion: Diagnosis and management of spontaneous hypoglycemia syndromes merit insulin immunoassays using both undiluted and diluted serum and serial / periodic continuous glucose monitoring.

Abstract #314

PROLONGED HYPOGLYCEMIA FROM GLARGINE OVERDOSE: AN APPROACH TO INVESTIGATION

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Case Presentation: A 50 year old woman was brought to the emergency department for severe hypoglycemia. She has a history of type 2 diabetes mellitus for which she is on 60 units Glargine insulin twice daily; however her last dose was 5 days prior to admission due to frequent hypoglycemia. At presentation she was unresponsive despite receiving Dextrose 50% and was intubated for airway protection. Her hemoglobin A1c was 8.9%, with normal metabolic panel and cortisol. Her hypoglycemic episodes persisted even after receiving multiple ampules of D50. As such, dextrose infusion was started, initially D5, then D10, then D20, and PRN boluses of D50. Enteral nutrition was initiated to obtain normoglycemia but with minimal avail. Blood was drawn during an episode of hypoglycemia of 45 mg/dL- concurrent insulin was 738 mIU/mL (reference range 2-27), C-peptide <0.1 ng/mL, negative insulin antibodies and sulfonylurea screen.

Because of persistent hypoglycemia, 1 mg Glucagon challenge was attempted; glucose responded from 55 mg/dL to 106 mg/dL. A single dose of Octreotide 50 mcg was given without appreciable improvement in glucose. Her clinical condition improved. She was maintained on Dextrose infusion, with PRN D50, and frequent meals. Mild hypoglycemia continued into her 5thday of hospitalization, 9 days after her last reported dose of Glargine, at which her glucose was documented to drop to 41 mg/dL, after which it eventually resolved.

Discussion: We present this case for two aspects. Firstly, this patient had unusually long hypoglycemia from exogenous insulin use. If her report was accurate, she had persistent hypoglycemia 9 days after her last dose of Glargine; even if her description was inaccurate, this was problematic into her 5thday of hospitalization. To the best of our knowledge, the longest duration of hypoglycemia in the literature is 4 days. Secondly, this provided a review of the diagnostic approach to hypoglycemia. The initial step is to fulfill Whipple’s triad. The next step is confirm if this is insulin-mediated, defined as having insulin levels >3 during a spell. This following step is to determine if the source is exogenous or endogenous. In the latter, a sulfonylureas drug screen should be performed to see if the hyperinsulinemia was induced pharmacologically. Insulin antibodies should be considered to rule out Hirata syndrome especially with markedly high insulin levels such as this.

Conclusion: Her response to Glucagon suggested she had normal glycogen stores while the lack of response to Octreotide suggested that this was not a result of endogenous hypersecretion by the pancreas, which is thus consistent with the patient’s clinical picture of exogenous insulin overdose.
Abstract #315
WERNICKE’S ENCEPHALOPATHY AS A COMPLICATION OF METABOLIC SURGERY
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Objective: We report a patient with type 1 diabetes and past metabolic surgery who developed Wernicke’s encephalopathy after treatment of hypoglycemia with dextrose, in the setting of severe thiamine deficiency.

Case Presentation: A 33 year old Black man with type 1 diabetes for 19 years, complicated by nephropathy and retinopathy, obesity, SLE, history of pancreatitis with partial pancreatectomy and Roux-en-Y gastric bypass (RYGB) was admitted with severe hypoglycemia and altered mental status (AMS). Prior to admission, he was independent, adherent to medications and diet, had no allergies, did not travel, use alcohol, tobacco or illicit drugs. He was lethargic and incoherent, with difficulty ambulating, and an undetectable glucose level by EMS (<30mg/dL). Home medications included Lantus 4 units hs, Aspart 2 units with meals, PO B12 supplements and a multivitamin. He was treated with IV D50% x 2 doses with improved glucose but not mental status. Vital signs were normal, physical exam was remarkable for stupor, spontaneous eye opening, and response to noxious stimuli. Vestibulo-ocular, deep tendon reflexes as well as plantar responses were normal. CT head showed partial opacification of mastoid air cells suggestive of mastoiditis and no evidence of hemorrhage, mass effect or ischemia. After ICU admission, glycemic control (80-180mg/dL) was established and maintained via a continuous insulin and dextrose infusions, electrolyte abnormalities were corrected, and enteral nutrition and hydration were provided via nasogastric tube. Broad spectrum antibiotics for presumed infection had no clinical effect and were stopped when cultures yielded no growth. Non-invasive hemoglobin 6.5% and no evidence of hemorrhage. Glucose for 20 days of presentation.

Conclusion: Nutritional deficiencies post malabsorptive metabolic surgeries, such as RYGB and biliopancreatic diversion, are common and often unnoticed. Glucose administration, without prior thiamine supplementation, can lead to poor outcomes. Based on our experience, we encourage physicians to carefully monitor electrolytes and nutritional status post metabolic surgery. In the setting of AMS with no readily identifiable cause, nutritional deficiencies should be highly considered in this group of patients.

Abstract #316
SEVERE HYPOINSULINEMIC HYPOGLYCAEMIA IN BECKWITH-WIEDEMANN SYNDROME (BWS): POTENTIAL MECHANISMS AND THERAPEUTIC IMPLICATIONS
Kalleshwar Chandrika, Reshma V, Sumathi K, Sri Srikanta, Thummala Kamala, Tejeswini Deepak

Objective: To describe a challenging case of persistent severe hypoinsulinemic hypoglycaemia in an infant with Beckwith Wiedemann Syndrome [BWS].

Methods: A male baby born [full term normal delivery; birth weight 2500 G] to a 30 year mother [para 4; no consanguinity; no hypertension or gestational diabetes], presented on day 5 with neonatal hypoglycaemia [lacthaery, refusal of feeds, uprolling of eyes, involuntary movements of hands and legs, seizures - recurrent]. Severe symptomatic hypoglycaemia continues to persist even till day 90 [BG: blood glucose 17 – 53 mg/dl], despite intermittent 2 hourly oral feeds [breast milk + supplements], and occasional IV glucose for emergencies. Urine ketones absent. A normal metabolic screen [tandem mass spectrometry]. Serum insulin: repeatedly < 2 IU/ml [simultaneous BG 17 -32mg/dl]. 18 F DOPA PET CT – whole body: positive for multiple midline retroperitoneal lesions, ? neuroblastomas; no focal pancreatic mass lesion; liver normal. Reports of serum IGF-2 (insulin growth factor - 2) and pituitary function tests are awaited. TSH normal. Inborn errors of metabolism screen [tandem mass spectrometry] normal.

Liver function tests: bilirubin direct 8.7 and total 17 mg/dl, SGOT 450 and SGPT 114 u/l, alk phosphatase 628 u/l, serial tests improving; Ultrasound abdomen: uncomplicated left inguinal hernia, mildly prominent left adrenal gland, no hepatic mass lesion. EKG: Abnormal; ECHO: atrial septum PFO, left > right shunt, EF 60%. S Alpha fetoprotein: 23399 IU/ml [5-15 ] - ? neonatal hepatitis.
Discussion: Hypoglycaemia reported in 30-50% of neonates with BWS, is usually transient and occasionally persisting. The classically reported mechanism is hyperinsulinemia and islet cell hyperplasia, at times very severe requiring partial pancreatectomy. Hypoinsulinemic hypoglycaemia in BWS is extremely rare, possible mechanisms include: secretion of IGF-2 from neuroblastomas; increased glucose consumption by embryonic tumors; and associated hypopituitarism or liver dysfunction.

Conclusion: The common cause of neonatal hypoglycaemia in BWS is hyperinsulinemia, very rarely hypoinsulinemic hypoglycaemia due to different mechanisms can occur, with corresponding significant therapeutic implications.
LIPID/CARDIOVASCULAR DISORDERS/HYPERTENSION

Abstract #400

INHIBITION OF ABCA1 PROTEIN EXPRESSION AND CHOLESTEROL EFFLUX BY TNF α IN MLO-Y4 OSTEOCYTES

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Objective: Hip fracture and myocardial infarction cause significant morbidity and mortality. In vivo studies raising serum cholesterol levels as well as pro-inflammatory cytokines such as TNF α manifest bone loss and atherosclerotic vascular disease, suggesting that abnormalities of cholesterol transport may contribute to osteoporosis.

Methods: We used the mouse osteocyte cell line (MLO-Y4) to investigate the effects of TNF α on the expression of cholesterol acceptor proteins such as apolipoprotein A-I and apolipoprotein E, as well as on ATP-binding cassette-1 (ABCA1) and scavenger receptor class B type 1 (SRB1).

Results: MLO-Y4 cells do not express apolipoprotein A-I or apolipoprotein E; however, they do express the cholesterol transporters ABCA1 and SRB1. Treatment of MLO-Y4 cells with TNF α had no effect on osteocalcin levels; however, TNF α reduced ABCA1 protein levels and cholesterol efflux to apolipoprotein A-I. Interestingly, TNF α treatment increased ABCA1 mRNA levels 1.8-fold and increased liver-X-receptor α protein expression but had no effect on retinoid-X-receptor α and retinoic acid receptor β protein levels. TNF α treatment suppressed SRB1 mRNA levels (18%) but there was no change in SRB1 protein expression. TNF α induced p38 mitogen-activated protein (MAP) kinase activity, but had little effect on c-jun N-terminal kinase 1 and extracellular regulated kinase 1/2. Pharmacological inhibition of p38 MAP kinase restored ABCA1 protein levels.

Conclusion: These results suggest that pro-inflammatory cytokines regulate cholesterol metabolism in osteocytes.

Abstract #401

ABSTRACT WITHDRAWN

Abstract #402

BETA BLOCKERS SUPPRESS DEXTROSE-INDUCED ENDOPLASMIC RETICULUM STRESS, OXIDATIVE STRESS AND APOPTOSIS IN HUMAN CORONARY ARTERY ENDOTHELIAL CELLS.

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Methods: To determine if beta blockers can also prevent dextrose-induced endoplasmic reticulum (ER) stress in addition to their anti-oxidative effects, human coronary artery endothelial cells and hepatocyte-derived HepG2 cells were treated with 27.5 mM dextrose for 24 hours in the presence of carvedilol (a lipophilic beta blockers with alpha blocking activity), propranolol (a lipophilic non selective beta blockers) and atenolol (a water-soluble selective beta blockers) and ER stress, oxidative stress and cell death were measured. ER stress was measured using the placental alkaline phosphatase assay and western blot analysis of glucose regulated protein 78, c-jun-N-terminal kinase (JNK), phospho-JNK, eukaryotic initiating factor 2α (eIF2α) and phospho-eIF2α and measurement of X-box binding protein 1 (XBP1) mRNA splicing using reverse transcriptase-polymerase chain reaction. Superoxide (SO) generation was measured using the superoxide-reactive probe 2-methyl-6-(4-methoxyphenyl)-3,7-dihydroimidazo[1,2-A]pyrazin-3-one hydrochloride (MCLA) chemiluminescence. Cell viability was measured by propidium iodide (PI) staining method.

Results: The ER stress, SO production and cell death induced by 27.5 mM dextrose was inhibited by all three beta blockers tested. The antioxidative and ER stress reducing effects of beta blockers were also observed in HepG2 cells.

Conclusion: The salutary effects of beta blockers on endothelial cells in reducing both ER stress and oxidative stress may contribute to the cardioprotective effects of these agents.

Abstract #403

THE GLUTATHIONE MIMIC EBSELEN INHIBITS OXIDATIVE STRESS BUT NOT ENDOPLASMIC RETICULUM STRESS IN ENDOTHELIAL CELLS.

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University of Florida

Objective: Reactive oxygen species are associated with cardiovascular disease, diabetes, and atherosclerosis, yet use of antioxidants in clinical trials has been ineffective at
improving outcomes. In endothelial cells, hyperglycemia-induced oxidative stress and endoplasmic reticulum stress promotes endothelial dysfunction leading to the recruitment and activation of peripheral blood lymphocytes and the breakdown of barrier function.

Ebselen, a glutathione peroxidase 1 (GPX1) mimic, has been shown to improve b-cell function in diabetes and prevent atherosclerosis.

Methods: To determine if ebselen inhibits both oxidative stress and endoplasmic reticulum (ER) stress in endothelial cells, we examined its effects in human umbilical vein endothelial cells (HUVEC) and human coronary artery endothelial cells (HCAEC) with and without hyperglycemia. Oxidative stress and ER stress were measured by MCLA chemiluminescence and ES-TRAP, respectively. GPX1 over-expression and knockdown were performed by transfecting cells with a GPX1 expression construct or a GPX1-specific siRNA, respectively.

Results: Ebselen inhibited hyperglycemia-induced oxidative stress but not ER stress in both HUVEC and HCAEC. Ebselen also had no effect on tunicamycin-induced ER stress in HCAEC. Furthermore, augmentation of GPX1 activity directly by sodium selenite supplementation or transfection of a GPX1 expression plasmid decreased hyperglycemia-induced oxidative stress but not ER stress, while GPX1 knockout enhanced oxidative stress but had no effect on ER stress.

Discussion: These results suggest that ebselen targets only oxidative stress but not ER stress.

Conclusion: Ebselen inhibited hyperglycemia-induced oxidative stress but not ER stress in both HUVEC and HCAEC. Ebselen also had no effect on tunicamycin-induced ER stress in HCAEC. Furthermore, augmentation of GPX1 activity directly by sodium selenite supplementation or transfection of a GPX1 expression plasmid decreased hyperglycemia-induced oxidative stress but not ER stress, while GPX1 knockout enhanced oxidative stress but had no effect on ER stress.

Abstract #404

STATIN-RELATED MYOPATHY IN VETERANS WITH LOW VITAMIN D LEVELS

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Objective: Statins reduce risk for cardiovascular disease, the major cause of morbidity and mortality in veterans. 5-10% of patients develop statin-related myopathy (SRM), defined as muscle pain/weakness with a normal creatine kinase (CK) level (myalgia), elevated CK (myositis) or >10 times elevated CK (rhabdomyolysis). Risk factors are advanced age, use of medications altering statin metabolism, liver, kidney disease, and hypothyroidism. Low vitamin D levels were associated with risk for SRM with reports of SRM being resolved upon vitamin D repletion. Our objective was to compare clinical characteristics of veterans without and with SRM, for whom electronic consults for vitamin D repletion were requested from the Endocrine Service between January 2nd and March 26th 2013.

Methods: Of 281 consults, 123 patients received statins. Among them 105 patients (93% males) had no SRM and 18 patients or 15% (89% males) had a history of SRM. The significance of the difference between the groups was tested with t-test (parametric variables) and z-test (proportions).

Results: In the group with SRM 10 (56%) patients had myalgia, 5 (28%) myositis, 1 (6%) rhabdomyolysis, and 2 (11%) had SRM with no documented CK; simvastatin was related to SRM in 13 (72%) patients, followed by atorvastatin (3 or 17%), lovastatin (2 or 11%) and pravastatin (1 or 6%). 10 (56%) of patients were not taking any statin at the time of the consult due to a history of SRM. Group without SRM was significantly older than the group with SRM (69.6±13.0vs.62.7±11.8years, p=0.039); group with SRM had higher proportion of African Americans (0.14vs.0.39, p=0.012) and patients taking medications altering statin metabolism such as warfarin, digoxin, amiodipine, diltiazem, verapamil, colchicine, fibrates, and niacin (0.23vs.0.56, p=0.004). There was no significant difference in vitamin D level (15.3±6.0vs.13.5±3.7ng/mL, p=0.091), BMI, tobacco/illicit drug use, presence of liver, kidney disease, diabetes, number of prescribed medications, TSH, or calcium levels between the groups.

Discussion: Low vitamin D level is a potential risk factor for SRM. Our study did not show significant difference in vitamin D levels between the groups, however all patients had low vitamin D and there was a trend towards even lower levels in the group with SRM. While a previous trial in veterans taking high-dose simvastatin showed association of SRM and younger age as well, we also showed that African American veterans are at a potentially higher risk for SRM in the setting of a low vitamin D level.

Conclusion: Low vitamin D level is a potentially significant and correctible risk factor for statin-related myopathy in veterans.
Abstract #405

CLINICAL COURSE OF ERUPTIVE XANTHOMAS AND HYPERTRIGLYCERIDEMIA

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Case Presentation: A 33 year-old Hispanic male with minimal prior medical care presented to a primary care facility for a routine exam. His father died of rapidly progressive kidney failure in his 50s and mother was living in her 50s without known problems. The patient had no siblings and was unaware of early coronary disease or sudden cardiac death in his extended family. He did not use any prescription, OTC, illicit drugs, or tobacco and drank 10 beers one night per weekend. He did not exercise and worked in the fast food industry. On exam he had centripetal obesity, BMI of 37 kg/m2, otherwise unremarkable without skin findings. Laboratory studies showed a HgbA1c of 7.3% and a triglyceride (TG) level of 1373 mg/dL with total cholesterol (TC) 202 mg/dL and HDL 21 mg/dL; he was started on metformin and gemfibrozil. Eight months later he presented to the same clinic with a new onset white rash on his arms, thighs, and back which was not-pruritic and not present in close contacts. He had no history of abdominal pain. His exam showed clusters of pearly papules white to yellow in color closely grouped measuring less than 5 mm on areas described and an obese non-tender abdomen. Repeat fasting laboratory studies showed a HgbA1c of 7.7% and a TG level of 6770 mg/dL with TC 620 mg/dL and HDL 35 mg/dL. He was counseled on diet including limiting alcohol and signs of pancreatitis and referred to our endocrinology clinic for further care three months later. Clinical photographs consistent with the prior exam were obtained; repeat fasting laboratory studies showed a TG level of 1956 mg/dL with TC 309 mg/dL, HDL particle number 32.9 (24.0-49.1 mmol/L), HDL size 8.8 (8.5-10.5 nm), LDL particle number 332 (low risk range < 1000 nmol/L), LDL size 19.6 (19.7-21.9 nm), VLDL particle number 170.7 (6.8-126.1 mmol/L), VLDL size 83.9 (36.9-68.8 nm), apoAI 118 (104-202 mg/dL), apoB 99 (66-113 mg/dL), and HgbA1c10.6%. CBC including MCV, vitamin B12, and folate were normal. ALT was elevated 55 (0-41 U/L), AST and alkaline phosphatase were normal, and GGT was elevated 85 (0-59 U/L). The patient was started on glargine insulin 15 units nightly, transitioned from gemfibrozil to fenofibrate 145 mg daily, and will be tracked monthly going forward with stepwise addition of statin therapy and omega 3 fatty acids.

Conclusion: This patient presented with eruptive xanthomas without pancreatitis and triglycerides > 6000 mg/dL consistent with Fredrickson Type V hyperlipidemia exacerbated by secondary causes including diet, obesity, and type 2 DM.

Abstract #406

MANAGEMENT OF CHYLOMICRONEMIA INDUCED PANCREATITIS WITH INTRAVENOUS (IV) INSULIN

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Objective: To demonstrate successful management of chylomicronemia induced acute pancreatitis in a patient whose triglyceride levels decreased with IV insulin.

Methods: We present a case of a 40 year old male with past medical history of Diabetes and Dyslipidemia who was admitted with complaints of severe mid-epigastric pain, nausea and vomiting. Patient consumes 5 alcoholic drinks daily. He takes metformin 500 mg orally daily, he could not recall other medications. His glycated hemoglobin was 8.1 percent. On examination, vitals were normal. He had diffuse left upper abdominal tenderness with decreased bowel sounds. He had eruptive xanthomas on his lower back. Significant laboratory findings were: Glucose 260 mg/dl, Total cholesterol 522 mg/dl, triglycerides 4731 mg/dl. Amylase and lipase were normal. Abdominal Computed tomography scan was consistent with acute pancreatitis. Patient was kept on bowel rest and IV fluids. He was started on IV insulin for his hypertriglyceridemia.

Case Presentation: Triglycerides trended down to near normal levels after 6 days. IV insulin was continued for two days until triglycerides were less than 1000mg/dl. Subcutaneous insulin was then started along with fibrate therapy. Abdominal pain also noted to resolve within the first 3 days of admission.

Discussion: Chylomicronemia syndrome is considered when triglyceride levels exceed 1000 mg/dl and can be associated with eruptive xanthomata, abdominal pain and lipemia retinalis. There have been case reports linking it to Multi Organ Dysfunction Syndrome. IV insulin is a recognized way of treating chylomicronemia with other modalities such as iv heparin and plasmapheresis. IV insulin is less expensive and more readily available then plasmapheresis in most centers.

Conclusion: IV insulin is an effective treatment for the chylomicronemia syndrome in the setting of acute pancreatitis.
Abstract #407

HYPERTRIGLYCERIDEMIA-INDUCED RECURRENT PANCREATITIS TREATED WITH PLASMAPHERESIS AND INSULIN DRIP

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Objective: A serum triglyceride level of more than 1000 mg/dl is a well-recognized risk factor for pancreatitis. We are reporting a case of hypertriglyceridemia-induced recurrent pancreatitis in a patient with familial hypertriglyceridemia successfully treated with plasmapheresis and insulin drip.

Case Presentation: A 33-year-old Hispanic man presented with recurrent pancreatitis. His laboratory work on presentation showed: triglyceride 9312 mg/dl, lipase 131 U/L, total cholesterol 891 mg/dl, hemoglobin A1C 9.7%. Many lab work were not attainable due to grossly lipemic specimen. The patient was kept NPO and treated with intravenous fluid, intravenous morphine for pain control, insulin drip with intravenous 5% dextrose infusion to maintain blood sugar 150-200 mg/dl. Plasmapheresis was started the following day to rapidly remove serum triglyceride. The patient received 3 sessions of plasmapheresis (replaced with albumin) done on a daily basis for three consecutive days. His triglyceride decrease to 462 mg/dl after the 3rd session. Insulin infusion was discontinued after triglyceride < 500 mg/dl. The patient’s symptoms improved significantly.

Repeat lipid profile 7 days later showed: total cholesterol 117 mg/dl, triglyceride 307 mg/dl, HDL 29 mg/dl, LDL 27 mg/dl. Diet was gradually advanced and the patient was discharged home.

Discussion: Recurrent episodes of pancreatitis in a patient with familial hypertriglyceridemia are usually precipitated by dietary fat, alcohol abuse or medication noncompliance. It has been noted that serum pancreatic enzymes may be normal or only minimally elevated, even in the presence of severe pancreatitis by imaging studies. The mainstay treatment of hypertriglyceridemia-induced pancreatitis includes intravenous fluid, analgesia, insulin drip which decreases serum triglyceride by enhancing lipoprotein lipase activity. Heparin has also been reported to have some effect in stimulating endothelial lipoprotein lipase release. However the effect is transient and is followed by enhanced hepatic degradation which contributes to depletion of plasma lipoprotein lipase. Therefore the role of heparin is controversial in the treatment of hypertriglyceridemia.

Conclusion: Plasmapheresis is a safe and highly effective way to rapidly remove serum triglyceride.

Abstract #408

MACHO MAN: ACUTE MYOCARDIAL INFARCTION IN A MALE BODY BUILDER RECEIVING TESTOSTERONE INJECTIONS

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Objective: Testosterone therapy has shown to improve intermediate outcomes and cardiac risk factors but recent studies show an increased risk of cardiovascular events in patients receiving testosterone. The following case highlights this growing concern.

Case Presentation: A 51-year-old male bodybuilder with no known past medical history presented with a sudden onset of substernal chest pain with dyspnea, diaphoresis, nausea and vomiting. He had a similar episode three weeks back and a cardiac catheterization showed 20% occlusion of one artery. He was prescribed aspirin along with testosterone injections which he has been taking for the past 10 years. He denied any toxic habits or family history of heart disease. Physical exam was unremarkable aside from his muscular physique. EKG showed inferior lead ST elevations with reciprocal depressions in the anterior leads. Laboratory tests showed elevated CPK and negative troponin-T. He underwent an emergent cardiac catheterization showing 100% mid right coronary artery lesion. He received one bare metal stent with significant improvement in his symptoms and EKG post procedure.

Discussion: In the last few years attention has been placed on the effects of testosterone therapy on cardiovascular outcomes and mortality. A retrospective study in JAMA found that men taking testosterone replacement therapy had a higher risk of death, myocardial infarction or stroke. Another study found that older and young men with pre-existing heart disease had increased risk for non-fatal myocardial infarction after starting testosterone therapy. Exogenous testosterone use was associated with increased risk of cardiovascular events, especially in studies not...
funded by pharmaceuticals. These findings are significant because previous trials have shown that testosterone therapy improves many intermediate outcomes and cardiac risk factors. Furthermore, previous meta-analysis found that testosterone therapy increases hematocrit and reduces HDL, but did not find a significant association with cardiovascular risk. In light of these findings, consumer advocacy groups petitioned the FDA to add black box warnings to testosterone formulations. Also, the endocrine society recommends that middle-aged and older men who are taking or considering testosterone therapy be advised of the potential risk of cardiovascular events.

Conclusion: Testosterone replacement therapy might be associated with increased cardiovascular risk and prospective, randomized controlled trials are needed to determine the risks and benefits of testosterone therapy.

Abstract #409

MEAN ARTERIAL PRESSURE, PULSE PRESSURE IN DIABETIC AND NON DIABETIC MALE AFRICAN POPULATION: A COMPARATIVE STUDY.

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Objective: Mean arterial pressure (MAP) and pulse pressure (PP) are important parameters that predicts cardiovascular risk both in diabetics and non diabetic population in both gender. Data on this subject area in Nigeria, Africa and worldwide are few. The aim of this paper is to examine the pattern of MAP and PP in a diabetic male population compared to a general population of males in Africans. Is the pattern of MAP and PP the same in both diabetic and non diabetic? Does any significant disparity exist?

Methods: This is a preliminary prospective study. Randomly, the blood pressure of 20 men from the general Lagos population were taken at heart level using a mercurial sphygmomanometer during a free medical screening exercise in Surulere. Similarly, the blood pressure of 20 consecutive known diabetic men were taken at heart level using a mercurial sphygmomanometer. The diabetic patients were recruited from the endocrinology clinic of the Lagos State University Teaching Hospital, Ikeja, Lagos, Nigeria. Individual consent was obtained from both group of participants. The PP of each individual was computed by subtracting the diastolic blood pressure from the systolic blood pressure. The MAP of each individuals was computed by adding one third of the PP to the diastolic blood pressure. The limitation of this study include the very small size of the study population and Africans are not well represented in the sample size.

Results: The age range of the non diabetic was 31 to 70 years while the age range of the diabetics was 31 to 82 years. The mean (average) pulse pressure among the non diabetic was 46.5 mmHg while the average pulse pressure among the diabetics was 67.7 mmHg. Among the non diabetic the mean of the MAP was 103.20 mmHg while among the diabetics it was 96.97 mmHg. The highest MAP among the diabetic group was 133.33 mmHg while the highest among the non diabetic was 150 mmHg.

Discussion: This paper shows that the average MAP is higher in the general African male population than among diabetic male Africans. This supports autopsy finding in literature that haemorrhagic cerebrovascular accident occurs slightly more commonly in non diabetic compared to diabetics while cerebral infarction occurs more in diabetic subjects compared to non diabetics. Similarly, it was noticed in the study that African male diabetics tend to have higher pulse pressure than the general African population.

Conclusion: MAP is lower in male African diabetics compared to the general African male population. Conversely, PP is higher among male African diabetics compared to the general African male population.

Abstract #410

ASSOCIATION BETWEEN CONTROLLED BLOOD GLUCOSE AND THE COMPONENTS OF FASTING LIPID PROFILE AMONGST PATIENTS WITH DIABETES AND DYSLIPIDEMIA ON LIPID LOWERING PHARMACOTHERAPY

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Objective: To evaluate the association between the target level of HgbA1c and the status of components of fasting lipid profile including LDL-C, non-HDL-C, HDL-C, and triglycerides in patients with diabetes and dyslipidemia on lipid lowering pharmacotherapy.

Methods: Components of fasting lipid profile including LDL-C, non-HDL-C, HDL-C, and triglycerides were obtained for a sub-cohort of patients with diabetes in a Canadian database of patients with dyslipidemia on lipid lowering pharmacotherapy. Linear and logistic regression models were employed to evaluate the correlation between the components of fasting lipid profile and the target level of HgbA1c.

Results: 198 patients (101 men and 97 women) with diabetes and dyslipidemia were included in this analysis. The average HgbA1c was 6.8% (1.2) [mean (SD)] in this cohort. Average age was 64 (10) year-old for the cohort. No significant correlation between the level of HgbA1c and components of fasting lipid profile was observed.
including LDL-C Goal [odds ratio = 0.97 (95% confidence interval: 0.75, 1.27)], LDL-C level (P=0.80), HDL-C level (P=0.90), triglyceride level (P=0.80) and non-HDL-C level (P=0.90).

**Conclusion:** In this cohort of patients with diabetes and dyslipidemia on lipid lowering pharmacotherapy who mostly had an acceptable average blood glucose control, there was no correlation between the level of HgbA1c and fasting lipid profile components.

**Abstract #411**

SEVERE HYPERTRIGLYCERIDEMIA IN A PATIENT OF 36 YEARS OF AGE WITH DIABETIC KETOACIDOSIS AS DEBUT OF TYPE 2 DIABETES MELLITUS

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**Objective:** To report a case of severe hypertriglyceridemia (HTG) in a patient with DKA as debut of T2DM.

**Methods:** Clinical and paraclinical characteristics of a young adult with severe HTG and DKA as debut of T2DM are presented.

**Case Presentation:** Male, 36 years, diagnosis of rosacea; father with DM2 from the 40th. He weighed 110Kg, IMC 35.5Kg / m2. until 09 mo since then refers progressive decrease in weight of 20kg; 04 mo ago polydipsia, polyuria, polyphagia and nocturia will increase 02 days prior hiporexia presents, nausea, abdominal pain and vomiting (8-9 episodes a day) is added; went to private clinic diagnosed DKA (pH: 7.1; HCO3: 3.5; Sodium: 139; Potassium: 4; Glicemia: 400mg%, ketonuria (++), glucosuria (+++), amylase, cardiac enzymes , liver profile: NL); He was treated with hydration and insulin infusion EV, being then transferred from 12h to the emergence of our hospital. On examination: BMI: 30; No xanthomas, lipemia retinalis present. Analysis: G: 234mg%, pH: 7.38; HbA1c 14.1% Peptide C: 1,27mg/ml; ChT/HDL/ Tg: 922/16/2344 mg/dl; TSH: 0,6uUI/ml; FT4: 1ng/dl; AntiGAD: negative; blood count, liver and renal function, amylase / lipase unchanged. EV hydration and VO, vegan diet for 5 days and then count CHO diet was indicated; Mixed SC insulin (NPH 40IU/d + R 15IU/d), metformin 2550 mg/d, combination therapy with atorvastatin 40 mg/d gemfibrozil 1200mg/d. At the 5th day of hospitalization: ChT/HDL/VLDL/Tg: 658/27/219/1096 mg%; 10th day: ChT/HDL/VLDL/Tg: 322/30/63/314 mg% and 15°d: ChT/HDL/VLDL/Tg/LDL: 196/30/36/179/124mg%.

**Discussion:** The HTG is a common abnormality of lipid metabolism. The primary forms represent less than 5% of the HTG. Most patients with HTG has at least one underlying factor. However, not all patients with a similar exposure to triggers develop the same degree of dyslipidemia. Patients with triglyceride concentrations >2000 mg% practically have a secondary HTG associated with genetic. Secondary causes, there are several that could cause severe HTG (>500mg%), among which are The DM and DKA; alcohol, hypothyroidism drugs (oestrogens, protease inhibitors, olanzapine, mirtazapine and isotretinoin). In patients with Tg> 1000mg there is an increased risk of developing acute pancreatitis so their management requires a rapid and effective decrease of Tg having reported using insulin or heparin IV infusion and plasmapheresis.

**Conclusion:** In our case the strict nutritional regimen in the management of blood glucose and lipid lowering therapy combined allowed normalize glycemia and almost all lipoprotein parameters.

**Abstract #412**

ABSTRACT WITHDRAWN

**Abstract #413**

LIPID LOWERING TREATMENT TRENDS AMONG DIABETES PATIENTS WITH VERY HIGH CARDIOVASCULAR DISEASE RISK: A REAL-WORLD STUDY

Ruben Quek, PhD1, Kathleen Fox, MHS, PhD2, Li Wang, MA, MBA, PhD3, Lu Li, MS3, Shravanthi Gandra, MBA, PhD4, Nathan Wong, PhD, FACC, FANA


**Objective:** Statins are the treatment of choice to prevent cardiovascular diseases (CVD) in type 2 diabetes mellitus (T2DM) patients. This study examined lipid-lowering treatment (LLT) trends among T2DM patients with very high CVD risk.

**Methods:** For this retrospective cohort study, adult (≥18 years) patients diagnosed with T2DM who initiated LLT (statin and/or ezetimibe) from 01/01/2007-06/30/2011 were identified from the IMS LifeLink Pharmetrics Plus commercial claims database. By adapting the 2012 AACE guidelines’ definition of CVD risk categories, T2DM patients were classified in two very high risk cohorts: 1: prior CVD; 2: no prior CVD with two risk factors (age [men ≥45; women ≥55 years] and hypertension [diagnosis or antihypertensive medication]). Patients had continuous health plan enrollment at least 1 year pre- and post-index date (initial LLT prescription date). Primary outcomes were initiation of statin according to intensity across the
study years, first treatment modification (e.g. switch, reinitiation after temporary discontinuation of >60 days, permanent discontinuation from all LLT) and time-to-first treatment modification. Patients in each cohort were stratified by age groups (<65 and ≥65 years).

Results: A total of 9,823 (cohort 1) and 62,049 (cohort 2) patients were included for analysis. Among patients aged <65, 90.0-90.5% were prescribed statin monotherapy, 65.6-77.6% a moderate-intensity statin and 7.2-22.4% a high-intensity statin on the index date. In cohorts 1 and 2, 20.5% and 25.1% reinitiated same LLT (most frequent first treatment modification), 17.5% and 12.8% switched to a new statin, 11.7% and 12.4% permanently discontinued all LLT and 2.6% and 2.4% switched to a non-statin LLT, respectively, as their first treatment modification. The average number of days to any first treatment modification ranged from 190-329 days. Additionally, 44.4-51.8% of patients with one treatment modification had a second treatment modification. A similar trend was observed among patients aged ≥65.

Discussion: Although at very high CVD risk, less than 23% of T2DM patients initiated treatment with a high-intensity statin. The trend did not change from 2007-2011. Almost 75.6-81.4% of patients who initiated statin therapy modified their index treatment, potentially implying intolerability and/or ineffectiveness associated with index therapy.

Conclusion: Among T2DM patients at very high CVD risk, index statin treatment modifications that potentially imply statin intolerability and/or ineffectiveness are frequent; high-intensity statin therapy initiation is low, potentially resulting in an increased risk of CVD.

Abstract #414

A CASE OF CENTRAL VENOUS SINUS THRombosis IN TYPE 2 DIABETES WITH SEVERE HYPERTRIGLYCERIDEMIA

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Objective: While the increased risk of thrombosis in the arterial tree among individuals with diabetes has been well appreciated, little is known about equivalent risk in the venous system outside the settings of hyperosmolarity or ketoacidosis.

Case Presentation: A 40 year old Indian male with type 2 diabetes(T2DM) since 10 years presented initially with diffuse abdominal pain associated with nausea, vomiting & constipation was diagnosed to have acute pancreatitis with bulky pancreas and fatty liver revealed by CT and ultrasonography. Eye fundus examination revealed lipemia retinalis. Baseline test revealed milky white serum with extremely high serum triglyceride(TG) level - 3580 mg/dL and glycated hemoglobin(HbA1c)-8%. Nine months later, he developed left parietal hemorrhagic infarct due to superior sagittal sinus thrombosis as revealed by CT brain angiogram. Further MRI of brain & Magnetic Resonance venogram showed “Subacute hemorrhagic infarct in left parietal lobe with almost complete occlusion of superior sagittal sinus sparing only posterior aspect”. Screening for coagulopathies and auto-immune disorders revealed no other abnormalities. Further history taking revealed that the patient was non-compliant with his medications. Based on above diagnostic tests and medication adherence history of the patient, a final diagnosis of “left parietal hemorrhagic infarct due to superior sagittal sinus thrombosis in a case of T2DM & hypertriglyceridemia” was made.

Discussion: Our case report suggests that major risk factors for CVST are associated with T2DM and extremely high triglyceridemia. Published literature on CVST and diabetes are confined to case reports predominantly among patients with type 1 diabetes and is in the context of diabetic ketoacidosis (DKA), dehydration or hyperosmolarity. In association with T2DM, two cases of CVST are reported: one presenting with DKA while the other patient had transverse sinus aplasia. In our case hypertriglyceridemia is another pre-disposing factor for developing CVST. A meta-analysis of 11 studies measured TG investigating its effect on Venous Thromboembolism (VTE). In most studies, patients with VTE had higher TG levels than that of control population. To our knowledge, this is the first report of CVST in association with uncontrolled T2DM and hypertriglyceridemia but in the absence of concomitant ketoacidosis or any known pro-thrombotic conditions.

Conclusion: Our case highlights the need for clinicians to consider CVST among patients with T2D and hypertriglyceridemia. If such a relationship were to be found, new diagnostic measures might be warranted and this may also have an implication on the risk of recurrence and duration of anti-coagulation in this group of patients.
Abstract #415

VYTORIN INHIBITS AND REVERSES THE PRO-INFLAMMATORY EFFECTS OF CREAM ON PERIPHERAL BLOOD MONONUCLEAR CELLS IN TYPE 2 DIABETIC PATIENTS

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Objective: Our previous work has shown that the ingestion of cream induces an increase in reactive oxygen species (ROS) generation and other cellular and molecular indices of inflammation by peripheral blood mononuclear cells (MNC). Similar increases are observed after the intake of a high fat high carbohydrate meal. Since vytorin (combination of simvastatin and ezetamibe) has a profound effect on lowering plasma concentrations of LDLc, which exerts a pro-inflammatory effect, we hypothesized that vytorin intake in type 2 diabetic patients may exert an anti-inflammatory effect and also inhibit the pro-inflammatory effect of cream.

Methods: Twenty type 2 diabetic patients were randomized to either vytorin or placebo treatment for 6 weeks. Patients in both groups ingested 33g of cream (= 300 Calories) containing a large amount of saturated fat and fasting and post-cream challenge blood samples were obtained at baseline and at 6 weeks.

Results: The two treatment arms had comparable, age, BMI, HbA1c and gender distribution at baseline. Total cholesterol and LDLc concentrations were lowered significantly at 6 weeks following vytorin (P<0.05). Cream induced significant increases in MNC expression of IL-1β(by 105±18%), TNFα(by 97±12%), CD68(by 48±8%), PECAM(by 66±10%), TLR-4(by 84±11%) and TLR-2(by 67±9%) at 0 week. The MNC expression of IL-1β and CD68 expression both fell in the fasting state(by 21±7 and 24±10, P<0.05) compared to baseline at 0 week and following cream(by 74±15% and 68±13%, respectively, compared to increase at 0 week, P<0.05) in the vytorin group. The increase in expression of TNFα and PECAM following cream was also suppressed significantly(by 67±14% and 45±9%, respectively, compared to the increase at 0 week) in the vytorin group. In addition, there was a paradoxical suppression of the expression of Cream induced increases in expression of TLR-2 and TLR-4(by 21±8% and 18±7%, respectively, vs baseline) following cream at 6 weeks in vytorin group. Vytorin treatment also suppressed fasting and cream induced increase in LPS concentrations in plasma (by 24% and 26%, P<0.05, vs baseline at 0 week). Fasting concentrations of CRP, FFA and IL-18 also fell by 32±11%, 19±8% 15±4%, respectively, (p<0.05) following vytorin treatment.

Conclusion: We conclude that vytorin exerts a powerful anti-inflammatory effect, reduces expression of pro-inflammatory mediators following cream challenge and reverses the action of cream from one of induction of TLR-4 and TLR-2 to one of paradoxical suppression of the expression of these receptors. Our data do not indicate whether it is the simvastatin or ezetamibe responsible for these intriguing and potent effects. This issue will need further investigation.

Abstract #416

FAMILIAL HYPERCHOLESTEROLEMIA REGISTRY IN THE MIDDLE EAST AND NORTH AFRICA REGION

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Objective: Familial hypercholesterolemia (FH) is a well understood Mendelian disorder that increases the risk of cardiovascular disease (CVD), a leading cause of mortality in Middle Eastern and North African (MENA) countries. In the MENA region, the prevalence of FH is currently unknown. Thus, we gather available FH cases and instigate an urgent screening strategy.

Methods: FH mutations were collected across MENA countries. Statistics data pertaining to CVD were analyzed. A comparison between statistics of FH mutations reported in MENA countries and countries with established FH registries were done. Finally, a systemic and strategic method for building a MENA FH registry was proposed.

Case Presentation: Only 57 mutations were reported in 17 MENA countries in comparison to over 500 mutations reported in 3 Western countries. Mortality rates due to CVD were significantly higher in MENA countries compared to Western countries.

Discussion: The relatively low reporting of FH mutations in the consanguineous MENA communities with higher prevalence of CVD indicates poor awareness of CVD genetic risk and warrants a registry to prevent premature CVD due to FH.

Conclusion: This registry will help in identifying novel mutations, which will have clinical and research benefits to MENA countries.
Abstract #417

THE EFFECT OF BLACK SEED (NIGELLA SATIVA) EXTRACT ON LIPID METABOLISM IN HEPG2 CELLS

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Objective: Black seed extract has been shown to modulate cholesterol and triglyceride metabolism in animal studies. We recently demonstrated that black seed extract induces apo A-I gene expression in hepatocytes and intestinal cells, presumably by inducing peroxisome proliferator-activated receptor α (PPARα) and retinoid-x-receptor α (RXRα). To extend these observations, we examined the effects of black seed extract on lipid metabolism and expression of lipid-responsive genes.

Methods: PPARα, PPARγ, RXRα, and TRβ expression were measured by Western blot. Expression of PPARα-responsive genes was measured by quantitative real-time polymerase chain reaction. Hepatic lipid content was measured by staining with oil-red-O.

Results: Treatment with black seed extract increased PPARα and RXRα expression as described previously but inhibited PPARγ expression. This was accompanied by increased CPT1 and ACOX1 expression, two PPARα-dependent genes that are key regulators of fatty acid oxidation. This was accompanied by decreased lipid storage inside the hepatocytes.

Conclusion: These findings suggest that black seed extract induces fatty acid oxidation in hepatocytes and up-regulates the expression of enzymes involved in lipid oxidation.

Abstract #418

EFFECT OF TESTOSTERONE (T) REPLACEMENT WITH A T-GEL OR A NEW ORAL T FORMULATION (REXTORO) ON SELECTED BIOMARKERS OF ENDOTHELIAL INJURY AND IMMUNE RESPONSE TO LIPIDS

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Objective: To characterize the effects of T replacement in hypogonadal men with either an investigational oral testosterone replacement therapy (REXTORO) or T-gel (AndroGel®) on cardiovascular biomarkers associated with increased cardiovascular risk due to endothelial injury [e.g., secretory phospholipase A2 (sPLA2) and phosphocholine oxidized phospholipids (PC OxPL)] or immune response factors to modified lipid fractions [e.g., IgG- and IgM-Immune complexes to ApoB (ApoB-IC), and IgG- and IgM-auto-antibodies to malondialdehyde (MDA)].

Methods: Study CLAR-09007 was an open-label, 2-arm, 1-year study in hypogonadal men who were randomized to either REXTORO [oral testosterone undecanoate (TU)] or AndroGel. In a sub-study at three study sites, 57 patients (28 REXTORO and 29 T-gel) had samples drawn at Days 0, 90, 180, and 365 for assay of the CV biomarkers.

Results: Most of the cardiovascular biomarkers evaluated in this sub-study did not change in a statistically significant manner during the 365 days of therapy. However, there were changes in the following biomarkers: PC OxPL exhibited a statistically significant decrease (favorable) in REXTORO treated patients versus an increase (unfavorable) in T gel patients. PC oxPL values in the REXTORO group decreased from a mean (SD) of 4.09 (0.78) at day 0 to 3.37 (0.81) by Day 365, while in the T-gel group, PC OxPL increased from a baseline of 3.49 (0.65) to 5.02 (1.03) by Day 365.

Immunoglobulin G class immune complexes to apolipoprotein-B1 exhibited a statistically significant decrease (favorable) in both treatment groups. Levels of IgG ApoB-IC expressed as Relative Light Units (RLU) showed a decrease from a mean (SD) of 1390 (97) (Rextoro) and 1362 (92) (T-Gel) at Day 0 to 979 (89) and 1062 (99), respectively, at Day 365.

Discussion: A number of epidemiological studies link hypogonadism to adverse cardiovascular (CV) outcomes and increased mortality in men; although, there is uncertainty regarding CV benefits of TRT. Most of the biomarkers of CV risk measured in this sub-study did not show statistically significant changes; however, two that did are PC OxPL and IgG IC to ApoB. Elevated levels are associated with increased risk of CAD events. In this sub-study, these antibody concentrations decreased in both groups, suggesting a potential benefit of T replacement.

Conclusion: This exploratory biomarker analysis suggests that TRT, with either oral TU or transdermal T does not substantially change the CV risk based on the biomarker analysis; however, larger studies are needed to confirm these results.
Abstract #419

ANALYSING ENDOTHELIAL DYSFUNCTION IN TYPE 2 DIABETES MELLITUS PATIENTS USING FLOW MEDIATED DILATATION SCORE.

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Diacare

Objective: To determine early stage CVD risk in type 2 DM patient using FMD (flow mediated dilatation) score – correlating it with acceleration of inflammatory process of vascular injury.

The risk of CVD in type 2 diabetes mellitus is 4% higher than in healthy counterparts. The first stage to CVD is endothelial dysfunction along with vascular injury leading to atherosclerotic changes in the tunica intima of the arteries. Endothelial dysfunction can be analysed to diagnose early atherosclerotic changes and arterial stiffness. Roles of hyperglycemia, diabetic dyslipidemia and inflammation in the acceleration of vascular injury can be detected earlier and treated so as to avoid severe cardiac events.

Methods: A total of 50 (36 F and 14 M) patients with type 2 DM of more than 10 years with age above 50 years were screened for FMD score along with 30 (17 F 13 M) healthy controls, using Angiodefender (Everist Genomics Ann Arbor, MI, USA). Pro-inflammatory cytokines- TNF alpha, IL-6, IL-1 were measured using standard ELISA kits. As surrogates for disease activity C-reactive protein and ESR levels were determined. A Framingham risk score was also assessed in order to evaluate coronary heart disease risk at 10 years in percent.

Case Presentation: The FMD score in 50 type 2 DM patients showed that 70% (n=35) patients suffered from impaired endothelial function and increased arterial thickness; 16% (n=8) patients suffered from endothelial dysfunction, arterial stiffness and atherosclerosis whereas the remaining 14% had normal endothelial function. On the other hand in the healthy counterparts, the FMD score was normal in 80% (n=24) patients. The pro-inflammatory cytokines were either normal or high in the patients with impaired endothelial function. C-reactive proteins and ESR levels also varied from high to normal in patients with endothelial dysfunction. The Framingham risk score also matched with 20% high risk in patients with lower flow mediated dilatation.

Conclusion: The flow mediated dilatation score can be effectively used as a marker to determine the vascular injury and endothelial dysfunction in patients with type 2 DM.

Abstract #420

CLINICAL OBSERVATIONAL STUDY EVALUATING EFFICACY OF SAROGLITAZAR IN TYPE 2 DM PATIENTS HAVING HYPERTRIGLYCERIDEMIA AT TERTIARY CARE CENTRE IN INDIA.

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Diacare

Objective: To evaluate the efficacy of Saroglitazar in type 2 diabetes mellitus patients having hypertriglyceridemia. ‘Diabetic Dyslipidemia’ (combination of raised triglyceride levels (200-499 mg/dl), raised small dense Low-density lipoprotein particles (160-189 mg/dl) and low high-density lipoprotein cholesterol levels (<40 mg/dl men, <50 mg/dl women)) is the most prominent risk factor of atherosclerosis and cardiovascular disease. Saroglitazar is a novel dual Peroxisome Proliferator-Activated Receptors-α/γ agonist and the first glitazar approved in the world for the treatment of diabetic dyslipidemia by Drug Controller General of India in June 2013. It has emerged with a new hope to effectively reducing diabetic dyslipidemia, free of side effects, especially with no increase of body weight.

Methods: In this experience based clinical observation, a total of 200 patients (117 male, 83 Female) having hypertriglyceridemia with type 2 diabetes mellitus (hypertriglyceridemia: TG > 250 mg/dl; glycosylated hemoglobin [HbA1c] >7 to 9%, BMI > 23 kg/m2) were observed in a tertiary care centre, India. The final end point was change in plasma triglyceride level at week 24. The secondary end points were change in BMI, LFT and RFT parameters at week 24. Patients who received saroglitazar 4 mg and had undergone at least 1 post baseline efficacy evaluation were observed in the efficacy analysis.

Results: At Week 24, saroglitazar 4 mg helped achieve the target plasma triglyceride level < 150 mg/dl in overall 93% (n=186) patients, while another 7% (n=14) patients did not achieve target triglyceride level (TG: 150-200) within 24 weeks of observation period with better glycemic control. Saroglitazar did not show any clinically relevant findings in clinical laboratory investigations of LFT and RFT. No adverse events were reported.

Conclusion: Saroglitazar appeared to be an effective therapeutic option for improving hypertriglyceridemia in patients with T2DM.
Abstract #421

SILENT PREGNANCY ASSOCIATED VERY SEVERE HYPERTRIGLYCERIDEMIA AND PROMPT REMISSION POSTPARTUM


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Objective: To describe a rare case of very severe, but totally asymptomatic and clinically silent pregnancy associated hypertriglyceridemia and hypercholesterolemia, with prompt remission postpartum.

Methods: 26 year pregnant woman with 30 weeks of gestation was referred for further management of severe hypercholesterolemia [754 mg/dl] and very severe hypertriglyceridemia [3885 mg/dl] – lipemia noticed by lab technician during OGTT. No family history of lipid disorders, atherosclerotic vascular disease or pancreatitis.

Case Presentation: Normal glucose tolerance, blood glucose 93 mg/dl, HbA1c 4.5% , euthyroid TSH 2.9 mIU/ml [on L thyroxine 25 ug/day]. Hyperbilirubinemia total bilirubin 3.4 mg/dl, with normal liver enzymes. Gestational hypertension of nifedipine. Ultrasound abdomen: hepatosplenomegaly with gravid uterus. During rest of the pregnancy there was progressive increase in S cholesterol from 754 to 1563 mg/dl and S triglyceride from 3885 to 7356 mg/dl. Despite presence of progressive hypertriglyceridemia, surprisingly patient did not manifest any evidence of chylomicronemia syndrome [eruptive xanthomas, pancreatitis, neuropathy etc]. She was treated with low fat diet and omega 3 fatty acids. She had an uneventful pregnancy and delivered a normal healthy female baby. Lipid profile dramatically improved / normalised 36 hours post partum [S cholesterol 103 and S triglyceride 461 mg/dl] ! - [received enoxaparin 40 mg SC 2 doses for postpartum thromboprophylaxis].

Discussion: Pregnancy-related hypertriglyceridemia is rare, but it can be life threatening in some patients with genetic susceptibility [mutations in LPL, APOE, and APOC2 genes]. Complications can include acute pancreatitis, hyperviscosity syndrome, and possibly preeclampsia. Besides, genetic defects, very few cases of autoimmune hyperchylomicronemia have also been described [circulating inhibitors and autoantibodies to lipoprotein lipase and apolipoprotein C II].

Conclusion: Pregnancy associated very severe hypertriglyceridemia and severe hypercholesterolemia can be totally asymptomatic and clinically silent, followed by prompt remission postpartum, and likely recurrence in subsequent pregnancies. Hitherto unidentified genetic and/ or non-genetic “protective” factors are likely responsible for the non-development of acute pancreatitis and other manifestations of chylomicronemia syndrome in selected patients [despite very severe hypertriglyceridemia], like the one illustrated in our case.
METABOLIC BONE DISEASE

Abstract #500

OSTEOPOROSIS PREVENTIVE MEASURES IN PATIENTS RECEIVING GLUCOCORTICOIDS – ARE THEY BEING PRACTICED?

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MSU

Objective: To determine the adherence to American College of Rheumatology (ACR) guidelines 2010 in patients receiving glucocorticoids (GC).

Methods: Data was collected from patients receiving Prednisone >5 mg from March 2003 through March 2014 by a retrospective chart review. Data was compared before and after 2010 to assess the impact of guidelines. Age, sex, steroid dose, vitamin D levels, vitamin D supplementation, bone mineral density (BMD) and administration of antiresorptive therapy was recorded.

Results: There were 62 patients who had received Prednisone >5 mg for more than 3 months, 28 before 2010 and 34 after 2010. Age range for patients was 23-97. There were 27 females and 35 males. 9 out of 28 patients (32.1%) were on calcium supplements before 2010 and 6 out of 34 patients (17.6%) received calcium supplements after 2010. 11 out of 28 patients (39.2%) were receiving vitamin D supplements before 2010 and 6 out of 34 (17.6%) were started on vitamin D after 2010. Baseline Vitamin D levels, before starting prednisone were checked in 1 patient (3.5%) before 2010 and 5 patients (14.7%) after 2010. Only 7 out of 28 patients (25%) had vitamin D levels checked during the treatment before 2010 and 5 out of 34 patients (14.7%) after 2010. 13 out of 28 patients (46.4%) had baseline BMD determined before 2010 and 8 out of 34 patients (23.5%) after 2010. Among those who had a determination of BMD, 76.6% had osteopenia or osteoporosis. 9 out of 28 patients (32.1%) patients had received antiresorptive therapy before 2010 whereas these numbers were 5 out of 34 patients (14.7%) after 2010. Although it may appear that fewer patients had determination of BMD and vitamin D levels, and received supplements of Calcium, vitamin D and antiresorptive therapy after 2010, compared to before 2010, none of these differences were statistically significant.

Discussion: ACR guidelines recommend antiresorptive agents be considered when patients are treated with prednisone of 7.5 mg daily or more for more than 3 months and if patients are at high risk of osteoporotic fracture therapy should be started at any GC dose. We expected the measures to prevent osteoporosis in patients receiving GC to increase, but that was not the case.

Conclusion: The ACR guidelines for prevention of osteoporosis in patients receiving GC are not being followed, at least at our institution. We observed no differences in the practice to prevent osteoporosis in patients receiving glucocorticoids even after the ACR guidelines were issued. More studies are needed to confirm or refute our findings. We are introducing a “GC alert” in EMR system to evaluate if this will improve adherence to the guidelines.

Abstract #501

OSTEOPOROSIS IN AN ADULT WITH BECKER MUSCULAR DYSTROPHY

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Cooper University Hospital

Objective: To present a case demonstrating osteoporosis in an adult with Becker muscular dystrophy in the absence of glucocorticoid therapy.

Case Presentation: A 44-year-old male with history of type 2 diabetes mellitus, hypovitaminosis D and recently diagnosed Becker muscular dystrophy (BMD) presented after a mechanical fall and was found to have a left acetabulum fracture. Prior to this fall, he suffered from lower extremity weakness but was able to perform activities of daily living and ambulated with a cane. He had no history of taking corticosteroids. Presurgical lab abnormalities revealed total testosterone 101 ng/dL (250-1100 ng/dL), total vitamin D 25-OH 15 ng/mL (30-100 ng/mL), PTH 27 pg/mL (15-65 pg/mL) and hemoglobin A1c 8.1%. A DEXA seventeen months prior showed osteopenia with Z-score of -2.1 at the left total hip. He underwent open reduction and internal fixation of the left acetabulum. Medications at the time of discharge included insulin and vitamin D with dosages unchanged from his home regimen. Two months later, a follow-up DEXA revealed osteoporosis of the right total hip with Z-score of -2.5. Total testosterone had normalized to 439 pg/mL, total vitamin D 25-OH was 33 ng/mL and hemoglobin A1c was 6.1%. For treatment of osteoporosis, he was started on ibandronate 150 mg daily. Three months later, he was weight bearing and back to his functional status prior to his fall.

Discussion: Osteoporosis is a common manifestation of Duchenne muscular dystrophy (DMD) with up to one third of patients affected by pathologic vertebral and long-bone fractures. Unfortunately, such data is lacking for BMD. The only therapy which has been shown to be effective in the treatment of DMD are glucocorticoids which with long-term use can lead to reduced bone mineral density. This case demonstrates that osteoporosis can precede glucocorticoid therapy in BMD, however, the mechanisms involved in bone demineralization are not well understood.
It is thought that interleukin 6, an inflammatory cytokine found to be elevated in DMD, may contribute to reduced osteoblast activity and increased osteoclast activity. Other contributing factors may include reduced free and total serum testosterone levels which can lead to decreased proliferation and differentiation of osteoblasts with reduced inhibition of osteoclast activity. In addition, immobilization and malnutrition can further worsen an existing predisposition to reduced bone mineral density.

**Conclusion:** Osteoporosis is a known complication of dystrophinopathies, however, the onset of bone demineralization in the absence of glucocorticoid therapy is still unclear. Guidelines regarding screening for osteoporosis in patients with dystrophinopathies should be established.

**Abstract #502**

**RATE OF OSTEOPOROSIS SCREENING IN MEN VS WOMEN IN AN ACADEMIC OUTPATIENT INTERNAL MEDICINE CLINIC**

Amer Issa, MD, Mohamad Sirri Tarazi, MD, Leela Mary Mathew, MD

Unity Health System

**Objective:** Osteoporosis affects 10 million Americans and causes 1.5 million fractures with a direct cost of 20 billion dollars a year. It is a silent disease until complicated by a fracture. One in two women and one in five men will suffer an osteoporotic fracture in their lifetime. The National osteoporosis foundation (NOF) clinical guidelines recommend bone density screening (DEXA scan) in women at age 65 and men at age 70 in average risk individuals. The objective of this study is to assess the adherence to these recommendations in an academic longitudinal outpatient Internal Medicine clinic at Unity Health System in Rochester, NY.

**Methods:** All males aged 70-85 and females 65-85 years of age were included. The clinic is a Resident run, Faculty supervised setting. All available medical records were reviewed for documentation of DEXA screening; through radiology reports, progress and consultation notes and previous medical records. All secondary risk factors for osteoporosis other than age were identified, ie fractures, chronic steroids use and hypogonadism.

**Results:** The study included 454 patients, 290 females (64%) and 164 males (36%). Documentation for osteoporosis screening was found in 136 females (47 %) as compared to 11 males (6.5 %). All 11 (100%) of screened men had identified secondary risk factors other than age. In contradistinction, only 15 women (10.5 %) screened had secondary risk factors other than age. Age remained the primary mainstay of screening in women (90%).

**Discussion:** There is limited data regarding average screening rate in men. In 2008, the American College of Physicians (ACP) identified osteoporosis as an underreported disease in men and called for improvement in the rates of diagnosis. Osteoporosis is universally viewed as a women’s disease and data shows that while women perceive osteoporosis as a serious disease, men perceive it as a women’s disease. Our study shows a dismal rate of screening in men and done only when other risk factors were identified. Despite coverage under Medicare, bone density tests are grossly underutilized. In 2005, an estimated 30 % of women and 4 % of men on Medicare received the DEXA scan. A 2006 cross sectional study in a family practice setting showed that 50 % of women aged >65 had received a DEXA scan.

**Conclusion:** There continues to be a major gap in the quality of care in bone health provided, especially among men. Public education and awareness remains key in closing this gap. On the medical side, performance improvement measures, EMR screening reminders and patient education at point of care needs to be reinforced and included as part of a Quality measure.

**Abstract #503**

**INSUFFICIENCY FRACTURES: IT’S NOT WHAT YOU THINK!**

Swapnil Khare, MD, Jonathan Anolik, MD

Temple University Hospital

**Objective:** Fanconi syndrome (FS) is rarely seen with aminoglycosides. When present it resolves on discontinuation of drug. We report an unusual case of aminoglycoside associated FS with bone manifestations which persisted months after discontinuation of drug.

**Case Presentation:** 53 year old male was referred for Endocrine evaluation for persistently high bone specific alkaline phosphatase (ALP). His history was significant for recent staphylococcal endocarditis requiring AVR, prolonged antibiotics including gentamicin and brief dialysis. Later he developed lower extremity weakness and rigidity. High bone specific ALP was high and continued to rise. It was associated with significant hypophosphatemia. His renal failure resolved. Extensive work up in next few months revealed normal calcium, potassium, chloride, uric acid, magnesium, AST, ALT and albumin on repeated measurements. TSH, 25 and 1,25 hydroxy Vitamin D, PTH and testosterone were also...
normal. Parathyroid uptake scan and malignancy work up were negative. DEXA revealed osteoporosis. Bone scan and MRI showed AVN or insufficiency fractures requiring arthroplasty. Osteogenic osteomalacia and aluminum poisoning were ruled out with normal FGF 23 and aluminum levels. Evaluation for FS revealed high urinary phosphate despite low serum phosphate. However, other features of classic FS including aminoaciduria and glycosuria were absent. He was thereby diagnosed with selective FS. Aminoglycoside was suspected secondary to temporal association. He was placed on oral phosphate and Vitamin D supplements with gradual improvement in symptoms and biochemical markers.

**Discussion:** Hypophosphatemia is uncommon in hospitalized patients. It is usually mild and asymptomatic. When symptomatic it presents as muscle weakness and osteomalacia as in our case. Usual causes are hyperparathyroidism, malignancy, Vitamin D and magnesium deficiency. FS is a rare cause of hypophosphatemia. It can be secondary to inherited errors of carbohydrate metabolism or acquired secondary to medications. FS secondary to aminoglycoside exposure is extremely rare. When present it usually resolves in 4-6 days after cessation of offending drug. To our knowledge ours is the only patient with persistent hypophosphatemia months after cessation of aminoglycoside exposure. Once recognized treatment is cessation of offending drug and phosphate repletion.

**Conclusion:** FS should be suspected in patients with hypophosphatemia and aminoglycoside exposure when usual suspects have been ruled out. Awareness of this disorder is important as these antibiotics are used in critically ill patients and recognition will help in their management and outcomes.

**Abstract #504**

**HYPERCALCEMIA IN NECROBITIC XANTHO-GRANULOMA: FIRST REPORTED CASE AND INSIGHT ON TREATMENT**

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Lankenau Medical Center

**Objective:** Necrobiotic Xanthogranuloma (NXG) is a rare systemic and progressive granulomatous disease first described in 1980. Given no established first-line therapy, treatment focuses on control of skin lesions and associated complications. Hypercalcemia has not been reported to complicate this chronic condition.

**Case Presentation:** An 83 y.o. woman with a history of breast cancer treated with a lumpectomy 16 years ago, hypertension, type 2 diabetes, IgG lambda paraproteinemia and NXG presents with a three-week history of progressive weakness and fatigue. On examination the patient appears frail and chronically ill; she has a normal gait and no muscle weakness but is unable to ambulate without assistance. She has crusting and ulcerating lesions on the face and all extremities in sun exposed distribution. One of the facial lesions extends to the full-thickness of the skin and penetrates the oral cavity. Laboratory workup reveals: serum calcium of 15.5 mg/dL, albumin of 2.6 g/dL, ionized calcium of 1.88 mmol/L, phosphorus of 2.4 mg/dL, PTH of 6.6 pg/mL, PTH-rp of 29 pg/mL, 25(OH) vitamin D of 27 ng/mL and 1,25(OH) vitamin D of 96 pg/mL. SPEP shows a stable IgG lambda monoclonal spike. A skeletal survey does not show lytic or blastic lesions. After aggressive hydration with normal saline, intravenous calcitonin is started at 90 mcg twice a day and continued for 48 hours. On day 7 she is discharged home with a calcium of 9.7 mg/dL. On one-month office follow up calcium has increased to 13.0 mg/dL; she is thus started on prednisone at 30 mg daily. Serum calcium normalizes within 4 weeks of therapy and remains within normal limits after slow titration of prednisone down to 7.5 mg daily over the following 8 months. Her skin lesions have also improved with no new eruptions noted despite decrease in steroid dose.

**Conclusion:** NXG has been described as a separate subtype of Non-Langerhans Cell Histiocytosis based on the clinical presentation and course. It is commonly associated with paraproteinemia (80-90%) and can rarely progress to lymphoproliferative diseases such as myeloma or lymphoma. Despite it being a granulomatous disease, NXG has not been associated with hypercalcemia. About 130 cases of NXG have been reported but to our knowledge this is the first case to be complicated by hypercalcemia. Our case confirms a granulomatous disease mediated production of 1α-hydroxylase leading to increased synthesis of 1,25(OH) vitamin D and subsequent hypercalcemia. Based on this pathophysiology, we elected to start systemic corticosteroids, titrated to clinical and metabolic response. Steroid-sparing agents need to be considered to avoid long-term complications but continue controlling this granulomatous disease.
Abstract #505

PREVALENCE OF OSTEOPOROSIS AND VERTEBRAL FRACTURES IN WOMEN WITH IMPAIRED GLUCOSE METABOLISM: A POPULATION BASED STUDY OF LATIN AMERICAN VERTEBRAL OSTEOPOROSIS STUDY (LA VOS)-PUERTO RICO SITE

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1. Endowed Health Services Research Center, School of Medicine, University of Puerto Rico, Medical Sciences Campus, 2. University of Puerto Rico, Medical Sciences Campus, Department of Internal Medicine, Endocrinology, Diabetes and Metabolism Division,

Objective: According with CDC 2010 data, Hispanics adults living in USA and PR showed twice the prevalence rate of Diabetes Mellitus II (DM2) than Caucasian Americans. Several studies have found an association between DM2 and high bone minerals densities (BMD) with a high risk of fracture. This is the first study that compares the prevalence of osteoporosis and vertebral fractures (VF) among women living in Puerto Rico with different glycemic status.

Methods: Clinical parameters, including BMD of the spine and hip by DXA and lateral dorsolumbar x-rays results were extracted from LA VOS database. Women were classified as diabetics, pre-diabetics and normal women, according to glycemic status and medical history. WHO criteria were used to classify women as: osteoporotic, osteopenic and normal. Overall and age-specific prevalence were estimated using the direct method of standardization weighting for the population size according to the 2000 Census. Comparison of BMD mean between glycemic groups were based on ANOVA. For all test a p value <0.05 was considered statistically significant.

Results: A total of four hundred women aged 50 y/o and over were evaluated: 115 (38.9%) diabetics’ women, 135 (33.8%) pre-diabetics and 149 (37.3%) normal. The overall prevalence of VF among diabetics was 2.9%, pre-diabetics 3.3% and normal 4.2%. Age-specific weighted prevalence of VF among women living in Puerto Rico with different glycemic status were as follows: 4.5% (50-59 y/o group), 2% (60-69 y/o), 8.2% (70-79 y/o), and 4.7% among the ≥80 y/o group. A high weighted prevalence of VF was found in 60-69 y/o normal groups (11.7%). The overall weighted prevalence of osteoporosis in spine for diabetics, pre-diabetics and normal participants were 5.1%, 9.1% and 10.2%, respectively. Diabetics women showed the highest mean of BMD in spine (0.925 ± 0.17), followed by pre-diabetics (0.892 ± 0.17), and normal (0.870 ± 0.16) (p-value=0.20). A marginally significance difference between glycemic groups and BMD of total hip was observed. Diabetic women showed highest mean of total hip (0.82 ± 0.14) and normal group showed the lowest mean of BMD total hip (0.79 ±0.14) (p-value=0.07). Compared with diabetics and pre-diabetics, normal groups showed the overall highest weighted prevalence of osteoporosis in femoral neck (5.4%) and total hip (4.8%). Furthermore, the highest age-specific weighted prevalence of osteoporosis was in pre-diabetics women aged 70-79 (9.4%).

Conclusion: Although not statistically significant, we found that Puerto Rican women with diabetes had high BMD, consistent with previous studies. We also found low prevalence of VF among 60-69 y/o diabetics’ women, revealing DM2 as a protective factor for VF in this age group.

Abstract #506

HYPOPARATHYROIDISM IN BETA THALASSEMIA MAJOR

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University of South Florida

Objective: To report a case of hypoparathyroidism as a cause of hypocalcemia in the setting of transfusion dependent beta thalassemia major.

Methods: Clinical exam, laboratory and hormonal studies, literature review.

Case Presentation: 26 year old male who was admitted to the hospital with complaints of diffuse joint pains with associated numbness and tingling of his feet. He reported a history of beta thalassemia major for which he has required blood transfusions since age 3 and now these are required every 3-5 weeks. Physical examination on admission was remarkable for tachycardia of 110 bpm, tenderness to palpation of knees and elbows, as well as paresthesias of upper and lower extremities, but negative Chvostek’s sign. Laboratory results were remarkable for calcium of 6.4 mg/dL, sodium 129 mEq/L, chloride 95 mEq/L, albumin 3.5 g/dL, ionized calcium 0.90 mmol/L. Electrocardiogram had no QT segment prolongation. He was admitted to the general medical ward for further care. Sodium and chloride abnormalities corrected after hydration with normal saline. He was given IV calcium gluconate with symptomatic improvement but intermittent correction of his serum calcium. Endocrinology service was consulted with further work up revealing a parathyroid hormone level of 11.7 ng/mL, calcium 6.0 mg/dL, ionized calcium 0.89 mmol/L, phosphorus 6.5 mg/dL, magnesium 1.4 mg/dL, 25-hydroxy vitamin D 23.4 ng/mL, and 1,25-hydroxy vitamin D 58 pg/mL. Previous
iron studies showed a ferritin of 9999.3 ng/mL, serum iron of 277 mcg/dL, total iron binding capacity of 265.7 mcg/dL, and serum transferrin saturation of 104%. A diagnosis of hypoparathyroidism secondary to potential infiltration of the parathyroid glands from iron overload was made. He was started on scheduled replacement therapy with oral calcium citrate as well as magnesium oxide.

Discussion: Patients with beta thalassemia major undergo frequent blood transfusions as part of their treatment regimen which results in iron deposition of multiple organs leading to potential endocrinopathies. Serum ferritin level has been studied as a predictive marker for progression of endocrine dysfunction in this patient population. Although a rare complication, hypoparathyroidism with resultant hypocalcemia can occur from iron infiltration into the glands. This is an under recognized association in these patients with some studies suggesting a prevalence of 4-10%.

Conclusion: Parathyroid hormone profile should be checked regularly in all patients with transfusion dependent beta thalassemia major as this will allow for earlier detection and management of hypoparathyroidism.

Abstract #507

UNUSUAL PRESENTATION OF PARATHYROID CARCINOMA IN A YOUNG PATIENT

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Case Presentation: Parathyroid carcinoma is one of the rarest known malignancies. It is estimated that a palpable neck mass is present in 40-70% of the cases and typically between 45-59 years of age. Imaging studies like TC-99 MIBI Scintigraphy are used to help localize disease. We report the case of a young patient with parathyroid carcinoma who had a negative TC-99 MIBI Scintigraphy and whose tumor presented in an unusual location for parathyroid tissue.

A 30-year-old Caucasian man with a history of beta thalassemia major was suffering from recurrent metatarsal stress fractures, with bilateral, spontaneous, nontraumatic, nonhealing metatarsal stress fractures over 6 months and subnormal serum ALP activity at 26 to 32 IU/L since the onset of his stress fractures. Serum bone-specific ALP (TNSALP). Adult HPP presents histomorphometrically as osteomalacia but a subset of these patients may have decreased bone remodeling when the disorder first manifests clinically. We describe the dynamic bone histomorphometry findings of a man with features of HPP and one defective TNSALP allele who was suffering from recurrent metatarsal stress fractures, an early complication of adult HPP.

Methods: A 30-year-old Caucasian man with a history of juvenile osteochondritis dessicans of the knee presented with bilateral, spontaneous, nontraumatic, nonhealing metatarsal stress fractures over 6 months and subnormal serum ALP activity at 26 to 32 IU/L (ref,32-91) since the onset of his stress fractures. Serum bone-specific ALP of 4.9 mcg/L (ref,6.5-20.1) was also low, with low urine N-terminal telopeptide of 17 nM BCE/mM creatinine (ref,21-83). Serum C-terminal telopeptide improved. He underwent ultrasound of the neck which showed complex left neck mass extrinsic to thyroid gland measuring 4.2 cm at its largest dimension. CT neck and chest revealed heterogeneous solid and cystic structure within the left anterior neck lateral to the upper aspect of the thyroid cartilage, anterior to the carotid space and sternoclavistemastoidast. There were also at least two rib masses that later were confirmed by FNA as brown tumors. Patient also underwent Sestamibi scan. Surprisingly no abnormal increased uptake was found in the patient’s known left neck mass; however, there was increased chest wall uptake consistent with known rib lesions. Patient will later undergo left superior parathyroidectomy. Surgical pathology confirmed diagnosis of parathyroid carcinoma. After surgery PTH level came down to 21.74 pg/mL.

Conclusion: The present case adds to the limited previous reports of parathyroid carcinoma in ectopic locations. It also highlight the fact that false negative Sestamibi scans can occur even in large tumors with high levels of PTH and the importance of increased clinical suspicion for parathyroid carcinoma despite a negative scan.

Abstract #508

ADULT HYPOPHOSPHATASIA PRESENTING WITH A LOW BONE REMODELING RATE

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Objective: Hypophosphatasia (HPP) is characterized by impaired bone and/or tooth mineralization in the setting of low alkaline phosphatase (ALP) activity. The etiology is loss-of-function mutations within the gene encoding the tissue-nonspecific ALP (TNSALP). Adult HPP presents histomorphometrically as osteomalacia but a subset of these patients may have decreased bone remodeling when the disorder first manifests clinically. We describe the dynamic bone histomorphometry findings of a man with features of HPP and one defective TNSALP allele who was suffering from recurrent metatarsal stress fractures, an early complication of adult HPP.

Methods: A 30-year-old Caucasian man with a history of juvenile osteochondritis dessicans of the knee presented with bilateral, spontaneous, nontraumatic, nonhealing metatarsal stress fractures over 6 months and subnormal serum ALP activity at 26 to 32 IU/L (ref,32-91) since the onset of his stress fractures. Serum bone-specific ALP of 4.9 mcg/L (ref,6.5-20.1) was also low, with low urine N-terminal telopeptide of 17 nM BCE/mM creatinine (ref,21-83). Serum C-terminal telopeptide
was normal. 25-hydroxyvitamin D was 22.8 ng/ml (ref, 30-74). Intact parathyroid hormone was low at 12 pg/ml (ref, 14-72) despite having normal serum calcium of 9.6 mg/dl (ref, 8.3-10.5). Serum pyridoxal 5'-phosphate was markedly elevated at 108.2 ng/dl (ref, 4-12) after vitamin B6 supplementation was discontinued for 2 months. We found a single heterozygous TNSALP missense mutation (c.406C>T, p.R136C) in exon 5 identified in a different patient with odontohypophosphatasia.

Case Presentation: Transiliac bone biopsy after tetracycline labeling showed no osteomalacia but quiescent bone remodeling with very low osteoid volume of 0.08% (ref, 0.8-2.6), low osteoid thickness of 3.2% (ref, 6.1-8.8), and low osteoid surface of 1.95% (ref, 6.7-17.6). The trabecular bone volume was normal and the 2-dimensional measures of microanatomy showed a slight increase in the trabecular number of 2.1% (ref, 1.5-1.8) with a reduction in trabecular separation of 459% (ref, 529-678), which were internally consistent. There were no tetracycline labels present in the trabeculae but a small number were found in the cortical bone indicating compliance with the labeling protocol. The findings indicated very low bone remodeling rate.

Conclusion: Histomorphometric characteristics of adult HPP have been described in the literature. Our findings indicate that patients manifesting early symptoms may present early on with decreased bone remodeling. There is no approved medical treatment available for HPP. Knowing more about its histomorphometric presentation may aid in evaluating and choosing treatment for this inborn error of metabolism.

Abstract #509

DEMOGRAPHIC AND CLINICAL PROFILE OF PATIENTS WITH PRIMARY HYPERPARATHYROIDISM IN THE LAST 20 YEARS: A SINGLE CENTRE STUDY

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Santa Croce and Carle

Objective: Over the last 50 years the clinical profile of primary hyperparathyroidism (PHPT) has shifted from a symptomatic disorder, characterized by symptoms of hypercalcemia, nephrolithiasis, and overt bone disease, towards a less symptomatic or asymptomatic disorder. Further variations in the clinical profile of PHPT over the last decades, and their therapeutic implications, are poorly known. Therefore, we retrospectively evaluated the demographic and clinical characteristics of a large series of PHPT patients diagnosed over the past 20 years.

Methods: From 1994 to 2013, 348 consecutive patients were evaluated. Patients were grouped into four five-year periods. We recorded mean age, percentage of women and percentage of asymptomatic patients. In asymptomatic patients, we evaluated the presence of surgical criteria recommended by the 2013 guidelines, and changes in the frequency of the criteria for surgery over the five-years periods.

Results: We found a stable gender involvement, with an F:M ratio of about 3:1. The mean age at diagnosis varied between 6th and 7th decade. The percentage of asymptomatic patients remained unchanged over the last three five-year periods (43% - 45%). In asymptomatic patients, from the first to the last five-year period, the percentage of cases meeting surgical criteria significantly increased (from 56.9% to 87.8%; p <0.05).

We found differences in the percentage of asymptomatic patients meeting surgical criteria for bone mineral density (T score <-2.5 at any site and/or previous fractures; p<0,001), serum calcium (> 1 mg/dl above the upper normal limit; p<0,001) and creatinine clearance (<60 ml / min; p<0,001). In particular, the percentage of asymptomatic patients with osteoporosis showed a significant gradual upward trend from the first to the last five year period.

Discussion: With the exception of the first five-year period, we observed a slight predominance of symptomatic forms of the disease, which remained stable over the last 15 years. We hypothesize that routine renal and bone imaging contributed to identify as symptomatic some apparently asymptomatic patients.

Conclusion: In conclusion, our data show a substantial stability in the clinical and demographic profile of PHPT. Nevertheless, among asymptomatic patients, we observed a rise in the frequency of osteoporosis and an increase in patients meeting surgical criteria.

Abstract #510

VITAMIN D LEVELS AMONG VETERANS FROM THE NORTH EAST USA WITH DIABETES AND/OR KIDNEY DISEASE

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Objective: Vitamin D is known for its role in calcium homeostasis for optimal skeletal health. The best marker of vitamin D status is the serum 25-hydroxyvitamin D concentration. The aim of this study was to evaluate the prevalence of vitamin D deficiency and its relation to diabetes and kidney disease in Veterans residing in the Northeast USA (VISN 2).
Methods: In this retrospective study, we used data from the computerized patient record system at Stratton Veterans Health Administration (VHA) for those patients who had 25-hydroxyvitamin D levels and 1,25 (OH) vitamin D levels measured between 2006 and 2009. We collected demographic information including age, sex, body mass index, and race; clinical data, including diabetes, hypertension, and CAD; and laboratory data, including calcium, creatinine, and PTH (intact). Vitamin D deficiency is defined as a serum 25-hydroxyvitamin D level of less than 20 ng per mL (50 nmol per L), and insufficiency is defined as a serum 25-hydroxyvitamin D level of 20 to 30 ng per mL (50 to 75 nmol per L).

Results: Data was available for approximately 68,000 subjects. We identified 64,144 subjects for analysis after exclusion of duplicates. Among them, 27,098 had diabetes. The mean age of subjects with diabetes was 68 ± 11 and BMI of 32 ± 7 with duration of diabetes of 5.6 ± 3.2 years. Vitamin D levels (25(OH) vitamin D) among subjects with diabetes was 27 ± 11.6. We divided the subjects with diabetes into two groups: those with e-GFR < 50, and those with e-GFR > 50. There was no significant difference in 25 (OH) vitamin D levels between the two groups, but 1,25 (OH) vitamin D levels were significantly lower (22) and PTH-intact was significantly elevated (163) in subjects with e-GFR < 50 compared to those with e-GFR > 50 (1,25 Vitamin D of 34 and PTH-intact of 69) [p= 1.14E-26 & 9.2 E-226 respectively]. (1,25 Vitamin D of 34 and PTH-intact of 69) [p= 1.14E-26 & 9.2 E-226 respectively]. Of the 64,144 subjects, 580 had end-stage renal disease. Of those, 407 had diabetes and 173 did not. Vitamin D levels in both groups were in the insufficiency range and there was no significant difference irrespective of presence or absence of diabetes. Subjects with Vitamin D levels less than 20ng per mL had a higher BMI and mildly elevated PTH, and their Hba1C levels were significantly higher. Conclusion: We conclude that we need to keep a close eye on Vitamin D levels in subjects with mild CKD as well as those with moderate control of diabetes.

Abstract #511

LEAST SIGNIFICANT CHANGE, MOST SIGNIFICANT CLINICAL VALUE

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Case Presentation: A 67 yo white female was seen for second opinion of osteoporosis and treatment options. In 2001, she was diagnosed with osteoporosis and began alendronate. Over 13 years, she had further bone mineral density (BMD) loss with varying stability as measured by DXA, and took various bisphosphonates, including risedronate, ibandronate, and again alendronate, which were rotated due to side effects. Historically, she also took estrogen replacement, calcium and vitamin D. She was treated with anastrozole for infiltrating ductal carcinoma, which was discontinued 2.5 years later due to side effects. After two MI's, calcium was stopped.

Upon evaluation in our clinic, her risk factors for osteoporosis included height loss, post-menopausal, weight below 127 lbs, prior high risk drug use, and calcium poor diet.

Results were obtained from 7 prior DXA’s done at the same facility over the past 8 years, and substantial differences were seen in patient positioning. Also, no facility least significant change (LSC) was reported, making it impossible to conclude if a clinically relevant change in BMD had occurred. A lack of reliable measurements, and DXA data that could not be meaningfully compared, lead to the question of possible treatment failure, or did inaccurate DXA analysis lead to incorrect clinical decisions.

These discrepancies lead to the referral and incited an extensive work-up to establish fracture risk, determine clinically significant bone loss, and apply appropriate clinical interventions.

Discussion: DXA has become the gold standard to assess BMD. Interpretation of serial DXA scans depends on multiple factors, such as patient positioning, machine used, and measurement site. It has been reported that the most influence on DXA measurement precision is due to technician related factors. A typical calculated LSC is around 4%, and as much as a 10-15% difference in BMD has been noted due to positioning error. It is thus vital that each testing facility provide precision assessment to determine their own LSC. This can then direct clinicians to properly respond to changes in therapy if needed.

While likely that our patient had post-menopausal osteoporosis, we were not driven by DXA data, and were prompted to obtain work-up for secondary causes, as well as labs for increased bone turn-over, with noted serum NTX of 22.1 (normal range 6.2 - 19.0 nM BCE). It was decided that denosumab would be drug of choice due to side effect profile.

Conclusion: Clinicians must recognize the importance of the LSC, and demand this data from their interpreting clinician. Failure to understand this analysis can often cause misconception of the presence of disease, and inappropriate clinical interventions.
Abstract #512

PARATHYROID CARCINOMA: A DIAGNOSTIC AND THERAPEUTIC CHALLENGE

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Objective: To report a rare case of parathyroid carcinoma (PC) presenting as a thyroid nodule with a benign features of primary hyperparathyroidism

Case Presentation: A 59 year-old man who initially presented with constipation and forgetfulness, was found to have primary hyperparathyroidism with hypercalcemia of 11.2 mg/dL, PTH of 415 pg/mL; and Vit-D deficiency with 25-OH Vit-D of 7 ng/mL. In the outside healthcare facility, patient had underwent parathyroid scintigraphy which revealed right thyroid lobe enlargement concerning for thyroid nodule and no definitive evidence of parathyroid adenoma. He also had thyroid ultrasound that showed 3.5 x 2.4 x 2.8 cm solid right thyroid lower lobe nodule, and heterogeneous gland. He underwent right lower thyroid nodule FNA that was initially interpreted as chronic lymphocytic thyroiditis, but re-evaluation of FNA slides at our institute rendered a diagnosis of parathyroid neoplasm. It was thought that patient has large right inferior parathyroid adenoma after re-evaluation of ultrasound images and parathyroid scintigraphy images as well. Patient underwent right inferior parathyroidectomy since he was also found to have osteoporosis in DXA scan. Histopathological evaluation of the surgical specimen revealed a hypercellular parathyroid neoplasm with multiple foci of vascular invasion, concerning PC. Post-operatively, PTH dropped to 8 pg/mL and calcium down to 9.8 mg/dL. However PTH level started trending up to 160-200 pg/mL at 2-week post-operation along with relatively low normal calcium level. Patient was treated with calcitriol 1mcg daily and ergocalciferol 50,000 IU twice a week, eventually his PTH level has decreased to 69 pg/mL and 25-OH Vit-D level has increased to 33 ng/mL. If PTH levels returned to normal with adequacy of Vit-D persistently, this may indicate that cure of cancer; patient may not need to get en block right thyroid lobectomy with central neck lymph node dissection.

Discussion: First PC case was described by F. D. Quervain in 1904. Since then, the pathogenesis, diagnosis and treatment of PC is still not well defined. Due to its rarity, difficulty in diagnosis, and limited cases described in literature, the knowledge about treatment and post-operative management is limited. In our case, both initial diagnostic studies have missed the detection of parathyroid carcinoma prior to surgery.

Conclusion: PC is a rare disease, and it can be extremely difficult to diagnose it preoperatively, due to clinical features shared with benign causes of hyperparathyroidism and that there is no diagnostic method to help define the malignancy potential of the mass. FNA of parathyroid tumors may also be difficult to distinguish from thyroid tissue.

Abstract #514

PAMIDRONATE FOR BONE HYPERRESORPTION IN CHRONIC CRITICAL ILLNESS IS ASSOCIATED WITH IMPROVED OUTCOMES AND RENAL PARAMETERS

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Objective: Chronic Critical Illness (CCI) designates a subset of patients requiring prolonged mechanical ventilation and tracheostomy, with associated multi-organ dysfunction. Bone hyperresorption has previously been identified as a frequent component of the CCI syndrome, and has been shown to abate after treatment with IV bisphosphonates. Our study assessed the impact of pamidronate use on outcomes in a CCI population.

Methods: A retrospective case series of 148 patients admitted to The Mount Sinai Hospital Respiratory Care Unit (RCU) from 2009-2010, identified patients with CCI who did (n=31) or did not (n=117) receive IV pamidronate (30-90 mg). Both groups included patients with normal renal function and all levels of CKD. Criteria for administration included either 1) 24 hour urine NTx ≥70 nmol BCE/mmol Cr (n=7), 2) serum NTx ≥ 40 nMBCE/L (n=3), 3) 24 hour urine collagen cross linked ≥ 103 nmol BCE/mmol Cr (n=7), 2) serum NTx ≥ 40 nMBCE/L (n=3), 4) 24 hour urine calcium ≥ 250 mg (n=11) or 5) ionized calcium > 1.29 mmol/L (n=2). All RCU patients received calcium carbonate, ergocalciferol and calcitriol (in the absence of hypercalcemia).

Results: RCU and 1-year mortality were significantly lower in the pamidronate group (0% and 23%) compared to non-receivers (19% and 55%), respectively (p=0.0079 and p=0.0015). A Cox proportional hazards model revealed an increased likelihood of ventilator liberation after pamidronate with a hazard ratio of 1.87 (95% CI: 0.84-4.15, p=0.1254). Within the subgroup of pamidronate users, creatinine was significantly lower 7 days following pamidronate administration (p=0.0025), and with no significant difference at 14 days compared to baseline. The
change in mean GFR from RCU admission to discharge increased for pamidronate users (65.37 to 69.75) and decreased for non-users (62.35 to 61.38), without reaching significance (p=0.3382). There was greater improvement in mean albumin levels from RCU admission to discharge for pamidronate users (2.50 to 3.23 g/dL) compared to non-users (2.49 to 2.72 g/dL), adjusting for length of stay and admission albumin levels; p<0.0001.

Discussion: Our retrospective study is the first to demonstrate an association of pamidronate use with improved outcomes including mortality and ventilator liberation in a CCI population. The most common hesitation for use of IV bisphosphonates in the hospital setting is concern over renal function deterioration and our study showed not only stability but mild improvements in renal parameters. Improved albumin levels in pamidronate users may reflect an overall decrease in inflammatory mediators.

Conclusion: Pamidronate use was associated with improved outcomes and renal parameters in a CCI cohort.

Abstract #515

FAMILIAL HYPOCALCIURIC HYPERCALCEMIA IN THE ELDERLY TREATED WITH CINACALCET

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Objective: To present a case of suspected familial hypocalciuric hypercalcemia (FHH) in the elderly that improved with Cinacalcet

Case Presentation: An 86 year old man with a history of chronic atrophic left kidney, furosemide therapy for chronic lower extremity edema, and no known personal or family history of hypercalcemia, was first noted to have a mildly elevated calcium level of 10.5 mg/dL in 2004. Repeat labs demonstrated a calcium level of 10.2 mg/dL and an iPTH of 176 pg/ml. From 2004 to 2012, calcium levels remained stable in the upper limit of normal. By early 2013, the calcium level had increased to 11.8 mg/dL, and he was referred for an endocrine assessment. Lab results were: Ca 12 mg/dL, iPTH 369, 24 hour urine calcium 60mg/24hr, 25-OH Vitamin D 46 ng/mL, and a creatinine of 2.05 mg/dL. The calculated Ca/Cr clearance ratio was 0.0077. Thyroid ultrasound showed multiple thyroid nodules and a Sestamibi scan localized activity to the right lower thyroid region. Repeat lab results were: Ca 11.6 mg/dL and 24 hour urine calcium 74mg/24hr. Calculated Ca/Cr clearance ratio was 0.01.

Patient had surgery in September 2013 for removal of an intrathyroidal right superior mediastinal parathyroid and right thyroid lobectomy. Intra-operative PTH decreased by more than 50%. Histology of the specimens revealed a hypercellular parathyroid with fibrous bands. However, subsequent post-operative laboratory studies revealed consistently elevated iPTH (max 453 pg/ml) and calcium levels (max 11.5 mg/dl). He started Cinacalcet 60mg and has had good response to therapy with calcium levels decreasing to 9.3-10.5 mg/dl.

Discussion: FHH is an autosomal dominant mutation in calcium sensing receptors that decrease sensitivity of the receptor to the levels of calcium in the body. It is a benign condition and parathyroidectomy is not indicated. FHH is characterized by a low 24 hour urine calcium excretion and a Ca/Cr clearance ratio < 0.01 in the absence of Vitamin D deficiency. In our case, the elevated calcium and PTH levels had its first manifestation at an elderly age. A diagnosis of FHH is suggested by low urinary calcium concentration, decreased Ca/Cr clearance ratio (<0.01) in a vitamin D replete patient, hypercellular parathyroid, and consistently elevated iPTH and calcium levels even after surgery. However, genetic testing is necessary to confirm the suspected diagnosis of FHH.

Conclusion: FHH should be considered as a differential diagnosis even in elderly patients without a family history of the disorder. Medical treatment with Cinacalcet is a reasonable therapeutic option in this situation.

Abstract #516

FRACTURE AND SURGICAL BURDEN IN PEDIATRIC AND ADULT PATIENTS WITH HYPOPHOSPHATASIA: RESULTS FROM PATIENT-REPORTED OUTCOME SURVEYS

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Objective: Hypophosphatasia (HPP) is a rare disease caused by loss-of-function mutation(s) in the tissue-nonspecific alkaline phosphatase gene. HPP is characterized by defective skeletal mineralization and diverse complications that may include proximal muscle weakness, pain, and pathological fractures (Fx). Here, we describe the fracture and surgical burden of HPP as assessed by 2 surveys specific to HPP symptomology.

Methods: The Hypophosphatasia Impact Patient Survey (HIPS, internet-based) and Hypophosphatasia Outcomes Study Telephone interview (HOST) were designed to assess the burden of disease in patients (pts) with HPP. Outreach from 2009-2011 by pt advocacy groups or physicians provided awareness of the surveys to pts or caregivers and invited participation. Data are expressed as the percentage of pts who responded to each item;
questions common to both surveys were pooled.

**Results:** 184 pts responded to the surveys: 59 children (mean[SD] age 7.6[5.1] yrs); 125 adults (mean[SD] age 45.0[14.3] yrs). Fx (mean, min-max) were reported in 42% of children (1, 0 8) and 86% of adults (11.6, 0-100). 15% of children had ≥2 Fx; 74% of adults experienced multiple (≥2) Fx, with 47% adults experiencing ≥6 Fx. Children in HIPS (n=44) reported pseudo- (7%) and nonhealing (2%) Fx. 36% of children did require some surgery, most commonly skull (21%) and osteotomy (11%). Adults in HIPS (n=89) reported higher rates of pseudo- (44%) and nonhealing (36%) Fx, with 74% and 44% of HIPS adults requiring surgery and Fx fixation, respectively; other common surgeries included osteotomy (15%) and joint replacement (11%).

**Discussion:** Fx and surgeries are common in both children and adults with HPP. The majority of adults report pathological and/or multiple Fx, possibly reflecting greater time with disease.

**Conclusion:** As reported by patients/caregivers, HPP is associated with a high burden of disease. High lifetime incidence of fractures and surgeries in adults suggests progressive morbidity with age.

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**Abstract #517**

**PREDICTING RISK OF OSTEOPOROTIC FRACTURE BY BONE ULTRASONOGRAPHY IN TYPE 2 DIABETES MELLITUS**

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**Objective:** Diabetes mellitus type 2 (DM2) is a disease that may be associated with osteoporosis and fractures. The X-ray bone densitometry (DXA) has given disappointing results in measuring the risk of fracture in patients with DM2. In the general population, bone ultrasound (QUS) has demonstrated a predictive power of osteoporotic fracture equal to that of DXA. The aim of our study was to evaluate the risk of osteoporotic fracture by QUS of the calcaneal bone in patients with DM2.

**Methods:** A retrospective case note analysis of 15 patients with symptomatic PHPT who underwent parathyroid resection in a single center from 2011-2014. Following biochemical diagnosis of PHPT, they underwent imaging with Ultrasonography (US), Computed tomography (CT) and TC99 Sestamibi scan for preoperative localization. Histology was reviewed and correlated with the radiological and surgical diagnosis. Statistical analysis was done using SPSS version 22 and 2×2 tables.

**Results:** Among the 15 patients 10 (66.6%) were females and 5 (33.3%) were males. Mean age at presentation was 47±12.5 years. Commonest clinical presentation was nephrolithiasis, which occurred in 7 patients (46.7%). PHPT was confirmed biochemically with elevated total calcium (mean 3.02±0.45 mmol/L) and parathyroid
hormone (PTH). Mean PTH was 758±655 pg/mL. Preoperative localization with imaging favored single gland disease in 14 (93.3%) patients and multi-gland disease in one (6.66%) patient. All 3 imaging scans showed concordant results in 6 (40%) patients and 5 (26.6%) patients had two concordant imaging. Only one out of the three imaging was positive in 4 (33.3%) patients. Three patients underwent three and half gland removal while 12 underwent single gland removal. Histology confirmed multigland disease due to hyperplasia in one patient who underwent three and half gland removal and 13 patients had single parathyroid adenoma. One patient was confirmed with parathyroid carcinoma by histology.

Discussion: In this series CT neck had the highest sensitivity, which was 92% while Tc99 Sestamibi had a sensitivity of 83%. US neck had the lowest sensitivity, which was 75%. When US had combined with CT neck or Tc99Sestamibi scan this increased to 88% in both instances. Specificity was not calculated since there was no control group and none of the histology was normal.

Conclusion: According to our series US has a lower sensitivity in detecting parathyroid gland abnormality compared to CT and Tc99 Sestamibi. However, this is an operator dependent test. Since none of the imaging is 100% sensitive combining at least two tests can ensure accurate preoperative localization. Although many experts prefer Tc99 Sestamibi combined with US neck, combination of US with CT neck also has similar sensitivity and can be used specially in resource poor setting, which will facilitate minimally invasive surgery.

Abstract #519

ROUTINE 4-GLAND EXPLORATION REMAINS UNNECESSARY IN MODERN PARATHYROID SURGERY

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Objective: Conventional four-gland exploration has long been considered the gold standard operation for patients with primary hyperparathyroidism (PHPT). Recent improvements in perioperative adjuncts such as advanced imaging techniques and intraoperative parathyroid hormone (IOPTH) assays have made single-gland, minimally invasive parathyroidectomy (MIP) the preferred option for most patients requiring parathyroid surgery. Despite this, the need for 4-gland exploration in all patients has recently been advocated. This study compares the long-term outcomes and durable cure rates of MIP with conventional four-gland exploration in patients with PHPT.

Methods: A prospectively-maintained database of patients undergoing parathyroid surgery from 2003-2013 in a tertiary endocrine surgery practice was interrogated, and all patients undergoing an initial MIP for sporadic PHPT were identified. Parameters assessed included demographic data, biochemical profiles, surgical procedures, complication rates, duration of follow-up and post-surgical outcomes. These rates were compared with published results of conventional four-gland exploration.

Results: 561 patients had parathyroid surgery during the study period; 338 had surgery for previously untreated PHPT and 283 of these patients met inclusion criteria. The mean age was 58.7 years, and 79.9% of subjects were female. The median duration of follow-up was 28 months. The mean preoperative calcium was 11.1 mg/dL, and the mean postoperative calcium was 9.6 mg/dL. A single adenoma was identified in 85.2% of cases. Preoperative imaging studies were co-localizing in 198 patients (70%), and 159 (80.3%) of these patients only required single-gland surgery. Imaging studies did not co-localize in 85 patients, yet 41 (48.2%) of these patients were still able to be cured with unilateral surgery. Preoperative imaging accurately predicted multi-gland disease in 35.7% of cases where more than 1 gland was abnormal. The cure rate for patients undergoing MIP was 98.6%, with a recurrence rate of <2%.

Conclusion: When coupled with the IOPTH assay, patients with at least one preoperative localizing study can undergo MIP and anticipate a cure rate of 99%, which is as good as or better than the published rates for conventional bilateral exploration. We therefore conclude that most patients do not require a planned four-gland exploration to achieve optimal cure rates in the surgical treatment of PHPT.

Abstract #520

LAZARUS: A METABOLIC PROBLEM ARISING 13 YEARS AFTER THE PREDISPOSING EVENT

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Objective: We present a rare case of a 48 year old female who underwent a successful parathyroidectomy for Primary Hyperparathyroidism who remained normocalcemic and asymptomatic for 13 years who suddenly developed hypoparathyroidism.

Case Presentation: We present a case of a 48 year old female who was diagnosed with Multinodular Goiter and Primary Hyperparathyroidism and underwent total thyroidectomy with subtotal parathyroidectomy in 2001. After a successful parathyroidectomy with the
removal of a single parathyroid adenoma, the patient was asymptomatic with normal serum calcium (8.9 mg/dL). She remained asymptomatic without the need for replacement over the next thirteen years. On the day of admission, the patient developed acute numbness of the face and extremities with generalized body malaise and associated with carpopedal spasm and positive Chvostek’s sign. Work up revealed low serum calcium of 5.7 mg/dL and a low intact PTH of 6.21 pg/ml consistent with Hypoparathyroidism. Other laboratory parameters ruled out other causes of hypocalcemia.

Discussion: A possible explanation for our patient developing spontaneous hypocalcemia and hypoparathyroidism after an apparent cure from parathyroidectomy is an acquired form of hypoparathyroidism not related to surgery and this is most often an autoimmune disease. Permanent hypoparathyroidism can result from immune-mediated destruction of the parathyroid glands. Alternatively, hypoparathyroidism can result from activating antibodies to the calcium sensing receptor leading to a reduction in PTH secretion.

Conclusion: After extensive literature search, this is the first reported case of an apparent cure of hypercalcemia due to hyperparathyroidism secondary to a parathyroid adenoma that subsequently led to hypocalcemia with low parathyroid hormone consistent with hypoparathyroidism after 13 years. The most likely scenario explaining this phenomenon is an autoimmune destruction of the remaining parathyroid tissue post parathyroidectomy: A destructive Lazarus rising from the grave.

Abstract #522

CALCITIROL MEDIATED HYPERCALCEMIA IN A PATIENT WITH SILICONE GRANULOMAS DUE TO COSMETIC INJECTIONS: CLINICAL CASE

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Reading Hospital

Case Presentation: A 41 year old female with past medical history of hypertension, hypothyroidism and one previous episode of urolithiasis was admitted by psychiatry due to severe depression. Medicine was consulted due to an incidental finding of hypercalcemia with values between
12.5 and 14 mg/dl (normal 8.5-10.5). All the workup was ordered showing normal creatinine, low phosphorus 2.2 mg/dl (normal 2.5-4.6), low PTH 7 pg/ml (normal 15-88), low 25-hydroxyvitamin D 9 ng/ml (normal 25-80) and high 1,25 Dihydroxyvitamin D 84 pg/ml (normal 18-78) with normal PTH-RP 0.4 pmol/Lt (normal <2). CT reported: Normal chest, bilateral hydronephrosis with obstructing bilateral calculi and subcutaneous and intramuscular nodules throughout the lower pelvis, gluteal area, and lower anterior abdominal wall. After these findings patient admitted cosmetic silicone injections 15 year previous. Biopsy of one nodule confirmed a silicone granuloma. Patient was treated successfully with intravenous fluids and Pamidronate, as temporary measure, with improved calcium levels. Now she is scheduled for other therapeutic options.

Discussion: Among the different causes of hypercalcemia the most common ones are malignancy and hyperparathyroidism in more than 90%. Calcitriol mediated hypercalcemia is a very uncommon cause with evidence limited only to case series or case reports. Usually this non PTH related hypercalcemia have been reported in different granulomatosis diseases like Tuberculosis, Sarcoidosis, Leprosy, Beriliosis and disseminated fungal disease; however in our case we present a patient with hypercalcemia related to iatrogenic granulomatosis due to silicone injections for cosmetic purposes. In the last decades the increase use of silicones for cosmetic purposes have become less expensive and attractive even for clandestine use, as a consequence the complications have been also increasing. These complications can be local or systemic ranging from changes in color of the skin and formation of nodules/granulomas to necrosis, scarring, deformities, sepsis and death. Silicone provoke a tissue reaction named sclerosing lipogranulomatosis (previously described as siliconoma) sometimes reported as high as 20% in patients that received these injections, however not all granulomas are associated with hypercalcemia. This report would be the 4th one in the literature where the increase production in 1,25 dihydroxyvitamin D associated with silicone granulomas causes hypercalcemia with PTH suppression and severe urolithiasis.

Conclusion: When a patient presents with hypercalcemia non PTH related and increase 1,25 dihydroxyvitamin D clinicians should have a high suspicion for different granulomatosis included siliconomas.
A 63-year-old white woman, 1
8.9 ng/dl (normal, 8.4 to 10.2), s25(OH)D 56ng/ml, serum
osteocalcin 12.1 ng/ml (normal, 3-22), serum calcium (sCA)
up to 306), sCTX 209 pg/ml (normal 59-679), serum
alkaline phosphatase (sALP) 97U/L (normal, 32-92), serum
parathormone (sPTH) 25 pg/ml (normal, 15-65). At the end of the second year a radiographic callus at the fracture site was seen, with femoral neck (FN) bone mineral density (BMD) (T score -1.6), lumbar spine (LS) BMD (T score -2.5). After the third dose of 5 mg zolendronate she suffered another fracture in the middle 1/3 of the right femur with no history of trauma. Serum CTX was 190 pg/ml, serum osteocalcin 8.2ng/ml, sALP 78U/L and SR 2g/day was started. After two months of SR, sCTX and osteocalcin were increased by 100% and 125%, respectively, with total closure of the fracture. After 5 years on SR, the patient had a normal life and had experienced no fractures. There was an increase in LSBMD of 18% and in FNBMD of 4.5%, with values for serum CTX and osteocalcin of 125 pg/ml and 10 ng/ml, respectively.

Discussion: These data suggest a predominantly osteoanabolic effect of SR following AFF which was evident during the first months of therapy. This was accompanied by marked increases in bone markers along with rapid closure of the fracture line which was sustained and durable over five years.

Conclusion: This case illustrates a favorable long-term effect of SR after BP-associated AFF.

Abstract #525

TRANSIENT PRIMARY HYPERPARATHYROIDISM, A CASE REPORT

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Objective: To describe a case of transient hyperparathyroidism.

Methods: We describe the clinical, laboratory and radiologic finding in a patient with an unusual clinical course of primary hyperparathyroidism.

Case Presentation: A 48 year old morbidly obese male with a past medical history of OSA, dyslipidemia and HTN was referred by his primary care physician for evaluation of a parathyroid adenoma in Jan 2012. His recent blood work showed elevated serum calcium 11.6 mg/dL, iPTH 124 pg/dL and 25OHD 15.2 ng/mL. He had no prior history of hypercalcemia or kidney stone and his calcium level 3 months prior was 10.1mg/dL. Repeat calcium was 11.8 mg/dL, iPTH 161 pg/dL, 25OHD 23 ng/mL and 24 hour urine calcium 604 mg. Thyroid sonogram showed a 1.6 x 1.3 x 1.2 cm solid hypoechoic nodule contiguous with lateral margin of the left thyroid pole, consistent with parathyroid adenoma. Sestamibi Scan showed a focal area of increased activity at the left mid pole region.
slightly medially, suggestive of a parathyroid adenoma. Patient then was referred to surgery for minimal invasive parathyroidectomy. Repeat blood test in Dec 2012, just before surgery showed calcium 9.6 mg/dL, iPTH 64 pg/dL, and 25OHDL 25 ng/mL. The surgery was cancelled and a repeat calcium level in May 2013 was 9.6 mg/dL. A repeat thyroid sonogram showed a smaller nodule at the same location of the previous adenoma. Patient’s calcium level remained normal in May 2014.

Discussion: The diagnosis of primary hyperparathyroidism is confirmed by hypercalcemia, hypercalciuria, elevated iPTH and positive parathyroid scan. The etiology of transient hyperparathyroidism remains unknown at present. The short duration of hypercalcemia and repeated thyroid sonogram showed a decrease in parathyroid adenoma size, supporting the possible diagnosis of parathyroiditis. Our patient’s PTH remained slightly elevated despite normal calcium level, which might reflect the occult parathyroid disease and vitamin D deficiency. Another possibility is a parathyroid adenoma infarction or bleeding.

Conclusion: This case illustrates that hypercalcemia and elevated iPTH levels in primary hyperparathyroidism can be transient. Repeat calcium and iPTH levels before parathyroidectomy might be necessary to avoid unnecessary surgery.

Abstract #526

RARE CASE OF SEVERE SYMPTOMATIC HYPERCALCEMIA IN PATIENT WITH CONCOMITANT PRIMARY HYPERPARATHYROIDISM AND HIGH GRADE DIFFUSE LARGE B-CELL LYMPHOMA

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Objective: In clinical practice evaluation of hypercalcemia usually starts with assessment of intact Parathyroid hormone (iPTH) level as a key step in the development of differential diagnosis. We present a rare and diagnostically challenging case of severe persistent hypercalcemia due to primary hyperparathyroidism (PHPT) and Diffuse Large B-cell lymphoma (DLBCL).

Case Presentation: A 77 year old female was admitted with a change in mental status. Eight years ago she was diagnosed with PHPT and refused surgery. On admission her Calcium (Ca) was 16.3, Cr 1.8, Albumin (Alb) 3.9, iPTH 152, and 25(OH)VitD 22.7. Severe symptomatic hypercalcemia was explained by untreated PHPT exacerbated by recently started hydrochlorothiazide and dehydration. Her mental status improved with IV fluids and Zoledronic acid. She again refused surgery and was discharged on Cinacalcet 30mg daily. Patient was readmitted with similar symptoms due to severe hypercalcemia. Parathyroid scan/CT revealed a 3.2 cm right parathyroid adenoma and large neck mass. Further workup revealed diffuse adenopathy. Biopsy of the left neck and retroperitoneal lymph nodes showed DLBCL. She underwent parathyroidectomy with rapid iPTH decline from 85 to 27 pg/ml. Pathology confirmed parathyroid adenoma, but Ca remained mildly elevated. Outpatient chemotherapy was scheduled. Three weeks later she was readmitted with confusion and Ca 11.5, Alb 2.7, and suppressed iPTH (7). Her PTHrp was not elevated, 25(OH) VitD was 15.7, and 1,25(OH)2 Vit D was 209 (normal 18-72 pg/ml). Diagnosis of DLBCL associated hypercalcemia due to overproduction of calcitriol was suspected. Initiation of Chemotherapy and Steroids resulted in a rapid decline in Ca level.

Discussion: Hypercalcemia due to lymphoma associated extra-renal production of calcitriol is uncommon but described in medical literature. In one study of 219 patients with Non-Hodgkin Lymphoma (NHL), 4.1% of newly diagnosed patients presented with hypercalcemia. The mechanism associated with NHL related extra-renal 25(OH)Vit D hydroxylation to Calcitriol is not well understood. One of the proposed mechanisms is stimulation of 1α-Hydroxylase in macrophages by the cytokines. We found only two cases of hypercalcemia of this rare and diagnostically challenging coexistence of PHPT and NHL medicated calcitriol excess.

Conclusion: Evaluation and differential diagnosis of severe hypercalcemia (Ca >13) due to PHPT (iPTH mediated) should consider a possible coexisting secondary etiology. In cases with persistent hypercalcemia and appropriately low iPTH after parathyroidectomy, the evaluation for other non-PHTH mediated coexisting etiologies should be considered.

Abstract #527

SEVERE HYPOCALCEMIA FOLLOWING ADMINISTRATION OF ZOLEDRONIC ACID IN AN OSTEOPOROTIC PATIENT WITH A HISTORY OF ROUX-EN-Y GASTRIC BYPASS

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Objective: To report the first described case of severe hypocalcemia in a post Roux-En-Y Gastric bypass patient after receiving a bisphosphonate for osteoporosis.

Methods: We present the clinical and laboratory findings from a case of severe hypocalcemia in a post gastric bypass patient who received zoledronic acid for the
treatment of osteoporosis.

**Case Presentation:** We present a 63 year old female with history of renal disease, osteoporosis, secondary hyperparathyroidism, and multiple micronutrient deficiencies after Roux-En-Y gastric bypass. She was known to be calcium deficient with prior 24hr urine calcium level of 36.9mg/24hr. After obtaining a repeat DXA, showing worsening bone density, the patient was given zoledronic acid by her primary care physician. Two days later the patient began to experience peri-oral tingling and paresthesias. Ten days after infusion the patient obtained labs that revealed a calcium of 5.4mg/dL and parathyroid hormone (PTH) of 1058pg/mL. The patient was sent to the emergency department and found to have a positive Chvostek’s sign and EKG with prolonged QTc (468msec). She was admitted to the ICU, treated with IV calcium and monitored until symptoms, labs, and EKG findings normalized. She was discharged with an outpatient regimen of 4.8grams of calcium citrate daily, 0.25mcg of calcitriol, and 400mg of magnesium oxide which has maintained her calcium homeostasis. Two weeks after discharge the patient’s calcium, PTH, 25OH vitamin D, and magnesium were within normal limits.

**Discussion:** Bisphosphonates are known to cause hypocalcemia in 5-10% of individuals. The risk of hypocalcemia is higher in individuals with hypoparathyroidism, and those with preexisting vitamin D or calcium deficiency. In the normal individual osteoclasts, through action of PTH, release calcium into circulation. Bisphosphonates work by inhibiting osteoclastic activity in favor of osteoblastic activity to help restore bone mass. Following bisphosphonate therapy, our patient could no longer restore calcium levels through this mechanism as osteoclastic activity was blocked by the bisphosphonate, resulting in hypocalcemia.

**Conclusion:** Bariatric surgery is known to cause calcium malabsorption, leading to reliance on calcium release from the bone. The use of a bisphosphonate in our patient led to hypocalcemia, as she was unable to release calcium from her bones. To our knowledge this is the first reported case of severe hypocalcemia following the use of bisphosphonates in a post gastric bypass patient. Increased awareness of this adverse reaction with bisphosphonates in this patient population is needed to avoid further morbidity.
OBESITY

Abstract #600

EFFECT OF BODY MASS INDEX (BMI) AND LIPIDS ON COLORECTAL CANCER SURVIVAL

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Objective: Obesity is an established risk factor for colorectal cancer (CRC). The relationship between body fat deposition and the pathogenesis of cancer has been the subject of many studies; however, no clear consensus has emerged linking these two biological processes. The aim of this study was to investigate whether BMI or hyperlipidemia have any impact on survival, when studied at the different stages of cancer treatment.

Methods: We retrospectively reviewed the records of all patients diagnosed with CRC at our institution from 2011 to 2013. Data analyzed included: demographics, lipid profiles and BMI at diagnosis, at the time of surgery and before chemotherapy. Kaplan-Meier and Cox proportional were used for survival and multivariate analysis.

Results: There were 376 patients; mean age at diagnosis was 65 years. There were more males than females, 57% (214) vs. 43% (162) (p<0.04). The average BMI at diagnosis was 28 (range: 16-53), at the time of surgery was 25 (17-45) and before chemotherapy was 24 (14-44). At diagnosis, a mean LDL of 101 (53-180), HDL of 38 (20-75), and triglycerides of 106 (15-350). Of comorbidities reviewed, 45% (170) had hypertension, 35% (133) hyperlipidemia, 28% (104) diabetes mellitus and 16% (62) coronary arterial disease. Regarding treatment, 81% (304) of the patients underwent surgery and 63% (237) received chemotherapy. Overall median survival was 25.7 months (95%CI: 23.3-28.0). There was a significant difference in overall survival between patients with a BMI<20 compared to a BMI>20 at the time of surgery, 20.3 months (95%CI: 11.4-22.0) vs. 26.1 (95%CI: 18.4-29.1) (p<0.04), respectively. BMI>28 at diagnosis (OR: 1.23, p<0.03) and statin use (OR: 0.89, p<0.01) were independent and significant predictors of survival. History of hyperlipidemia was not a predictor of survival by univariate or multivariate analysis.

Discussion: Our data suggests that a BMI<20 at the time of surgery is associated with increased mortality. Moreover, a paradoxical effect was observed, where patients with a BMI>28 at the time of diagnosis had also an increased risk of mortality. Statin use has been linked to decreased mortality in CRC patients in previous studies and this was seen in our group of patients as well.

Conclusion: The effect of BMI on CRC varies upon cancer treatment stage. While obesity tends to increase mortality when present at the time of diagnosis, lower BMI at the time of surgery has a similar effect on overall survival. As lower BMI has been correlated with more advanced disease, it might be expected that our findings of BMI<20 at the time of surgery leads to increased mortality. Further studies regarding the effect of BMI in CRC are necessary as this could impact management.

Abstract #601

WAIST CIRCUMFERENCE DISPARITY: A COMPARISON OF AMERICAN, EUROPEAN AND ASIAN CUT OFFS AMONG AFRICANS.

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Objective: The world is a constellation of Homo sapiens with different orientation to life. These disparity in orientation had been of genetic, physiologic and phenotypic importance even before the times of Hippocrates. Due to phenotypic differences in waist circumference, different continents of the world notably Americans, Europeans and Asians have different scientifically generated cut off values for people of their origin or descent. The same cannot be said of Africans.

The aim of this study is to analyse the disparity in applying the American, European and Asian waist circumference cut offs to Africans.

Methods: This preliminary prospective study was carried out in Lagos, Nigeria, the most populous black African nation. The umbilicus was used as the land mark for measurement of waist circumference using a non stretch tape. The exclusion criteria used are pregnancy, ascites, abdominal mass from any cause, puerperium. Demographic data were obtained excluding name.

Results: The population of this cohort was 126. The age range was 18-88years. Males formed 40.48% while female formed 59.52%.

By using the American cut off of >102cm for male and >88cm for female as high waist circumference, it was noticed that 68.25% of the cohort studied were normal while 31.75% were abnormal.

By using the European waist circumference cut off of 94cm for male and 80cm for female, it was noticed that 43.65% of the cohorts studied was normal while 56.35% abnormal.

By using the Asian cut off of >90cm for male and >80cm for female, it was noticed that 59.52% were abnormal.

Discussion: The disparity in using the different cut off for Africa is glaring. Both Asian and European cut off gave same percentage of abnormal waist circumference in the general population 56.35% in African, but with disparity genderwise. The difference in cut off for female using Asian and European
cut off is less than one, yet it translated to a difference of 10% in the female African population with large waist circumference! Hence using other races cut off will definitely bring about error in diagnosis in Africans either overdiagnosing or underdiagnosing since the sensitivity, specificity and predictive value of other races cut offs is/are not known in Africans.

**Conclusion:** Africans need to research and generate an indigenous African descent based cut offs for better prediction of cardiovascular risk amongst Africans. Awake O Africans!

**Abstract #602**

**COMPENSATORY PANCREATIC β-CELL FUNCTION IN HEALTHY NORMOGLYCEMIC MEN MODIFIES BUT DOES NOT FULLY CORRECT THE DISRUPTED GLUCOSE HOMEOSTASIS INDUCED BY INCREASING BODY FAT IN FASTING AND FED STATES**

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1. Lewis Gale Montgomery Regional, 2. Mayo Clinic, 3. Salem VAMC

**Objective:** This study was intended to assess the glucose regulatory status in healthy men of variable total body fat mass.

**Methods:** Eighty one men aged 18-78 years with BMIs of 18-39 kg/m\(^2\) were studied on 2 randomly ordered occasions after an overnight fast, followed by ingestion of either 75 grams of dextrose solution or equal volume of water. Sessions started between the hrs of 0800-0900 and continued for 6.5 hrs, with blood collected at 10-min intervals for the measurements of glucose and insulin. Adiponectin concentration was assayed in the first blood sample. Total body fat was determined by DXA. Fat mass index (FMI: kg/m\(^2\)) was calculated using total body fat (kg) and height (m). Parameters of interest were fasting concentrations of glucose and insulin, mean and areas under the 6.5 hr concentration time series (AUC), peak concentrations and time to peaks after dextrose ingestion. Linear regression was used to relate hormone data to body-composition variables.

**Results:** Regression analysis revealed significant positive correlation (r coefficient:P value) between FMI and each of: FBG (0.26:<0.0017), 6.5 hrs water-day mean glucose (0.23:<0.043) and AUC (0.22:0.047), 6.5 hr dextrose-day mean glucose (0.42:<0.0001) and AUC (0.42:<0.0001), post-dextrose peak glucose (0.42:0.0001), and time to peak glucose (0.26:0.019). FMI also was positively correlated with insulin levels in the fasting state (0.6:<0.0001), 6.5 hrs water-day mean (0.63:<0.0001) and AUC (0.64:<0.0001), 6.5 hr dextrose-day mean (0.53:<0.0001) and AUC (0.53:<0.0001), and post-dextrose peak insulin (0.45:<0.0001). Adiponectin had significant negative correlation with FMI (-0.22:0.044).

**Discussion:** Increased body fat is known to induce insulin resistance, and increase β-cell insulin secretion. Such compensatory mechanisms are believed to maintain initially normal glucose homeostasis. The present study identifies altered glucose metabolism albeit within the normal range with increasing body fat, as characterized by relatively higher blood glucose in the fasting state, and more pronounced increases in all measures of glucose concentrations after dextrose ingestion, including peak and time to peak glucose levels.

**Conclusion:** Quantitatively impaired glucose disposal associated with increasing body fat in healthy men, despite compensatory augmentation of β-cell function, identifies compromised glucose regulation, which could be inferred as a precursor to the development of subclinical and clinical diabetes. Having a negative correlation with fat mass, hypoadiponectinemia could be proposed as a contributory factor.

**Abstract #603**

**ABSTRACT WITHDRAWN**

**Abstract #604**

**DETECTION OF CARDIOVASCULAR RISK FACTORS BY ANTHROPOMETRIC MEASURES IN ADULTS LIVING IN AN URBAN SETTING IN SRI LANKA.**

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**Objective:** To report the prevalence of obesity, Metabolic syndrome and to evaluate the relationship between anthropometric indices of obesity and metabolic risk factors among adults living in an urban community in Sri Lanka.

**Methods:** Using a stratified random sampling method, 369 subjects(116 men; 253 women) aged 18 years and above, representative of all socio-economic strata, were tested by 75g Oral Glucose Tolerance Test, HbA1c and lipid profile. Demographic and anthropometric details were recorded using a standard proforma. Receiver-operating characteristic(ROC) curves were
generated and area under the curve (AUC) was calculated to identify the optimal measurement of obesity among BMI, waist circumference (WC), neck circumference (NC) and waist to height ratio (WHtR), for the prediction of metabolic risk factors.

**Results:** The overall prevalence of obesity was 17.93%, while 39.89% of the population was overweight. According to the WC, central obesity was prevalent in 52.52% while MetS was prevalent in 24.69%.

Although, all 4 anthropometric indices significantly predicted MetS, the area under the ROC curve for WC (0.700) and WHtR (0.673) were higher than BMI (0.666) and NC (0.621). Similarly, all 4 indices were predictive of Diabetes Mellitus (DM), with the highest predictive AUC seen in NC (0.646) and WC (0.622). On the other hand, only NC significantly predicted hypertension (HT).

Low HDL (male <40, female <50 mg/dl) showed no significant correlation with any of the anthropometric measures, while hypertriglyceridemia (≥ 150 mg/dl) had significant correlation with all 4 anthropometric indices. Of the 4 obesity indices, NC (r=0.231, p<0.001) and WC (r=0.219, p<0.001) showed the strongest correlation with hypertriglyceridemia, while BMI had the weakest correlation (r=0.166, p=0.01).

**Discussion:** Sri Lanka has been experiencing rapid urbanization with lifestyle changes that may contribute to increased CV risk. This study identified a high prevalence of obesity and metabolic risks in Sri Lankan adults living in an urban community.

There is little consensus on the best obesity index associated with metabolic risk factors among South Asians. MetS is defined by WC and hence will have the best correlation with WC and WHtR. Although, BMI was a significant predictor of MetS, it was a poor predictor of DM and HT with weak correlation to low HDL and hypertriglyceridemia.

**Conclusion:** Along with the changes in the sociodemographic status, the metabolic profile of the Sri Lankan adult has transformed, with a high prevalence of obesity and Metabolic Syndrome. Waist circumference and Neck circumference can be used as simple and effective anthropometric predictors of obesity associated metabolic risks compared to conventional BMI.

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**Abstract #605**

**ANTHROPOMETRIC INDICES AMONG HIV INFECTED PATIENTS IN KANO, NORTH WESTERN NIGERIA**

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**Objective:** To determine the anthropometric indices of HIV patients, and to compare these indices between HAART exposed and HAART naïve participants.

**Methods:** HIV positive patients attending the Aminu Kano Teaching Hospital HIV Specialist clinic were evaluated. Their anthropometric indices were determined and body mass index (BMI) calculated using the Quetelet’s equation. Waist circumference (WC) and waist-hip ratio (WHR) were defined using the NCEP-ATP III criteria.

**Results:** A total of 300 HIV seropositive patients (150 HAART exposed and 150 HAART naïve) were assessed. The mean±SD age of study participants was 35.7±10.0 years (HAART exposed) and 34.0±9.7 years (HAART naïve). The mean BMI of the HAART exposed and HAART naïve participants was 24.0±6.0kg/m² and 22.0±5.6kg/m² respectively, (p=0.001). Among the HAART exposed participants, 15.3% were obese, 16.7% overweight, 55.3% were of normal weight while 12.7% were underweight. In the HAART naïve group, 8.0% were obese, 14.0% overweight, 47.3% of normal weight and 30.7% underweight. Among the male participants, the mean±SD WC for HAART exposed and HAART naïve groups was 89.6±11.7cm and 77.1±14.0cm respectively, (p<0.05). Among the female participants, the mean±SD WC for HAART exposed and HAART naïve groups was 82.9±15.4cm and 78.4±13.3cm respectively, (p=0.032); the mean±SD HC was 94.5±15.0cm and 90.9±13.2cm respectively, (p=0.08); while the mean±SD WHR was 0.94±0.09 and 0.90±0.09 respectively, (p=0.05). Among the male participants, the mean±SD WHR was found to be associated with increase prevalence of obesity and raised waist circumference. This could be as a result of lipodystrophy which is a complication of HAART. The difference between HAART exposed and HAART naïve groups for HC and WHR was more pronounced in males than in females.

**Conclusion:** HAART exposure was found to be associated with increase prevalence of obesity and raised waist circumference. This could be as a result of lipodystrophy which is a complication of HAART. The difference between HAART exposed and HAART naïve groups for HC and WHR was more pronounced in males than in females.
could have a negative metabolic and social consequence on HIV patients exposed to it. Regular monitoring of the anthropometric indices of HIV patients is therefore of paramount importance for early detection.

**Abstract #606**

**NECK CIRCUMFERENCE - A MORE INFORMATIVE INDICATOR FOR METABOLIC DISTURBANCES COMPARED TO WAIST CIRCUMFERENCE?**

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**Objective:** Obesity is one of the most important risk factors for cardiometabolic diseases. Waist circumference (WC) has often been used as a surrogate marker for abdominal fat mass and thus as a predictor for metabolic risk. The predictive potential of neck circumference (NC) for such risks remains uncertain. The aim of this study was to evaluate whether NC independently contributes to the prediction of metabolic risk beyond WC and to compare the two anthropometric measures in a population of obese subjects.

**Methods:** A total of 168 obese subjects (BMI ≥30 kg/m²) recruited from 2013-2014 in a University Hospital setting participated in the study. Anthropometric measures included WC, NC, weight, height. Biochemical measurements included HbA1c, liver enzymes, uric acid (UA), lipids. Standard OGTT with immunoreactive insulin (IRI) measurement were performed where Type 2 Diabetes Mellitus (T2DM) was not already diagnosed. FINDRISC questionnaire was applied. Reciever operating characteristic (ROC), logistic regression and partial correlation analyses were employed to determine the association of WC and NC to metabolic disturbances, separately by gender.

**Results:** Median age was 52 yrs [IQR=15], median BMI was 35 kg/m² [IQR=6.62]. 50(29.8%) of the study participants were male. 69 (41%) of the patients had T2DM; 71 (42.3%) patients had prediabetes according to the ADA criteria; 28 (16.7%) patients had normal glucose tolerance. The prevalence of Metabolic Syndrome (MS) based on the IDF criteria was 86.9%. Adjusted for age NC correlated better than WC with IRI (r=0.300 vs. r=0.200), UA (r=0.354 vs. r=0.269), HOMA-IR (r=0.345 vs. r=0.223), ALT (r=0.385 vs. r=0.256), TG (r=0.245 vs. r=0.177) in females. WC correlated better than NC with HbA1c (r=0.368 vs. r=0.150), FINDRISC (r=0.323 vs r=0.232) in females. AUCs for WC and NC were as follows: MS (r=0.732 vs. r=0.717), T2DM (r=0.712 vs. r=0.683), dyslipidaemia (r=0.697 vs. r=0.663) in females.

**Discussion:** WC is an established method for evaluating abdominal fat but it has several disadvantages particularly in severely-obese individuals. NC contributes to metabolic risk evaluation beyond WC and is easier to measure.

**Conclusion:** NC is an anthropometric parameter that might be of greater value than WC as an indicator for metabolic risk.

**Abstract #607**

**EARLY RESPONDERS TO LIRAGLUTIDE 3.0 MG AS ADJUNCT TO DIET AND EXERCISE FROM THE SCALE OBESITY AND PREDIABETES TRIAL: EFFICACY AND SAFETY RESULTS**

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**Objective:** To explore the clinical impact of an early response to liraglutide 3.0 mg treatment in overweight/obese individuals.

**Methods:** This was a 56-week, randomized, double-blind trial that evaluated the efficacy and safety of liraglutide 3.0 mg (n=2487) vs. placebo (n=1244) in overweight/obese individuals (BMI ≥27 kg/m² with ≥1 comorbidity or ≥30 kg/m²) without T2D. Mean baseline characteristics were age 45 years, 79% female, body weight 106 kg, BMI 38 kg/m². This sub-analysis compared outcomes at 56 weeks of liraglutide 3.0 mg early responders (≥4% weight loss at 16 weeks) vs. early non-responders (<4% weight loss at 16 weeks). Data are from completers (FAS, LS means; SAS). Placebo data not shown.

**Results:** At 16 weeks, 80.2% and 33.1% of individuals treated with liraglutide 3.0 mg vs. placebo achieved ≥4% weight loss. At 56 weeks, body weight was reduced by 10.8% (11.2 kg) in early responders, compared with 3.0% (3.2 kg) in early non-responders. Waist circumference was reduced by 10.5 and 4.8 cm. Consistent with these findings, greater improvements were observed in glycemic outcomes, CV risk markers and quality of life (QoL) in
Abstract #608

CLINICAL PRACTICE GAP ANALYSIS OF OBESITY TREATMENT IN THE MODERN ERA

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Objective: Obesity is a major public health crisis. In the past 10 years, prevalence in the United States has increased from 20.0% to 35.7%. Despite recognition as a disease, obesity remains undertreated. This study’s objective was to assess current clinical practices of primary care physicians (PCPs), endocrinologists, and obstetricians/gynecologists (OB/GYNs) in obesity management to identify knowledge, competency, and practice gaps and barriers to improving patient care.

Methods: A survey instrument including multiple choice and knowledge- and case-based questions was developed to assess educational needs. The survey instrument was made available online to healthcare providers without monetary compensation or charge. Respondent confidentiality was maintained and responses were de-identified and aggregated prior to analyses. The survey launched on June 26, 2014 and responses collected through July 31, 2014.

Results: In total, 945 physicians responded to the survey, including 487 PCPs, 85 endocrinologists, and 78 OB/GYNs. When presented with patient case scenarios involving a need for obesity treatment, physicians demonstrated gaps in: mechanism of action of anti-obesity agents (43-48% correct responses), efficacy expectations (28-41% correct responses), contraindications (42-66% correct responses), dosing and titration schedule (60-75% correct responses), successful dietary interventions (62-78% correct responses), eligibility for bariatric surgery (78-85% correct responses), and weight loss needed for clinical benefits (79-98% correct responses).

Many physicians indicated that they are less than confident in their ability to manage patients with obesity: PCPs (36%), endocrinologists (33%), and OB/GYNs (55%). The greatest clinical challenges with respect to the management of patients with obesity included time (26-34%), lack of knowledge of current therapeutic guidelines (15-29%), lack of resources to educate patients (14-27%), and lack of training (13-15%).

Discussion: Physicians demonstrated a need for education on several obesity treatment-related topics. Of barriers to treatment, many could be addressed with continuing medical education (CME), including lack of knowledge of current therapeutic guidelines, lack of resources to educate patients, and lack of training.

Conclusion: With the goal of improving physician practices and patient care, this assessment of healthcare providers’ clinical practices identified knowledge and competency gaps among (PCPs), endocrinologists, and OB/GYNs in several key areas in the evaluation and treatment of patients with obesity. Further assessment of physicians after participating in educational interventions is planned to demonstrate improvement in clinical practice.

Abstract #609

ABSTRACT WITHDRAWN
Abstract #610

IMPROVEMENTS IN HEALTH-RELATED QUALITY OF LIFE WITH LIRAGLUTIDE 3.0 MG COMPARED WITH PLACEBO FOR WEIGHT MANAGEMENT

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Objective: Obesity has a negative impact on health-related quality of life (HRQoL), the degree of which is dependent upon the severity of obesity. The Satiety and Clinical Adiposity - Liraglutide Evidence (SCALE) Obesity and Prediabetes study aimed to investigate the effect of liraglutide 3.0 mg, as adjunct to diet and exercise, on HRQoL in non-diabetic obese or overweight subjects, with or without pre-diabetes.

Methods: Individuals (BMI ≥27 kg/m2 with ≥1 comorbidity or ≥30 kg/m2) were advised on a 500 kcal/day deficit diet and a 150 min/week exercise program, and randomized 2:1 to once-daily s.c. liraglutide 3.0 mg (n=2487) or placebo (n=1244). HRQoL outcomes, assessed in subjects from countries with validated translations (82% of randomized) at baseline, 6 months and 1 year (end of trial), utilized Impact of Weight on Quality of Life-Lite (IWQOL-Lite) and Short-Form 36 (SF-36) questionnaires. The Treatment-Related Impact Measure-Weight (TRIM-Weight) was completed at 6 months and end of trial. Data were reported as observed means±SD and estimated treatment differences (ED), derived using ANCOVA with LOCF.

Results: Baseline characteristics: 78.5% female, age 45.1 years, weight 106.2 kg, BMI 38.3 kg/m2 (all means). Individuals on liraglutide 3.0 mg had significantly greater improvements in IWQOL-Lite total score ([10.6±13.3] vs. placebo [7.6±12.8; ED 3.1 [95%CI: 2.2;4.0]; p<0.0001]) and SF-36 physical (PCS) and mental component (MCS) summary scores (PCS, 3.6±6.8; MCS, 0.2±8.1) vs. placebo (PCS, 2.2±7.7; MCS, -0.9±9.1) (ED PCS 1.7 [95%CI: 1.2;2.2], p<0.0001; and MCS 0.9 [95%CI: 0.3;1.5, p=0.003]), which accompanied greater weight loss from baseline (-8.0±6.7%) compared with placebo (-2.6±5.7%; ED -5.4% [95%CI: -5.8;5.0]; p<0.0001)). All sub-domain scores of the IWQOL-Lite and SF-36 were significantly improved with liraglutide 3.0 mg vs. placebo. Odds of achieving a minimally clinically important improvement were higher with liraglutide 3.0 mg vs. placebo for IWQOL-Lite total score (1.59 [1.35;1.88], p<0.001) and SF-36 PCS (1.69 [1.43; 2.00] p=0.0001). The TRIM-Weight total score was also higher at end of trial with liraglutide 3.0 mg (83.1±10.7) vs. placebo (81.0±9.4; ED 2.1 [95%CI: 1.3;3.0], p<0.0001).

Discussion: Use of liraglutide 3.0 mg, in addition to diet and exercise, was associated with clinically meaningful improvements in physical domains of HRQoL vs. placebo.

Conclusion: Treatment with liraglutide 3.0 mg significantly improves HRQoL, including physical function and mental health, in patients who are overweight or have obesity, compared with placebo.

Abstract #611

THE IMPACT OF GASTROINTESTINAL ADVERSE EVENTS ON WEIGHT LOSS WITH LIRAGLUTIDE 3.0 MG AS ADJUNCT TO A DIET AND EXERCISE PROGRAM

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Objective: To explore any associations between gastrointestinal adverse events (GI AEs) and weight loss with liraglutide 3.0 mg/day in addition to a diet and exercise program in individuals without type 2 diabetes who were obese (BMI ≥30 kg/m2) or overweight (BMI 27–29.9 kg/m2) with at least one comorbidity.

Methods: The SCALE Obesity and Prediabetes trial was a randomized, double-blind, multi-center trial in which individuals (mean age 45.1 years, 78.5% female, mean weight 106.2 kg, mean BMI 38.3 kg/m2, 61% with prediabetes) were enrolled in a long-term weight management program and randomized to liraglutide 3.0 mg (n=2487) or placebo (n=1244). These data are from an exploratory analysis based on groups of individuals defined by occurrence of GI AEs (0–16 weeks, 0–56 weeks). Weight loss at week 56 is presented as least squares means using LOCF, with p-values denoting whether or not GI AEs had a significant effect on treatment.

Results: Overall, liraglutide 3.0 mg was associated with a greater weight loss from baseline than placebo (8.0% vs. 2.6%, respectively, p<0.0001). As expected, more individuals on liraglutide 3.0 mg (68.3%) compared with placebo (40.3%) reported GI AEs; the most prevalent GI AEs were nausea (40.2% vs. 14.7%), diarrhea (20.9% vs. 9.3%), constipation (20.0% vs. 8.7%) and vomiting (16.3 vs. 4.1%), occurring mostly within the first 16 weeks of treatment. There was no significant difference in weight loss between individuals who did or did not experience ≥1 episode of nausea/vomiting during 0–56 weeks, regardless of treatment (liraglutide 3.0 mg: nausea/vomiting, -7.8%,.
no nausea/vomiting, -8.1%; placebo: nausea/vomiting -2.5%, no nausea/vomiting -2.6%, p=0.81). Similar results were seen if all other types of GI AE combined were included. Moreover, no significant differences were observed at week 56 for weight loss in individuals who experienced 0, 1, 2-3, or ≥4 GI AEs in the first 16 weeks (7.7–8.2% with liraglutide 3.0 mg vs. 2.3–3.0% with placebo, p=0.24), or during the entire 56 weeks of treatment (7.7–8.4% with liraglutide 3.0 mg vs. 2.4-3.2% with placebo, p=0.55). Although those experiencing 0 GI AEs appeared to perform slightly better than the other groups, this may be explained by the higher withdrawal rate as the number of GI AE increase. These results were further supported by comparable mean weight loss profiles over time across the 0, 1, 2-3, or ≥4 GI AE groups.

Conclusion: The weight loss observed with liraglutide 3.0 mg is not explained by the occurrence of GI AEs, including nausea/vomiting.

Abstract #612

EFFICACY AND SAFETY OF LIRAGLUTIDE 3.0 MG FOR WEIGHT MANAGEMENT ARE SIMILAR ACROSS RACE

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Objective: Obesity is a significant public health challenge both in the Western world and in developing countries. Black/African-Americans (BAA) are disproportionately affected compared with white individuals. Further, BAA generally achieve lower weight loss using standard behavioral interventions. Thus it is important to evaluate emerging weight loss therapies in different racial subgroups for comparative efficacy and safety.

Methods: This was a post hoc analysis of pooled data from one 52-week Phase 2 trial and the 4 Phase 3 SCALE trials (3 of 56 weeks’ duration, one 32 weeks). We compared the efficacy and safety of liraglutide 3.0 mg vs. placebo, as adjunct to diet and exercise, in different racial subgroups: white (n=4945), BAA (n=580), Asian (n=172) and other (n=116). The population of the randomized double-blinded trials was adults who were overweight or obese with (n=844; 14.5%) or without (n=4969; 85.5%) type 2 diabetes (T2D).

Results: Across the racial subgroups, most participants (~60-80%) were female. Mean age ranged between 40.8 and 47.5 years. Mean BMI and body weight were lowest in Asians (35.8 kg/m2 and 95.1 kg) and highest in BAA (39.5 kg/m2 and 109.9 kg). In each subgroup greater mean weight loss from baseline to end of treatment was achieved with liraglutide 3.0 mg vs. placebo: white, -7.74 vs. -2.35% (estimated treatment difference [ETD] 5.25% [95%CI -5.6; 4.9]; BAA, -6.29 vs. -1.36% (ETD -4.78% [-5.9; 3.7]); Asian, -6.29 vs. 2.52% (ETD -4.02% [-6.1; -2.0]); other, -7.31 vs. 0.49% (ETD 6.81% [ 9.3; -4.3]) (p<0.0001 for all, last observation carried forward). In each subgroup more individuals lost ≥5% of their baseline weight in the liraglutide 3.0 mg group (range 52 62%) vs. the placebo group (8.7 25%) and more lost >10% weight with liraglutide (range 22 33%) vs. placebo (0-8.9%) (p<0.02 for all). All mean and categorical weight loss effects were race independent (p>0.05). Greater improvements in systolic and diastolic BP, lipids and A1C in individuals with and without T2D were generally seen with liraglutide 3.0 mg vs. placebo across racial subgroups; the treatment effects were independent of race (p>0.05). The proportion of individuals reporting adverse events (AEs) and serious AEs was similar across racial subgroups. Gastrointestinal events were reported more frequently with liraglutide 3.0 mg (59.1-76.3% across racial subgroups) than placebo (31.4-40.1%) and were largely similar across the subgroups.

Conclusion: Effects of liraglutide 3.0 mg, as adjunct to diet and exercise, on weight loss, associated metabolic effects and clinical safety profile were generally consistent across racial subgroups, including black/African Americans, a group with higher rates of obesity.

Abstract #613

THE BEST ANTHROPOMETRIC INDEX FOR CENTRAL OBESITY IN SAGAMU AND ISARA, NIGERIA

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Objective: Central or abdominal obesity is recognized as a risk factor for cardiovascular disease (CVD), and listed as a criterion for diagnosing metabolic syndrome by some authorities. While the IDF and NCEP ATP III recommended the use of waist circumference (WC), the WHO recommended waist-to-hip ratio (WHR) as a measure of central obesity. Recently, waist-to-height
ratio (WHR) was proposed as a good measure of central obesity. The purpose of this study was to determine the correlation between three measures of central obesity and the body mass index (BMI), and the best measure of central obesity which identifies individuals with general obesity in Sagamu and Isara, Nigeria.

Methods: Nine hundred and sixteen (916) participants of a community health survey in Sagamu and Remo-North Local Government Areas of Ogun State, Nigeria were included in the study. The BMI, WC, WHR and WHtR of the participants were determined by standard protocols. General obesity was defined as BMI ≥ 30kg/m2. Pearson correlation between BMI and the three central obesity indices was determined. The area under curve (AUC) on the ROC was used to determine the best measure of central obesity which identifies individuals with general obesity.

Results: The participants were made up of 443 (48.4%) males, mean age (40.56± 13.59 years) and 473 (51.6%) females, mean age (46.8±15.49 years). The mean BMI, WC, WHR, and WHtR of the male participants were 23.65±3.96kg/m2, 83.08±11.76cm, 0.91±0.07, and 0.49±0.07 respectively, while the corresponding values for the female participants were 25.79±6.12 kg/m2, 85.76±13.97cm, 0.89±0.07, 0.55±0.09 respectively. The female participants were significantly older, and had greater BMI, WC, WHR, and WHtR than their male counterparts (p=0.002 for WC, and p<0.001 for BMI, WHR and WHtR). The correlation between BMI vs WC, BMI vs WHR, and BMI vs WHtR were 0.874, 0.377, and 0.878 respectively, (p<0.001).

In the male participants, the AUC on the ROC for WHtR, WC, and WHR respectively were 0.972 (95%CI, 0.950-0.994, p<0.001), 0.966 (95% CI, 0.943-0.989, p< 0.001), 0.785 (0.703-0.866, p<0.001). In the female participants, the AUC on the ROC for WHR, WC, and WHR respectively were 0.973(95% CI, 0.959-0.987, p<0.001), 0.969 (95% CI, 0.954-0.983, p<0.001), 0.744 (95% CI, 0.690-0.797, p<0.001).

Discussion: Consistent with previous studies, there was a significant correlation between BMI and the three measures of central obesity. However, the correlation was best with WHR. The ROC showed that WHtR identified participants with generalized obesity better than WC and WHR.

Conclusion: WHtR is better than WC and WHR in identifying individuals with obesity and may also be a good criterion to diagnose metabolic syndrome.

Abstract #614

SECOND PROSPECTIVE, PHARMACOEPIDEMIOLOGIC DATABASE ANALYSIS OF QSYMIA® (PHENTERMINE AND TOPIRAMATE EXTENDED-RELEASE) USAGE FROM A REPRESENTATIVE US SAMPLE OF PATIENTS

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VIVUS, Inc.

Objective: Qsymia® (phentermine and topiramate extended-release [PHEN/TPM ER]) capsules CIV was approved by the US FDA in July 2012 for chronic weight management in combination with lifestyle modifications in adults with a body mass index (BMI) of ≥30 or ≥27kg/m² and ≥1 weight-related comorbidity. This second interim analysis of a Phase 4 post-marketing study assessed medical appropriateness of prescribed PHEN/TPM ER by examining the total number of PHEN/TPM ER patients, their demographics, weight-related comorbidities, and concomitant medication over 18 months post-approval.

Methods: The purpose of this prospective, pharmacoepidemiologic database analysis was to determine the total number of PHEN/TPM ER patients, and to determine patient demographics. Data were collected from two databases; the Qsymia Certified Pharmacy Network (QCPN) database provided information on age and gender of all patients with ≥1 recorded PHEN/TPM ER prescription, while the Humedica Electronic Health Record (HEHR) database collected age, gender, race, BMI, weight-related comorbidities, and concomitant medication use. Data included in this analysis were acquired between 17 September 2012 and 28 February 2014.

Results: In total, there were 160,853 patients in the QCPN database and 5253 patients in the HEHR database. In the HEHR database, mean age was 47 years, 80% were female, 80% were Caucasian, 12% African American, 1.0% Asian, and 7% unknown/other. Mean age and gender collected from the QCPN database was similar. Mean BMI (kg/m²) in the HEHR database was 36 (84% had BMI ≥30 and 56% BMI ≥35) with <2% of patients having BMI ≤25. In the HEHR database, 42% had dyslipidemia, 39% had hypertension, and 19% had type 2 diabetes mellitus (T2DM). In addition, 49% were prescribed antihypertensive medications, 28% antidiabetic medications, and 23% antidepressants (including SSRIs and SNRIs). Among those patients with a BMI ≥35, 45% had dyslipidemia, 48% had hypertension, and 25% had T2DM.

Discussion: These data demonstrate consistencies between patient demographics, weight-related comorbidities, and concomitant medication use among real world patients...
prescribed PHEN/TPM ER, subjects randomized in the Phase 3 CONQUER clinical trial, and the labeled indication.  

**Conclusion:** Over 18 months post-approval by the US FDA, this analysis of database data indicates that medically appropriate individuals are utilizing PHEN/TPM ER as intended for chronic weight management.

**Abstract #615**

**HISPANIC PEOPLE ACHIEVE CLINICALLY SIGNIFICANT WEIGHT LOSS WITH LIRAGLUTIDE 3.0 MG FOR WEIGHT MANAGEMENT**

Patrick O’Neil, PhD1, W. Timothy Garvey, MD2, J. Michael Gonzalez-Campoy, MD, PhD, FACE3, Pablo Mora, MD, FACE4, Rafael Violante Ortiz, MD, PhD5, Birgitte Claudius, MD, PhD6, German Guerrero, MD7, Xavier Pi-Sunyer, MD, MPH8


**Objective:** The prevalence of overweight and obesity in the US is higher in the Hispanic/Latino population than in white individuals. Few data are available on weight-loss interventions in the Hispanic population, which may be less prone to weight loss using lifestyle intervention than the general population.

**Methods:** This post hoc analysis of pooled data from the 4 global Phase 3 randomized double-blinded SCALE trials (3 of 56 weeks’ duration, one 32 weeks) compared the efficacy and safety of liraglutide 3.0 mg vs. placebo, as adjunct to a reduced-calorie diet and physical activity, in Hispanic vs. non-Hispanic subgroups. The trials were conducted in adults who were overweight/obese with (n=844; 15.8%) or without (n=4500; 84.2%) type 2 diabetes (T2D). Ethnicity was self-reported.

**Results:** Baseline characteristics were: Hispanic (n=551, 76% female, age 41.5 years, weight 99.7 kg and BMI 37.1 kg/m2 [means]); non-Hispanic (n=4790, 70% female, age 47.6 years, weight 107.2 kg, BMI 38.0 kg/m2). Both subgroups achieved clinically significant mean weight loss at end of treatment with liraglutide 3.0 mg vs. placebo: Hispanic, -6.95 vs. -5.13% (ETD [-4.8] vs. [-3.3]; p<0.0001 for both, LOCF). In both subgroups more individuals lost ≥5% of their baseline weight in the liraglutide 3.0 mg group (56 and 61%) vs. the placebo group (16 and 24%) and more lost >10% weight with liraglutide 3.0 mg (28 and 31%) vs. placebo (4.6 and 8.6%) (p<0.0001 for all). The weight-loss effects were all independent of ethnicity (p>0.05). Improvements in systolic BP with liraglutide 3.0 mg vs. placebo were also comparable between Hispanic (ETD -2.9 mmHg, p=0.003) and non-Hispanic (ETD -2.9 mmHg, p<0.0001) subgroups. In individuals with overweight/obesity who had T2D (A1C ~7.9%), improvements in A1C were observed in both Hispanic (ETD -1.2%) and non-Hispanic (ETD -0.9%) subgroups with liraglutide 3.0 mg vs. placebo (p<0.0001 for both). The changes in systolic BP and A1C were independent of ethnicity (p>0.05). In the liraglutide 3.0 mg group, the proportions of people reporting adverse events (AEs) and serious AEs were similar for Hispanic and non-Hispanic individuals. Gastrointestinal events were reported more frequently with liraglutide 3.0 mg (67.4 and 67.7% for Hispanic and non-Hispanic) than placebo (33.2 and 40.0%) in both subgroups.

**Conclusion:** In the Hispanic subgroup (which comprised ~10% of the full population and tends to have higher rates of obesity), treatment with liraglutide 3.0 mg was effective. The treatment effects on efficacy and safety were consistent overall between Hispanic and non-Hispanic subgroups.

**Abstract #616**

**NECK CIRCUMFERENCE: CORRELATION WITH BODY MASS INDEX, WAIST CIRCUMFERENCE, WAIST HIP RATIO OF BANGLADESHI MEN AND WOMEN.**

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1. United Hospital Limited, 2. BIRDEM

**Objective:** To evaluate whether neck circumference(NC) correlate with body mass index(BMI), waist circumference(WC) and waist hip ratio(WHR).

**Methods:** This cross sectional observational study conducted with ethical permission, July 2013- June 2014, among randomly collected Bangladeshi male=496(56.9%), female=375(43.1%), aged >18 years, who visited OPD of United Hospital, BIRDEM, Primary centers of Gazipur and among healthy subjects of respective centers. Those having goiter, cervical lymphadenopathy, cystic or mass in neck or anatomical abnormality of neck, waist, hip, ascitis, organomegaly, intra- or extra-abdominal mass lesion, kyphosis, scoliosis, pregnant, severe co-morbid conditions were excluded. Primary outcome included NC in cm,WC and waist hip ratio(WHR).

**Methods:** This cross sectional observational study conducted with ethical permission, July 2013- June 2014, among randomly collected Bangladeshi male=496(56.9%), female=375(43.1%), aged >18 years, who visited OPD of United Hospital, BIRDEM, Primary centers of Gazipur and among healthy subjects of respective centers. Those having goiter, cervical lymphadenopathy, cystic or mass in neck or anatomical abnormality of neck, waist, hip, ascitis, organomegaly, intra- or extra-abdominal mass lesion, kyphosis, scoliosis, pregnant, severe co-morbid conditions were excluded. Primary outcome included NC in cm,WC and waist hip ratio(WHR).
to the long axis of the neck. BMI ≥ 23 overweight and BMI ≥ 27.5 obesity [(WPRO) of WHO]. HC >90 cm (male) and >80 cm (female) defined abdominal obesity. Data were collected in pre-formed record form, analyzed with IBM SPSS for Windows ver 20.

Results: 35.1% (men=31.9%, women=39.5%) were overweight and 9.2% (men=6.3%, women=13.1%) were obese. As per WC, 16.9% men and 49.1% women had abdominal obesity. As mean± SD, men had age (yrs): 30.81±10.24, height (m): 1.64±.06, weight (kg): 59.89±9.82, BMI (kg/m2): 22.17±3.23, SBP (mmHg): 116.17±12.44, DBP (mmHg): 75.84±7.72, WC (cm): 82.32±7.87, HC(cm): 90.20±6.90, WHR: 0.91±0.05 and NC (cm): 34.16±1.95. As mean± SD, women had age (yrs): 31.18±11.37, height (m): 1.56±.06, weight (kg): 57.02±9.21, BMI (kg/m2): 23.42±3.70, SBP (mmHg): 115.57±14.36, DBP (mmHg): 74.99±8.51, WC (cm): 81.62±9.20, HC(cm): 90.43±7.98, WHR: 0.90±0.065 and NC (cm): 32.50±2.20.

Pearson's correlation coefficient indicated significant positive association between NC and height (men, r=0.33; women, r=0.28; each, p <0.0001), weight (men, r=0.61; women, r=0.55; each, p <0.0001), BMI (men, r=0.51; women, r=0.41; each, p <0.0001), WC (men, r=0.61; women, r=0.46; each p <0.0001), HC (men, r=0.61; women, r=0.44; each p <0.0001), WHR (men, r=0.22; women, r=0.18; each p <0.0001) and SBP (men, r=0.09, p 0.03; women, r=0.16, p <0.001), DBP (men, r=0.16; women, r=0.19; each p <0.0001).

Discussion: NC was positively correlated with height, weight, BMI, WC, HC, WHR of Bangladeshi men and women (p<0.001).

Conclusion: NC can be a simple, potentially useful initial screening tool for evaluating upper body fat distribution, overweight and obesity.
ECOTOPIC PTH: A RARE CAUSE OF HYPERCALCEMIA IN MALIGNANCY

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Case Presentation: Hypercalcemia is seen frequently in the setting of malignancy. Hypercalcemia of malignancy from ectopic production of PTH is rare. We describe a patient with metastatic colon cancer who developed refractory hypercalcemia from this unusual cause.

58 year old male with complaints of abdominal pain and hematochezia was found to have a mass during colonoscopy. A biopsy was positive for malignancy. Upon initial staging there was no evidence of metastatic disease. He underwent surgery, and pathology revealed a high-grade adenocarcinoma of the colon. He received chemotherapy with FOLFOX.

Two months after completing chemotherapy he developed acute kidney injury and hypercalcemia. He had no previous history of hypercalcemia. At that time labs showed: calcium 16.1 mg/dL, phosphorus 1.9 mg/dL, albumin 3.9 mg/dL, creatinine 2.7 mg/dL and BUN 29 mg/dL. He was treated with IV fluids, calcitonin and bisphosphonates.

His work up included the following: PTH: 672.8 pg/ mL (14-72 pg/ mL), PTHrp: 0.93 pmol/L (<2 pmol/L), Vitamin D 25-OH 16.7 ng/mL (30-100 ng/mL), Vitamin D 1, 25-OH 26.4 ng/mL (10-75 ng/mL), 24 hr urinary calcium: 775.8 mg/24 hr. SPEP and UPEP were unremarkable. A parathyroid scan did not identify an enlarged parathyroid gland. Imaging studies showed new bilateral pulmonary nodules and a 9 cm right hepatic mass without any osseous lesions. Patient had IR guided core biopsy of liver mass, which was reported as high-grade carcinoma with focal neuroendocrine differentiation, compatible with colon primary. Pathology stained positive for PTH.

He began chemotherapy with carboplatin and etoposide. After his first cycle PTH levels trended down from 543.30 to 367.5 pg/ mL. Patient developed hypercalcemia requiring admission again in 2 occasions. The patient elected to pursue palliative care after second cycle of chemotherapy and expired 3 weeks after.

Conclusion: Hypercalcemia in the setting of malignancy is seen frequently due to osseous lesions, secretion of PTHrp or cytokines. In these settings the PTH level is usually suppressed. Hypercalcemia due to ectopic PTH production is uncommon. It has been described from tumors arising from different organs such as kidney, lung and pancreas. It’s less often reported in association to endocrine tumors. Our patient had colon cancer and presented with hypercalcemia with very elevated PTH levels. In some of the previously described cases the PTH and calcium levels improved after tumor removal, which was the source of the ectopic hormone production. Our patient did not undergo surgery for his liver lesion however PTH levels decreased after chemotherapy suggesting response to treatment.

PATIENTS WITH MCCUNE-ALBRIGHT SYNDROME ARE PREDISPOSE TO PANCREATIC CANCER? SHOULD WE SCREEN THEM FOR THAT?

Ricardo Correa, MD, Silvia Cuadra Mongalo, MD

1. NIH, 2. University of South Carolina

Objective: Describe association between McCune-Albright syndrome and the likelihood of presenting pancreatic cancer.

Case Presentation: 55-ya-male with McCune-Albright syndrome with multiple manifestations including polyostotic fibrous dysplasia, thyroid involvement, history of Leydig cell tumor, and cafe-au-lait spot presented with recurrent episodes of pancreatitis with a pancreatic cyst.

The patient’s history is significant for recurrent episodes of pancreatitis. The first one dates back to 1998 and a subsequent episode was documented in 2003. He recalls undergoing upper endoscopy that demonstrated pancreatic cysts. In this context, the patient denies a history of alcohol consumption or cholelithiasis. During the admission, liver function test and lipase and amylase were within normal limits. MRI abdomen plus MRCP showed dilatation of the extrahepatic common bile duct and pancreatic duct, with replacement of pancreatic parenchyma by dilated side branches or pancreatic cyst. These findings are concerning for intraductal papillary mucinous neoplasm (mixed type). An upper endoscopy with ultrasound of the pancreatic area was performed and multiple cysts were seen and biopsied. As per pathology report, there was mucin and CEA was 124, no malignancy identified on the cytology.

Discussion: Somatic activating GNAS mutations have been reported in various hepatobiliary and pancreatic neoplasm such as hepatocellular adenoma, hepatocellular carcinoma and pancreatic intraductal papillary mucinous neoplasm (IPMN). cAMP pathway is involved in the pathophysiology of this neoplasm. The prevalence of IPMN is poorly know but has been estimated to be only 25/100000. Idiopathic pancreatitis has been described in patients with MAS and could possibly be explained by IPMN, since mild pancreatitis is a classic mode of discover these neoplasm. In our patient, the pancreatic cyst was found because he had 2 episode of pancreatitis and imaging was performed. Sebastien G et al published a small observational study were they describe the new association between MAS and pancreatic neoplasm (IPMN). In that study, 32% of the patients were found to have hepatic, pancreatic or biliary lesions. 3 of 6 patients in the series had numerous branch-duct IPMN. That study strongly suggests that cAMP...
pathway is involved in IPMN tumorigenesis. Given the long-term malignant potential of IPMN, all MAS patients might be offered routine screening by MRI.

**Conclusion:** All detected lesions in MAS, should benefit from a multidisciplinary counseling and management with follow, biopsy and surgical indications should be advised. If no lesion is found, MRI might be performed every 5 years.

**Abstract #702**

**AN UNCOMMON CASE OF DISSEMINATED COCCIDIOIDOMYCOSIS ASSOCIATED WITH HYPERCALCEMIA**

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**Case Presentation:** Hypercalcemia is rarely associated with granulomatous diseases such as sarcoidosis, tuberculosis (TB), and other fungal infections. While it has been established that the mechanism for hypercalcemia in sarcoidosis and TB is driven by macrophages producing 1, 25-dihydroxyvitamin D, the pathogenesis for hypercalcemia in Coccidioidomycosis remains unclear. We present the case of a 51-year-old previously healthy female, who presented with altered mental status and flu-like symptoms for 4-8 weeks. MRI of the brain revealed multiple enhancing lesions consistent with meningo-encephalitis. She was diagnosed with disseminated Coccidioidomycosis based on a trans-bronchial biopsy which revealed necrotizing granulomas with fungal organisms consistent with Coccidioides antibodies in the serum. She was started on fluconazole. The hospital course was complicated with recurrent hypercalcemia. Her laboratory work-up showed; parathyroid hormone (PTH) 14.8 pg/mL (11-68 pg/mL), 25-hydroxyvitamin D 17ng/mL (30-100 ng/mL), 1, 25-dihydroxyvitamin D 60.1 pg/mL (10-75 pg/mL), parathyroid hormone-related peptide (PTHrP) <0.74 (<2 pg/mL), angiotensin-converting enzyme 32 U/L (14-82 U/L), urinary calcium 279 mg/24hrs (100-250 mg/24hrs), and SPEP/UPEP were negative. Tests for other causes of granulomatous diseases were negative. Her calcium normalized with saline, pamidronate, and calcitonin. She was discharged to a long term care facility due to chronic respiratory failure and was continued on the treatment for disseminated Coccidioidomycosis. She was readmitted 3 months later with increasing somnolence and severe hypercalcemia with corrected calcium of 14.3 mg/dL. Her laboratory work-up was unchanged from prior, and she was also found to have left sided nephrocalcinosis with a normal GFR. She was treated with normal saline, zolendronate, and prednisone. Her calcium improved to 11.8 mg/dL on the day of discharge.

**Conclusion:** This patient presented with recurrent non-PTH mediated hypercalcemia related to disseminated Coccidioidomycosis exacerbated by long term immobilization. The patient had a suppressed PTH, low 25-hydroxyvitamin D, normal 1, 25-dihydroxyvitamin D, and hypercalcuria which is consistent with other reported cases. The patient’s serum calcium normalized with normal saline and an IV bisphosphonate. This raises the question with a suppressed PTH, low PTHrP if there are other humoral or cytokine factors that are stimulating osteoclast bone resorption. We also raise the question if a high normal 1, 25-dihydroxyvitamin D in the setting of non-PTH mediated hypercalcemia is driven by overproduction by macrophages as seen in TB and sarcoidosis.

**Abstract #703**

**AN ADULT PATIENT WITH SEVERE HYPOCALCIURIC HYPERCALCEMIA WITH NEGATIVE CASR GENE MUTATION**

*Grace Kim, MD, Michael Marchese, MD, Hassan Shawa, MD, Matthew Leinung, MD, Sara Clark, MD*

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**Objective:** Familial hypocalciuric hypercalcemia (FHH) is an autosomal dominant disorder with 3 known subtypes. 2/3 of the cases are associated with a heterogeneous germline-inactivating mutation in the CaSR gene leading to its hallmark features of hypercalcemia, nl/elevated PTH and reduced FEca <0.01. FHH type 2 and 3 are associated with mutations in the GNA11 or AP2S1 gene, respectively. In up to 10% of FHH patients, genetic screening can be false negative. While hypercalcemia is usually mild in FHH, severe hypercalcemia mimicking primary hyperparathyroidism (PHPT) has been reported. FHH’s treatment differs from PHPT as parathyroidectomy is not indicated in FHH.

**Case Presentation:** We present a 66-yo Caucasian F with PMHx of HTN, congenital solitary kidney and PTH-mediated hypercalcemia. She was initially diagnosed with PHPT in 1994 after presenting with hypercalcemia and nephrolithiasis resulting in a L. inferior parathyroidectomy. Pathology was consistent with parathyroid adenoma. She subsequently developed recurrent hypercalcemia (13.5 mg/dL), elevated PTH (735 pg/mL) and clinical symptoms. Sestamibi scan and neck ultrasound were negative, but MRI neck revealed a possible left parathyroid adenoma near the L. sternocleidomastoid muscle. Neck exploration was performed in Dec-2013 but the proposed adenoma could not be identified. Consequently, the three remaining glands were removed but intraoperative PTH did not drop. In May 2014 another neck exploration was performed. A
left inferior parathyroid adenoma was re-identified and removed resulting in >50% drop in the intra-operative PTH and normalization calcium level. A month later, she developed recurrent PTH-mediated hypercalcemia with Calcium of 11.6 mg/dL, ionized Ca. 1.58 and PTH 215 pg/mL, with associated 25 OH Vit D level of 23.8 ng/mL, 1,25 OH Vit D level of 40 pg/mL, phos 3.2 and a 24 hr urine calcium of <37 mg/24hr on 2 separate occasions with a FEca <0.01. 4D CT neck in Oct-2014 revealed 2 hyperenhancing nodules suspicious for parathyroid tissue. CaSR mutation was found to be negative. Further genetic testing for the GNA11 and AP2S1 gene is being processed. Patient is currently managed with Cinacalcet 30 mg TID and Zolendric acid infusions.

Conclusion: This patient’s biochemical testing was consistent with FHH. However, the clinical picture is atypical for heterogeneous and more consistent with homozygous inactivating mutation. This case highlights the importance of checking 24-hour urinary calcium while approaching PTH-mediated hypercalcemia cases even in settings of severe hypercalcemia. Genetic testing can be helpful in confirming the diagnosis. However, novel mutations may not be detected in the traditional CaSR gene sequencing.

Abstract #704

HEMATOCHEOZIA IN A CHILD WITH TURNER SYNDROME TREATED WITH TRANSDERMAL ESTROGEN PATCH: A CASE REPORT

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Objective: Children with Turner syndrome (TS) are at increased risk of gastrointestinal arteriovenous malformations and telangiectasias. While gastrointestinal bleeding in patients with TS is relatively rare, it does occur in approximately 7% of patients. Two case reports have been published using oral contraceptive pills (OCPs) and/or conjugated estrogen as a means of treating gastrointestinal bleeding in adolescents with TS. We present the first case of a prepubertal 10 year old girl with TS who presented with hematochezia and was successfully treated with transdermal estrogen patch.

Case Presentation: The patient had a 1 day history of non-bloody, non-bilious emesis and abdominal pain followed by dark red hematochezia, likely secondary to viral gastroenteritis as her sibling had a similar illness without GI bleed. This was followed by another episode of frank bright red blood per rectum prompting admission. The patient was made NPO, given IV hydration, proton pump inhibitors, and treated with 12.5 mcg estradiol patch. Colonoscopy performed four days later was normal. Her hematochezia resolved on estrogen therapy and there have been no further episodes of bleeding. She did not develop breast or vaginal bleeding while using the estradiol patch.

Conclusion: Previous case reports have shown successful treatment of gastrointestinal bleeding with Premarin, and OCPs in pubertal children. There have also been reports of equivalent efficacy between the estradiol patch and conjugated estrogen. The estradiol patch is more physiologic, which likely contributes to its effectiveness. Our case is unique in that we had to consider the risks and benefits of treating with estrogen in a growing, prepubertal child with very short stature (SD -2.98) given that estrogen closes the epiphyseal growth plates, initiates puberty, and increases the risk of thrombosis. We used the lowest dose possible, 12.5 mcg estradiol patch (half of a standard patch) with no resulting breast development or other signs of estrogen effect; indicating this was effective in controlling the GI bleeding without causing adverse effects. To our knowledge, this is the first known case of a young, prepubertal patient with TS and GI bleed to be treated with transdermal estrogen.

Abstract #705

AUTOIMMUNE LIMBIC ENCEPHALITIS ASSOCIATED WITH ANTI-GAD ANTIBODIES

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Case Presentation: A 30 year old female with no significant past medical history presented in 2012 with 2 years of gradually worsening anterograde amnesia affecting her school grades and routine. She was diagnosed with simple partial seizures a year later. There was no history of headaches, anxiety, muscle weakness, paresthesias or numbness in the extremities. Physical examination was unremarkable except for diminished memory and difficulty remembering objects. Brain MRI revealed an infiltrative non-enhancing mass involving the posterior temporal lobe on the left side extending to the hippocampus/amygdala complex. A PET CT scan of the brain indicated an infiltrative hypermetabolic lesion involving the left hippocampus. A brain biopsy done to rule out malignancy showed evidence of limbic encephalitis. An autoimmune work up was positive for very high levels of Anti-GAD antibodies (>5000 U/ml) in serum, CSF also showed high anti-GAD levels. Incidentally, PET scan also revealed an increased foci uptake in the thyroid gland. A thyroid sonogram reported multiple nodules in the thyroid and subsequent fine needle aspiration of dominant nodule
was suggestive of papillary thyroid cancer. She underwent a total thyroidectomy and was found to have four foci of micro papillary carcinoma, largest being 7 mm with no evidence of capsular, vascular or lymph node invasion. For treatment of persistent memory of loss associated with high GAD65 antibody in serum and CSF the patient underwent plasmapheresis treatment with no significant improvement. The patient is currently on intra-venous immune globulin treatment every three weeks for more than a year with modest improvement in her anterograde amnesia. Her anti-GAD levels have improved significantly between 80-150 U/ml range on most recent evaluations.

**Discussion:** Limbic encephalitis is usually paraneoplastic, but rarely has been associated with auto-antibodies like anti-GAD, anti-NMDA and anti-VGKC complex. In a recent large prospective review of 138 patients with etiologically unclear recent-onset epilepsy, 53 patients were identified to have limbic encephalitis, 9 patients had GAD positivity and 9/9 presented initially with seizures. The case presented therefore represents a rare presentation of nonparaneoplastic autoimmune limbic encephalitis (NPALE) with severe memory loss; partial seizures developed only during later stage of the disease.

**Conclusion:** Autoimmune limbic encephalitis is a rare condition, however should be in our differential diagnosis in adults patients with encephalopathy; therapeutic responsiveness of this condition reiterates the importance of the diagnosis and timely intervention to avoid permanent cognitive deficits.

**Abstract #706**

**DIFFERENTIATING BENIGN PRIMARY HYPER-PARATHYROIDISM FROM PARATHYROID CARCINOMA: A CHALLENGING DIAGNOSIS.**

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The Ohio State University Wexner Medical Center

**Objective:** Parathyroid carcinoma is a rare disease with a high rate of local recurrence but prolonged survival. However, differentiating between parathyroid adenoma and carcinoma can be difficult.

**Case Presentation:** A 66 year old African female was referred to the Emergency Department for calcium 17.5 mg/dL (reference range, 8.6-10.5) on outpatient labs. She endorsed severe fatigue, bone pain, and intermittent episodes of sharp abdominal pain. She denied urinary difficulty but reported a history of nephrolithiasis. A large right neck mass was palpable without tenderness or erythema that she reported was stable in size.

Two years ago, workup for hypercalcemia in Ghana showed an intact PTH (iPTH) of 971 pg/ml, and CT neck showed an enhancing mass in the right thyroid lobe. She had previously been treated with weekly alendronate. There was no known family history of calcium or thyroid problems. On admission, tests revealed calcium 16.0, iPTH 1374.8 pg/ml (14.0-72.0), ionized calcium 8.5 mg/dl (4.60-5.30), phosphorous 2.2 mg/dl (2.2-4.6), and normal renal and thyroid function tests. She was treated with intravenous fluids, calcitonin, and one dose of IV zoledronic acid. Calcium trended down to 9-10 mg/dL. Thyroid ultrasound confirmed a heterogeneous intrathyroidal mass measuring 3.0x3.8x4.7 cm with variably increased vascularity. A 99m-technitium Sestamibi scintigraphy with single proton energy computerized tomography showed a radiotracer avid mass within the right thyroid lobe which persisted on 2 hour imaging measuring 3.9x3.9x5.1 cm. Biopsy was deferred and she underwent right hemi-thyroidectomy via an en-bloc resection. During surgery, no extrathyroidal parathyroid glands were identified on the right side and there was no overt invasion of the firm mass into surrounding tissues. Intraoperative iPTH decreased from 1235.3 to 126.5 pg/ml over 12 minutes. She developed mild post-operative hungry bone syndrome responding to 2.4 g elemental calcium daily. The tumor measured 4.4 cm and microscopic examination revealed unequivocal areas of capsular invasion but without areas of angiolymphatic invasion. Final diagnosis was an atypical parathyroid adenoma with uncertain malignant potential. She remains on calcium supplementation with close outpatient follow up.

**Conclusion:** Our patient has numerous clinical features suggestive of parathyroid carcinoma, including markedly elevated calcium and PTH levels, palpable neck mass, skeletal and renal involvement, and capsular invasion. It is crucial to consider the full clinical presentation, laboratory tests, and imaging studies to determine likelihood of malignancy, extent of surgical resection, and need for long term follow up.

**Abstract #707**

**WHEN IMAGING FAILS: PREOPERATIVE SELECTIVE VENOUS SAMPLING TO LOCALIZE OCCULT PARATHYROID ADENOMA CAN SUCCESSFULLY FACILITATE FOCUSED PARATHYROIDECTOMY**

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University of Kansas Medical Center

**Objective:** To describe the utilization of selective venous sampling to precisely locate an occult parathyroid adenoma in a case of elusive primary hyperparathyroidism with negative imaging
**Case Presentation:** A 52 year old female with a history of hypertension and type 2 diabetes mellitus presented with recurrent nephrolithiasis. Hypercalcemia and elevated PTH was noted during her acute nephrolithiasis workup. Unfortunately, neck ultrasound, sestamibi scan, and 4D CT neck failed to localize a parathyroid adenoma. Given high clinical suspicion of primary hyperparathyroidism, the patient was referred for selective venous sampling for parathyroid adenoma localization. Venous samples were obtained from her bilateral proximal, mid, distal jugular veins, middle thyroid vein, bilateral facial veins, and branches of innominate vein including thymic vein. This proved successful in localizing a gradient of over 1000 to the left lower neck in the proximal jugular vein. She underwent a subsequent focused left parathyroidectomy with intraoperative ultrasound and parathyroid hormone monitoring. After a left inferior parathyroid adenoma was removed, PTH levels decreased from 1735 pg/mL at baseline to 22.0 pg/mL at 5 minutes, 14.9 pg/mL at 10 minutes, and 13.1 pg/mL at 15 minutes. At follow up her calcium normalized and she has not demonstrated further nephrolithiasis.

**Discussion:** Primary hyperparathyroidism is a common disease encountered with incidence of 66 (female) and 25 (male) per 100,000 patients. It is usually caused by a solitary benign adenoma in 80-85% of cases. Multiple pre-operative localization techniques are available to identify the over functioning adenoma. 99mTc-sestamibi scintigraphy does not preclude primary hyperparathyroidism in 12-25% of patients. Sestamibi single photon emission computed tomography (SPECT) identifies abnormal parathyroid gland 96% of adenomas. Neck ultrasound is highly a sensitive study in experienced centers. 4-D computed tomography is particularly useful in the reoperative setting after initial negative imaging. Currently there are few recent case reports describing use of preoperative selective venous PTH sampling to identify primary hyperparathyroidism when imaging fails to localize an adenoma when searched through standard databases. Importantly, this diagnostic provides an option for preoperative evaluation of primary hyperparathyroidism when clinical suspicion is high despite negative non-invasive imaging studies.

**Conclusion:** Preoperative venous sampling provides a novel approach in the preoperative evaluation of primary hyperparathyroidism when clinical suspicion is high but traditional imaging techniques fail to localize a parathyroid adenoma.
the differential diagnosis of CDI and hypothalamic-pituitary dysfunction. Evaluation with MRI brain, TSH, free T4, prolactin, testosterone (males), LH, FSH, morning serum cortisol, and urine osmolality is warranted for all patients with ECD. Endocrinologists need to participate in the multidisciplinary team for diagnosis and treatment of ECD.

Abstract #709

E-CONSULTS: A NOVEL APPROACH TO INCREASE ACCESS TO SUBSPECIALTY CARE IN ENDOCRINOLOGY

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Mayo Clinic

Objective: Mayo Clinic instituted the concept of electronic consults (E-consult) in 2012. E-consults can be ordered by Mayo physicians to address targeted clinical questions in both medical and surgical subspecialty fields without the need for the consultant to physically meet with the patient. This study reviews the use of E-consults in the division of endocrinology for the last 3 years.

Methods: The Mayo Clinic electronic health record for the Florida campus was queried for all E-consults ordered for the division of endocrinology between January 2012 and December 2014. Orders required a clinical diagnosis subcategory and a clinical question to be entered. Categories included thyroid, osteoporosis, calcium/parathyroid, pituitary, lipid, and “other” disorders. Endocrinology consultants reviewed the electronic chart including available notes, labs, imaging, and pathology to answer the clinical question. Recommendations were then placed in the chart in <48 hours, including a recommendation for an in person consultation if appropriate. Charts were reviewed for follow up of recommendations as well as occurrence of in person consultations. All consultants were surveyed on the average time spent on the E-consult process.

Results: 273 E-consults were placed between 2012 and 2014 which resulted in a total of 51 in person consults. The number of E-consults doubled from 2012 to 2014. The majority of E-consults were thyroid (40%) or osteoporosis related (15%) and the lowest number was in lipids. Clinical questions included evaluation/follow up for thyroid nodules, evaluation of hypercalcemia, use of osteoporosis medications and testosterone replacement. Most of the e-consults were ordered by primary care providers (PCP) and consultants on average spent about 30 minutes for each E-consult.

Discussion: Currently there is a shortage of nearly 1500 adult endocrinologists in the United States to accommodate the demand for services due to the rise of chronic diseases. The current wait time for an endocrinology consultation often ranges from weeks to months. E-consults provide benefits to both the patient and the PCP including faster access to subspecialty care, potential reduction in health care costs, more targeted referrals, and transfer of information. They can be used as a method to help improve subspecialty access in the setting of the shortage of endocrinologists. Given the repetition of some clinical questions, E-consult data can be used to develop educational information for referring providers.

Conclusion: E-consults appear to reduce the need for in person physician consultations by >80%, provide benefits to both patients and primary providers and can be used as an approach to help deal with limited access to subspecialists.

Abstract #710

IMPACT OF ETHNIC BACKGROUND ON CLINICAL CHARACTERISTICS AND CARDIOVASCULAR RISK FACTORS AMONG PATIENTS WITH PRIMARY HYPERPARATHYROIDISM

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Rutgers Robert Wood Johnson Medical School

Objective: To compare metabolic characteristics and cardiovascular risk factors (CVRF) among patients with primary hyperparathyroidism (PHPT) from different ethnic backgrounds.

Methods: In this retrospective study, 500 charts of patients with PHPT were reviewed. 46 African Americans (AA), 31 Asians (A), 19 Hispanics (H) and 404 Caucasians (C) were included. The following characteristics were compared between the four groups at initial presentation to endocrinology or surgery clinic: BMI, serum calcium, iPTH, 25(OH)D, 24-hr urine calcium and parathyroid adenoma weight. CVRF including BMI, DM and HTN were also used for comparison. χ2 test and ANOVA test were used for comparison.

Results: Adjusted for age and gender, AA have lower mean 25(OH)D (20.4ng/mL vs 29.7ng/mL, P<0.05) and higher iPTH (189.8pg/mL vs 158.3pg/mL, P<0.05) compared to C. AA also tend to have higher serum Ca (11.3mg/dL vs 11.1mg/dL) and lower 24-hr urine Ca (309.9mg/24hr vs 369mg/24hr) when compared to C, but these differences were not significant. The adenoma weight is heavier in AA (1.7g) compared to C and A (1g and 0.6g, P<0.05). Similar to AA, H also have lower 25(OH)D, 24-hr urine calcium and parathyroid adenoma weight. CVRF including BMI, DM and HTN were also used for comparison. χ2 test and ANOVA test were used for comparison.

Results: Adjusted for age and gender, AA have lower mean 25(OH)D (20.4ng/mL vs 29.7ng/mL, P<0.05) and higher iPTH (189.8pg/mL vs 158.3pg/mL, P<0.05) compared to C. AA also tend to have higher serum Ca (11.3mg/dL vs 11.1mg/dL) and lower 24-hr urine Ca (309.9mg/24hr vs 369mg/24hr) when compared to C, but these differences were not significant. The adenoma weight is heavier in AA (1.7g) compared to C and A (1g and 0.6g, P<0.05). Similar to AA, H also have lower 25(OH)D 24.7ng/mL, higher iPTH 178.6pg/mL when compared to C, but these findings were not significant. iPTH was 167.7pg/mL, serum Ca
Objective: Neuroendocrine tumors (NETs) are neoplasms of enterochromaffin cell origin; these neoplasms are often slow-growing and can cause a variety of nonspecific symptoms. The annual incidence of NET is 8.4 per 100,000; yet many of these tumors remain asymptomatic and are often found after metastasis has occurred. The aim of this study was to investigate the clinical characteristics and predictors of survival in primary colorectal NETs.

Methods: We reviewed the records of all patients (pts) diagnosed with colorectal NET at our institution from 2000 to 2013. Demographics, tumor characteristics, recurrence and survival were analyzed. Kaplan-Meier and Cox regression were used for survival and multivariate analysis.

Results: A total of 27 pts with primary colorectal NET were identified. Mean age at diagnosis was 61 years (23-86). There was a higher prevalence in females than males (67% vs. 33%, p<0.03). The most common initial presentations were: gastrointestinal bleeding (28%), weight loss (20%) or abdominal pain (11%). Pts were more likely to have recto-sigmoidal tumors than all other tumor locations combined (71% vs. 29%, p<0.006). Only 36% of the NETs were >2cm in diameter. Regarding histologic grade, 74% were poorly differentiated vs. 26% were well to moderately differentiated tumors (p<0.001). At diagnosis, 55% (15) of the pts were stage IV; with liver (68%) representing the most common site of distant metastasis. 63% of the pts underwent surgery with 47% of the pts having positive margins after resection. Median overall survival was 58 months (95%CI: 37-78). There was a significant difference in survival upon tumor location, being 74 months for recto-sigmoidal tumors (95%CI: 47-102) and 38 months for right-sided tumors (95%CI: 12-63), p<0.03. Female gender (OR: 0.14, p<0.02), negative margins (OR: 0.18, p<0.04) and tumor location (0.41, p<0.0001) were independent predictors of survival by multivariate analysis. In 59% (16) of the pts, this cancer was the primary cause of death.

Discussion: In our cohort, we observed that colorectal NETs are very aggressive malignancies, as evidence by 55% presenting at stage IV and being the primary cause of death in 59% of the pts. Tumor location was a detrimental factor in survival. Overall, right sided tumors survival was 35 months less when compared with recto-sigmoidal tumors. This difference in survival could be explained by the early onset of symptoms in recto-sigmoidal tumors, due to decreased left colonic diameter.

Conclusion: Presentation of NETs tends to be very unspecific, making diagnosis in an early stage a challenge. Further research should aim to elucidate the basis of these differences, as this could potentially impact management and improve survival.

Abstract #712

ASSESSMENT OF THE PRACTICE, COMFORT LEVEL AND KNOWLEDGE AMONG ENDOCRINOLOGISTS CARING FOR CHILDHOOD CANCER SURVIVORS - A SURVEY STUDY

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Objective: To assess the practice, comfort and knowledge level of endocrinologists in their care for childhood cancer survivors (CCS), specifically evaluating their awareness
of Long Term Follow-Up (LTFU) guidelines. 

**Methods:** After IRB approval, a web based RedCap survey was sent via email to the members of Pediatric Endocrine Society and American Association of Clinical endocrinologists. Responses to the 19 survey questions (5 on demographic data, 10 on provider characteristics, and 4 based on 2 clinical vignettes) were captured anonymously.

**Results:** During the 6 weeks when our study was open, 294 surveys were received of which 274 were complete/near-complete. Among the survey respondents, 231 (84%) were Pediatric Endocrinologists (PE) following either predominantly pediatric patients or a mixture of both pediatric and adult patients, and 43 (16%) were Adult Endocrinologists (AE) having predominantly adult patients in their practice. Of these, 78% of PE vs. 35% of AE practiced in academic institutions; 64% of PE vs. only 19% of AE currently followed 6 or more CCS in their practice; 54% of PE reported having an endocrine focus clinic for CCS while none of the AE reported having such a focus clinic in their practice (all p values < 0.001). Fertility issues and sex steroid deficiency were identified by more than 70% of both pediatric and adult endocrinologists as the most challenging to address in CCS. Overall, AE reported significant lack of adequate training and confidence in caring of CCS and majority (84% AE vs. 16% PE) reported lack of awareness of the LTFU guidelines (p<0.0001).

For clinical vignette questions, 76% of PE vs. 50% of AE (p=.001) correctly recognized GH as the most susceptible to cranial radiation (CR), and 28% vs. only 13% recognized the ovarian failure risks (p=0.048). There were no significant difference between PE and AE in % of correct responses for questions regarding evaluation for hypopituitarism following CR (38% vs. 23%), and male fertility/ hypogonadism risks following cancer therapy (39% vs. 31%).

**Discussion:** AE in our survey report lack of adequate training and confidence in caring for CCS compared to PE. This could be attributed to differences in practice setting (academic vs. private), years since completion of training, number of CCS followed, and presence of endocrine focus clinic for CCS care in their practice. AE also had higher % of incorrect responses to 2 out 4 clinical vignette questions compared to PE.

**Conclusion:** About 1:640 young adults living in the U.S are CCS, of whom ~40% will have one or more endocrine disorder. It is essential to incorporate adequate training and resources among endocrinologists to empower them in their care for CCS.
received little attention, they can cause much distress and may induce a variety of psychosocial reactions. It should be considered as a possible causative factor in patients complaining of body malodor.

Abstract #714

SEVERE PRIMARY HYPERPARATHYROIDISM WITH CYSTIC PARATHYROID GLAND

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Case Presentation: 34 y/o F presented with 1 mo h/o of headache, polyuria and polydipsia. She had a palpable R thyroid nodule. Ca 13.3 mg/dl(8.6-10.2), albumin 3.9 g/dl(3.6-5.1), corr Ca 13.4,P 1.2 mg/dl(2.5-4.5),Alkp 127 U/L(33-115), Cr 0.69, GFR 114, ionized Ca 6.5,PTH 314 pg/ml(10-65), 25 OH vit D 21 ng/ml(30-100). She was treated with IVF, IV furosemide and IV pamidronate for hypercalcemia from primary hyperparathyroidism(PHPT). US neck showed R mid thyroid cystic nodule 2.1x1.6x1.6 cm and mixed echogenic nodule in R inf thyroid 2.1 x 1.7 x 1.9 cm, with several hypoechoic areas suggesting cystic changes. No parathyroid gland was seen in typical location; L thyroid lobe was normal. Sestamibi scan showed focus of increased activity in R inferior thyroid. She underwent USGFNA of both nodules to rule out malignancy preop. FNA cytology showed clusters of parathyroid cells consistent with parathyroid hyperplasia in R inf nodule and was non-diagnostic in R mid nodule. PTH needle washout was sent to confirm the location given the atypical imaging phenotype. iPTH from FNA 900 and 3 pg/ml for inferior and mid nodules respectively. She underwent R hemi-thyroidectomy with parathyroid gland removal avoiding cyst rupture. Pathology showed nodular goiter and hyperplastic parathyroid without atypical features. PTH postop day 1 was 13.

Discussion: Parathyroid adenoma normally appears as well defined, homogenous, hypoechoic, oval lesion on US typically posterior to thyroid(1). Cystic parathyroid lesions (CPL) are very rare and only 300 cases are reported. In the largest published series of patients undergoing para-thyroidectomy for PHPT, CPL was found in 3%. CPL are functional parathyroid cysts or non-functional parathyroid cysts and can be differentiated by PTH from FNA. Functional parathyroid cysts are often due to cystic degeneration of an adenoma and rarely hyperplasia, as was in our case. Care should be taken not to rupture CPL’s during surgery to facilitate complete resection and avoid parathyromatosis. Cyst rupture can cause elevated initial post resection intra-op PTH and can prolong surgery(2).

Conclusion: CPLs are an uncommon finding in patients undergoing parathyroidectomy for PHPT. US and USGFNA are sensitive tools to diagnose these lesions preop. Cyst rupture should be avoided during surgery to avoid parathyromatosis and skewed elevation of intraop PTH. Atypical parathyroid adenomas (US phenotype: heterogenous echogenecity, cystic change, calcification) are associated with higher incidence of malignancy and should be monitored closely.

Abstract #715

MAGNETIC RESONANCE IMAGING (MRI) INDUCED VERTIGO

Andrew Fong, Ankur Gupta, MD
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Objective: We report a case of vertigo that began during a brain MRI and continued post imaging. MRI induced vertigo has been previously described in the literature. Several mechanisms have been postulated but the cause is unknown.

Case Presentation: A 75-year-old man underwent a pituitary protocol MRI for evaluation of central hypogonadism. During the MRI procedure, the patient experienced the onset of the sensation of the room moving and disorientation accompanied with nausea. The patient started having episodes of disequilibrium and room spinning that could last for up to an hour daily. The symptoms were worst during first 24 hours after the MRI. The patient denied ear pain or discharge. The patient denied history of vertigo. He does have a history of hearing loss and waterfall like tinnitus that began in 1959 after the loud noise injury from extensive radio telephone use in 1959.

During physical examination the patient had vitals within normal limits and a neck examination was unremarkable. Both ears had a normal external and internal auditory canal. The patient’s tympanic membranes were gray and in neutral positions without effusions. The Dix Hallpike maneuver was performed showing a positive result with the head to the left. The Epley maneuver was performed twice and showed nystagmus in all positions which became milder with repetition. Cranial nerves II through XII were found to be normal without any deficits. He was evaluated by ENT and was recommended vestibular exercises.

Discussion: MRI induced vertigo can be produced by the effect of magnetic fields in the inner ear during and/or after the imaging. The mechanism is unknown. Zee et al., 2011, indicated that the interaction between magnetic field and naturally occurring ionic currents in the labyrinthine endolymph fluid could result in generation of Lorentz force. This force can lead to nystagmus and vertigo by
exerting pressure on the semi-circular canal cupula. The patient in our case had no prior history of vertigo and had onset of vertigo symptoms during his MRI procedure. He had a positive Dix Hallpike maneuver upon subsequent examination. Alternatively, positioning during the MRI could have caused cervicogenic vertigo with history of degenerative disc disease in the cervical spine.

**Conclusion:** MRI induced vertigo is under-recognized. Clinicians should be aware of this potential complication of the MRI.

**Abstract #716**

**THE VASOPRESSIN WITHDRAWL SYNDROME**

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**Objective:** To report a case of massive polyuria and increasing serum sodium after withdrawal of vasopressin infusion in a patient after shock.

**Case Presentation:** 33 year old male with nonischemic cardiomyopathy, depression and bipolar disorder initially presented to an outside hospital with confusion and multiple falls for one day. Patient’s mother reported that he might have overdosed on one of his home medications. On initial evaluation systolic blood pressure was found in the 40s. He was given 7 L of intravenous fluids. Due to the concern for beta blocker toxicity he was started on glucagon and insulin drip. He was transferred to our hospital on dopamine, levophed and vasopressin for pressure support. Levophed and dopamine was slowly weaned off and vasopressin infusion was continued for 3 days. Serum sodium on day 2 dropped down to 122 from 133 on admission. Serum osmolality at that time was 262, urine osmolality was 692 and urine sodium was 187. Hypertonic saline was started for hyponatremia. Vasopressin infusion was withdrawn over 8 hours. Within 3 hours of discontinuing vasopressin infusion patient’s urine output increased to more than 1 liter per hour without any medication changes, and oral fluid intake was around 50 to 250 mL per hour. No diuretics had been administered for at least 24 hours. On hypertonic saline serum sodium increased to 129 over 24 hours. During excess urine output, serum sodium increased from 129 to 136. Serum osmolality and urine osmolality were not checked at that time. The excretion of large volume of dilute urine with increasing serum sodium was consistent with diabetes insipidus. On administration of 1 mcg of DDAVP, urine output decreased to 75-150 per hour suggesting the diagnosis of central diabetes insipidus. Patient received DDAVP for a total of 2 days before resolution.

**Discussion:** In this report, we speculate that the withdrawal of vasopressin infusion resulted in a transient form of central diabetes insipidus, causing polyuria and increasing serum sodium level. The occurrence of transient diabetes insipidus could have been secondary to the negative feedback inhibition of the endogenous vasopressin production and release. Or endogenously synthesized vasopressin in this patient might have been depleted because of increased demand from the prior hypovolemic state, and withdrawal of exogenous vasopressin unmasked this deficit.

**Conclusion:** This case emphasizes the need to consider the very uncommon occurrence of central diabetes insipidus after vasopressin withdrawal and early intervention to prevent hypernatremia.

**Abstract #717**

**ECTOPIC ACTH FROM BRONCHIAL CARCINOID PRESENTING AS DEXAMETHASONE SUPPRESSIBLE CUSHING’S SYNDROME**

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Cooper University Hospital

**Objective:** Bronchial carcinoids are among the most common causes of ectopic ACTH syndrome (EAS). High dose dexamethasone suppression test usually points to pituitary Cushing’s syndrome. We present a rare case of dexamethasone suppressible Cushing’s syndrome from bronchial carcinoid.

**Case Presentation:** A 36 year-old 5’4”, 179 lbs African American woman with recent onset of type-2 diabetes and hypertension, who initially presented to ER for palpitations and shortness of breath. She had negative cardiopulmonary workup but revealed a stable 10 mm centrally located right upper lung nodule (compared to prior CT scan in 2012). Subsequent referral to endocrine clinic revealed cushingoid woman with hyperglycemia, central hypothyroidism, and normokalemia. Biochemical workup revealed elevated 24 hr urine free cortisol 250-300ug/24hr, late night salivary cortisol 0.477-0.951ug/dL with baseline morning cortisol 29.7ug/dL and elevated ACTH 167pg/ml, and failure to suppress with 1 mg dexamethasone suppression test. Her plasma cortisol suppressed after overnight 8 mg dexamethasone to 5.6ug/dL. MRI of pituitary gland showed possibility of 1-2mm lesion. She was started on ketoconazole, insulin and metformin. She underwent PET CT scan which did not show abnormal activity in lung lesion. Repeat MRI pituitary with 3-Tesla magnet did not reveal any definite pituitary lesion. Given difficult to biopsy central location of the pulmonary nodule, she underwent robotic assisted thorascopic wedge
The objective is to analyze the Endocrine disorders seen in our clinic and compare the pattern with that seen about a decade earlier. There is no difference in the pattern of Endocrinopathies seen in the Lagos University Teaching Hospital’s Endocrine unit over a 10 year period.

Methods: This was a review of Endocrinopathies recorded in the register of the Endocrine clinic of Lagos University Teaching Hospital, Lagos, Nigeria. All patients referred to the Endocrine service and whose records appear in the register were included in the analysis. Patients with Diabetes Mellitus were excluded from this analysis. Information sought included age, sex, anthropometric indices and type of Endocrinopathies. Statistical analysis was done using SPSS version 17.

Results: Four hundred and forty eight cases were seen during the period of review (68 males, 380 females). Male to female ratio was 1:5.6. The (SD) age was 45.10 ± 6.67 years. Minimum age was 11 years while maximum age was 86 years. Thyroid disorders were the commonest accounting for 86.8%.

Graves’ disease was 52.0%, Nodular goitre 21% and Hypothyroidism 13.8%. Dyslipidemia and diseases of the pituitary ranked next, accounting for about 3.5% each.

The was followed by Addison’s disease 1.8%, Bone disease 1.1%, Metabolic syndrome 0.9%, Phaeochromocytoma 0.7%, Reproductive disorder accounted for 0.6%, Obesity 0.2%. Uncommon Endocrinopathies seen include Precocious puberty, Intersex and Achondroplasia.

Conclusion: Excluding Diabetes Mellitus, Thyroid disorders were the most common Endocrinopathies seen in the Lagos University Teaching Hospital Endocrine clinic with Graves’ disease being the most frequent thyroid disorder.

Most other Endocrine disorders are not frequently seen. This may be due to high threshold for referral of Endocrine cases to specialist centres. Subspecialization in Endocrinology may also encourage diagnostic awareness.

Abstract #719

LATE DEVELOPMENT OF PARATHYROID HARMON DEPENDENT HYPERCALCEMIA IN A PATIENT WITH SEPSIS

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Objective: Critical surgical illness, accompanied by shock, sepsis, multiple transfusions and renal failure, is commonly associated with low total serum calcium and low / normal ionized calcium, with resultant compensatory increases in parathyroid hormone (PTH) secretion. Two previous case series have, however, identified subsets of such critically ill patients who developed overt hypercalcaemia accompanied by frankly elevated PTH levels characteristic of primary hyperparathyroidism. We recently observed such a case of acute development of apparent primary hyperparathyroidism in a patient with a bowel perforation and sepsis.

Case Presentation: A 71-year old woman was admitted to the ICU with acute abdominal pain having medical history of hypertension, coronary artery disease, sleep apnea, atrial fibrillation, and hypothyroidism. A left knee prosthetic joint replacement had been removed because of recurrent
infection. She had no known history of hypercalcemia, renal stone, peptic ulcer disease or osteoporosis. On admission, CT imaging revealed that mesh from a previous ventral hernia repair had migrated, causing a bowel perforation. She underwent laparotomy and repair. In the post operative period she developed E. coli sepsis, thrombocytopenia and enterocutaneous fistula. She was treated with aggressive fluid resuscitation and broad spectrum antibiotics. During the first eighteen days of her hospital course serum calcium levels (corrected for hypoalbuminemia) were normal. Her total serum calcium then progressively rose to a maximum corrected value of 12.6 mg/dl. PTH level at that time was 165 pg/ml (normal: 7.5-53.5) and repeat testing confirmed elevated PTH and calcium (both corrected total values and measurements of ionized calcium) with normal 25-hydroxyvitamin D3 levels. Renal function (creatinine 0.86 mg/dl) and adrenal and thyroid tests were normal.

Volume expansion and loop diuretic therapy had minimal effect on calcium levels and she was administered a single dose of pamidronate (60 mg) IV. Serum calcium levels declined to corrected values of 10.8 mg/dl. Despite surgical attempts to repair an enteric perforation, sepsis persisted and the patient expired.

**Conclusion:** PTH dependent hypercalcemia is most commonly due to a single parathyroid adenoma, although multiple gland disease can occur, particularly in the setting of heritable disease. Parathyroid autonomy can also develop in the setting of renal failure and lead to hypercalcemic state with elevated PTH. Both these conditions exhibit chronic courses. The case presented here likely represents the less common entity of acute onset of hypercalcemia driven by PTH in the setting of sepsis. The mechanisms for PTH hypersecretion in this setting are unknown.

**Abstract #720**

**INSULIN AND HYDROCORTISONE COMBINATION AS AN ANTI-INFLAMMATORY COCKTAIL**

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**Objective:** Glucocorticoids have been used as the major class of anti-inflammatory agents for over 60 years. However, they have well known side effects including weight gain, adiposity, and a series of catabolic effects with loss of musculature osteoporosis and diabetogenicity. We have recently described the induction of expression of specific pro-inflammatory genes including HMG-B1, TLRs, LIGHT, LTBR and MMP-9 by a single large dose of hydrocortisone (HC). In addition, these subjects experienced a significant increase in plasma glucose and FFA concentrations. Thus, the infusion of insulin at a low dose with a high dose of HC or other corticosteroids may constitute an ideal anti-inflammatory cocktail in the in-patient setting. Since our group discovered the anti-inflammatory actions of insulin in 2001, we have now hypothesized that a combination of insulin with a high dose of a glucocorticoid may neutralize the pro-inflammatory effects of HC and offer an ideal and safe anti-inflammatory combination.

**Methods:** Healthy subjects were randomized into a cross over study to be injected in two separate days (a week apart) with 300 mg of hydrocortisone (= 60 mg prednisolone) intravenously with or without an infusion of 2U/h of insulin with 5% dextrose for 8 hours.

**Results:** HC injection alone induced a significant anti-inflammatory effect including suppression of CCR-2 (by 69±6%), IL-4 (by 52±7%) and TNF-α (by 55±8%) expression in mononuclear cells (MNC) and plasma MCP-1 (by 64±9%) and TNF-α (by 32±8%) concentrations. However, the HC injection also induced an increase in the MNC expression of HMG-B1, TLR-2, TLR-9 and LIGHT (by 102±13%, 67±11%, 84±7% and 126±14% over the baseline, respectively, P<0.05) and in plasma levels of MMP-9, LIGHT and TGF-b1 (by 186±15%, 94±9% and 167±17% over the baseline, respectively, P<0.05). Plasma glucose and FFA concentrations also increased significantly following the HC injection alone. Insulin infusion along with the HC injection increased the magnitude of the overall anti-inflammatory effect and completely inhibited the increase in glucose and FFA. In addition, the infusion of insulin with HC injection inhibited the HC induced increase in TLR-2 and TLR-9 expression and significantly reduced the HC induced increases in the MNC expression of HMG-B1 and LIGHT (to only 21±11% and 34±14% over the baseline, respectively, NS) and in plasma LIGHT and TGF-b1 concentrations (to only 21±12% and 12±10% over the baseline, respectively, NS) but not in plasma MMP-9 levels.

**Conclusion:** Thus, the infusion of insulin at a low dose with a high dose of HC or other corticosteroids may constitute an ideal anti-inflammatory cocktail in the in-patient setting.
Abstract #721

NEUROENDOCRINE TUMORS: AN EPIDEMIOLOGICAL STUDY IN FRIULI VENEZIA GIULIA

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Objective: Given the increased incidence of neuroendocrine neoplasms (NEN) in recent years it was decided to do an epidemiological study on patients with NEN referred to the Endocrinology and Metabolic Diseases Unit of the Hospital in Udine, the referral center for this disease in the Region Friuli Venezia Giulia.

Methods: Data were collected on 344 patients diagnosed with NEN between 1990 and 2013 regarding: town of residence, age at diagnosis, type of NEN, survival, metastases at diagnosis, the length of the clinical course, diagnostic tools used, specialist visits and prescribed therapies. Survival and progression-free survival (PFS) were analyzed according to sex, type of NEN, and the presence of metastases at diagnosis.

Results: The average age at diagnosis was 59.8 years (range 19-87 yrs), 50.3% males and 49.7% females. Most of the patients came from the Udine province, the most populous. The two sites most affected by NENs were lungs and pancreas; the most frequent was the non-functioning of the pancreas, followed by a typical pulmonary carcinoid. The number of diagnoses of NEN per year increased progressively to over 30 cases a year from 2009 onwards, the highest increase in GEP-NEN compared to T-NEN. In the period 2003-2013 there were 19.7 cases per 100 000 inhabitants; 20.8% of patients had liver metastases at diagnosis. The survival ranged from 1 month to 23.7 years; 31.6% of patients had died, and of these 71.1% due to the disease.

We compared the length of the clinical course of patients diagnosed prior to 2006 with those diagnosed from 2006 onwards (the year a Network was started to provide information about NEN at the local medical level). In the first group, the percentage of patients seen by the endocrinologist within 3 months of diagnosis, was 44.9%, but in the second group it was 68.8%. Computed Tomography was the most frequent test (63.1%) for diagnosis; 44.5% of patients did not receive any medical treatment; of the remaining, 40.7% were treated with somatostatin analogues (24.1% with Octreotide and 16.6% with Lanreotide). Survival and PFS were more frequent in females than in males, in patients without liver metastases at diagnosis and in patients with typical carcinoid. Among all kinds of NEN the typical carcinoid is the one with the greatest survival time.

Conclusion: The data obtained confirm the increased incidence of NEN in our Region and provide additional information on the epidemiology and natural history of these tumors. The implementation of projects of information about the NET has proven useful in reducing the time of the clinical pathway of care while improving the service offered to the patient.

Abstract #722

MICROPENIS: NEW EXPERIENCE WITH TESTOSTERONE COMBO PREPARATION

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BIRDEM

Objective: Micropenis is a clinical term used to describe a very small penis. The generally accepted definition of a micropenis is a penis that is “more than 2.5 standard deviations” below the average penis length for the age of the individual. There is age matched SD. Most often the cause of a Micropenis is chromosomal and hormonal. May be idiopathic. The exact prevalence is not known, but it is noticed that prevalence is increasing possibly due to increased awareness and increasing childhood obesity. Many as one- third of people born with micropenis don’t fit into an easily identifiable category to explain the cause of it.

Methods: A retrospective data was analyzed. Children diagnosed as Micropenis, penile length was <2.5 SD of that age. All patients are given Inj. Testosterone 0.3 ml monthly, which contains 250 mg/ml of combo Testosterone Enanthate, Undecoinate and Cipionate. All children are followed before each Injection monthly. Stretched Penile Length(SPL), Testicular Volume(TV), Pubic Hair(PH), Height were measured.

Results: Consecutive 42 subjects were recorded. Mean age 9±2.6 year and height 116 ±9 cm. Before Inj. Testosterone 0.3 ml IM Stretched Penile Length 3.1±1.1 cm, Testicular Volume <4ml and Pubic hair stage 1. After one month 29(69.05%) subjects had SPL 3.8± 1.6 cm and rest 13 dont have significant improvement. TV and PH don't change significantly. Among the rest 13 subjects, 8 (61.54%) after 2nd Injection SPL was 3.6±1.3 cm. TV in all cases after 2nd Injection were < 4ml.

Discussion: Micropenis in children is concerned issue specially the parents. Possibly prevalence increasing due to obesity. Many of them are idiopathic. Treatment with Androgen Injection corrects in all cases. Usually 3-6 Injections (monthly for 3-6 months) are prescribed at a dose 100 mg per dose of Testosterone Enanthate or
Combination (where Enanthate is not available). Many of the cases patients are not followed up monthly. They are usually asked to follow up after 3-4 months. 

**Conclusion:** Testosterone Injection is very effective in micropenis. If Testosterone Enanthate is not available, Combo Testosterone Injection 75 mg (0.3 ml) monthly can be given as short course 1-2 Injection. Many of them (~90%) don’t require more than one or two injections. All patients should be followed up monthly (prior to next injection). Current dose and schedule usually in practice seems excess. Larger RCT study is necessary to formulate guideline for proper dose and duration.

**Abstract #723**

**METABOLIC SYNDROME AND QUALITY OF LIFE ASSESSMENT: EXPERIENCE FROM TERTIARY CARE HEALTH CENTER**

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**Objective:** To assess levels of stress (Anxiety/Depressive symptoms) and Quality of Life in patients of Metabolic Syndrome and compare it with healthy controls and to study the relation of Anxiety/Depressive symptoms and Quality of Life with various parameters of metabolic syndrome if any.

**Methods:** This prospective observational cross section study was conducted on 100 metabolic syndrome patients (according to Harmonizing definition 2009) and equal number of age, sex and social status matched controls enrolled from endocrine OPD & IPD over a period of one year in a north Indian tertiary care center. The cases & controls were subjected to thorough history, clinical & biochemical examination, screening questionnaires General Health Questionnaire & Hospital Anxiety and Depression Scale, and severity questionnaires Hamilton Rating Scale for Depression (HAM-D), Hamilton Rating Scale for Anxiety (HAM-A) and World Health Organization – Quality of Life – BREF Version.

**Results:** On GHQ significantly higher (p<0.001) proportion of Controls (62%) had GHQ Scores upto 10 (suggestive of no distress) as compared to Cases (19%). A significant positive association between GHQ Scores and Waist circumference (p<0.001), SBP (p<0.001), DBP (p=0.004), Triglycerides (p<0.001) and Fasting Plasma glucose levels (p<0.001) while a significant negative association between GHQ Scores and HDL Cholesterol levels (p<0.001) was observed. A significantly higher (p<0.001) proportion of Controls (79%) had HADS-Anxiety scores in the category 0-7 (suggestive of no anxiety) as compared to Cases (57%). Only two parameters of metabolic syndrome (waist circumference (p=0.008) and triglyceride levels (p=0.029)) at different HADS-Anxiety grades was statistically significant.

**Discussion:** The relationship of depression, anxiety and psychological distress with chronic metabolic disease such as diabetes mellitus, insulin resistance and dyslipidemia has been established. There are conflicting results about probable association of Metabolic Syndrome with psychological problems. Therefore, we aimed in this study to investigate association of depression, anxiety, psychological distress and quality of life with metabolic syndrome in a sample of Indian population.

**Conclusion:** This study proves the higher prevalence of depression as compared to anxiety and impaired quality of life in cases of metabolic syndrome.

**Abstract #724**

**PARATHYROIDECTOMY: MEDICAL TOURISM WITHIN THE UNITED STATES**

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**Objective:** Parathyroid surgery is increasingly being performed by high-volume centers demonstrating higher cure rates, fewer complications, lower mortality, and shorter hospital stays. The University Health System Consortium (UHC) database was interrogated to generate a descriptive report of trends in parathyroidectomy volume in the US. The UHC represents 90% of non-profit academic medical centers and more than 300 of their affiliated hospitals.

**Methods:** UHC data from 2010 to 2013 were compiled. 27,181 patients undergoing parathyroid surgery in the US were identified. The patient’s state of residence versus surgery, age, sex, race, insurance, comorbidities, complications, discharge status, length of stay, and hospital admission were collected.

**Results:** Eighty-two percent of Americans undergoing parathyroidectomy did so in their home state. Six states performed over 50% of cases. Only 32.9% of parathyroidectomy patients were from these same six states. States performing less than the 20th percentile of parathyroid surgery (per capita) experienced a larger proportion of patients leaving the state for surgery (P<0.05). Complications and deaths were reported in less than 0.5% (n=130) and 0.1% (n=23), respectively. When patients traveled out of the state for care, Florida was the state traveled to most often (79%) had HADS-Anxiety scores in the category (79%) had HADS-Anxiety scores in the category.
most frequent destination (43.6%), which increased the state’s parathyroidectomy case volume by an additional 62.1% (less than 1% of Florida residents traveled to another state for surgery).

**Conclusion:** This dataset represents the largest series of geographic-specific parathyroid volume in the US. The vast majority of Americans undergoing parathyroidectomy choose surgeons in their home state. Future research is focused on how consolidation of parathyroid surgery into higher-volume centers impacts patient care.

Abstract #725

**HUMORAL HYPERCALCEMIA OF MALIGNANCY (HHM): “THE HOOK EFFECT” IN MEASUREMENT OF PTH-RP**

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**Objective:** Ovarian cancer is the most common female genital tract malignancy that is associated with HHM. Clear cell carcinoma of the ovary - an uncommon tumor that accounts for 5% of all ovarian cancers, is associated with HHM in 5%-10% of the cases. We present a rare case of hypercalcemia of malignancy associated with simultaneous elevation of serum PTH rP and 1,25-dihydroxyvitamin D in a patient with clear cell ovarian adenocarcinoma.

**Case Presentation:** A 48 year old Caucasian female with past medical history of hypertension and obesity presented to her PCP for fatigue, decreased appetite and weight loss of about 22 pounds in few months. On exam patient was found to be hypotensive and dehydrated. Patient was sent to ED and laboratory findings revealed hypercalcemia with a corrected Calcium level of 14.9mg/dL and intact PTH of <3 pg/ml (normal 14-72). She was treated with intravenous fluids, calcitonin and zoledronic acid. Calcium levels improved to 10.9. Subsequent workup revealed Vitamin A level of 23 ug/dL (20-120 ug/dL) 1,25 Dihydroxyvitamin D 104 pg/ml (15 to 75), 25-OH vitamin D level of 14.4 ng/ml (30-100), Serum and urine protein electrophoresis were negative, PTHrP initially was 3.1 pmol/L (normal <2) and Ca-125 was 232units/ml (normal 0-35). Given suppressed iPTH levels and very high level of calcium, malignancy was high on the differential. Pt. underwent an abdominal/pelvic CT scan which was concerning for a large low density pelvic mass. Subsequently she underwent an exploratory laparotomy, hysterectomy and bilateral salpingo-oophorectomy. Pathology reported stage IIIC Clear Cell Adenocarcinoma of the ovaries. Hypercalcemia of ovarian malignancy is usually associated with PTHrP, however, as the initial level was not very high (3.1), PTHrP was rechecked with dilution to rule out the hook’ effect and was found to be elevated at 21 pmol/L (normal <2). Patient was subsequently hospitalized for worsening weakness, decreased appetite, and was found to have a corrected calcium level of 11.8. Pt. was treated with intravenous fluid and prednisone 40mg daily. Calcium levels improved with glucocorticoid therapy but with extensive metastatic disease, decision was made to pursue comfort care with hospice.

**Conclusion:** Malignancy is high in the differential with hypercalcemia that is iPPTH independent. Paraneoplastic hypercalcemia, although commonly associated with squamous cell malignancy, is a rare presentation in clear cell adenocarcinoma of the ovaries. Clinicians should be aware of the hook effect and when suspected, dilution testing of PTH-rP samples may clarify the diagnosis. Our patient presented with hypercalcemia associated with concomitant elevation of PTH-rP and 1,25 Dihydroxyvitamin D.

Abstract #726

**PRIMARY HYPERPARATHYROIDISM AND THE RELATIONSHIP BETWEEN 25-VITAMIN D, 1,25 VITAMIN D AND PARATHYROID HORMONE: A PROSPECTIVE CASE SERIES**

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**Objective:** Primary hyperparathyroidism (PHPT) is a common endocrinological disease with an evolving clinical presentation. Vitamin D deficiency is more common in PHPT than the general population, partly related to the elevated parathyroid hormone (PTH) converting 25-hydroxyvitaminD into 1,25-dihydroxyvitaminD. Observational studies have shown that a low 25-hydroxyvitaminD is associated with reduced BMD, post-op hypocalcaemia and elevated PTH. In a small RCT 25-hydroxyvitaminD replacement decreased PTH and increased lumbar BMD without increasing adverse events. The role of 1,25-dihydroxyvitaminD was not investigated. We analysed the data of patients with PHPT looking for correlations between PTH, calcium, 25-hydroxyvitaminD, 1,25-dihydroxyvitaminD and 25-hydroxyvitaminD replacement.

**Methods:** We performed a prospective case series of all patients referred to a regional hospital endocrine outpatients clinic with PHPT.

**Results:** 40 patients were diagnosed with PHPT. Average corrected calcium in the PHPT group, expressed as mmol/L above normal, was 0.2. The average PTH, expressed...
as a multiple above normal, was 1.73. The average 25-hydroxyvitaminD was 61nmol/L (50-150), the average 1,25-dihydroxyvitaminD was elevated at 173pmol/L (40-150). There was a statistically significant difference in PTH level between vitamin D replete and deficient groups, 1.51 and 2.45 times normal respectively (p=0.003) without a difference in corrected calcium. The correlation factor of PTH and 25-vitaminD was -0.56. The correlation factor of PTH and 1,25-vitaminD was 0.43. There was a negative correlation between 25-vitaminD and 1,25-vitaminD (r=-0.64). Replacing vitamin D did not alter hypercalcaemia.

Discussion: The current guidelines are to give supplemental vitamin D in patients with PHPT whose vitamin D levels are less than 50nmol/L. The theoretical basis for this is that increasing the 25-vitamin D level will lead to an increased 1,25-vitamin D level which will then suppress the secretion of PTH. Our findings of an inverse relationship between 25- and 1,25-vitamin D and a positive correlation between 1,25-vitaminD and PTH suggests that increasing the 1,25-vitaminD level does not suppress PTH. There has also been concern that vitamin D supplementation alters the clinical outcome of patients with PHPT.

Abstract #727

DIABETES DETECTION IN THE DENTAL OFFICE (DIDDO): A PROMISING EMERGING OPPORTUNITY FOR SCREENING FOR UNDIAGNOSED PREDIABETES AND DIABETES

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Objective: As a part of campaigns to alleviate the health and financial burdens of undiagnosed diabetes, and because many Americans regularly visit their dentists but not medical doctors, diabetes screening in dental offices has emerged as a promising screening opportunity. Recently published related studies had methodological limitations, and did not include a customized screening survey convenient to dental offices. This study was conducted to design and validate a dental-office-friendly screening score (survey) as an effective strategy for early detection of prediabetes (PreDM) and early diabetes (DM) in dental patients.

Methods: Consecutive adult dental patients attending a private dental practice in Holt, Michigan, without history of PreDM or DM, were given a customized 14-question survey. Subsequently they underwent finger sticks for A1c measurement, using a unique, validated capillary testing, performed at the NGSP’s Laboratory in Columbia, Missouri.

Results: A total of 500 patients completed the study, 302 women and 198 men, with a mean age of 48 years. The prevalence rates of PreDM and DM were 19.2% and 1.2%, respectively. Predictors of PreDM or DM included age; above 10% ideal body weight; waist size above 40” for men or 35” for women; hypertension; abnormal lipids; tingling of hands or feet; and visual symptoms or conditions (blurring; cataracts; glaucoma)

Discussion: Our study confirmed findings of prior studies affirming the effectiveness of the dental office in detection of undiagnosed PreDM and DM. The rate of undiagnosed PreDM in this study is in keeping with other studies, and with the general population risk. However, the low rate of DM is believed to be due to demographic causes, as well as to the unique health preventive and educational activities of the study’s dental practice. In addition, this uniquely designed study introduces a newly developed customized PreDM and DM screening tool designed for dental offices. This newly introduced screening survey requires no body weighing or BMI calculation, that are considered inconvenient and undesirable in dental offices. This is hoped to assist the dental care provider in determining when it is appropriate screen for PreDM/DM, and to apply a simple screening test for DM/PreDM, such as point of care A1c measurement.

Conclusion: A newly developed simplified and dental-office-friendly screening score is proposed for use in dental offices. This is important since dental offices encounter a significant proportion of the population, who do not regularly visit their physicians. Given the high rates of undiagnosed PreDM and DM in the general population, such dental patients with potentially similar risk, would therefore otherwise remain undiagnosed.
Abstract #728

SEVERE HYPOMAGNESEMIA AND BREAK-THROUGH SEIZURE WITH PROTON PUMP INHIBITORS USE

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Objective: Proton pump inhibitors (PPIs), as a class, are one of the most prescribed medications. Side effects are estimated to be in 5% of the patients. However, literature reviews show more and more accounts of people having adverse reactions to these medications, including electrolyte disturbances.

Case Presentation: A 72 year old female presented to the ED with three witnessed seizures. She had a medical history of Parkinson’s disease, seizure disorder, dyslipidemia, COPD, GERD, ulcerative colitis, hypotension, and fibromyalgia. Initially her calcium (Ca++) was found to be 5.8 (corrected 7.0), ionized Ca++ 0.78mEq/L and Potassium of 3.5mEq/L. Magnesium (Mg) levels were undetectable (less than 0.2mEq/L). Records showed she was on esomeprazole for about six months. Two months prior, her Ca++ level was 8.4 and at that time esomeprazole was changed from 20 mg to 40 mg daily. She was also on Mg oxide 800mg twice a day, cholecalciferol 2000units a day and multivitamins. Vitamin D metabolites, thyroid function tests, creatine kinase and phosphorus levels were normal. Intact Parathyroid hormone (PTH) of 52pg/ml, was on keppra and lamotrigine, levels of both were therapeutic. EKG exhibited tachycardia and prolonged QT interval. She was obtunded with eyelids twitching and tetanic contractures of upper extremities. PPI was stopped; magnesium and calcium were replaced IV and then orally when levels normalized, within 48 hours. Her spasms resolved and her magnesium levels remained steady throughout the rest of her hospitalization without any more seizure.

Conclusion: Magnesium, one of the most common intracellular cation, is essential for the maintenance of electrolytes and PTH release. Estimates show that half the population of the US is believed to be deficient in their daily dietary consumption of magnesium. Approximately one third of the consumed magnesium is absorbed in the bowel. The gastric acidity is believed to keep magnesium salts suspended and allows for better absorption. With PPIs the acidity is decreased and thus absorption. Although it is a class effect, omeprazole and esomeprazole are evidently the most common offenders causing hypomagnesemia. Magnesium citrate might be a better option for replacement because of better bioavailability. This patient experienced severe hypomagnesemia within 6 months of PPI use which usually happens with longer use.

PPIs are generally considered safe medications but they have wide range of side effects including iron deficiency, vitamin B12 deficiency, fractures, rhabdomyolysis, pneumonia, thrombocytopenia, clostridium difficile infections and nephrotoxicity. Appropriate use of PPIs is warranted to avoid these side effects.

Abstract #729

ECTOPIC ACTH-PRODUCING ATYPICAL CARCINOID

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Objective: To present a rare case of secondary hypertension due to ectopic ACTH-producing carcinoid.

Methods: A 23 year-old male presented with a 6-month history of uncontrolled hypertension on three agents with unintentional weight gain. He reported generalized fatigue, lower extremity edema, easy bruising, nocturia, insomnia, and irritability.

Case Presentation: Physical examination revealed truncal obesity, moon facies, dorsocervical fat pad and violaceous striae. Laboratory results: 1-mg DST (cortisol 32.7 mcg/dL), 24-hour UFC 1643 ug, midnight plasma cortisol 38.68 mcg/dL, late night salivary cortisol 1.016 mcg/dL (0.010-0.090), ACTH 290 pg/mL (ref 7.2-63.3), hyperglycemia, hypokalemia, and 8-mg DST (cortisol 37.56 mcg/dL). Pituitary MRI was normal. A chest CT, PET and Octreoscan showed a 3 x 6 cm hypermetabolic mass within the left lower lobe with left hilar lymphadenopathy with somatostatin receptor avidity. Bronchoscopy failed to reveal any intraluminal masses. Patient underwent resection of the left lower mass by lobectomy and lymph node dissection. Pathology revealed a 5.0 cm, grade 2 atypical carcinoid tumor with 10 out of 10 positive lymph nodes consistent with Stage IIIA neuroendocrine carcinoma (negative ACTH immunostain). Adjunctive studies including thyroid function tests, aldosterone:renin ratios, plasma and 24-hour urine metanephrines, serotonin, chromogranin A and 5-Hydroxyindoleacetic acid, were all normal. In the immediate post-operative period, patient reported near complete resolution of his presenting symptoms with a 26-pound weight loss and normalized ACTH level (24.1 pg/mL) and 24-hour UFC.

Discussion: In a recent study, the lung appears to be the major site of ectopic ACTH-secreting tumor (47.5%), with the majority of cases being bronchial carcinoid tumors (30%) followed by small cell lung cancers (17.5%) (1). Although carcinoid tumors are generally considered a...
low-grade malignancy, some reports indicate that atypical, hormonally-active tumors – specifically – ACTH-secreting bronchial carcinoids – are more aggressive with greater metastatic potential than quiescent typical carcinoids (2). For this reason, surgical approach with anatomic resection and routine lymph node dissection is warranted. For patients with recurrent, non-resectable, or metastatic disease, radiofrequency ablation and chemotherapy can be offered (3). Our patient had follow-up PET/CT and Octreoscan which revealed residual tumors; therefore, the patient was referred for evaluation of chemotherapy with/without radiation.

**Conclusion:** This case demonstrated the importance of early recognition of Cushing syndrome and its cause in order to intervene appropriately and effectively.

**Abstract #730**

**IMPACT OF DIABETES EDUCATION PROGRAM ON KNOWLEDGE AND PERCEPTION AMONG TYPE 2 DIABETES IN BANGLADESH**

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**Objective:** Bangladesh has one of the highest numbers of diabetes population in the world and knowledge-based education is the most feasible strategy to prevent diabetes and its complications in this low resource society. Realizing this fact, Diabetic Association of Bangladesh has emphasized on the diabetes education program. The present study was undertaken to see the impact of diabetes education program on knowledge and perception among type 2 diabetes in Bangladesh.

**Methods:** A total of 500 type 2 diabetes patients (male 43%, female 57%) attending the structured diabetes education program (such as face to face and group discussion using leaflet, flipchart and posters) in the BIRDEM were included in the study. Data were collected by a pre-designed, interviewer-administered questionnaire. Baseline data were collected before providing education and the follow-up data were collected after 12 months of providing diabetes education.

**Results:** At the follow up, fasting (mean±SD, mmol/l 9.8±4 vs 8.2±3; p=0.0001) and after break fast (mmol/L, 14±5 vs 11.8±4; p=0.0001) serum glucose level were significantly reduced. Knowledge and perception scores of the patients, (% 56±15 vs 68.4±11 and 78±5 vs 85.8±6 respectively; p=0.0001) were significantly increased after intervention. Before receiving diabetes education better knowledge was associated with better perception (r=0.29, p=0.0001). After receiving education this associations {knowledge vs perception (r=0.23; p=0.0001)} became stronger. Age, sex, habitat, religion, year of education, occupation, and monthly income, family history of diabetes and diabetes education were tested in a multiple regression model with knowledge and perception score as the dependent variable. Age (b=0.09, p=0.04) showed a significant negative association with knowledge score. Year of education (b=0.27, p=0.0001) and diabetes education (b=0.13, p=0.01) showed a significant positive association with knowledge score. Diabetes education (b=0.21, p=0.0001) and number of education class (b=0.11, p=0.03) showed a significant positive association with perception score.

**Conclusion:** Diabetes Education Program is associated with improved glycemic control and increased Knowledge and perception. The present data also show that better knowledge leads to better perception and a diabetes education program has positive effect in increasing knowledge and perception.

**Abstract #731**

**HYPOVITAMINOSIS D IN EARLY PREGNANCY AS A PREDICTOR OF GESTATIONAL DIABETES MELLITUS**

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**Objective:** Gestational Diabetes Mellitus affects 3 to 10% of pregnancies, depending on the population studied. The progressive increase of insulin resistance observed in pregnancy contributes to the pathophysiology of gestational diabetes mellitus (GDM). There is controversy whether vitamin D deficiency contributes to abnormal glycemic regulation in pregnancy.

**Methods:** We tested the associations between first trimester 25-hydroxyvitamin D3(25OHD3) levels and the risk of developing GDM in a large hospital-based prospective cohort of pregnant women. Participants (n=200) were seen at first (6–13 weeks) and second (24–28 weeks) trimesters for blood samples. Each participant was selected in their first trimester and demographic parameters were recorded. Their Height, weight & BMI was calculated as weight (kg)/height (m2). Family history of Diabetes, Obstetric score for gravidity, history of previous abortion and previous history of GDM were recorded. Fasting blood sugar was measured and in those with >92mg/dl HbA1c was done and those with >6.5% were excluded. Those with FBS < 92mg/dl were included directly. In these patients 25 (OH) Vitamin D3 was estimated using Enhanced Chemiluminescence assay. Irrespective of Vitamin D level all the enrolled subjects underwent Oral glucose challenge test with 50gm glucose
(GCT) during their second trimester (24-28 weeks) of pregnancy. In those with 2hrs glucose value of >140mg/dl, Oral Glucose tolerance test (OGTT) was done and diagnosed as GDM or NGT based on ACOG criteria.

**Results:** Based on ACOG criteria, 18 participants (9%) developed GDM. 25(OH) Vitamin D level was deficient in 190 participants (95%) and sub group analysis revealed 25(OH) Vitamin D3 level of <20nmol/l in 48% of participants. On logistic regression analysis for GDM risk factors, Advancing age, Increased BMI and 25(OH) Vitamin D3 level of <20nmol/l were significantly associated with risk of GDM. 25(OH) Vitamin D3 level <20nmol/l was found to be significantly associated with increased risk of GDM. In our study this risk was evident only in advanced maternal age (29.07 ± 1.68).

**Conclusion:** Advancing age, Increased BMI and 25(OH) Vitamin D3 level of <20nmol/l were significantly associated with risk of GDM. We recommend that every woman in early pregnancy should be screened for 25(OH) Vitamin D3 levels & if significantly low <20nmol/l then should be observed for development of GDM.

**Abstract #732**

**AGGRESSIVE PRESENTATION OF CLINICALLY PALPABLE PARATHYROID ADENOMAS**

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**Objective:** A palpable parathyroid tumor in patients of primary hyperparathyroidism is presumed to be parathyroid carcinoma until proven otherwise, with other less common causes including parathyroid cysts and adenomas. The features of primary hyperparathyroidism (PHPT) in developing countries have rarely been examined. More cases of symptomatic PHPT are presented in younger age group and some time large adenomas can presented a palpable neck swelling.

**Methods:** Retrospective analysis of 147 patients of symptomatic PHPT who presented in tertiary teaching hospital in last 10 years.

**Results:** 14 cases of parathyroid tumors who presented with clinically palpable swelling in out of 147 cases. In all palpable parathyroid cases except one proved benign adenomas. All 13 cases of parathyroid adenoma had ostetis fibrosa cystica with median symptoms duration of 2.6 (range 1-21) years. In all cases serum calcium and alkaline phosphatase (ALP) were raised more than 10 folds. In most of cases of primary hyperparathyroidism coexistence of vitamin D deficiency was found.

**Discussion:** Only parathyroid carcinoma can presented as clinically palpable neck swelling but this is not true according to this series. Most common cause of clinically palpable parathyroid adenomas are delayed diagnosis, socioeconomic factors and ignorance.

**Abstract #733**

**TESTOSTERONE OVER 2200: REAL OR FAKE?**

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**Objective:** Endocrinologists often struggle with serum testosterone assays, in view of various intervening factors. We report a case of an extremely high serum testosterone level in a patient on androgen replacement, with no clinical manifestations of hyperandrogenism. We discuss the challenges of interpreting these conflicting parameters.

**Case Presentation:** A 72-year-old male was followed in the endocrinology clinic for panhypopituitarism following transphenoidal hypophysectomy for a large pituitary macroadenoma. After replacing thyroid and steroid hormones, he was started on androgen replacement. He was started on Androgel 1% gel (50mg/5gm), applying 2 puffs (25 mg) a day, with instructions for proper application. Testosterone levels were measured 2 months later, demonstrating impressively high levels of free testosterone of 84 ng/dl (9-30 ng/dl) and total testosterone of 2260 ng/dl (240-950 ng/dl). Strangely, he denied any excessive libido, aggressive behavior or changes in body hair growth. As we struggled to explain the asymptomatic elevated testosterone levels, we speculated a lab error. The patient then stated that he had a theory: He stated that his blood was drawn from the antecubital fossa region, soon after the application of the gel. He also stated he would routinely rub the gel from the top of the shoulder throughout his arm, speculating possible contamination from gel residual at the site of the blood draw. Free and total testosterone levels were subsequently measured before gel application and were in fact very low, confirming the patient’s theory. Upon dose titration, serum testosterone levels were normalized.

**Discussion:** Only few cases have been reported where testosterone levels were spuriously elevated as a result of blood drawn adjacent to the site of topical application. Health care providers and patients should be aware of this pitfall, to avoid inaccurate lab results and unnecessary correction of a normal level.
**Conclusion:** Venous sampling near the site of the application of topical testosterone may lead to erroneous levels of measured testosterone as a result of contamination. Clinicians should be aware of this pitfall, to avoid needless correction to testosterone therapy.

**Abstract #734**

**METABOLIC ABNORMALITIES IN PATIENTS TREATED WITH ANTIRETROVIRAL THERAPY**

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**Objective:** To evaluate metabolic abnormalities in Antiretroviral therapy (ART) treated HIV patients.

**Methods:** A total of 98 HIV patients (82 on Antiretroviral therapy, 16 therapy naive HIV cases) were studied. After clinical examinations & auxology, investigations such as blood glucose, glycosylated hb, complete lipid profiles and Dual Energy X-ray Absorptiometry (DEXA) were performed. Adipokines and cytokines were also analysed. For analysis Antiretroviral therapy treated patients were divided into protease inhibitor (PI) & non-PI (d4T) subgroup.

**Results:** In non-PI (d4T) subgroup of Antiretroviral therapy treated patients, 51 out of 82 (62.19%) patients had TG >150 mg/dL, 6 patients had impaired fasting glucose (IFG i.e. FBS >100 mg/dL) & 27 of 82 (32.92%) patients developed lipoatrophy. Among 22 patients in PI subgroup, 6 (27.27%) had TG >150 mg/dL, 9 (40.9 %) patients had low HDL (<40 mg/dL for males & <50 mg/dL for females) while 5 had elevated LDL of >100 mg/dL. IFG was seen in 9 (40.9%) out of 22 patients in PI subgroup, while 1 patient developed frank diabetes. In PI subgroup 11 (50%) patients had central obesity (waist circumference >80 cm in females, >90 cm for males), while 21 on 22 (95.45%) patients had total body fat >25%.

**Conclusion:** PI therapy was associated with significant abnormalities of lipid profile, impaired glucose tolerance & abnormal body fat composition. In non-PI (d4T) treated patients lipoatrophy was the commonest abnormality followed by hypertriglyceridemia.

**Abstract #735**

**FUNCTIONAL GIANT PARATHYROID CYST: RARE CAUSE OF PRIMARY HYPERPARATHYROIDISM**

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**Objective:** Primary hyperparathyroidism (PHPT) is rarely caused by parathyroid cyst (PC). We report a case of a giant functioning symptomatic PC in a 70-year-old woman.

**Methods:** A 70 years old woman presented with a history of generalized weakness, urolithiasis, and renal colic. Palpation revealed a left sided neck mass which was discrete, moved with deglutition. Based on the clinical presentation she was investigated for hyperparathyroidism.

**Case Presentation:** Biochemical evaluation confirmed the diagnosis of PHPT, corrected s.calciump: 11.5 mg/dL, s.phosphorus: 2.3 mg/dL, s. iPTH: 291.6 pg/mL, s. creatinine: 0.8 mg/dL, s.25(OH)Vit D: 32.01 ng/mL. Thyroid function tests were normal. USG of neck showed a large cystic mass (7.5 x2.9 x3.5 cm) in left paratracheal region with multiple hypoechoic nodules in both lobes of thyroid. Tc99m-Sestamibi scan showed no demonstrable evidence of SestaMIBI avid lesion. CT scan of neck and mediastinum revealed a multi-septate cystic lesion (7.3x4.5x3.4 cm). The diagnosis of PC was based on the elevated levels of PTH (2500 pg/mL) in the fluid extracted from the cyst. USG guided FNAC of right thyroid lobe nodule was colloid nodule. She underwent cyst excision (Weight- 80 gms) with total thyroidectomy. She had more than 50% drop in iPTH at 10 minute from baseline with normalization of PTH level at 15 minutes indicating biochemical cure. Postoperatively she had smooth recovery. The histopathology revealed giant parathyroid cyst with nodular colloid goiter. Post op the patient had uneventful course.

**Discussion:** PC is a very rare cause of cervical mass. All functioning PC are histologically identified by cystic degeneration of a preexisting parathyroid adenoma or rarely, parathyroid carcinoma. The diagnostic workup includes neck USG, Tc99m-Sestamibi scintigraphy, CT scan, MRI and FNAC- iPTH estimation. The overactivity of a PC should be assessed by the calcium and PTH levels in the patient’s serum. Parathyroid cyst aspiration and PTH estimation in the aspirated fluid can be diagnostic. The surgical excision of the cyst is always the first option in a functioning cyst. The intraoperative rupture of the cyst is not uncommon and special techniques should be followed in order to avoid parathyromatosis. Intraoperative measurements of PTH levels is a useful tool for evaluating the success of the surgery, as in our case.
Conclusion: Functioning PC can present as PHPT. The diagnosis can be established by high PTH in the aspirated fluid. Tc99m-Sestamibi scintigraphy may be negative in a parathyroid cyst. A functioning cyst requires surgical excision. The thyroid pathology should be dealt as per the published standard thyroid guidelines.

Abstract #736

A RARE CASE OF AN ECTOPIC PARATHYROID ADENOMA MIMICKING A PARATHYROID CARCINOMA

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Objective: The most common cause of hypercalcaemia is primary hyperparathyroidism, caused in the majority of cases by parathyroid adenoma, followed by four gland hyperplasia. Parathyroid Carcinoma (PC) is rarely the cause of PHPT, however, this diagnosis may be considered in patients with severe hypercalcaemia and PTH levels 5 to 10 times upper limit of normal (ULN).

Case Presentation: 44 year old female presented to the ED complaining of 4 days of non-radiating, right flank pain. Her history was notable for anemia and hyperparathyroidism. Review of systems was significant for 3 months of polyuria, polydipsia and nocturia. Physical exam relevant for tachycardia 101 beats/min, and costovertebral tenderness. Initial work up revealed hypercalcaemia 14.8mg/dl, hypokalemia 3.5mmol/L, hypophosphatemia 1.7mg/dl, normal renal function, increased alkaline phosphatase 1445U/L and iPTH level >2500pg/ml. Abdomen CT showed bilateral, non-obstructive nephrolithiasis and diffusely sclerotic bones with multiple lytic lesions. Patient was admitted to the ICU for severe hypercalcaemia, which improved with IV fluids, calcitonin, biphosphonate and electrolytes replacement. Tc99m-sestamibi parathyroid scan showed a large focal area of intense radiotracer activity in the mediastinum suggesting an ectopic parathyroid tissue. Subsequent Chest CT showed an anterior superior mediastinal mass and extensive lytic bony lesions consistent with brown tumor. In view of the extremely high iPTH and hypercalcaemia parathyroid carcinoma was suspected. She underwent ectopic parathyroidectomy and thymectomy. Pathology revealed parathyroid adenoma.

Discussion: Patients with PHP are often asymptomatic. However patients with PC are symptomatic and often have concomitant bone and renal. An iPTH >10 times the ULN was reported as highly predictive for this condition. If malignancy is suspected, aggressive surgical excision needs to be done. Preoperative localization studies are indicated to identify possible ectopic locations of the lesions. In our patient, the studies showed an ectopic parathyroid in the mediastinum, which was significantly larger compared to a normal parathyroid gland. Interestingly, pathology results demonstrated a benign condition.

Conclusion: Parathyroid adenoma is a rare cause of markedly elevated PTH, or associated with metabolic or clinical disease. The presence of these should prompt aggressive work up given the implications of PC as a likely diagnosis. Our patient presentation was significant for severe hypercalcaemia, extremely high iPTH >38 times ULN, extensive metabolic bone disease and nephrolithiasis suggesting this diagnosis. However pathology was consistent with parathyroid adenoma.

Abstract #737

MULTIPLE LIVER-DIRECTED THERAPY INCLUDING THERASPHERES FOR RECURRENT METASTATIC CARCINOID TUMOR.

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King Faisal Specialist Hospital & Research Center

Objective: We present long-term 18-yrs. course of a pt. w/ liver metastases from midgut carcinoid. She had successful outcome following multimodal therapy consisting of repeated liver resection, RF ablation, octreotide radionucleotide, & therasphere therapy (TT) in succession.Minimally invasive therapy of TT using transarterial Y90 can be used safely for recurrent liver mets of neuroendocrine tumor (NET).

Methods: Liver resection, RF ablation, Imaging (MRI, octreoscan), Liver Bx, CGA, Y90 radioembolization.

Case Presentation: A 61-yr. old female w/ liver metastases from non-functioning jejunal carcinoid, had resection of 25 cm of small bowel containing 5 cm of carcinoid tumor, resection of mesenteric metastatic lymph node, & hepatic segments 3 & 4 containing 232 G tumor. This was followed 10 yrs. later by resection & radioablation of recurrent liver mets. Two yrs. later images showed multiple liver mets, & abnormal serum CGA (100 ng/ml;Ref. <93) while receiving on going monthly octreotide Rx. Four yrs. later liver mets progressed w/ additional lesions. Liver bx: metastatic neuroendocrine NET grade 2 tumor. She received TT. Y90 tumor dose 164 Gy was injected into lt. hepatic artery. Pt. tolerated it well w/ no side effects. A yr. later MRI showed resolution of tumor w/ atrophic lt. lobe, & hypertrophic rt. lobe.
ABSTRACTS – Other

Discussion: Majority of pts. w/ NET harbor liver mets at presentation, posing therapeutic challenge. Multiple liver-directed Rx modalities have been employed w/ variable success. TheraSphere is an emerging, well-tolerated Y-90 glass microsphere Rx for transarterial radioembolization in liver-dominant metastatic NETs. It consists of millions of small glass microspheres containing radioactive Y-90. TheraSphere, a localized, minimally embolic therapy, capitalizes on hypervasculature nature of tumors delivering, a source of beta energy, via hepatic artery to tumor bed. The distribution of blood flow is 3 to 7 X greater within the tumor than surrounding normal tissue. Consequently, there is preferential delivery of microspheres to tumor capillary bed allowing for higher doses of radiation to be delivered to tumor relative to surrounding parenchyma. This form of Rx keeps future Rx options open should liver mets progress. However, pt. selection is important & following criteria are considered contraindications for TT; infiltrative tumor type, tumor volume > 50% of target liver volume, combined w/ an albumin < 3 g/dL, AST/ALT > 5 times ULN, bilirubin>2 mg/dL, or significant hepatopulmonary shunt.

Conclusion: Majority of pts. w/ NETs present w/ liver metastases. Despite therapeutic challenge hepatic metastases can be meaningfully managed by a combination of surgical, radioablation, medical Rx & radioembolization using Y90.

Abstract #738

RETROPERITONEAL FUNCTIONING PARAGANGLIOMA: CASE REPORT

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Case Presentation: We present the case of a young male patient of 45 years old, who was admitted for hypertensive crisis (the highest systolic blood pressure 190 mmHg), headache and palpitations, symptoms that have emerged during the last month. His family history was positive for type 2 diabetes and his medical history included medically controlled type 2 diabetes mellitus, diagnosed 6 months ago. Hormonal evaluation revealed elevated urinary metanephrines and normetanephrines, with mainly increased normetanephrines (1693 pg/ml). Plasmatic metanephrines were in normal range, but levels of plasmatic normetanephrines were elevated. Also the endocrine evaluation revealed elevated levels of serum chromogranin A and neuron-specific enolase. The assessment of pituitary, thyroid, parathyroid hormones and aldosterone-renin axis values were within normal limits. Abdominal computed tomography showed expansive solid retroperitoneal tumor, located above the left renal hilum of 45/50 mm with heterogeneous aspect and in contact with the inferior part of the tail of the pancreas and with the medial arm of the left adrenal gland. The patient was transferred to the general surgery ward of the University Hospital Floreasca, where the surgeons practiced a laparoscopic tumorectomy with left adrenalectomy. Histopathologic and immunohistochemical examination diagnose parangglioma, without invasion of adjacent tissues. The patient evolution was favorable, with the remission of the symptoms and normalization of hormonal markers.

Discussion: Retroperitoneal neoplasms are rare and easily misdiagnosed in the current medical practice. These tumors are often discovered incidentally during imaging studies. Paranggliomas are rare neuroendocrine tumors that arise from the extra-adrenal autonomic paraganglia, which can derive from either parasympathetic or sympathetic paraganglia. They can be functional when they secrete catecholamines or non-functional. Most paranggliomas are located in the head and neck and less than 5% of these tumors are endocrinologically active. We report the case of a patient who had a retroperitoneal parangglioma manifested with symptoms of catecholamine excess.

Conclusion: In conclusion, we present the case of a young patient with functional retroperitoneal parangglioma, who presented with symptoms of pheochromocytoma. Compared to pheochromocytomas, paranggliomas are more often asymptomatic and non-functional. Specialized investigations allowed the proper diagnosis and the therapeutic approach above was the result of a multidisciplinary cooperation.

Abstract #739

GERMINOMA AND DIABETES INSIPIDUS WITH ABSENT THIRST MECHANISM

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Objective: To describe a rare case of suprasellar germinoma with resulting diabetes insipidus and absent thirst mechanism.

Case Presentation: A 16-year-old male, with no past medical history, presented with 18 months of intermittent polyuria associated with generalized weakness, impaired short-term memory and visual disturbances. Physical exam
was notable for bitemporal hemianopsia, microphallus, and infantile genitalia. Laboratory tests revealed that ACTH, cortisol, LH, FSH, testosterone, and growth hormone levels were undetectable. Pituitary MRI showed predominantly solid but partially cystic tumor involving the sella turcica and suprasellar cistern. The tumor measured 4.7 cm in maximal superior-inferior diameter x 4 cm in right-left diameter and 4.5 cm in anterior-posterior diameter. An open brain biopsy was performed and confirmed the diagnosis of germinoma. The patient was discharged home on post-op day 6 with Na level of 147 and on desmopressin 0.2mg q12hrs PO, hydrocortisone taper and levothyroxine 100mcg. During an outpatient office visit 6 days post-discharge, the patient’s Na was 170 despite compliance with desmopressin. He was readmitted to the hospital for hypernatremia but denied ever feeling thirsty. Desmopressin was switched to subcutaneous route as the initial thought was that the patient had impaired absorption and this was contributing to his resistant hypernatremia. However, sodium did not decrease when desmopressin was given subcutaneously. 12 hours after holding desmopressin, urine output increased to 350 ml/hour. It fell to 50 ml/hour within one hour of oral desmopressin, confirming that his kidneys responded to it. Therefore, patient’s problem was the lack of thirst in response to hyperosmolality and possibly partial osmoreceptor destruction by germinoma. The patient was placed on fixed hourly water intake corresponding to the urine volume while maintaining the same dose of PO desmopressin, and Na gradually decreased to 149. Patient eventually received proton beam radiation and chemotherapy.

Discussion: Suprasellar germinomas usually present with hypothalamic/pituitary dysfunction which most commonly includes Diabetes Insipidus. Our patient’s large tumor may have affected the hypothalamus and thus altered thirst mechanisms and partially destroyed the osmoreceptors.

Conclusion: Clinicians should be aware of potential lack of thirst mechanism in patients with large germinomas and watch closely for the development of unexplained hypernatremia. The patients should also be educated about adequate oral water intake and daily weight measurements.

Abstract #740

HEMOSIDERIN ENDOCRINOPATHIES AND CARDIAC CONDUCTION ABNORMALITIES IN PATIENTS WITH HEMOGLOBINOPATHIES.

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Objective: We report 2 cases of hemoglobinopathies (HGP) who received chronic blood transfusion therapy (BTT) resulting in Fe overload-related endocrinopathies, & cardiac conduction abnormality that resulted in death in one.

Methods: Hb electrophoresis, serum Ferritin, detailed endocrine tests, Holter monitor, electrophysiological test, MRI pituitary.

Case Presentation: Two males both aged 16 yrs. presented w/ growth retardation (GR) & failure of sexual maturation (Tanner stage 1-2). They had received BTT since birth for sickle cell disease (pt.A), & beta-thalassemia (Pt. B).Their serum ferritin were abnormal 950 & 8724 ug/l (RR: 30-400) respectively. Both had evidence of GH deficiency (flat response on triple dynamic testing) & central hypogonadism. Both had normal thyroid function & normal synacthen test, but Pt. B lacked cortisol response to ITT. LFTs were abnormal, & pts. were not diabetic. MRI pituitary T1&T2 images in both showed hypoplastic gland w/ diffuse signal devoid. Bone age was retarded in both (13 yrs).

Additional data: PT A: IGF1 175 ng/ml(RR: 247-482), IGF binding protein 3 of 4.0 mg/l (RR: 3.4-9.5), testosterone(T) 6.1 nmo/l (RR: 9.9-27),FSH 5 IU/l(RR: 1.5-12.4) LH 4.4 IU /l (1.7-8.6),
Pt. B: had hypocalcemic carpopedal spasms,(low ca ++ 1.73 mmol/l, high Po4 2.76 mmol/l, PTH 21 ng/l (10-65), T <0.7 mmol/l, FSH 2 IU /l, LH <1 IU/l. He suffered recurrent symptomatic palpitations & 24-hr Holter monitor revealed complex multifocal atrial tachycardia/ flutter for 23 hrs. w/ Electrophysiological study :recurrent unstable atrial tachycardia originating from 3 ectopic sites, precluding catheter mapping & ablation.However, arrhythmia was controlled on antiarrhymic agents. Both pts. received Rx consisting of GH, & testosterone. Pt. B received ca++ & calcitriol w/ normalization of ca ++. However, he suffered sudden demise at home, presumed to be arrhythmic death.

Discussion: BTT has enhanced quality of life & helped prolong survival in pts. w/ HGP, albeit at the expense of Fe overload. The resultant hemosiderosis may affect several endocrine & other organs. Fe deposition in pituitary, parathyroids, & beta-cells of pancreas results in GH deficiency, central hypogonadism, primary
hypoparathyroidism, diabetes mellitus & heart.  

**Conclusion:** Iron deposition leading to organ dysfunction involves endocrine & non-endocrine tissues. Pituitary involvement results in GH deficiency, ACTH-cortisol axis dysfunction, & central hypogonadism. Parathyroid involvement results in primary hypoparathyroidism. Cardiac conduction abnormalities can result in death. A systematic & longitudinal F/U studies to uncover a constellation of abnormalities are warranted in order to improve the quality of life for pts. w/ hemosiderin deposition.

**Abstract #741**  

**VITAMIN D DEFICIENCY IN PSYCHIATRIC DISORDERS**

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Dr Layla Onaizi Polyclinic

**Objective:** From time of discover Vitamin D is well known for its role in calcium homeostasis and bone health, while inadequate levels of vitamin D have been associated with bone disorders such as rickets and osteoporosis.

**Methods:** Vitamin D status is assessed by measuring the serum concentration of 25-hydroxyvitamin D: Deficiency < 10, Insufficiency 10-30, Sufficiency 30-100, Toxicity > 100. Screening by lab test of 300 patients male and female. Collecting data about psychiatric history. Following treatment of supplement vitamin D to all patients who have insufficiencyand deficiency of vitamin D.

**Results:** In our study performed on 300 Saudi patients 160 patients with psychiatric disorders. The other 140 patients are free of psychiatric illnesses, for whom questionnaire, physical exam, and routine laboratory test, and serum 25-hydroxyvit.D [25(OH)D was done. We found in the first group 83.9% were vitamin D deficient and 7.4% insufficient. In the second group 70.4% were vitamin D deficient and 19.7% insufficient, it was noted that deficiency of vitamin D was more common in patients diagnosed with depression and schizophrenia. We could not recognize if the deficiency was already present prior to the psychiatric illness. However we can assume that vitamin d deficiency contributes indirectly to the psychiatric disease.

**Discussion:** Clinical data suggest that Vit. D(3) insufficiency is associated with an increased risk of several CNS diseases, seasonal affective disorder and schizophrenia. In a cross-section of older adults, vitamin D deficiency was associated with low mood and with impairment on two of four measures of cognitive performance. It appears to be a relation between serum levels of 25(OH)D and symptoms of depression. Supplementation with high doses of vitamin D seems to ameliorate these symptoms indicating a possible causal relationship. Ecological studies support a potential role for vit.D in schizophrenia.

**Conclusion:** In healthy adults at low risk for vitamin D deficiency, routine vitamin D supplementation daily is recommended. Routine screening is recommended to all psychiatric patients. Supplementation helpful in pschiatric disorders. However, until results from additional prospective studies are available, there is little harm in recommending that individuals with depressive symptoms and other psychiatric disorder consume the newly recommended dose of 1,000 – 2,000 IU of vitamin D per day and attain modest sun exposure, given the overall health benefits of vitamin D and low risk of toxicity at these doses.
Abstract #800

MALIGNANT PITUITARY ADENOMA WITH PAPILLARY THYROID CARCINOMA.

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Case Presentation: It is been now known that pituitary tumor transforming gene (PTTG) plays important role in tumor initiation, progression and stimulation of fibroblast growth factor (FGF)-2 expression. New reports of role of PTTG in thyroid cancer with expression of p27, Ki-67 in thyroid cancer are being reported. We present a rare case of co existence of malignant pituitary adenoma with papillary thyroid carcinoma in a patient.

48 y/o Burmese female with a history of metastatic pituitary adenoma which was initially diagnosed in 2002 and resected in Thailand. Since she underwent a total of 3 cranietomies - 2002, 2003 and 2004, followed by a transsphenoidal surgery in 2006 for recurrent disease; pathology was consistent with pituitary adenoma with atypical features with greater than 50% staining for Ki-67. She has received several courses of radiation therapy to pituitary tumor and gamma knife surgery of pituitary adenoma from 2004-2011. She was then found to have metastatic disease in her lumbar and thoracic spine for which she underwent radiation therapy and then went on Hospice. She was also seen at Roswell Park for a 2nd opinion and was started on oral chemotherapy with Temozolamide in 4/13 for leptomeningal spread with cauda equina involvement. She responded well and came off Hospice. She completed 12 cycles of her chemotherapy. Unfortunately in 10/2014 she was found to have multinodular goiter on thyroid sonogram and FNA was consistent with papillary thyroid carcinoma. A conservative approach was taken considering her comorbidities and functional status and she was left with one more cycle of chemotherapy. She has been monitored with thyroid sonography and so far it is stable.

Conclusion: This is a rare case of a patient with pituitary and papillary cancer who was exposed to external beam radiation and has positive staining for Ki-67 on pituitary tissue. Ki-67 staining pattern indicates an extremely high proliferation index that is unusual even in atypical adenomas and raises the possibility of carcinoma. Radiation therapy can be a catalyzing factor. Based on these reports, our questions are: will patients treated with external beam radiation benefit from potassium iodine for thyroid protections, and is implementation of earlier thyroid sonogram surveillance needed in patients with pituitary tumors?

Abstract #801

PARTIAL HYPOPITUITARISM WITHOUT RADIOGRAPHICALLY DETECTABLE HYPOPHYSISIS DURING TREATMENT WITH IPILIMUMAB

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Case Presentation: A 59-year-old male was receiving induction dosing of ipilimumab (Ipi), a humanized monoclonal cytotoxic T-lymphocyte associated antigen-4 (CTLA-4) antibody, for management of metastatic melanoma. Shortly after the fourth dose, he presented to his oncologist with subacute onset frontal headache and lethargy. MRI of the sella turcica failed to show pituitary metastases or enlargement indicative of hypophysitis. The patient was treated empirically with a 5 d methylprednisolone taper, and symptoms abated. However, headache and fatigue recurred, prompting two additional 5 d treatment courses in the 4 weeks between symptoms onset and endocrinology referral. Pituitary function was evaluated 2 weeks after the last dose of methylprednisolone and notable for 8 AM cortisol 0.4 μg/dL (6.2-19.4), ACTH < 5 pg/mL (0-46), free T4 0.70 ng/dL (0.93-1.70), and TSH 0.62 mIU/L (0.27-4.20). Prolactin was low (2.4 ng/mL, 4.0-15.2), but morning testosterone (331 ng/dL, 193-740) and LH level (4.5 mIU/mL, 1.7-8.6) were unremarkable. Partial Ipi-induced hypopituitarism was diagnosed, and the patient was started on hydrocortisone followed by levothyroxine one week later. Headache and fatigue completely resolved, and the patient started Ipi maintenance therapy.

Discussion: CTLA-4 antibodies are checkpoint inhibitors that disrupt immune tolerance to antigens on tumor cells. However, immune-related adverse events may occur as a consequence of T-cell activation including hypophysitis. In a recently published retrospective review, hypophysitis occurred in 11% of Ipi treated patients, and male gender and advanced age were risk factors. Central hypothyroidism occurred in all patients, central hypogonadism was present in all cases where evaluation was performed, and central adrenal insufficiency occurred in half of patients. Mild to moderate pituitary enlargement was demonstrated on MRI in all cases in the series. Animal studies have found CTLA-4 expression on anterior pituitary cells, lymphocytic infiltration of the pituitary, and antipituitary antibodies after injection of CTLA-4 antibodies.

Conclusion: Hypophysitis and varying degrees of hypopituitarism occur in approximately 10% of patients treated with Ipi. This case is unusual for two reasons: 1) no pituitary enlargement was apparent on MRI, and 2) gonadotrope function was preserved. Ipi-induced hypophysitis should be investigated promptly when patients develop provocative
symptoms and appropriate hormone replacement started based on anterior pituitary function. This case illustrates that Ipi-induced hypophysitis can occur even in the absence of obvious pituitary enlargement.

Abstract #802

WHOOPING COUGH ASSOCIATED RIB FRACTURES: SHOULD WE LOOK DEEPER? A CASE REPORT OF CUSHING’S DISEASE

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Objective: An atypical presentation of Cushing’s disease. Case Presentation: A 36 year old man presented to the Emergency Department complaining of persistent cough for 3 weeks. Chest x-ray showed clear lungs, and incidentally found were right 7th and 8th rib fractures. Assay for B. pertussis was positive. He was admitted for uncontrolled blood pressure. He had gained 72 lbs. over the last 12 months. Blood pressure was 160/105 mmHg with a normal pulse, respirations and temperature. Weight was 382 lbs. and BMI 49 kg/m2. Physical exam remarkable for moon facies, bibasilar rhonchi, central obesity, large abdominal bruising in the right upper quadrant, purple colored abdominal striae, bilateral lower extremity pitting edema, and the presence of supra-clavicular fat pads. CBC and chemistries were normal except for mild leukocytosis with neutrophilia. HgbA1c was 6.2%. Morning cortisol was 24.1 ug/dL. A 1 mg dexamethasone overnight suppression test gave a morning cortisol of 22.3ug/dL, whereas an 8mg suppression test led to a morning cortisol of 9.5 ug/dL. The 11pm salivary Cortisol was 0.9 mcg/dL. Distal radius DEXA was within normal range. Pituitary MRI showed a small partially cystic left-sided pituitary lesion. He underwent bilateral petrosal sinus sampling which confirmed the diagnosis of left sellar Cushing’s disease and he underwent successful transphenoidal hypophysectomy surgery.

Discussion: Prolonged hypercortisolism causes immunosuppression via broad effects on the immune system, while also inducing bone losses, mostly trabecular. Vertebral and rib fractures are commonly seen in patients with Cushing’s syndrome, while according to the Centers of Disease Control, only 4% of children and adults with whooping cough may develop rib fractures. Kwon et al, found that 62% of immunocompromised hosts lose pertussis immunity despite vaccination. As a result, we hypothesize that hypercortisolism played a major role as risk factor for susceptibility to pertussis and rib fractures. It is also important to be aware of infections as a presentation of Cushing’s syndrome. To our knowledge, there is no literature associating risk of B. pertussis infections and hypercortisolism. We did not confirm presence of trabecular bone loss in this patient and recognize that pertussis cases have risen in the US in recent years and in the patient’s age group.

Conclusion: Cushing’s disease is a potential risk factor for whooping cough, associated with rib fractures.

Abstract #803

CUSHING DISEASE DUE TO PITUITARY MACROADENOMA: BIOCHEMICAL CHARACTERISTICS IN A PEDIATRIC COHORT

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NIH

Objective: Demonstrate the biochemical behavior of Cushing disease due to pituitary macroadenomas in a pediatric population.

Methods: A retrospective review of all patients <18 years of age admitted to the National Institute of Health (NIH), with the diagnosis of CD confirmed by pathology between 1997-2014 was performed.

Results: Of 87 patients identified, 13 were determined to have pituitary macroadenoma and 74 microadenoma based on imaging; 9/13 (69%) in the macroadenoma group and 43/74 (58%) in the microadenoma group were females. The mean age±SD in both groups were similar (14±6.4 vs 14±5.4yr). The mean BMI±SD was also similar in both groups (31.8±7.5 kg/m2 for macroadenoma and 30.2±15.4 kg/m2 for microadenoma group). The median (25%-75%) baseline 24-hr urine UFC was 263.60 mcg/24hr (170.7-528.0) for macroadenomas and 371.6 mcg/24hr (244.2-625.3) for microadenomas (P=0.47). The baseline median 24-hr urinary 17-hydroxysteroid excretion was 12.6 mg/24 hr (range 8.9-42.5) and 31.6 mg/24 hr (range 4.3-39.9) for macroadenomas and microadenomas, respectively. Mean 0800-0900 hr serum cortisol was 38.9±40.4 mcg/dl in macroadenomas compared to 20.2±15.8 mcg/dl in microadenomas (P=0.16). Basal plasma ACTH 0800-0900 hr (mean±SD) was 106.3±112.3 pg/ml for macroadenomas and 49.9±44.3 pg/ml for microadenomas (P=0.11). In the ACTH responses to ovine CRH test there were also no statistically significant differences. Using the high dose dexamethasone suppression test, 58% (7/12) suppressed more than 69% in the macroadenoma group compared to 69% (44/64) in the microadenoma group (P=0.51).

Discussion: Studies in adult patients have demonstrated that
macroadenomas have less glucocorticoid suppressibility after the high-dose dexamethasone suppression test and attenuated ACTH response to CRH compared to pituitary microadenomas. However, the present study shows that this is not true in children; although patients with macroadenomas had a tendency for higher baseline serum ACTH and cortisol levels, their responses to dynamic testing were similar to those with microadenomas.

**Conclusion:** Biochemical behavior of Cushing disease due to pituitary macroadenoma is different in pediatric population compared with adult population.

**Abstract #804**

**COMPREHENSIVE EVALUATION OF THYROTROPINOMAS: EMORY UNIVERSITY 20-YEAR EXPERIENCE**

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**Objective:** Historically, thyrotropinomas (TSHomas) represent 1% of pituitary adenomas, but up to 4% in recent series. Data on silent TSHomas is sparse. Classic presentation includes tumor mass effect and hyperthyroidism often incorrectly treated with thyroid surgery/ablation. We present a single center review of TSHomas.

**Methods:** Retrospective case series of histopathologically-proven TSH-adenomas operated between 1993-2013. TSHomas were classified as active (group A) and silent (group B) based on biochemical evidence of central hyperthyroidism (elevated thyroid hormones along with inappropriately normal/high TSH).

**Results:** Among 1628 operated pituitary adenomas, 20 were TSHomas (1.2%). In increments of 5 years, proportion of TSHomas was 1%, 1%, 0.04% and 1.77% respectively. Two thirds of active TSHomas were operated between 2009-2013.

**Group A:** 6 patients (5 men), age 41±12, presented with hyperthyroidism (3), incidentally discovered tumor (2) and acromegaly (1). One patient with incidentaloma was diagnosed with acromegaly and 10 months later developed hyperthyroidism. Preoperatively, 3 patients received somatostatin analogs (SSA), 1 antithyroid drugs (ATD) and 2 SSA/ATD. None had thyroid surgery/ablation. Mean FT4 was 2.68±2.73 ng/dL; TSH 6.50±3.68 mIU/L. Glycoprotein alpha subunit (GSU obtained in 5 cases) was uniformly high. IGF-1 was high in 2 and prolactin (PRL) in 1 case. Tumor diameter was 2.1±1.2 cm. All adenomas were plurihormonal and 5 stained for GH. Postoperatively, 4 patients became euthyroid, 1 had high TSH/normal T4 and 1 remained hyperthyroid. Residual tumor was identified in the latter who received SSA, ATD and radiation.

**Group B:** 14 patients (7 men), age 47±14 presented with acromegaly (6), mass effect (4), incidentaloma (3) and galactorrhea (1). Mean FT4 (1.00±0.24 ng/dL) and TSH (2.02±1.65 mIU/L) were lower than in group A (p<0.01). GSU (measured in 5 cases) was uniformly elevated; IGF-1 was high in 9 and PRL in 6. Tumor diameter was 2.0±1.0 cm. All adenomas were plurihormonal and 12 stained for GH. Postoperatively, 2 patients had residual tumor; 1 underwent radiation and 1 reoperation. One patient had recurrence at one year and received SSA and radiation.

**Discussion:** In our surgical series, active TSHomas have been detected with greater frequency in recent years. Silent TSHomas may secrete insufficient amounts of TSH to induce hyperthyroidism but exhibit high GSU. TSHomas frequently co-secrete GH, which may be clinically apparent.

**Conclusion:** TSHomas have a wide spectrum of manifestations and often require multimodality treatment. Correct biochemical diagnosis is essential for early detection and may improve outcomes.

**Abstract #805**

**RECURRENT MANTLE CELL LYMPHOMA PRESENTING AS A SELlar MASS**

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**Objective:** The differential diagnosis of sellar masses in adults is broad, including pituitary adenomas, craniopharyngiomas, cysts, and malignancies. We describe a patient with a locally invasive sellar mass that proved to be metastatic mantle cell lymphoma.

**Case Presentation:** A 70 year old female, with mantle cell lymphoma in remission and primary hypothyroidism, presented to the referring hospital with vision changes followed by progressive confusion, nausea and hematemesis over two months. An MRI of the brain performed as an outpatient revealed a large sellar mass with extension into cavernous sinuses and encasing the internal carotid arteries bilaterally. An upper endoscopy additionally revealed a mass in the duodenum. High dose dexamethasone was started and the patient was referred to our hospital for further management. On admission, the patient was noted to have disorientation. An endocrine evaluation did not detect biochemical evidence of a prolactinoma or growth hormone secreting tumor, and her gonadotropin levels were normal. Her TSH was elevated,
the interpretation complicated by possible euthyroid sick syndrome and steroid administration. Her cortisol was low as expected on dexamethasone. Labs additionally showed hyponatremia, diagnosed as SIADH, which improved with fluid restriction. She underwent partial transphenoidal resection of the sellar mass. The pathology revealed atypical lymphocytes with flow cytometry positive for CD5, CD19, CD20, CD22 and negative for CD10 and TdT, consistent with a subsequent endoscopic biopsy of the duodenal mass. The patient began chemotherapy with intrathecal cytarabine and methotrexate via an Omaya catheter. Her hospital course was complicated by leukopenia and periods of altered mental status. Two months after admission, her steroids were tapered down and she was discharged on hydrocortisone and levothyroxine, with plans for continuation of chemotherapy and endocrine followup as an outpatient.

Discussion: Lymphoma in the central nervous system (CNS) may be of either primary or metastatic origin. Involvement of CNS occurs in 5-29% of cases of non-Hodgkin’s lymphoma (NHL). Review of the literature reveals lymphoma as the origin of metastatic cancer to the pituitary in <1% of cases. Lymphomas of the pituitary may cause hypopituitarism and neurologic deficits by mass effect and invasion of brain parenchyma. 

Conclusion: Lymphoma is a rare, albeit important, entity to consider in the differential diagnosis of sellar masses.

Abstract #806

THE UTILITY OF PITUITARY MAGNETIC RESONANCE IMAGING IN MEN WITH SECONDARY HYPOGONADISM

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Objective: In men with secondary hypogonadism, the utility of routinely obtaining a magnetic resonance imaging (MRI) to exclude hypothalamic-pituitary pathology is not well studied. We performed a retrospective study to evaluate the yield of pituitary MRI in men with secondary hypogonadism. We also determined if there were endocrinologic or hypothalamic-pituitary differences between men with and without metabolic syndrome (MetS) or type 2 diabetes (T2DM).

Methods: Eighty-eight men were evaluated in general endocrinology clinics and were included in this study if they had symptoms of hypogonadism as well as laboratory values consistent with secondary hypogonadism. Baseline total testosterone (TT), free testosterone (FT), follicle-stimulating hormone (FSH), luteinizing hormone (LH), and prolactin (PRL) were measured. All men received MRI of hypothalamic-pituitary region. Statistical analysis was performed using Mann-Whitney test for continuous variables and Fisher’s exact test for categorical variables.

Results: Of the 88 men, 16 (18%) had abnormal MRI. Adenoma was found in 9 (10%) men, and empty-sella in 7 (8%) men. Men with pituitary adenomas had significantly lower FT levels compared to those with normal MRI (18.7 pg/ml vs. 36.4 pg/ml). Men with empty-sella had significantly higher PRL compared to men with normal MRI (21.4 ng/ml vs. 11.2 ng/ml). Most of the men in the study (80%) had either MetS or T2DM. No endocrinologic differences were found between men with and without MetS or T2DM. In men without MetS or T2DM, 28% were found to have abnormal pituitary MRI, compared to 16% in men with MetS or T2DM, but this difference was not significant.

Discussion: The incidence of pituitary imaging abnormalities found in our study of men with secondary hypogonadism was not greater than the prevalence of pituitary adenomas in the general population, indicating that there is little value to routinely obtain MRI in the evaluation of men with secondary hypogonadism. Lower FT levels were found in men with pituitary adenomas, and higher PRL levels were found in men with empty sella syndrome. Men without MetS or T2DM had higher, but not significant, incidence of abnormal MRI.

Conclusion: We do not recommend the use of MRI for routine evaluation of all men with secondary hypogonadism. However, MRI is warranted in men with higher PRL or very low FT, both of which are associated with pituitary structural abnormalities.

Abstract #807

DIABETES INSIPIDUS IN LEUKEMIA: A COMPLICATION OR MARKER OF PROGRESSION

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Objective: Central diabetes insipidus (CDI) is a disorder characterized by inability to maximally concentrate urine secondary to deficiency or impairment of antidiuretic hormone. It is rarely observed in hematological malignancies such as acute leukemia and myelodysplastic syndrome. In leukemia, the reported incidence is less than 0.6%. The underlying causal mechanism in these malignancies remains unknown. We present one such challenging case of CDI in a patient
with chronic lymphocytic leukemia (CLL).

**Case Presentation:** A 67 year old female with history of hypertension and CLL presented with fever, chills, nausea, vomiting and malaise. She was diagnosed with autoimmune hemolytic anemia as a complication of CLL. Treatment with steroids, cyclophosphamide, ibrutinib and multiple blood transfusions showed no clinical improvement. She underwent plasmapheresis with improvement in symptoms. Her serum sodium gradually trended up to 150 mmol/L. Hypernatremia was considered secondary to fluid losses from polyuria not compensated by oral intake. Despite intravenous hydration, serum sodium remained in 145-150 mmol/L range and patient consistently had polydipsia. Careful monitoring of fluid balance revealed daily urine output of more than 3L with urine osmolality of 173 mOsm/Kg. Hypernatremia work up included a water deprivation test. Urine osmolality almost doubled following administration of 2 mcg of DDAVP (366 to 725mOsm/Kg). MRI brain revealed absence of hyperintensity signal in posterior pituitary. Anterior pituitary hormonal evaluation was unremarkable. Patient was diagnosed with CDI and desmopressin was started with improvement in urine output and osmolality, serum sodium levels and clinical symptoms.

**Conclusion:** The exact cause of CDI in leukemia is not fully understood. Leukemic cell infiltration of the hypothalamic-neurohypophyseal fibers, infection, hemorrhage and thrombosis of small vessels of the neurohypophysis are considered as potential underlying mechanisms. T1 weighted MRI brain may show pituitary stalk thickening and/or absence of hyperintense signals in posterior pituitary. CDI has been reported as a presenting symptom during relapse and has been associated with acceleration of disease in AML with a gravid course. In our patient, CDI also manifested when she presented with a well-recognized complication of CLL. Clinicians must remain vigilant of the possibility of CDI in patients with hematologic malignancies presenting with hypernatremia or DI symptoms as early diagnosis and treatment may prevent irreversible degeneration of the neurohypophysis.

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**Abstract #808**

**FUNCTIONAL GONADOTROPH PITUITARY ADENOMA PRESENTING WITH BITEMPORAL HEMIANOPIA**

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**Objective:** To present a case of a male patient who presented with bitemporal hemianopia and was found to have a functional pituitary gonadotroph macroadenoma secreting both FSH and LH with preserved testosterone, all three of which decreased dramatically post-resection.

**Case Presentation:** A 55-year-old man presented with bilateral peripheral vision loss and was found to have bitemporal hemianopia. He reported intermittent headaches and denied changes in weight, changes in hand or foot size, fatigue, easy bruising, thinning of skin, muscle weakness or decreased libido. Physical exam was otherwise unremarkable. An MRI revealed a 3.5x3.7x5.2cm well-circumscribed mass in the sella and suprasellar region with mass effect on the optic chiasm. Initial labs included prolactin 31.2ng/ml, IGF-1 126ng/mL, GH <0.1ng/mL, ACTH 23.5pg/mL, cortisol 3.9ug/dL, TSH 0.47uIU/mL, free thyroxine 0.83ng/dL, FSH 25.8mIU/mL, LH 7.2mIU/mL and testosterone 792ng/dL. Levothyroxine and twice daily hydrocortisone were started, and the patient was referred for transsphenoidal resection. Post-operative labs were unchanged except for FSH, LH and testosterone which drastically decreased to 1.4mIU/ml, 0.2mIU/mL and less then 2.5ng/dL, respectively. Repeat MRI showed a small amount of residual pituitary tissue with minimal distortion of the optic chiasm. Pathology staining showed pituitary adenomatous cells positive for FSH and LH.

**Discussion:** Gonadotroph adenomas represent about 35% of pituitary adenomas and are the most common type of nonfunctioning macroadenomas. The majority of gonadotroph adenomas are nonsecretory, and those that are secretory are associated with hypogonadism, which is thought to be secondary to a combination of hyperprolactinemia, mass effect on normal gonadotroph function and production of a non-functional gonadotroph. There are only a handful of published case reports of functional gonadotroph adenomas secreting FSH and LH resulting in preserved testosterone secretion. Like our patient, most presented with vision defects with one young boy presenting with precocious puberty. Only one other case report published by Dizon et al reported post-
operative testosterone levels similar to our patient. **Conclusion:** Although gonadotroph adenomas represent approximately a third of pituitary adenomas, most are nonfunctioning. We presented a case of a man with a large pituitary macroadenoma whose only symptom was vision loss and was found to have a functional gonadotroph adenoma with tumor-dependent preserved testosterone levels.

Abstract #809

SPONTANEOUS PITUITARY APOPLEXY IN THE SECOND TRIMESTER ASSOCIATED WITH SENSORY LOSS

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**Objective:** Pituitary apoplexy is characterized by spontaneous hemorrhage into the pituitary gland. We highlight a case which occurred at 23 weeks gestation associated with right sided weakness and sensory loss which subsequently resolved.

**Case Presentation:** A 32 year-old Hispanic woman (G6P4) at 23 weeks gestation presented with a right-sided headache which was severe, sharp and constant around her face and back of neck. This was associated with photophobia and a right-sided numbness of her body. At admission she denied nausea, vomiting, visual problems, menstrual irregularities, or galactorrhea. Examination revealed visual acuity 20/40 bilaterally with some blurriness on left side, decreased right V1-V2 facial sensation with midline splitting at forehead and nose, but other cranial nerves were normal. She had preserved 5/5 power in all groups except right upper (4/5) extremity, with decreased sensation over entire RUE and RLE to touch and pinprick. Labs suggested an elevated prolactin at 314.2 ng/ml (in setting of pregnancy), normal cortisol and ACTH (14 pg/ml), LH 0.19 (IU/L), IGF-1 low at 78 ng/ml (106-368), normal TSH (2.15 mIU/ml) and fT4 (0.69 ng/dl). MRI brain revealed enlargement of pituitary (1.7 cm), with layering hemorrhage posteriorly and mild compression of the optic nerve.

She described additional visual symptoms shortly after admission and emergent evacuation of pituitary hematoma was subsequently performed. Histology revealed minute fragments of adenohypophysis with hemorrhage and fibrosis. Post-operative MRI revealed resolution of optic nerve compression.

**Discussion:** Pituitary apoplexy most often results from spontaneous hemorrhage into a pituitary adenoma. Pregnancy is associated with a higher risk. The pituitary gland may grow by up to 40% in the 2nd trimester and 70% in 3rd trimester. In 80% of cases, pituitary apoplexy is the presenting sign of an underlying pituitary adenoma, with common symptoms including headache, nausea, decreased visual acuity, visual field deficits, ocular paresis and impaired mental status. Our patient had associated symptoms of right-sided weakness and sensory loss affecting the upper limb associated with the acute hemorrhage.

**Conclusion:** Pituitary apoplexy is rare in pregnancy. It is an endocrine emergency and must be considered in a pregnant patient presenting with sudden onset headache. This case provides a reminder of other less commonly associated neurological symptoms and signs in such patients.

Abstract #810

LAST GASP OF A DYING GLAND: STRESS CORTICOTROPH RESPONSE IN A CASE OF PITUITARY APOPLEXY

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SIU School of Medicine

**Case Presentation:** A 72-year-old man presented to the hospital with acute onset headache, diplopia, and vomiting. Examination was notable for hypertension and partial left third and sixth cranial nerve palsies. No stigmata of Cushing’s syndrome were observed. MRI revealed a 2.9 cm pituitary macroadenoma with acute hemorrhage extending into the left cavernous sinus. Evaluation of anterior pituitary function approximately 30 hr after admission revealed serum cortisol 56.4 μg/dL (8.7-22.4) and ACTH 337 pg/mL (7-69). TSH (0.92 mIU/L, 0.34-5.60), free T4 (1.0 ng/dL, 0.5-1.3), and IGF-1 (167 ng/mL, 36-215) were unremarkable, though prolactin level was low (1.0 ng/mL, 2.6-13.2). Over the next 4 d, serum cortisol ranged from 50-60 μg/dL, and 24 hr urine free cortisol was 1,883 μg (< 60). At hospital discharge 7 d after admission, cortisol (24.6 μg/dL) and ACTH (148 pg/mL) were falling, and at 15 d from admission early hypopituitarism had occurred [8 AM cortisol 5.7 μg/dL, ACTH 15 pg/mL, TSH 0.55 mIU/L, free T4 0.6 ng/dL, IGF-1 65 ng/mL, LH 2.2 mIU/mL (1.2-8.6), testosterone 76 ng/dL (270-1070)]. The adenoma was resected 6 wk after initial presentation, and postoperative histology revealed neuroendocrine cells in a background of fibrosis and pigment-laden macrophages but no staining for ACTH.

**Discussion:** Pituitary apoplexy usually occurs due to hemorrhage or infarction of an adenoma. Hypopituitarism often occurs either at time of presentation due to compromise of anterior pituitary blood flow or before
the event due to mass effect of the adenoma. Secondary adrenal insufficiency is reported in approximately 70% of pituitary apoplexy cases, but significant hypercortisolism is rare. Literature review identified only one published case of hypercortisolism during apoplexy in the setting of Cushing’s disease. In this case, hemorrhage of a corticotroph adenoma is unlikely as corticotroph macroadenomas are rare, the patient had no symptoms or signs of Cushing’s syndrome, and no immunohistochemical staining for ACTH was detected on histological evaluation of the tumor. Elevations of ACTH and cortisol most likely reflect stress activation of the hypothalamic-pituitary-adrenal axis, with subsequent central hypogonadism and declines in other pituitary functions reflecting subacute onset of hyponadotuitarism.

**Conclusion:** This case illustrates that pituitary apoplexy may provoke a stress glucocorticoid response if corticotrophs remain viable. There is little published to predict subsequent anterior pituitary function after hemorrhage when initial cortisol levels are elevated, though low prolactin level appears to have been a marker for eventual hyponadotuitarism as in more typical cases of apoplexy.

**Abstract #811**

**NELSON’S SYNDROME: THE DREADED COMPLICATION FOLLOWING BILATERAL ADRENALECTOMY FOR UNCONTROLLED CUSHING’S SYNDROME**

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Boston University School of Medicine

**Objective:** Nelson’s syndrome is a rare condition with an aggressive growth of an adrenocorticotropin (ACTH)—secreting pituitary adenoma that may occur following bilateral adrenalectomy for Cushing’s disease. There has been ongoing interest in identifying patients at risk for progression to Nelson’s syndrome as well as guidelines for diagnosis and management.

**Case Presentation:** A 55 year old male was treated at a teaching hospital in 1987 with transsphenoidal resection for an ACTH-secreting pituitary microadenoma, but pathology failed to show ACTH positive cells. In subsequent months he underwent bilateral adrenalectomy for persistent hypercortisolism; pathology showed adrenal hyperplasia of both glands. He returned to the same hospital twenty years later with hyperpigmentation and weakness. MRI revealed recurrence of 1.4 cm pituitary tumor. He had a second transsphenoidal resection in 2008; pathology showed ACTH-staining cells. He was lost for follow-up for five years and then seen at our hospital for evaluation of blurry vision and headache. His current presentation was notable for marked hyperpigmentation (palmar creases, buccal mucosa, gingiva, vermilion border), left ptosis and decreased visual acuity bilaterally. His biochemical evaluation was remarkable for an elevated ACTH 17.606 ng/L (while on glucocorticoid replacement). Brain MRI revealed a 4.7 cm suprasellar mass with extension into the clivus and 3rd ventricle, invasion of the cavernous sinus and encasement of the internal carotid arteries with significant compression of the optic chiasm and intracranial optic nerves. After multidisciplinary consultation he underwent third transsphenoidal resection in attempt to debulk his unresectable tumor. Post-operatively he had resolution of left ptosis and improvement in vision.

**Conclusion:** This case highlights the importance of close post-operative surveillance following resection of ACTH-secreting adenomas. In addition to risk-stratification after histopathological review, recommended follow-up includes ACTH, radiologic evaluation and careful consideration for neoadjuvant radiotherapy. Nelson’s Syndrome requires prompt evaluation and multidisciplinary approach to treatment because of the aggressive tumor growth and morbidity associated with late diagnosis.

**Abstract #812**

**PRIMARY B CELL LYMPHOMA OF PITUITARY PRESENTING WITH HYPOPITUITARISM AND DUAL NATREMIC ABNORMALITIES**

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**Objective:** To report a rare case of hypopituitarism caused by Primary central nervous system lymphoma (PCNSL), presenting with dual natremic abnormalities.

**Case Presentation:** A 75-year-old gentleman presented with complaints of several months of malaise, fatigue, confusion and weakness. He was found to be hyponatremic (sodium=127mmol/L) attributed to SIADH of unknown origin. Further workup of his hyponatremia and weakness revealed: TSH-0.33mcUnit/ml (0.4-5.0mcUnit/ml), free T3-1.8pg/ml (1.7-3.7pg/ml), free T4-0.79ng/dl (0.8-1.8ng/dl), and normal cortisol levels with normal ACTH stimulation test. He returned to the hospital 2 weeks later with the inability to read the left side of his newspaper. He was found to have left homonymous hemianopsia, worsening confusion, bradycardia and hypotension. Enhanced MRI was done, which revealed a lobulated enhancing suprasellar mass.
measuring 2.7 cm with involvement of the chiasm and 3 additional enhancing intracranial lesions. Sodium was elevated at 151 mmol/L with serum osmolality of 330 mOsm/kg and urine osmolality of 320 mOsm/kg, and low anti-diuretic hormone level 0.8 pg/ml (0-4.7 pg/ml). After desmopressin urine osmolality increased to 400 mOsm/kg, suggestive of central diabetes insipidus. Prolactin was elevated at 77.5 ng/ml (0-17.5 ng/ml) due to pituitary stalk effect. Parasagittal craniotomy and excisional biopsy of the frontal lesion showed high-grade large B cell lymphoma, CD20 positive. Further imagining was negative for systemic lymphoma. He could not tolerate the first cycle of methotrexate, procarbazine and vincristine and with his worsening condition, his family decided to pursue home hospice care.

Discussion: Pituitary adenoma is known as the most common cause of hypopituitarism. PCNSL is rare overall, and not high on the differential for hypopituitarism. PCNSL commonly presents with visual disturbances or neurological defects. However, our patient presented with vague symptoms of lethargy and malaise months before any such defects set in. SIADH and diabetes insipidus which are two extremes of sodium disorders occurring in succession has been rarely reported with PCNSL. Our case highlights the importance of the varied presentation of PCNSL, and a high index of suspicion is required when dealing with natrencic disorders and hypopituitarism. Early diagnosis and treatment of this aggressive tumor, have shown patients to respond hematologically with improvement in pituitary function. Conclusion: Recognition of this rare presentation of PCNSL in the differential diagnosis of sodium disturbances with partial hypopituitarism, will allow early diagnosis and prompt treatment.

Abstract #813

A CASE OF HYPOGONADISM IN A YOUNG MAN WITH AN EATING DISORDER

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Case Presentation: Severe restriction of nutritional intake leading to a low BMI, such as in anorexia nervosa (AN), is 10 times more common in females than males and is known to have a number of endocrine effects including hypogonadotrophic hypogonadism, hypercortisolism, growth hormone resistance, thyroid abnormalities, and bone loss. In patients that meet most of the criteria for AN, yet have a normal weight, the term “atypical anorexia nervosa” has been used. Atypical AN may be more prevalent than AN and those affected can also suffer from endocrinopathies.

We report the case of a 20 year-old man presenting with hypogonadism. Over a period of several months he noted a 30 lb weight loss, decreased libido and muscle mass, muscle fatigue, and a recent diagnosis of mononucleosis. Initial BMI was 21.6. Morning labs revealed: TSH: 7.8, FSH: 2.1, LH: 1.4, total testosterone: 130, prolactin: 10.4, FBG: 73, normal CMP and LFTs, Hb: 14.6, total IgA: 126 (normal), TTG: 6 (normal < 4), negative endomyseal antibody, total vitamin D: 39; and vitamin B12: 1191. A pituitary MRI was was obtained due to central hypogonadism and was unremarkable. Repeat labs showed a normal CMP, FBG, LFTs, TSH: 5.5, free T4: 1.1, negative TPO antibodies, AM cortisol: 28.8, ACTH: 64 (6-50), IGF-1: 151 (83-456), normal DHEA and estradiol, and a repeat AM testosterone: 147. On exam, his testicles had a normal volume. The abnormal thyroid studies were felt to be due to non-thyroidal illness, possibly from mononucleosis, with the mild cortisol elevation thought to be due to stress. The patient continued to experience weight loss, malaise and fatigue. After further questioning, he denied anabolic steroid use but did report college-related stress and that he was severely restricting calories while binging at times, to keep his weight down. The patient was counseled and referred to an eating disorder clinic. Over a period of 4 months, his weight increased from 127 to 175 lbs, and his thyroid studies, total testosterone, and cortisol level normalized with treatment of his eating disorder.

Conclusion: This case should raise awareness that males also suffer from eating disorders, and that even a patient with a normal weight can suffer from an endocrinopathy related to an eating disorder. The most common presenting endocrinopathy is hypogonadism, but patients also present with euthyroid sick syndrome and hypercortisolism. When a young adult presents with an otherwise unexplained endocrinopathy, it is good practice to obtain a diet, supplement, drug use, and mental health history.

Abstract #814

ANAPLASTIC INFILTRATING GLIOMA PRESENTING AS ISOLATED HYPERPROLACTINEMIA

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Case Presentation: While significant elevations in prolactin levels usually indicate a pituitary adenoma, it is
unusual for a primary brain tumor to present with isolated hyperprolactinemia. A 31-year-old female with three-month history of secondary amenorrhea was admitted to our institution after presenting with a thunderclap headache. CT scan of the head revealed a subarachnoid hemorrhage and an incidental pineal mass. A prolactin level was checked which was elevated at 64.9 ng/ml (2.8-29.2) and further brain imaging was consistent with a complex enhancing pineal infiltrative lesion. All other pituitary hormones were within normal. Given only the mild elevation in prolactin levels, hook’s effect was ruled out by a prolactin dilution assay. She underwent surgical resection and pathology was consistent with an infiltrative malignant glioma based with a high Ki-67 index. Metastases to the central nervous system were ruled out by cerebrospinal fluid cytological analysis. In the direct post-operative period, her prolactin level decreased to 41.5 ng/ml but then increased up to a peak of 100.8 ng/ml on her 3-month outpatient follow-up without resolution of her secondary amenorrhea. She was started on cabergoline which controlled her hyperprolactinemia (<0.3 ng/ml at 6 months) but did not restore her menstrual cycles. She thus required hormonal treatment which was problematic given the association of certain primary central nervous system tumors with positive estrogen and progesterone receptor status. **Conclusion:** The importance of elevated prolactin levels should be recognized and hyperprolactinemia should be worked up judiciously when no other identifiable cause exists as it can be telling of a much more morbid diagnosis.

**Abstract #815**

**GROWTH HORMONE, TSH CO SECRETING ATYPICAL PITUITARY MACROADENOMA IN AN ACROMEGALY PATIENT COMPPLICATED BY ACUTE THYROIDITIS**

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Makati Medical Center

**Case Presentation:** 37 year old male referred to the Endocrinology clinic due to elevated blood sugar. Upon examination frontal bossing, enlarged hands and feet with 2 cm diameter circumscribed mass at the right lobe of the thyroid gland were noted. 75 gram glucose stimulated Growth hormone was requested revealed: 0 hour 35.6 ng/ml(NV 0-3 ng/ml), first hour 32.6 ng/ml, second hour 34.6 ng/ml. MRI of the pituitary gland showed sellar/suprasellar mass with cystic and solid components measuring 2x2x2.2 cm without identifiable residual pituitary gland. Pre operative hormonal work up showed normal Prolactin: 7.85 ng/ml(NV 4.04-15.20 ng/ml), and cortisol: 10.66ug/dl(NV 6.2-19.4 ug/dl), low TSH: 0.22 pmol/L (NV: 0.25-4 pmol/L) High FT4: 27 pmol/L(NV: 11.5-23 ug/dl). Patient denies symptoms of palpitation, diarrhea, tremors or insomnia. Thyroid scan showed homogenous with hypo-functioning nodules in both lobes. Thyroid ultrasound showed enlarged homogenous thyroid with multiple solid and cystic nodule. Patient was given methimazole 5mg OD.

3 weeks prior to admission, patient complained of anterior neck pain at the area of the thyroid most prominent on head turning and swallowing. He had bout of colds few weeks before. Anti-TPO, ESR were normal, relieved with intake of NSAIDs.

Patient was admitted for transphenoidal surgery. Histopathology revealed large deeply stained irregular nuclei, reactive to synaptophysin, growth hormone, TSH and chromogranin, non reactive to CK20 and focally reactive to CK7. Diagnosis: Consistent with atypical pituitary adenoma growth hormone positive, TSH positive. **Conclusion:** Acromegaly is frequently associated with thyroid disorders. Manifestations of hyperthyroidism were not observed possibly masked by the features of acromegaly. This patient presented with acromegaly on top multiple thyroid disorders: acute thyroiditis, nodular goiter and TSH and Growth hormone secreting pituitary tumor.

**Abstract #816**

**LYMPHOCYTIC HYPOPHYSITIS PRESENTING WITH DIPLOPIA IN A NON-PREGNANT WOMAN**

**Halis Akturk, MD, Ana Maria Chindris, MD**

Mayo Clinic

**Case Presentation:** Lymphocytic hypophysitis is a rare, presumed autoimmune condition. It commonly affects young women in late pregnancy or in the early postpartum period. Here we report a case of a young woman without a history of pregnancy who presented with lymphocytic hypophysitis and was treated successfully with corticosteroids.

26 year old female presented with diplopia and headaches. MRI of the brain showed a diffuse enlargement of the pituitary gland of 2.2 X 1.2 cm and a pituitary stalk of 3.5 mm. Physical exam was consistent with left cranial nerve VI palsy. Neuroophthalmologic exam did not show any visual field deficits. Laboratory work up showed normal levels of FSH, LH, Prolactin, Cortisol, ACTH, TSH and fT4. AFP and HCG levels were also normal. In past medical history; she has hypothyroidism and she was on levothyroxine treatment. She reported a febrile diarrhea 4 weeks ago. She was started on dexamethasone 4 mg p.o. daily for 4 weeks and her symptoms dramatically
improved. Dexamethasone was tapered down successfully and at follow up she has normal pituitary hormone levels and no vision problem. **Discussion:** The clinical presentation of lymphocytic hypophysitis may mimic that of a pituitary adenoma. Imaging studies usually demonstrate a diffuse homogenous enlargement of pituitary gland and stalk with a characteristic ‘pear shape’ appearance. Corticosteroids are the first choice for treatment. Routine pituitary hormone studies and periodic MRI imaging are recommended for long term management. Lymphocytic hypophysitis is mostly encountered postpartum, and other autoimmune endocrine disorders can be seen with these patients. Germ cell tumors of sella also need to be ruled out for differential diagnosis. **Conclusion:** Lymphocytic Hypophysitis is a rare entity that needs to be considered in differential diagnosis of pituitary masses.

**Abstract #817**

**PITUITARY METASTASIS WITH AN UNKNOWN PRIMARY**

**Halis Akturk, MD, Kaniksha Desai, MD, Ana Maria Chindris, MD**

Mayo Clinic

**Case Presentation:** Pituitary metastasis accounts for less than 1% of sellar masses. The most common primary site in women is breast cancer and in men is lung cancer. We report a case of pituitary metastasis with an unknown primary site.

A 41-year-old female presented with progressive vision loss. Physical exam showed ptosis and severe vision loss in the left eye. Neuroophthalmologic exam revealed complete left cranial nerve III palsy, severe left optic neuropathy with no light perception vision on the left side and a temporal visual field defect in the right eye. MRI of the brain showed a 2.6 cm X 2.5 cm pituitary macroadenoma with cavernous sinus invasion. She was previously healthy until her vision loss. She had no evidence of hypopituitarism or diabetes insipidus at presentation. Laboratory work up showed normal levels of FSH, LH, TSH and fT4, but elevated prolactin 32.2 ng/mL (4.8-23.3 ng/mL). She underwent a transsphenoidal pituitary surgery and the pathology revealed poorly differentiated non-small cell carcinoma, consistent with pituitary metastasis. Immunostains showed that the tumor was strongly positive for keratin (AE1/AE3), but negative for CK20, CK7, CK5/6, S-100, Melan A, TTF-1, CDX-2, mammaglobin, synaptophysin, CD31 and EBV in-situ hybridization which supported the above diagnosis.

She had a chest/abdomen/pelvis CT and mammogram which were negative for primary lesion. Her postoperative course was complicated by new onset diabetes insipidus, panhypopituitarism, and an internal carotid artery thrombosis. She was treated with hydrocortisone, levothyroxine and desmopressin. She was also noted to have a pulmonary embolism and was anti-coagulated with a subsequent cerebral hemorrhage which led to her demise within 7 weeks of her initial presentation.

**Discussion:** Metastasis to the pituitary gland is a rare clinical entity which is most often found at autopsies after a primary site has been identified. Pituitary metastasis is typically seen in cases in which there is widespread metastasis and prognosis is poor. Symptomatic pituitary metastasis, especially as a first presentation is very rare. The most common reported symptom is polyuria with diabetes insipidus at presentation. However our patient presented with vision loss and ptosis without any signs of diabetes insipidus or panhypopituitarism.

**Conclusion:** Although metastasis to the pituitary gland is rare, it should be considered in the differential diagnosis of the sellar masses.

**Abstract #818**

**UNUSUAL PRESENTATION OF HYPOTHALAMIC-PITUITARY DYSFUNCTION**

**George Thott, M.D., Karen Herbst, Ph.D., M.D.**

University of Arizona

**Case Presentation:** A 24 year old healthy male presented to the university medical center after having complaints of right leg numbness with foot drop, visual disturbances, and excessive fatigue over the last two months. Upon furthering questioning the patient endorsed having progressive hair loss on his chest, arms, legs and erectile dysfunction over the last 5 months. Endocrine labs on admission showed low cortisol, testosterone, LH, FSH, free T4, but elevated prolactin and hypernatremia. MRI brain showed three well-defined intensely enhancing lesions, the first one within the suprasellar cistern measuring 26 x 20 x 22mm involving the optic chiasm, hypothalamic region and extending to the anterior/inferior portion of the 3rd ventricle. The pituitary is intact without mass effect, but the infundibulum showed mild deviation to the left side. The second mass encased the pineal gland measuring 13 x 15 x 10mm. The third mass within the Meckel’s cave measured 17 x 15 x 9mm. Lumbar puncture and CSF studies showed 26 WBCs with 98% lymphocytes with AFP <1 and elevated Beta-hCG. CSF cytology showed atypical cells unclear if malignant. Serotal US was normal and his MRI spine revealed leptomeningeal metastasis.
The findings are suggestive of intracranial germinoma. The patient was started on treatment with physiologic dose of hydrocortisone, and levothyroxine for panhypopituitarism. Hypernatremia was thought to be caused by diabetes insipidus from suppression of the thirst center and the patient was encouraged to increase his free water intake. Oncology was consulted and initiated chemotherapy shortly before discharge.

**Conclusion:** This case illustrates compromise of the hypothalamic pituitary axis by a very rare cancer in this patient’s age group. In addition, this patient exhibited a trifocal lesion with leptomeningeal metastasis which adds to the rarity of the presentation of this uncommon cancer.

**Abstract #819**

**AN UNUSUAL CAUSE OF FEVER**

Eng Keong Tan, MD

Baystate Medical Center

**Objective:** Fever has almost always been associated with infection. However, many causes other than infectious exist. We report an elderly adult whose persistent fever was due to pituitary adenoma.

**Case Presentation:** 71 years old male known hypertension presented with lethargy and a swollen right knee after fall. He was found to be tachycardia, febrile, temperature of 103 F with a right knee effusion, tender and warm. Laboratory revealed elevated WCC 21,000, CRP over 200. Despite of appropriate antibiotic for septic arthritis, patient remained febrile. Transthoracic echocardiogram, computed tomography (CT) of thorax and abdomen revealed no focal infection source. Incidentally CT head revealed pituitary macro adenoma. During knee washout operation, he developed hypotension requiring vasopressor support for 1 day. Post ICU discharge he was noted to have persistent fever despite of completing the appropriate course of antibiotic. Knee effusion fluid revealed pseudo gout crystal.

Patient was having urine output above 3L to 4.9L daily. With suspicion of diabetes insipidus (DI), pituitary function was investigated which revealed secondary hypothyroidism, hypogonadotropic hypogonadism with reduced ACTH and IGF-1. Cortisol level was inappropriately normal. Magnetic resonance imaging (MRI) of pituitary revealed large sellar mass extending into sphenoid sinus compressing optic chiasm. Thyroid and cortisol replacement was started urgently. Fever resolved subsequently. Patient underwent transsphenoidal resection of the tumor. Histochemical stains revealed gonadotrophic cell adenoma. He was discharged with hormonal replacement.

**Discussion:** Pituitary macro adenomas can rarely presented with persistent fever. Pituitary tumors may cause fever via inflammatory chemical meningitis or by activating hypothalamic noradrenergic pathways. Interestingly our patient has elevated serum IgG. IgG4-related disease can cause autoimmune hypophysitis, resulting in pituitary dysfunction, fever and DI. Reported cases responded to corticosteroid replacement alone with resolution of both fever and high urine output.

Pituitary tumor’s mass effect can resulted in pituitary apoplexy and panhypopituitarism, which could result in high mortality. Our patient’s gonadotropic cell adenoma had resulted panhypopituitarism secondary to apoplexy phenomenon. Transsphenoidal pituitary surgery in elderly has been proven to be safe and effective.

**Conclusion:** Pituitary macro adenomas can cause persistent fever and hypopituitarism. It may be subtle in presentation. Due to potential high morbidity and mortality physicians need a high index of suspicion in the appropriate circumstances.

**Abstract #820**

**IF AT FIRST YOU DON’T SUCCEED, TRY AND TRY AGAIN: A CASE OF REFRACTORY PROLACTINOMA**

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William Beaumont Hospital Royal Oak

**Objective:** To report a case of medically- and surgically-refractory prolactinoma and present indications for alternate or repeated treatment modalities.

**Case Presentation:** A fifty-one year old man with a long history of asymptomatic pituitary adenoma presented in 1998 with bitemporal hemianopsia. Prolactin (PRL) level was 27ng/mL. MRI demonstrated a 1.1 x 0.8cm sellar mass. Cabergoline was initiated with good effect. He remained stable for the next ten years.

In 2008, he had relapse of symptoms despite PRL <18ng/mL. MRI revealed herniation of the optic chiasm into the sella turcica so his cabergoline dose was reduced. In 2009, MRI showed a 2.2 x 1.8 x 2.0cm macroadenoma expanding the sella with marked compression of the optic chiasm. Despite medication escalation, PRL reached 680ng/mL. The patient underwent transphendoidal radical hypophysectomy with clean margins. Symptoms subsided only transiently, so he then proceeded with gamma knife radiosurgery (GKRS.)

In 2013, recurrent tumor prompted repeat endoscopic transphenoidal hypophysectomy, followed by fractionated radiation. This combination was effective in achieving remission. The patient is now on stable dose cabergoline and steroid replacement for panhypopituitarism. One year
later there has been no recurrence of tumor, and his most recent PRL in 2014 was 1.2 ng/mL. 

**Discussion:** The mainstay of treatment for prolactinomas is dopamine agonists, which work by inhibiting PRL secretion though dopamine receptor 2 (DRD2). Resistant prolactinoma is defined by an inability to normalize PRL and to reduce tumor size by 50% despite appropriate medical therapy. The mechanism may be linked to the loss of the DRD2 or post-receptor intracellular transduction mechanisms. Transphenoidal surgery is the most common surgical approach with remission rates of 73-90%. Our patient’s elevated pre-operative PRL and male sex statistically suggested a worsened prognosis. GKRS is another option with 30% success in normalizing PRL. It has lower remission rates in patients on concurrent dopamine agonist therapy due to decreased cell cycling. Fractionated radiation is considered a radiotherapy of last resort due to greater incidence of side effects. Had he failed this, temozolomide, an alkylating chemotherapeutic drug, has been shown to have some benefit.

**Conclusion:** Prolactinoma is generally regarded a treatable diagnosis; however, cases of refractory tumors have been reported. Tumor features, genetics, and male sex may portend a poor prognosis. Though usually benign, the symptoms associated with prolactinomas can be devastating. Our case highlights the potential benefit of alternate modalities, including GKRS, fractionated radiation, and repeat surgery in these rare cases.

**Abstract #821**

**ABSTRACT WITHDRAWN**

**Abstract #822**

**HYPOGONADISM AND HYPERPROLACTINEMIA ASSOCIATED WITH A PITUITARY MACROADENOMA AS AN INITIAL PRESENTATION OF PRIMARY HYPOTHYROIDISM**

Diane Elegino-Steffens, MD, Vinh Mai, MD, Babette Glistor, MD, Patrick Clyde, MD, K. M. Shakir, MD

Walter Reed National Military Medical Center

**Objective:** Pituitary thyrotroph hyperplasia is a rare presentation of primary hypothyroidism, observed most often after a prolonged period of TSH elevation and can present with concomitant elevation in prolactin levels. This chronic stimulation has been shown to cause pituitary enlargement that may be mimic a pituitary tumor. Here we present a case of anterior pituitary thyrotroph hyperplasia secondary to primary hypothyroidism, presenting primarily with hypogonadism and hyperprolactinemia, that resolved with levothyroxine treatment.

**Case Presentation:** A 29yo male presented for an infertility work-up after failing to impregnate his wife for past five years. He was initially evaluated by Urology and was found to have hypogonadotropic hypogonadism (Total testosterone 125 ng/dl, Free testosterone 11 pg/mL, FSH 3.91 mIU/mL, LH 1.25 mIU/mL). He endorsed fatigue and weight gain of approximately 30lbs, but denied erectile dysfunction or gynecomastia. Semen analysis demonstrated low semen volume and decreased sperm count with slowly progressive sperm. Laboratory evaluation revealed an impressive elevation in TSH (TSH >500 mu/L, FT4 0.10 pmol/L) and mildly elevated prolactin (55.4 ng/mL). ACTH stimulation test was normal. There was diffuse enlargement of the pituitary gland, measuring 1.5cm, on MRI. After treatment with levothyroxine therapy for primary hypothyroidism, his prolactin and testosterone levels trended toward normal. Repeat MRI after a 12 month interval showed marked improvement in the size of the pituitary gland with an essentially normal appearance.

**Conclusion:** In the setting of untreated, long-standing primary hypothyroidism, thyrotroph hyperplasia can result in the rare presentation of a pituitary mass and sella turcica enlargement. The incidence of hyperprolactinemia has been reported to be as high as 40% in these cases, but hypogonadism as a presentation is rarely reported in literature. This can lead to improper or delayed diagnosis and even unnecessary surgery. Replacement therapy with levothyroxine is the first line treatment and, in the absence of visual impairment, will lead to normalization of TSH, testosterone and prolactin levels, as well as interval resolution of the pituitary mass. Hence, a full clinical history and hormonal assessment is important for a clinician to ensure proper treatment and unwarranted surgical intervention.

**Abstract #823**

**ECTOPIC ACTH-SYNDROME: CLINICAL FEATURES, DIAGNOSIS, TREATMENT AND LONG-TERM OBSERVATION**

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**Objective:** The objective of this study was to analyze the clinical, biochemical, and radiological features, management, and treatment outcome of patients with EAS. It was a retrospective case-record study of 63 patients with EAS.
Methods: Clinical, biochemical, and radiological features and response to therapy and survival were measured.

Results: The median follow-up was 7 yr (range, 1–13 yr). None of the dynamic tests achieved 100% accuracy. Imaging correctly identified the lesion at first investigation in 85% of cases. Bronchial carcinoid tumors were the most common cause of EAS (n = 45; 71.43%), followed by other neuroendocrine tumors (n = 13, 20.63%). In 7.93% (5) of patients, the source of EAS was never found. Octreotide scintigraphy and whole-body venous sampling were of limited value. Surgical attempt at curative resection was successful in 85.71% (54 of 63) of all patients; 9 (14.28%) responded generally well to bilateral adrenalectomy by vital necessity. Tumor histology and the presence of distant metastases were the main predictors of overall survival (P < 0.05).

Conclusion: No single test provides to find the source of EAS correctly. Despite a variety of tests and imaging studies for the correct diagnosis of the EAS, up to 10% of cases present an occult EAS syndrome. These cases require a prolonged follow-up, review, and repetition of diagnostic tests and scans, but, if it is necessary, do bilateral adrenalectomy.

Abstract #824

CUSHING’S DISEASE: AN UNUSUAL PRESENTATION

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Objective: Describe Cushing’s disease (CD) diagnosed after pituitary apoplexy and repeatedly normal 24-hr urine free cortisol (UFC) levels.

Case Presentation: A 40-year-old woman presented for acute severe headache behind her right eye, double vision, and eyelid droop. MRI to further assess her CNIII palsy showed a 1.5 cm sellar mass with pituitary hemorrhage and extension into the right cavernous sinus. She did not require emergency surgery and within 4 days her diplopia and headache resolved. Physical exam revealed facial plethora, centripetal obesity, wide (>1cm) violaceous abdominal striae, and lower extremity edema. Initial biochemical testing for pituitary hyper/hypofunction was unremarkable except for persistently elevated plasma ACTH levels of 71 to 100pg/mL (reference range 6-50); this included two UFC levels. Further testing revealed elevated midnight salivary cortisol levels on 3 occasions and a low dose overnight dexamethasone test that failed to suppress morning cortisol. Six months after initial presentation, her UFC became markedly elevated to 421.8 mcg/24hr (reference range 36-137). Subsequent sellar MRI showed a decrease in the pituitary mass size but growth of the extension into the right cavernous sinus. Inferior petrosal sinus sampling revealed a central to peripheral ratio >10:1 with lateralization to the right, confirming CD. The patient received XRT as primary therapy because of the cavernous sinus extension. She also started adjuvant ketoconazole titrated to achieve normal UFC.

Discussion: Our case demonstrates several noteworthy points. Our patient presented with pituitary apoplexy and classic exam features suggestive of longstanding undiagnosed CD, but normal UFC results. Several months after resolution of her apoplexy, she demonstrated biochemical evidence enabling the diagnosis of CD. In screening patients for hypercortisolism, it is important to recognize the shortcomings of each screening test and pursue additional testing when clinical features strongly suggest the presence of disease. Additionally, a few case reports describe pituitary apoplexy causing temporary CD remission, which further illustrates the need for serial testing. This is the most likely explanation for our patient’s normal UFC results immediately following her presentation with apoplexy.

Conclusion: When clinical suspicion for hypercortisolism is high, serial biochemical testing should be performed, especially in the setting of pituitary apoplexy.

Abstract #825

ABSTRACT WITHDRAWN

Abstract #826

INCIDENTALLY FOUND MEN1 AFTER A MOTOR VEHICLE ACCIDENT

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Case Presentation: A 48-year-old male with nephrolithiasis and severe gastroesophageal reflux on a proton pump inhibitor was incidentally found to have hypercalcemia (11.5 mg/dL) during a hospitalization. A PTH was elevated at 113 pg/mL. The patient was lost to follow-up. He was admitted 8 months later after a motor vehicle accident. A head MR revealed facial plethora, centripetal obesity, wide (>1cm) violaceous abdominal striae, and lower extremity edema. Initial biochemical testing for pituitary hyper/hypofunction was unremarkable except for persistently elevated plasma ACTH levels of 71 to 100pg/mL (reference range 6-50); this included two UFC levels. Further testing revealed elevated midnight salivary cortisol levels on 3 occasions and a low dose overnight dexamethasone test that failed to suppress morning cortisol. Six months after initial presentation, her UFC became markedly elevated to 421.8 mcg/24hr (reference range 36-137). Subsequent sellar MRI showed a decrease in the pituitary mass size but growth of the extension into the right cavernous sinus. Inferior petrosal sinus sampling revealed a central to peripheral ratio >10:1 with lateralization to the right, confirming CD. The patient received XRT as primary therapy because of the cavernous sinus extension. She also started adjuvant ketoconazole titrated to achieve normal UFC.

Discussion: Our case demonstrates several noteworthy points. Our patient presented with pituitary apoplexy and classic exam features suggestive of longstanding undiagnosed CD, but normal UFC results. Several months after resolution of her apoplexy, she demonstrated biochemical evidence enabling the diagnosis of CD. In screening patients for hypercortisolism, it is important to recognize the shortcomings of each screening test and pursue additional testing when clinical features strongly suggest the presence of disease. Additionally, a few case reports describe pituitary apoplexy causing temporary CD remission, which further illustrates the need for serial testing. This is the most likely explanation for our patient’s normal UFC results immediately following her presentation with apoplexy.

Conclusion: When clinical suspicion for hypercortisolism is high, serial biochemical testing should be performed, especially in the setting of pituitary apoplexy.
cabergoline. At 2 months follow-up, prolactin decreased to 63 ng/mL, and MRI confirmed a decrease in the size of the prolactinoma to 4 x 1.8 cm, with resolved mass effect. A fine needle aspiration of the pancreatic mass revealed a neuroendocrine tumor. He underwent a combined subtotal parathyroidectomy and Whipple procedure. MEN1 gene testing was positive for c1022G>A mutation in exon 7.

**Discussion:** MEN1 is a rare disorder, characterized by primary hyperparathyroidism (90%), pancreatic neuroendocrine tumors (30-70%) and pituitary tumors (30-40%). A diagnosis can be made if a patient has two primary MEN1 tumors, a germline MEN1 mutation, or a MEN1 characteristic tumor with a first-degree relative with an MEN1 associated tumor. MEN1 is inherited in an autosomal dominant fashion. 8-14% of MEN1 patients have no known family history of MEN1. There is a 1-18% incidence of MEN1 in patients with primary hyperparathyroidism. In patients with MEN1, primary hyperparathyroidism presents about 20 years earlier than in those without MEN1. MEN1 patients who have a parathyroidectomy for primary hyperparathyroidism are at higher risk for recurrent hypercalcemia or hypocalemia. Adrenocortical and cutaneous tumors are also associated with MEN1. Surgical resection is indicated for nonmetastatic neuroendocrine pancreatic tumors.

**Conclusion:** MEN1 is a rare syndrome with autosomal dominant inheritance characterized by pituitary, parathyroid, and pancreatic tumors. Additional features include adrenocortical lesions, bronchial, thymic, and gastric carcinoids, and cutaneous tumors. Treatment includes surgical resection of tumors and medical treatment of prolactinoma. Because penetrance is almost 100 percent by age 50, genetic screening of first-degree relatives of patients with MEN1 is recommended for early diagnosis and intervention.

**Abstract #827**

**RECURRENT SEVERE HYponatREMIA AS INITIAL PRESENTATION FOR PANHYPOPitUITARISM WITH PARTIAL EMPTY SELLA SYNDROME**

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**Objective:** Hyponatremia with high urine osmolality in euvolemic patient is most commonly caused by syndrome of inappropriate ADH. However, SIADH is essentially indistinguishable from secondary hypoadrenalism from looking at case reports in the literature. We present a unique case for recurrent severe hyponatremia which was deemed to be SIADH of unknown etiology and found to have partial empty sella syndrome. Her subsequent work up showed panhypopituitarism with improvement in her hyponatremia after treatment with hydrocortisone

**Case Presentation:** A 59 y old thin cachetic female with history of a few episodes of severe hyponatremia thought to be secondary to SIADH was admitted for generalized weakness, malaise and lethargy. She had a couple of episode of hyponatremia in the past which transiently responded to fluid restriction. She had an extensive work up including CT scan of head, chest, and abdomen which did not reveal any etiology for SIADH with normal TSH level and cortisol levels in the past. She had repeat cortisol level performed which was 8 mcg/dl which was followed by cosyntropin stimulation test with appropriate response. Subsequently the patient had an MRI of brain which revealed partial empty sella syndrome. Further endocrinology workup revealed extremely low free T4 level, low prolactin level, undetectable IGF-1 level, Low FSH and LH. Levothyroxine was started on patient along with fluid restriction. Subsequently she was started on tolvaptan which is a competitive vasopressin receptor 2 antagonist with resolution of hyponatremia. She continued to have generalized weakness, malaise, lethargy and weight loss as an outpatient even after the resolution of hyponatremia and hypothyroidism. Due to suspicion for partial secondary adrenal insufficiency, an Insulin tolerance test was performed. It shows no significant change in cortical, ACTH or GH level from baseline confirming panhypopituitarism. She was started on hydrocortisone therapy which resolved her symptoms along with resolution of hyponatremia even after stopping tolvaptan therapy.

**Discussion:** Hyponatremia from partial secondary adrenal insufficiency with empty sella syndrome is rare in medical literature. The Postulated mechanism is that Anti diuretic hormone levels are elevated and does not suppress to plasma volume or osmolality in Cortisol deficient patients. Second possible mechanism is decrease in distal delivery with decrease cardiac output and renal blood flow. In many instances, hyponatremia does resolve after initiation of glucocorticoids in patients with secondary adrenal insufficiency.

**Conclusion:** We describe a rare case of hyponatremia with empty sella syndrome with partial secondary adrenal insufficiency presenting as SIADH.
We report four cases of idiopathic hyperprolactinemia.

**Case Presentation:** The inclusion criteria for this case series are elevated serum prolactin, (reference: 4.04 -15.2ng/mL) negative history of chest wall or spinal cord injury, liver or kidney disease, recent significant life stressors, or causative medications. Workup including thyroid function tests, renal function, liver function, AM cortisol, macroprolactin, and MRI sella was negative.

The first patient is a 43 year old male with erectile dysfunction found to have prolactin of 25ng/mL. He denied visual changes, headaches, or galactorrhea. Testosterone replacement was initiated but hypogonadal symptoms persisted with continuing hyperprolactinemia of 35ng/mL.

The second patient is a 47 year old female with two years of menometrorrhagia and prolactin of 24ng/mL. She denied headaches, visual changes, or galactorrhea and pregnancy testing was negative. Started empirically on cabergoline and menses returned to normal.

The third patient is a 21 year old male with gynecomastia and prolactin of 20ng/mL. He denied galactorrhea, headaches, or visual changes. Referred to general surgery and underwent bilateral breast liposuction for cosmetic reasons.

The fourth patient is a 65 year old male with decreased libido found to have prolactin of 111ng/mL. He denied headaches, visual changes, or galactorrhea. Cabergoline was empirically started and prolactin decreased to 43ng/mL with resolution of hypogonadal symptoms.

**Conclusion:** We present four cases of idiopathic hyperprolactinemia. Each of these patients suffers from clinical symptoms associated with elevated prolactin but comprehensive workup proved to be negative. There are no current guidelines for the management or surveillance of mild idiopathic hyperprolactinemia. This syndrome continues to pose a management dilemma for clinicians and we would like to propose recommendations for surveillance and treatment to include assessment of assay accuracy, repeat imaging, and medical therapy.

**Abstract #829**

**LYME DISEASE PRESENTING AS BITEMPORAL HEMIANOPSIA**

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**Objective:** Bitemporal hemianopsia is a common manifestation of optic chiasm dysfunction. Patients with bitemporal hemianopsia are frequently seen by Endocrinologists as sellar masses such as pituitary adenomas are the most common etiology. We present a rare case of Lyme disease induced bitemporal hemianopsia.

**Case Presentation:** A 57 year old male initially presented for a yearly eye exam with no specific visual disturbances. He did admit to intermittent dizziness, lightheadedness, confusion, difficulty concentrating and short term memory loss. His past medical history includes prior LASIK surgery. Visual Fields revealed bitemporal hemianopsia. No optic neuritis was noted on retinal exam.

He was subsequently referred to Endocrinology and underwent MRI and hormonal evaluation. His MRI demonstrated neither hypothalamic nor pituitary mass, nor any abnormality within or around the optic chiasm; it did show scattered nonspecific white matter abnormalities in the frontal and parietal lobes. Serum laboratory values demonstrated normal BMP, TSH, free T4, LH, prolactin, testosterone, cortisol and IGF-1 values.

He was next seen by Neurology and underwent a lumbar puncture. CSF evaluation demonstrated normal glucose, protein, albumin, VDRL, cryptococcus and oligoclonal bands, but was significant for an elevated Lyme IgM. With convincing evidence for a diagnosis of Lyme disease he was treated with oral doxycycline.

**Discussion:** Lyme disease is caused by the spirochete Borrelia burgdorferi a tick-borne obligate parasite whose normal reservoir includes small mammals, lizards and birds. Multiple ocular manifestations of Lyme disease have been previously reported in the literature. These include a single case of unilateral chiasmal optic neuritis, neuroretinitis, cranial nerve II, V, VI, and VII dysfunctions, keratitis, conjunctivitis, vitritis, uveitis, optic atrophy, disc edema.
and posterior scleritis. To our knowledge, this is the first reported case of Lyme induced bitemporal hemianopsia. Bitemporal hemianopsia, defined as bitemporal visual field defects that respect the vertical midline, is the hallmark of an optic chiasm dysfunction. The etiology of these chiasmal disorders includes sellar masses, infection, vascular abnormalities, autoimmune or inflammatory causes. Temporal defects that do not respect the vertical midline can be caused by a tilted or hypoplastic optic disc, sectoral retinitis pigmentosa or enlarged blind spots.

**Conclusion:** Lyme disease should be included in the differential diagnosis of bitemporal hemianopsia especially in cases of negative imaging or cases of optic chiasm neuritis.

**Abstract #830**

**DIABETES INSIPIDUS IN GRANULOMATOSIS WITH POLYANGITIS**

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**Case Presentation:** A 20 year old male with history of granulomatosis with polyangiitis (GPA) was admitted to the hospital for workup and management of fever, pleuritic chest pain, and worsening dyspnea initially concerning for infection. His GPA was being treated with high dose daily prednisone and monthly cyclophosphamide infusions. Computerized tomography (CT) of lungs showed increased size and number of air- and fluid-filled cavitary lesions bilaterally, biopsy of which demonstrated necrotizing granulomatous inflammation. During his hospitalization, the patient was noted to have hypernatremia; on questioning, he endorsed polyuria and polydipsia during the prior 2 months. He denied headaches, and was euvoemic on physical exam. Laboratory data showed sodium in 148-156 mmol/L range, with a urine osmolality of 75 mOsm/kg and urine sodium 40 mmol/L. He had normal electrolytes, creatinine 1.3 with GFR > 60, a normal prolactin level, and normal thyroid function. Urine output ranged from 3.5-5 L/day. A diagnosis of central diabetes insipidus (DI) was made. He was given IV desmopressin, with subsequent decrease in thirst, increase in urine osmolality (to 497), and normalization of sodium. Magnetic resonance imaging (MRI) of the pituitary showed a 13 x 6 mm hypointense heterogenous lesion with possible areas of infarction and microhemorrhage, as well as absence of the posterior pituitary bright spot. An extensive infectious workup was negative, and his presenting symptoms were attributed to active GPA due to subtherapeutic dosing of cyclophosphamide. His doses of prednisone and cyclophosphamide were increased, and he was discharged on oral desmopressin 0.1 mg daily, which he continues to require.

**Discussion:** Granuloma formation in GPA most commonly involves the upper and lower respiratory tracts and the kidneys, but any organ system can be affected. CNS involvement has been reported, most frequently presenting with stroke, menigitis, ophalmoplegia, seizures, or cerebritis. DI as a complication of GPA is rare, and is due to either vasculitis or granulomatous involvement of the hypothalamus. Vasculitis syndromes should be considered in the evaluation of patients with DI. Reversibility of DI after cytotoxic drug therapy has been reported, but is dependent on the amount of tissue necrosis present.

**Conclusion:** Central DI is a rare manifestation of central nervous system involvement from GPA and other type of vasculitides; symptoms of DI should be elicited during the evaluation.

**Abstract #831**

**REDUCTION IN BRAIN TISSUE PERFUSION WITH HIGH BLOOD SUGAR**

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SUNY at Buffalo

**Objective:** Hyperglycemia at the time of ischemic stroke presentation has been shown to be associated with poor clinical outcomes(1); however, the effect of hyperglycemia on cerebral blood flow patterns has not been studied. At our stroke unit, all patients presenting with symptoms of stroke undergo CT Stroke protocol study (CSPS) that includes a 360 slice brain scan, Perfusion CT and CT angiography. Perfusion CT delineates the ischemic tissue by showing increased time to peak (TTP), decreased cerebral blood flow (CBF) and normal or increased cerebral blood volume (CBV), whereas infarcted tissue manifests with markedly decreased CBF and CBV.

We hypothesized that hyperglycemia induces abnormal patterns of cerebral blood flow including diminished cerebral tissue perfusion as reflected in increased TTP in patients investigated for but not found to have ischemic stroke.

**Methods:** We studied the perfusion images of 75 patients who were not found to have stroke and correlated with their blood glucose level at admission (BGA). 25 patients with BGA <100mg/dl served as the control group whereas 25 with BGA 100-140mg/dl constituted Group A and 25 patients with BGA >140 formed Group B. Each group was then studied in detail for the cortical and hypothalamic blood flow parameters (CBV, CBF, TTP) using the Vitrea software.
Results: We found that the cortical TTP increased by 17% in both groups A (p=0.019) and B (p=0.033) when compared with the control and there was a statistically significant rise in TTP in each sector of the cortex in both hemispheres. Hypothalamic TTP also increased by 12% in group A (p=0.031) and by 1.8% in group B (p=0.386), when compared with the control group (BGA <100). There was no significant change in cortical or hypothalamic CBF or CBV.

Conclusion: We conclude that in patients without stroke, a blood glucose >100mg/dl, is associated with significant increases in TTP in the cortex and the hypothalamus. Since TTP is inversely related to cellular and tissue perfusion, our study shows for the first time a reduction in cerebral tissue perfusion with at glucose concentrations >100mg/dl. These observations have implications for the pathogenesis of adverse outcomes related to hyperglycemia in patients.

Abstract #832

A CASE OF CENTRAL DIABETES INSIPIDUS FOLLOWING INFLUENZA B VIRUS INFECTION

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Case Presentation: The common causes of central diabetes insipidus (CDI) are infiltrative or neoplastic lesions of the hypothalamus or pituitary gland, traumatic head injuries, pituitary or hypothalamic surgery. Rare causes include autoimmune inflammatory disease like Lymphocytic infundibuloneurohypophysitis (LINH) . CDI caused by infections, particularly viral infections are seldom seen. Here we describe the case of an 82 year old active female patient with only past medical history of well controlled hypothyroidism who presented with sudden onset polyuria and polydipsia 1 week after being diagnosed with flu secondary to Influenza B virus infection.

Patient was admitted to the hospital with flu like symptoms, Influenza B infection was confirmed by PCR, patient did not receive Oseltamivir as she had been symptomatic for more than 48 hours. She received supportive treatment and was discharged home. One week following the discharge patient started having sudden onset polyuria and polydipsia where she was drinking between 2-3 gallons(7-11 litres) of water /day. Workup revealed high serum osmolality (302 mOsm/L) and low urine osmolality (122 mOsm/L) with high serum cortisol levels (26.5). MRI was done which showed a 3-5mm pituitary microadenoma immediately posterior to the pituitary infundibulum. Further workup of anterior pituitary function was within normal limits. Patient was started on DDAVP with significant improvement in symptoms. Three months later when the patient was tapered off DDAVP she became symptomatic again and had to be restarted on DDAVP. To date patient remains asymptomatic with low dose DDAVP.

Conclusion: We present a very interesting case of central diabetes insipidus post Influenza B Virus infection requiring DDAVP treatment. The author could not find any case report of Influenza B virus. There is once case report from Japan dated 2011 of CDI following probable Influenza infection (not confirmed by PCR).

Abstract #833

SYNDROME OF INAPPROPRIATE ANTI-DIURETIC (SIADH) RELATED TO PROBABLE LUNG CANCER CORRECTED BY TREATMENT WITH A PROGESTERONE RECEPTOR ANTAGONIST

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Objective: To determine if the use of mifepristone, a progesterone receptor antagonist could provide enough tumor regression of apparent lung cancer to at least provide improvement of severe hyponatremia which was considered likely to be secondary to inappropriate secretion of arginine vasopression (the anti-diuretic hormone – ADH) by the multiple pulmonary nodules.

Methods: An 81 year old moribund woman was admitted to the hospital for marked dyspne from a pleural effusion with a serum sodium level of 118 mmol/L. There had been a steady decline in serum sodium over 3 months from 130 to the lowest at 118 mmol/L. A CT scan revealed multiple pulmonary nodules diagnosed by the radiologist as probable metastatic lung cancer. The patient refused a thorocotomy and biopsy and asked to be discharged to die at home after her sodium was temporarily increased by manipulating water intake and intravenous fluids. Her serum sodium quickly dropped again to 122. She agreed to try oral mifepristone tablets 200mg/day.

Case Presentation: Treatment with mifepristone has prevented the return of hyponatremia related to SIADH for 3 years. Her serum sodium levels have been as follows during this interval 136 1 month after mifepristone therapy to 141 mmol/L after 3 months of therapy and has remained between 141 to 144 mmol/L during 3 years of treatment. The prevention of hyponatremia by treating with mifepristone seemed to be related to its effect of causing a remission of her lung cancer since 2 months later a repeat CT scan showed complete disappearance of her pulmonary nodules. This has been associated with improved clinical status in that she is no longer short of
breath, her oxygen pressure was normal (which had been markedly low before) and she was no longer weak.

**Discussion:** Mifepristone, a progesterone receptor antagonist has been found to provide palliative relief for a variety of human cancers and spontaneous murine lung cancer. The mechanism is thought to be related to inhibiting the conversion of the 90 kDa parent progesterone induced blocking factor (PIBF) located in the centrosome to the intracytoplasmic immunomodulatory 34-36 kDa split variant. Presence of this intracytoplasmic split variant of PIBF is believed to confer immune protection of cancer cells from cellular immunity especially NK cells.

**Conclusion:** Mifepristone can correct hyponatremia from SIADH associated with lung cancer by causing regression of the cancer cells making excessive arginine vasopressin (ADH).

**Abstract #834**

**COMPLETE REVERSAL OF CLINICAL SYMPTOMS AND SIGNS OF THE HEREDITARY SPASTIC PARAPLEGIA SYNDROME FOLLOWING A SHORT COURSE OF SYMPATHOMIMETIC AMINE THERAPY**

Jerome Check, MD, PhD, Michael Dougherty, BA, Diane Check, BS, MT

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**Objective:** To determine if treatment with the sympathomimetic amine dextroamphetamine sulfate can ameliorate or reverse symptoms and signs of hereditary spastic paraplegia syndrome.

**Methods:** A 45 year old man who was diagnosed with hereditary spastic paraplegia syndrome by his neurologist was offered treatment with dextroamphetamine sulfate therapy (15mg extended release capsule). The diagnosis given to him by his neurologist based on the fact that his 59 year old brother has this condition, and based on the patient’s physician examination demonstrated an abnormal spastic gait, weakness in his lower extremities controlled by his iliopsoas muscle, tibialis anterior causing him dragging his right leg.

**Case Presentation:** Upon his return visit one month later the patient noted a complete reversal of his symptoms with full return of his muscle strength which allowed him to participate in strenuous physical activity, e.g., hill climbing and bicycle riding. His gait was perfectly normal and he no longer dragged his leg. The patient has maintained complete remission now after 4 months of treatment with this very low dosage of amphetamines.

**Discussion:** Hereditary spastic paraplegia syndrome is a genetic disorder (at least 30 different gene mutations). It is related to pyramidal tract dysfunction. In this case it was inherited as an autosomal dominant. Thus the hereditary spastic paraplegia syndrome seems to be part of the wide variety of pathological disorders lumped together based on response to treatment with sympathomimetic amines as the sympathetic neural hyperalgesia edema syndrome. Besides severe headaches, other neurologic conditions that have shown very good response to sympathomimetic amine therapy include the restless leg syndrome, and a remarkable case of a retired pharmacist who was wheelchair ridden completely unable to walk for 25 years diagnosed by muscle biopsy as to the form of muscular dystrophy known as the mitochondrial encephalopathy, lactic acid and stroke-like syndrome who was able to resume walking and gained all of her strength back also after just one month of treatment (presently 5 year remission). The hypothesized explanation is that the genetic disease makes the pyramidal tract more prone to permeability and thus unable to properly filter out unwanted chemicals and toxic agents that adversely effect the mitochondria. This is combined with inadequate dopamine secretion by sympathetic nerve fibers. The dextroamphetamine sulfate probably stimulate more of the dopamine neurotransmitter.

**Conclusion:** This is the first and only described effective treatment for the hereditary spastic paraplegia syndrome.

**Abstract #835**

**LONG STANDING POST-HERPETIC NEURALGIA RESISTANT TO STANDARD ANTI-NEUROPATHY MEDICATION SHOWING QUICK DRAMATIC IMPROVEMENT FOLLOWING TREATMENT WITH SYMPATHOMIMETIC AMINES**

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**Objective:** To determine if treatment with dextroamphetamine sulfate can alleviate severe chronic post-herpetic neuralgia that failed to respond to standard drugs typically used for neuropathy.

**Methods:** An 88 year old man with a 5 year history of severe post-herpetic neuralgia pain who had failed to respond to pregabalin, and duloxetine was offered 15 mg of amphetamine salts extended release capsules. Eventually he was increased to 30mg extended release capsules.

**Case Presentation:** Within the first month of treatment
there was significant relief of his pain with just 15mg extended release capsule. After 2 months the dosage was increased to 30mg extended release capsules and he has had at least a 90% reduction in pain which has lasted now 1 ½ years.

Discussion: Not only had this patient failed to respond to standard therapies for neuropathies, but he gained only marginal relief from lidocane patches, hydrocodine, oxydodone (all of which caused nausea), acupuncture and TENS units. He has had no adverse side effects from the dextroamphetamine sulfate. Though the exact mechanism of action is not known for sure, the main hypothesis for the etiology of the sympathetic neural hyperalgesia syndrome is that the sympathetic nervous system controls cellular permeability, and a sensitive tissue already showing signs of increased permeability allows chemicals and toxic elements to permeate these tissues resulting in inflammation. The permeability problem is further compromised by sympathetic hypofunction. Dextroamphetamine sulfate is thought to stimulate the neurotransmitter dopamine which corrects the problem.

Conclusion: Post-herpetic neuralgia can be added to the long list of pain syndromes that are refractory to most therapies, but respond quickly and efficiently to sympathomimetic amine therapy. Though one may consider giving a stimulant to an 88 year old person is somewhat risky, the pain had been so severe he stated he wanted to commit suicide.

Abstract #836

MARKED VARIATION IN SERUM CHROMOGRANIN A LEVELS IN A PATIENT ON CHRONIC OMEPRAZOLE THERAPY.

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Objective: Serum chromogranin A (CgA) is used as a standard marker in the diagnosis of neuroendocrine tumors. We report a case with wide fluctuation (more than 10-fold) in serum chromogranin A (CgA) levels in a patient on chronic omeprazole therapy.

Case Presentation: A 67-year-old woman with hypothyroidism presented for evaluation of facial flushing for 1 year. Flushing had increased in intensity over the past several months without any provocative factors. She denied any diarrhea, wheezing, headache, palpitations or facial erythema. Her home medications were aspirin, omeprazole, levothyroxine, and raloxifene. The patient reported no improvement in flushing on stopping raloxifene. Physical exam was unremarkable. On blood test, she was noted to have mildly elevated serum CgA 18.8 ng/ml (Range 1.9-15 ng/ml). Other endocrine testing including serum tryptase, 24 hour urine N-methylhistamine, 24 hour urine 5-hydroxyindoleacetic acid, metanephrines, catecholamines, serum calcitonin were unremarkable. Serum CgA was repeated because of her continued symptoms. Repeat blood test showed markedly increased CgA value (128 ng/ml). She underwent CT chest/abdomen/pelvis and octreotide scan. Octreotide scan showed uptake in the right axillary and subcarinal regions. She subsequently underwent endoscopic bronchial ultrasound and mediastinal biopsy of two lymph nodes. Biopsy was negative for any pathological process. PET scan was done to rule out occult malignancies and was negative. Echocardiogram was normal. She was also seen by Neurology with unremarkable work up. CgA levels were repeated and levels varied from 126 to 182 ng/ml. She was asked to hold omeprazole for 2 weeks and CgA levels dropped to 24 ng/ml. The patient resumed omeprazole due to worsening reflux. Repeat CgA level 3 months later on omeprazole was 18 ng/ml. Venlafaxine and paroxetine were tried for flushing but she could not tolerate due to side effects.

Discussion: It had been previously established that medications which stimulate neuroendocrine cells, in particular proton pump inhibitors (PPI) could lead to falsely elevated CgA levels. The interesting aspect in this case is increase in CgA more than 10-fold and the marked variation in CgA levels while on omeprazole (18-182 ng/ml).

Conclusion: There is marked variability in serum CgA levels in presence of PPI as seen in our case. Clinicians should consider repeat testing of CgA levels in setting of abnormal value and also consider stopping contributing medications before testing and making important clinical decisions.

Abstract #837

CASE REPORT: EFFECTIVENESS OF MEDICAL THERAPY WITH OCTREOTIDE IN MEN-1 PATIENT WITH NON-FUNCTIONAL PANCREATIC NEUROENDOCRINE TUMOR (NET)

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Objective: Pancreatic surgery for NET may lead to short and long term adverse health consequences. In this report, we present a patient with MEN-1 who developed an apparently non-functional pancreatic NET that was safely managed with long acting octreotide.

Case Presentation: A 40 year-old male with a history of primary hyperparathyroidism and prolactinoma was seen for routine surveillance. His paternal grandfather, father,
and sister also had MEN-1. The patient was asymptomatic, having undergone total parathyroidectomy with placement of parathyroid auto-grafts in both forearms, and normalization of serum prolactin after a brief course of cabergoline. Medications included calcitriol and calcium carbonate with vitamin D3. Testing for menin gene was positive for a heterozygous autosomal dominant mutation c.798+1G>A. Examination showed a clinically euthyroid and eugonadal male without Cushingoid features. Laboratory tests were normal, including serum gastrin, glucagon, insulin, vasoactive intestinal polypeptide, chromogranin A and anterior pituitary hormones with the exception of a mild hyperprolactinemia 18.8 (normal 4.0-15.2 ng/mL). Of note, pancreatic polypeptide levels had been elevated the past 2 years with a doubling rate 520 and 1198 (normal 70-430 pg/mL). A dedicated CT of the pancreas revealed several subcentimeter lesions (0.5 and 0.8 cm) in the tail, which correlated with pancreatic uptake in the subsequent 111-Indium octreotide scan. A sellar MRI was normal. The patient was treated with short acting octreotide for 2 weeks and then maintained on long acting octreotide depot for 6 months. His pancreatic polypeptide levels normalized to 62 pg/mL and 374 pg/mL at 1 and 6 month, respectively. Repeated CT showed stability of the pancreatic lesions without evidence of metastasis.

Discussion: Basal and meal-stimulated pancreatic polypeptide has been shown to be useful for early detection of pancreatic involvement in 75% of patients with MEN-1. Our patient’s basal pancreatic polypeptide levels were not only elevated but actually doubled at one year follow-up. As the benefits of pancreatic surgery for small lesions (<2cm) are not clear, the morbidity, mortality, and long term complications of surgery must be considered. Our patient was offered medical therapy with long acting octreotide, which was recently shown to provide 90% objective tumor response and stability in MEN-1 patients with early non-functional pancreatic NET.

Conclusion: Serum pancreatic polypeptide is a useful marker to screen for early non-functional pancreatic NET in MEN-1 patients. Long-acting octreotide can be safely and effectively used as first-line medical therapy to avoid the potential complications associated with pancreatic surgery.

Abstract #838

A CASE OF PRIMARY EMPTY SELLA IN FANCONI ANEMIA: AN ENIGMA OF FINDINGS & DILEMMA IN MANAGEMENT

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Objective: Fanconi anaemia (FA) is a rare haematological disorder of chromosomal instability. Of late there has been recognition of various endocrinological abnormalities which can be prevalent in 3/4th of these patients. We describe a similar case with complex endocrinological issues and probably for the first time in literature a case of primary empty sella (PES) in FA.

Case Presentation: A 12 year old male born of non-consanguineous union presented for evaluation of short stature. There was generalized hyperpigmentation, cafe au lait spots, low set ears, moderate pallor. The patient was a known case of FA and hypothyroidism on levothyroxine, folic acid and oxymethalon. Family history was significant for an elder sister died of bone marrow failure due to FA. On examination height of patient was 121 cm (SD of -3.4), growth velocity of 5.6 cm/yr since last 3 years, head circumference < 3rd percentile for age. Sexual maturity was discordant. Calculated bone age was 12 years. Peripheral stress cytogenetics demonstrated increased chromosomal breakage. MRI of hypothalamic pituitary region showed 2mm rim of pituitary tissue around sella turcica, normal stalk, septum pellucidum & corpus callosum.

Discussion: The above patient presents with four clinical endocrinological issues- hypothyroidism, short stature, discordant bone age, discordant puberty. PES has not been reported in FA patient previously. Anabolic steroids are reported to increase intracranial tension, a risk factor for PES. Benign intracranial hypertension (BIH) has strong association with PES, although tell-tale signs of raised ICT are absent. The issue of decreased predicted height due to rapid epiphyseal maturation vis a vis growth hormone secretory defect is leading to dilemma on starting GH therapy. The exact increase in predicted height after stopping of anabolic steroid or instituting GH is difficult to quantify. GH therapy in FA patients can be given either before or after bone marrow transplant. GH therapy after transplant has advantage of reduced rejection rate but decrease responsiveness. This has to be balanced with increased risk of malignancies as they are at increased risk of leukaemia and squamous cell carcinoma. No specific
guideline currently exist regarding institution of growth hormone therapy in these patients.

**Conclusion:** A child with FA presents with complex endocrinological issues. Hypothyroidism, hypoadrenalism, short stature, pubertal disruption along with effects of iatrogenic androgens and propensity to leukaemia on GH therapy require astute clinical decision making. To best of our knowledge PES - a finding in this patient, has not been previously described in English literature.

**Abstract #839**

**CYCLIC CUSHING’S DISEASE IN A WOMAN OF 32 YEARS WITH SEVERE HYPERCORTISOLISM**

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**Objective:** To report a case of cyclic hypercortisolism in Cushing’s disease (CD).

**Methods:** Clinical and paraclinical characteristics of a patient with CD are presented.

**Case Presentation:** Female, 32 years, with history of infertility, PCOS and DM treated with metformin and insulin; 22 d before admission, has altered behavior, doing activities that then no further recalls, palpitations, flushing. The day of admission to the ER presents psychomotor agitation, sensory disorder, and severe hypokalemia and hyperglicemia so is hospitalized. At examination: alert, cushingoid, weight: 60kg BMI: 23 PA: 120/60mmHg, FC: 92x’, FR 16x’; skin: moderate hirsutism, multiple bruises and no stretch marks. small bearings in supraclavicular fossa, small dorsal hump, edema ++ / +++ lower limbs. Analyses: Glicemia 459mg%, Na:149, K:1.99, F >50ug/dl, ACTH: 386pg/ml, TSH: 1.54 uU/ml, T4Libre: 0.54ng/dl; Peptide C: 0.27ng/ml, E2: 29pg/ml, Pg: 0.80ng/ml, LH: 0.10mIU/ml, PRL: 7.25ng/mL, Androstenedione >10ng/ml, DHEAS: 265ug/ml, free Testo: 3.20pg/ml, Basal UFC1: 919.35ug/d, basal UFC2: 1592.5ug/d, UFC post Dexam8: 132 ug/d. Serum F post Dexam8 >50ug/dl. EV infusion of Dexam7mg and IV catheterization (S:81%) with an ratio central/eripheral> 1.6 that guides us CD.

**Discussion:** CD is the most common cause of spontaneous CS with 60 to 70%, is the result of ACTH hypersecretion by a pituitary adenoma. CS is a cyclical pattern of hypercortisolism, wherein the biochemical production of cortisol fluctuate rhythmically. Clinical suspicion of CS, we demonstrate the presence of hypercortisolism, breaking the circadian cycle and the failure to exogenous corticosteroid withdrawal. In our patient, we show increased levels of UFC and serum F, UFC suppression > 90% post Dexam8, early suppression of serum F post IV infusion Dexam7mg and IV catheterization (S:81%) with an ratio central/eripheral> 1.6 that guides us CD.

**Conclusion:** We report a case with typical clinical and paraclinical Cushing’s disease associated with a fluctuating severe hypercortisolism.

**Abstract #840**

**MIFEPRISTONE RE-ESTABLISHED GLYCEMIC CONTROL IN A CUSHING’S SYNDROME PATIENT THAT RELAPSED AFTER A 21 MONTH INTERRUPTION**

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**Objective:** Mifepristone (MIFE, Korlym®, Corcept Therapeutics), a glucocorticoid receptor antagonist, was approved for the treatment of patients with Cushing’s syndrome (CS) based on SEISMIC, an open-label, multicenter study. Herein we report details on a study patient who had achieved significant glycemic control while on MIFE for 31 months but relapsed after study completion - when MIFE therapy was interrupted for 21 months.

**Case Presentation:** A 46 y/o man with Cushing’s syndrome (CS) and a failed transphenoidal surgery for an ACTH-secreting adenoma participated in SEISMIC and a study extension for a total of 31 months. MIFE was titrated over 2.5 months to a stable dose of 600 mg/d (300 – 900 mg/d range). Improvements in glycemic control were observed within the first few weeks of starting MIFE. After 6 months, fasting blood glucose decreased from 148 to 79 mg/dL, A1c decreased from 9.3 to 6.9%, and fasting insulin decreased from 186 to 168 µUnits/mL. Patient continued participation for an additional 25 months. With interruption in MIFE therapy post-study completion, patient’s hyperglycemia relapsed and worsened. Attempts to control it with a concomitant combination of anti-diabetic medications [metformin 1g BID, glimepiride 4mg BID, Levemir, Novolog] were unsuccessful. Fasting blood glucose worsened to 219 mg/dL and A1c increased to 11.1% during this 21 months interval without MIFE. MIFE was restarted and titrated to a stable dose of 900
mg/d within 3 months. After 3 months of therapy, fasting blood glucose decreased from 219 to 108 mg/dL and A1c decreased from 11.1 to 7.5%. An attempt to further improve glycemic control by increasing the dose to 1200 mg/d was not tolerated. The patient maintained glycemic control on 900 mg/d for another 6 months (fasting blood glucose of 105 mg/dL, A1c 8.0%) until he elected to undergo a second transphenoidal surgery to remove the residual pituitary adenoma.

**Conclusion:** This case highlights the contributions of MIFE in improving glucose parameters driven by hypercortisolemia and reinforces the importance of maintenance therapy. This patient initially achieved glycemic control while on MIFE but experienced significant deterioration after interruption of therapy. Conventional anti-diabetic medications were ineffective in this patient with CS and co-morbid diabetes mellitus. The re-introduction of MIFE 21 months later re-established glycemic control.

Abstract #841

**A SECOND CASE OF SUCCESSFUL TREATMENT OF RESTLESS LEGS SYNDROME USING THE SYMPATHOMIMETIC AMINE DEXTROAMPHETAMINE SULFATE**

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**Objective:** To try to corroborate the benefits of dextroamphetamine sulfate, a sympathomimetic amine, for alleviating symptoms of the restless legs syndrome.

**Methods:** Dextroamphetamine sulfate starting at 15 mg extended release capsules with the option of increasing the dosage if necessary was given to a 22-year-old young man who had chronic severe daily headaches attributed to 7 concussions from playing collegiate hockey.

**Case Presentation:** This man showed considerable improvement in 1 week after taking 15 mg dextroamphetamine sulfate. The restless legs syndrome of 2 years duration was almost completely dissipated after increasing the dosage of dextroamphetamine sulfate to 30 mg extended release capsules. The only time it would occur following treatment and to a much milder extent was when he had been subjected to extreme physical activity during the day. He also noted marked improvement of pain and swelling in his joints.

**Discussion:** A previous case was reported of a woman refractory to standard therapy of dopaminergic treatment and ropinirole who responded very well to dextroamphetamine sulfate. The question was this a spontaneous remission or was the dextroamphetamine sulfate the reason for improvement? The fact that dextroamphetamine sulfate has been tried in only 2 cases of restless legs syndrome and both responded quickly and effectively to this sympathomimetic amine, increases the likelihood that the sole response in cycle 1 was not merely fortuitous or a rare case of spontaneous improvement. Restless legs syndrome thus is another one of the clinical manifestation of sympathetic nervous system hypofunction that all respond to dextroamphetamine sulfate. The syndrome goes by various names including autonomic dystrophy and the sympathetic neural hyperalgesia edema syndrome.

**Conclusion:** Though only 2 cases, both have responded very well to small dosages of dextroamphetamine sulfate. This drug which is so widely tolerated and has a great safety profile should be considered first line therapy for restless legs syndrome. So far there are no known failures to this therapy.

Abstract #842

**POST-CONCUSSION HEADACHES RESPOND DRAMATICALLY FOLLOWING TREATMENT WITH DEXTROAMPHETAMINE SULFATE - CASE REPORT**

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**Objective:** To determine if severe chronic daily headaches resulting from multiple concussions could be ameliorated by treating with the sympathomimetic amine dextroamphetamine sulfate.

**Methods:** Dextroamphetamine sulfate starting at 15 mg extended release capsules with the option of increasing the dosage if necessary was given to a 22-year-old young man who had chronic severe daily headaches attributed to 7 concussions from playing collegiate hockey.

**Case Presentation:** Though he improved quickly with 15 mg dextroamphetamine sulfate, by increasing the dosage to 30 mg, his migraines have been reduced to a rare frequency and mild intensity.

**Discussion:** At the 2014 AACE meeting, a large series was presented of women who showed a rate of marked amelioration of chronic migraines that failed to respond to ergotamines, beta blockers, and topiramates. However, none of these women had a headache from a previous concussion.

**Conclusion:** This could show that the sympathomimetic amine dextroamphetamine sulfate can ameliorate headaches, even when related to concussions. Women are more susceptible sympathetic nervous system hypofunction than men, but men, as indicated in this
case, can also respond to sympathomimetic amines. The hypothesized mechanism is that the dextroamphetamine corrects a permeability defect, allowing absorption into brain tissue of unwanted chemicals, leading to inflammation and pain.

Abstract #843

RALOXIFENE FOR THE TREATMENT OF PROLACTINOMA

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Objective: We report the case of a 34 year old man with a giant prolactinoma in whom Raloxifene was added in attempt to normalize the prolactin levels still elevated on Cabergoline. 

Case Presentation: The patient presented to ophthalmology with impaired vision in the left eye and was found to have bitemporal hemianopsia due to a 6.0*4.1*3.0 cm partially cystic sellar mass with suprasellar and right temporal lobe extension. The hormonal evaluation showed a prolactin of 8193 ng/ml (2-14), DHEAS 659.7 ug/dl (10.0 - 319.0), IGFBP 67 ng/dl (89 - 350), TSH 0.996 uU/mL (0.400 - 5.500), free T4 1.1 ng/dL (0.7 - 1.8), basal cortisol of 16.3 ug/dL and hypogonadotropic hypogonadism with total testosterone 103 ng/dL (220 - 1000), LH 1.2 mU/mL (1.0 - 7.0), FSH 4.2 mU/mL (1 - 10). He was started on Cabergoline 1mg per week which was gradually increased to 2.5 mg over the course of one year with improvement in the visual fields, tumor shrinkage to 2.1*2.4*1.8 cm, decrease in the prolactin to 69.8 ng/ml and increase in total testosterone to 501 ng/dl. As he was still having low libido and he was on high dose of Cabergoline, Raloxifene 60 mg daily was started; prolactin decreased to 51.1 ng/ml. Later during his follow-up while on 3.5 mg Cabergoline weekly, he ran out of Raloxifene and the prolactin level increased from 42.6 to 74.9 ng/ml. The patient tolerated the medication well with no reported side effects.

Discussion: Prolactinoma is the most common functioning pituitary tumor and only a very small percentage is refractory to dopamine agonists. The usual approach is to escalate the dose, surgery or radiotherapy. Clinicopathologic studies showed that 60% of the prolactinomas in men and 67-90% of prolactinomas in women have estrogen receptors. Exposing prolactinoma rat cells to anti estrogenic agents suppressed their proliferation and the secretion of prolactin. About half of the men with prolactinoma under treatment remain hypogonadal and testosterone replacement via conversion to estrogen may stimulate the tumor growth and prolactinemia. Addition of an aromatase inhibitor or selective estrogen receptor modulator are attractive solutions to this issue with the latter having the advantage of protecting the bone health. In our case, Raloxifene had a very modest effect on prolactin reduction either because the patient has a prolactinoma without a significant number of estrogen receptors, was not very adherent to the therapy or just because it is not very effective.

Conclusion: To our best knowledge, this is the first report of Raloxifene used in the treatment of prolactinoma in humans. Further studies are needed to validate any efficacy of Raloxifene in the prolactinoma treatment.

Abstract #844

ISOLATED ACTH DEFICIENCY AND ACQUIRED LIPODYSTROPHY (ALD) ASSOCIATED WITH MULTIPLE ENDOCRINE AND NONENDOCRINE AUTOIMMUNITY.


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Objective: To describe a challenging case of isolated ACTH deficiency presenting as the intriguing syndrome of acquired lipodystrophy associated with multiple endocrine and non-endocrine autoimmune disorders.

Methods: A 35 year female [primary hypothyroidism past 6 years (TSH 41miu/ml) on L-thyroxine; Pregnancy 1, 6.5 years earlier, with gestational diabetes mellitus - GDM (blood glucose 400 mg/dl) treated with insulin, birth weight 2.6 kg; Pregnancy 2, 1.5 years earlier, without GDM, birth weight 1.9 kg (IUGR due to ? deficient nutrient supply), lactation failure after both pregnancies; always regular cyclic menses], presented with extreme weight loss of 6 years duration [50 to 37 kg in the 1st year itself], weakness, anorexia, nausea and recurrent diarrhea. No history of head injury or post partum hemorrhage.

Case Presentation: Lipodystrophy: Severe generalized lipoatrophy, prominent musculature and phlebomegaly, weight 37 kg, BMI 16.4 kg / m2. Pulse 75/min; BP 93/61 mm of Hg; vitiligo lips, past uveitis; post prandial blood glucose PPBG 94 mg/dl; Hba1c 5.4 %; Hb 10.2 g/dl, microcytic hypochromic, S Iron normal, eosinophilia 17%. Body fat composition DEXA: total fat 8.2 kg, total lean mass 28.2 kg; % total fat 22.5%, android 30% and
Severe secondary adrenocortical deficiency: Serum Cortisol Basal 0.06, post 250 mcg ACTH 0.23 mcg/ml; undetectable plasma ACTH <0.05 pg/ml (<45). Overt proteinuria; urine albumin : creatinine ratio >150 mcg/mg creatinine; low voltage ECG. Thyroid peroxidase and thyroglobulin antibodies negative. Antinuclear antibody: ANA positive (immunoflorescence); RA factor negative; complement C3 and C4 normal; serum protein electrophoresis normal. HIV Serology negative. BMD normal. CT Abdomen normal. MRI pituitary: Empty sella. Glucocorticoid replacement: Prednisolone 7.5 mg/day was added, resulting in dramatic and total improvement (weight increased back to 50 kg in 4 months). By 1 year follow up, weight further increased to 69 kg, with development of diabetes (HbA1c 9.5 %, PPBG 454 mg/dl) and hypertension (160/94 mm of Hg) requiring pharmacotherapy. Results of islet cell and GAD antibodies, C Peptide, and C3 Nephritic factor awaited.

Discussion: Isolated ACTH deficiency [likely a consequence of autoimmune lymphocytic hypophysitis] may present as ALD associated with multiple autoimmune disorders. Though ALD (both generalized and partial) itself has been suggested to represent autoimmune disease, the inciting factors (autoantigens and effector mechanisms) remain to be elucidated.

Conclusion: High index of suspicion and extensive evaluation are essential in diagnosis of the rare and complex acquired lipodystrophy syndromes. All cases of ALD possibly merit ACTH stimulated cortisol testing.

Abstract #845

FUNCTIONING GONADOTROPIC ADENOMA OF PITUITARY

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Objective: To present a case of functioning gonadotropin secreting adenoma of pituitary.

Case Presentation: 59 yr male presented with h/o painless loss of vision in the right eye for last 6 yrs, reduced vision in left eye on lateral aspect and undue fatigue for last 6 months. There was h/o being operated twice trans-sphenoidally for pituitary mass in other medical facility. Seeking medical attention in the first instance was for painless loss of vision in the right eye with early morning bifrontal headache, vision never recovered after the surgery. Prior to 2nd surgery, headache was the only complaint. Conscious, oriented male with stable vitals. Scantiness of hair was noted all over the body with fine wrinkling of face (around angle of mouth and around lateral canthi). Generalised decrease in muscle mass. Both Testes were soft with increased volume (>25 ml). Right sided pupil was dilated & non reacting. Perimetry revealed left superior quadrantanopia. Fundus: right optic atrophy, left normal. Hb: 10 gm/dl (14-18). Routine serum chemistry was normal. Hormone profile FT4: 0.59 ng/dl (0.89 – 1.76); FT3: 2.20 pg/ml (2.3 – 4.2); TSH: 1.54 µIU/ml (0.35-5.5); testosterone: 65.84 ng/dl (241-820); LH: 2.0 µIU/ml (1.5-9.3); FSH: 5.07 µIU/ml (1.4-18.1); prolactin: 9.29 ng/ml (2.1-17.7); IGF-1: 70.1 ng/ml (81-225); ACTH: <5 pg/ml (6-70); Cortisol: 8.65 µg/ml (4.3-22.5). Semen examination: volume decreased, counts normal, motility decreased. MRI: a large sellar mass with suprasellar, parasellar and infrasellar extension. Previous records revealed thyroid functions to be normal & a high testosterone value of 1216 ng/dl (normal: 241-820). Patient underwent trans-sphenoidal surgical removal of the tumor and was further advised for stereotactic radiotherapy (for residual tumor). Histopathology, revealed tumor cells that were immunopositive for LH & FSH (focally). A final diagnosis of recurrent pituitary macro adenoma (functioning gonadotropin secreting adenoma: FGA) with right optic atrophy and left superior temporal quadrantanopia with pan-hypopituitarism (hypothyroidism and hyposomatotropism, hypocortisolism) was made. He was started on appropriate hormone replacement and continues to do well.

Discussion: FGA are adenomas expressing and secreting biologically active gonadotropins and causing distinct clinical manifestations. In males, they cause macro-orchidism, increased testosterone & increase in semen parameters. FGA are clinically rare entity, are mostly macroadenomas requiring surgical decompression to prevent sinister complications.

Conclusion: Increased awareness is required for early diagnosis of this rare clinical entity in setting of pituitary macroadenomas.
Abstract #846

RECURRENT HYPOGLYCEMIA IN A YOUNG AMENORRHEIC FEMALE

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Objective: To present a case of recurrent hypoglycemia in a young non-diabetic amenorrheic female.

Case Presentation: 31 year old female presented with recurrent vomiting since 15 days and sudden onset slurring of speech followed by loss of consciousness. No H/O fever, seizures, head trauma, focal weakness, drug intake. Patient had a similar episode 2 days back which improved after intake of sugary drink. Last childbirth was 9 years back, full term normal vaginal delivery at home with H/O PPH requiring hospitalization & blood transfusion. This was followed by lactation failure. The patient resumed menstruation initially, but became amenorrheic for last 8 years. H/O dyspareunia present. No H/O Hypertension, DM, TB, other chronic illness. Patient is a non smoker & doesn’t consume alcohol. EXAMINATION: Patient was unconscious responding to painful stimuli with pulse 74/min, BP = 106/72. CNS – Pupils B/L NSNR, Plantar-B/L mute, DTRs were present normal, no meningeal signs. Respiratory, cardiac and abdominal examination was normal. Capillary Blood Glucose was 16 mg/dL for which immediately IV Glucose was given after which her sensorium improved. There was no goiter; axillary and pubic hair were absent. Breasts were atrophied with areolar hypopigmentation. Gynaecological examination showed pale vaginal mucosa with atrophy. INVESTIGATIONS: Hb 10.9gm/dl (12-16); TLC 8300/cumm (4000-11000); DLC P81L19; Platelet count 300,000/cumm (1,50,000 – 4,00,000); ESR 15 mm/1 hour (< 20); RBS 40mg/dL (70-110); Urea 15mg/dL (15-45); Creatinine 0.6mg/dL (0.6-1.2); LFTs were normal, Total proteins 5.9 mg/dL (6.0-8.0); albumin 3.4 mg/dL (3.5-5.5); globulins 2.5mg/dL (1.5-3.5); T. Chol 142 mg/dL; Triglycerides 85 mg/dL; Na/K 123/3.9; Ca/Phosphorous 7.9/2.4; Hormone Profile: TSH 3.2mcu/mL (0.5-5.5); T4 0.28mg/mL (0.6-2.2); FT3 1.2 pg/mL (2-4.4); IGF1 < 25 ng/ml (normal 115-307); FSH 7.8mIU/ml (1.3-23.4); LH 7.1mIU/mL (0.8-15.5); Estradiol 30pmol/L (97.5-1404); Prolactin 4.7ng/mL (3-18.6); 8 am Cortisol 5.1nmol/L (123-626). USG abdomen and pelvis was normal. DEXA scan showed LS Spine T score -1.5. CEMRI Brain revealed partial empty sella turcica. Thus a diagnosis of panhypopituitarism secondary to Sheehan’s syndrome was made. She was started on 5 mg prednisolone, L-Thyroxine 50 mcg OD PO, OCPs, Calcium and Vitamin D supplementation.

Discussion: This is a case of Sheehan’s syndrome wherein the hormonal deficiencies were present for a long time, yet the patient remained asymptomatic for 9 years.

Conclusion: Hypoglycemia can be the first alarming indicator of Sheehan’s syndrome even after many years of disease onset.

Abstract #847

ENDOCRINE CAUSES OF STROKE: GIANT PROLACTINOMA IN A FEMALE PATIENT

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UIC/Advocate Christ Medical Center

Case Presentation: Giant prolactinomas are very rare, representing only ~3% of all prolactin-secreting tumors. They occur more frequently in men than women, with a ratio of 9:1. Patients often present with endocrine symptoms but some can present with stroke associated with pituitary apoplexy. We report a case of giant prolactinoma without apoplexy presenting with a stroke. 79 year old female with history of HTN and hyperlipidemia presented to the ED with slurred speech, left sided facial droop, left arm and leg weakness and expressive aphasia. Review of symptoms was normal except for intermittent headaches. She had a history of regular menstrual periods, had four children and became menopausal at the age of 50. She denied any history of galactorrhea, weight changes, cold intolerance or visual disturbances. Vital signs were normal. Physical examination was notable for expressive aphasia and mild bitemporal hemianopsia on visual field testing. Head CT was negative for acute hemorrhage or ischemia but showed possible pituitary adenoma vs aneurysm. Brain MRI revealed 4.6 x 2.8 x 2.3 cm pituitary macroadenoma compressing the optic chiasm and extending into the inferior right frontal lobe. Her symptoms resolved after a few hours of presentation except for persistent expressive aphasia and slurred speech. Laboratory results were remarkable for a Prolactin level of 5,830 ng/ml, LH <01 munit/ml, FSH 0.3 munit/ml, GH 0.17 ng/ml, IGF-1 131 ng/ml, ACTH 7.5 pg/ml, Cortisol 13.7 mcg/dl, TSH 1.3 munit/ml, Free T4 0.9 ng/dl. Head/Neck CTA showed no aneurysms, significant stenosis or occlusion of the major neck arteries and large intracranial arteries. The patient was started on Cabergoline 0.5 mg biweekly. After two weeks the patient was seen in clinic, she was asymptomatic with no headaches or any neurological complaints. Her repeat Prolactin level was 227.3 ng/ml.

Discussion: Most prolactinomas are small and confined to the pituitary fossa. Giant prolactinomas are defined as large prolactinomas (>4 cm) presenting with a prolactinoma without apoplexy. We report a case of giant prolactinoma without apoplexy presenting with a stroke.

Abstract #845

PROLACTINOMA IN A FEMALE PATIENT

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Discussion: Most prolactinomas are small and confined to the pituitary fossa. Giant prolactinomas are defined as large prolactinomas (>4 cm) presenting with a prolactinoma without apoplexy. We report a case of giant prolactinoma without apoplexy presenting with a stroke.
level of >1000 and symptoms related to mass effect. Giant prolactinomas are rarely seen in women. When seen in women these usually present with endocrine symptoms in more than 75% of cases. Neurological changes occur from extension of the tumor, with visual symptoms present in 70% of cases. Few cases of stroke have been reported, always due to pituitary apoplexy, which was likely caused by tumor-induced vessel compression. To the best of our knowledge we report the first case of a patient with stroke associated with a giant prolactinoma with no evidence of pituitary apoplexy.

Abstract #848

A SECOND CASE OF COMPLETE ERADICATION OF HEADACHES AND PAPILLEDEMA FROM INTRACRANIAL HYPERTENSION (PSEUDOTUMOR CEREBRI) FOLLOWING TREATMENT WITH DEXTROAMPHETAMINE SULFATE

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Objective: To determine if treatment with the sympathomimetic amine dextroamphetamine sulfate could improve headaches from intracranial hypertension that was only partially relieved by acetazolamide.

Methods: A 33 year old woman with severe migraine headaches was diagnosed as having intracranial hypertension by a neuro-ophtalmologist on the basis of having papilledema with negative brain magnetic resonance imagining. The intensity of her headaches was described as an 8 out of 10. Treatment with acetazolamide decreased the frequency and intensity to an overall score of 5 out of 10. The woman sought a different therapy that would 1) be more effective, 2) not give her side effects of tingling in her fingers, and 3) be safe to take in pregnancy (she had been advised that acetazolamide was not safe). She was treated with 15mg dextroamphetamine sulfate extended release capsules which were increased to 25mg daily after 1 month of treatment.

Case Presentation: The 15mg dosage provided immediate relief of the headaches to a 1 of 10 intensity and frequency. The 25mg dosage completely eradicated her headaches. She no longer has papilledema.

Discussion: This is only the second known case of increased hypertension treated with dextroamphetamine sulfate. The previous one had not shown any improvement with acetazolamide yet had almost total eradication with dextroamphetamine sulfate. The second case has been headache free for 1 ½ years while taking 25mg dextroamphetamine extended release capsules once daily in the morning. Not only is dextroamphetamine sulfate safe to take in pregnancy it has been used to prevent miscarriage and help to achieve pregnancies in unexplained failures. The mechanism is believed to be related to correcting sympathetic nervous system hypofunction by stimulating dopamine. The hypothesized mechanism is that certain tissues that are susceptible to increase permeability for a variety of reasons (genetic, traumatic, etc.) are further compromised by decreased sympathetic tone since normal tone is needed to control cellular permeability. This allows absorption of unwanted chemicals leading to inflammation and subsequent pain. The increased permeability also leads to transudation of fluid causing edema where in this case involved edema of the optic nerve.

Conclusion: Based on the dramatic response to a very safe drug despite inadequate response to acetazolamide, dextroamphetamine sulfate should be given consideration as first line treatment for intracranial hypertension.

Abstract #849

IDENTIFICATION OF COLON CANCER IN PATIENTS WITH ACROMEGALY IN AN ONGOING OPEN-LABEL TRIAL OF PASIREOTIDE LAR

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Objective: A recently published meta-analysis reported increased colon cancer risk in acromegalic patients (14/304 [4.6%]) vs controls (8/627 [1.2%]). Here, we report the prevalence of colon cancer during a small open-label trial of acromegalic patients.

Methods: The ACCESS study is an ongoing open-label trial of acromegalic patients (N=27; ClinicalTrials.gov Identifier NCT01995734) that assesses the safety of pasireotide long-acting release (LAR; 40 mg every 28 days). Patients are excluded from enrollment if they have been diagnosed with active malignant disease within the previous 5 years or if their blood glucose is poorly controlled.

Case Presentation: Two men (7.4%) with growth hormone (GH)–secreting pituitary macroadenoma were incidentally diagnosed with stage 3 colon cancer after enrollment. Both cancer-related adverse events were considered to be unrelated to pasireotide. The first patient (36 years old) underwent transsphenoidal adenomectomy immediately after enrollment.
before enrollment. One week after enrollment, a routine colonoscopy revealed a 4.0-cm T1N1a adenocarcinoma in the descending colon and metastasis to a single lymph node. The tumor was resected, and the patient initiated chemotherapy with oxaliplatin and capecitabine. Normalization of insulin-like growth factor 1 (IGF-1) and GH levels was observed 4 months after enrollment. The second patient (50 years old) had a GH-secreting pituitary macroadenoma removed 21 months before enrollment. IGF-1 level was normalized 3 months after enrollment. Five months after enrollment, routine colonoscopy revealed 2 polyps, and a mass was removed. The patient received chemotherapy with oxaliplatin and capecitabine but withdrew from the ACCESS study because of surgical treatment for colon cancer.

Discussion: In this small study, 7.4% of acromegalic patients were diagnosed with colon cancer soon after enrollment. As colon cancer was diagnosed shortly after the patients had enrolled in ACCESS, development of this malignancy was considered to be unrelated to pasireotide LAR. Future studies will be necessary to determine the long-term consequences of uncontrolled acromegaly on colon cancer risk.

Conclusion: Long-term exposure to elevated IGF-1 and GH levels is associated with increased risks in patients with acromegaly. Therefore, there is an urgent need for treatment if these risks are to be mitigated.

Abstract #850

HIDING BEHIND A STROKE: MACROPROLACTINOMA IN A POSTMENOPAUSAL WOMAN

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Case Presentation: A 70-year-old female presented with a one day history of left-sided numbness and weakness. She denied headache, nausea, vomiting, vision changes and galactorrhea. She reported having two full-term pregnancies in the past. Physical exam showed left-sided limb weakness, slow coordination and a left Babinski sign. Head CT revealed a mass projecting into the right sphenoid sinus. MRI of the sella area showed a right pontine infarct and a 2.1 x 1.8 x 2.5cm pituitary mass encasing the right internal carotid artery (ICA) and encroaching upon the right cavernous sinus, but not compressing the optic chiasm. No visual field defects were found. Upon neurosurgical evaluation, intervention was not deemed necessary as brain/neck MRA showed no vascular narrowing from tumor encasement. Interestingly, a 6mm aneurysm emerging from the cavernous right ICA was visualized within the tumor. She received medical management for acute stroke. Further investigations revealed a serum prolactin of 3588ng/mL. TSH, free T4 and T3, FSH, LH, Cortisol, ACTH, IGF-1 and GH were within the normal range. A Cosyntropin test showed appropriate adrenal response. Cabergoline therapy was initiated at 1mg weekly, subsequently increased to 2mg weekly. Follow-up prolactin level 3 weeks after initiating therapy is 83ng/mL. A new MRI will be needed to reassess the size of the pituitary mass.

Discussion: Incidental pituitary macroadenomas are rare; prolactinomas are the most common of these. Large non-functioning tumors can cause hyperprolactinemia due to stalk compression, but prolactin levels >94ng/mL are usually indicative of a prolactinoma. Levels of prolactin generally correlate with tumor size and values >250ng/mL are highly suggestive of a macroadenoma. Other causes of hyperprolactinemia are certain medications and hypothyroidism, but these were excluded in our case. Although she had an elevated serum creatinine, renal failure usually provokes only a modest raise in prolactin as compared to the markedly elevated levels caused by macroadenomas. It is not clear for how long this macroadenoma has been growing, but the fact that she had two pregnancies suggests that she may not have had hyperscretion of prolactin at that time. It is remarkable that our patient’s tumor did not provoke any neurologic or clinical manifestations despite its large size, invasive nature, and the degree of hyperprolactinemia.

Conclusion: Our patient, who presented with clinical signs and symptoms of an acute ischemic stroke, was incidentally found to have a large asymptomatic macroprolactinoma with extensive extrasellar extension.

Abstract #851

INCREMENTAL HEALTHCARE RESOURCE UTILIZATION AND COST IN U.S. PATIENTS WITH CUSHING’S DISEASE COMPARED TO PATIENTS WITH DIABETES

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Objective: Cushing’s disease (CD) affects 8 people per million in the U.S. and is associated with increased morbidity and mortality. Healthcare cost and resource utilization for patients with CD have not been well-studied. We compared CD patients to matched patients with diabetes mellitus (DM) to characterize resource utilization and cost.

Methods: We conducted a matched cohort study using US insurance claims. CD patients were identified by a claim with Cushing’s syndrome and an additional claim
with pituitary neoplasm or pituitary surgery. From a 5% random sample of the same database, we identified DM patients (without CD) and matched by age, gender, region, and year in a 1:2 ratio. We compared utilization and cost during a 1-year timespan. Comparisons between cohorts were performed with chi-square and t-tests.

**Results:** There were 1,852 CD patients and 3,704 matched DM controls. Mean age 42.9 years and 78.2% were female. CD patients had significantly higher rates of infections, osteoporosis, depression/anxiety, kidney stones, and cardiovascular disease/stroke, compared to DM patients. CD patients were hospitalized significantly more frequently (19.3%) than DM patients (11.0%, p<.001). They visited the ED significantly more (25.4%) than DM patients (21.1%, p<.001). CD patients had a mean 19.1 office visits, compared to 10.7 for DM patients (p<.001). Mean total healthcare cost for CD patients was $26,269, versus $12,282 for DM patients (p<.001).

**Conclusion:** Cardiovascular disease and stroke, often associated with DM, were found to be even more common in CD patients than in DM controls. CD is a chronic condition and often requires long-term treatment. CD patients used significantly more healthcare resources than DM controls, including more hospitalizations, ED visits, and office visits. The cost of CD patient care was double that for DM patients. Better disease control has been linked to reduced comorbidities and may potentially also reduce healthcare cost.

**Abstract #852**

**CUSHING'S SYNDROME BEHAVING BIOCHEMICALLY AS ECTOPIC ACTH SYNDROME IN A PATIENT WITH AN EXISTING PITUITARY MACROADENOMA AND RESOLUTION OF THE SAME, FOLLOWING SPONTANEOUS INVOLUTION OF THE PITUITARY ADENOMA**

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**Case Presentation:** A 53 year old post menopausal lady was referred for hyperprolactinemia and minimal galactorrhea. Prolactin level was 40.6 (3-26 mcg/L). TSH was normal. AM Cortisol was 362 (185-624 nmol/L). MRI scan showed a 1.4 cm pituitary mass undergoing cystic degeneration. The hyperprolactinemia was thought to be due to stalk compression and no treatment was initiated. She didn’t look Cushingoid during the initial visit but developed signs of Cushing’s syndrome 5 months later. HbA1c was 7.0% and hypokalemia noted. 24 hour urine cortisol levels were elevated at 1904 and 1311 (<275 nmol/day). AM Cortisol was 798 (170-720 nmol/L). ACTH was 29.7 (0-10.1 pmol/L). Low dose dexamethasone suppression test reduced Cortisol to 774 nmol/L, ACTH remained high at 30.6 pmol/L. With high dose dexamethasone suppression test, Cortisol went down to 659 nmol/L and ACTH to 19.5 pmol/L. In view of these results, ectopic ACTH syndrome was considered in this chronic smoker. As she was symptomatic, Ketoconazole was initiated. Chest Xray, CT scan of the chest/abdomen were unremarkable. 24 hour urine 5 HIAA, Octreotide scan, Calcitonin and gastrin levels were normal. Over the next few months, she showed improvement and Ketoconazole was reduced and eventually stopped. Repeat MRI showed considerably smaller pituitary adenoma measuring 7 mm in size. Off the Ketoconazole, patient continues to show no clinical or biochemical evidence of Cushing’s syndrome.

**Discussion:** Five months after initial assessment of this postmenopausal patient for hyperprolactinemia and pituitary macroadenoma, she presented with Cushing’s syndrome. Initial impression was that she had developed Cushing’s disease but biochemically, she behaved like an ectopic ACTH syndrome. The high dose dexamethasone suppression test did not suppress the Cortisol level. ACTH levels were 3 times the upper limit of normal. Work up of ectopic ACTH syndrome did not show any culprit lesion. Although treated with Ketoconazole briefly, patient improved and Ketoconazole was stopped. This correlated with the spontaneous involution of the pituitary adenoma. The dexamethasone suppression test did not suppress the cortisol level possibly because the patient did not take the dexamethasone as directed. Inferior petrosal sinus sampling would have helped clarify matters but was not done as by then, patient was improving and there was involution of the pituitary adenoma.

**Conclusion:** This case history illustrates the difficulty in sometimes figuring out Cushing’s disease versus ectopic ACTH syndrome. It is likely that she had Cushing’s disease all along. It is also remarkable to note resolution of Cushing’s syndrome non surgically by spontaneous involution of the pituitary adenoma.
Abstract #853

RECURRENT SYNCOPE AND INTRACTABLE HEADACHE: AN ATYPICAL PRESENTATION OF AN ACTH PRODUCING PITUITARY MACROADENOMA IN A YOUNG WOMAN

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Objective: We report an unusual presentation of Cushing’s disease in which the diagnostic MRI was only obtained for persistent severe headache following a negative syncope workup.

Case Presentation: A 28-year-old healthy female presented with recurrent syncope. The patient also had severe frontal headaches. History obtained later was remarkable for weight gain, irregular menses, galactorrhea, and fatigue. Significant physical findings included hypertension, a BMI of 27, acne, moon facies, dorsal and supraclavicular fat pads and lower extremity violaceous striae. Initial cardiac and neurological workup including head CT was negative. Brain MRI, ordered for headache unresponsive to pain medication, revealed a 13x18x14mm pituitary macroadenoma, which partially encircled the carotid artery in the right cavernous sinus.

Laboratory results were significant for plasma ACTH 99 pg/mL (6-50), urine free cortisol (UFC) 563 mcg/24h (4-50), late night salivary cortisol 1.91 mcg/dL (<0.9), AM cortisol post 1 mg dexamethasone 20.52 mcg/dL (<1.9); post 8 mg dexamethasone 3.51 mcg/dL. Abdominal CT showed bilateral adrenal nodular thickening, possible hyperplasia. There was no laboratory evidence of hypopituitarism. The patient underwent transsphenoidal surgery. Pathology was negative syncope workup.

Discussion: Cushing’s disease, hypercortisolism due to an ACTH pituitary adenoma, is rare with 2.2-1.7 cases per million a year, only 4-10% of which are associated with a macroadenoma (>10mm). Although our patient had classic signs and symptoms of central obesity, facial rounding, hypertension, acne, striae and subjective weakness, syncope brought her to medical attention. We found no cases in the medical literature of Cushing’s disease associated with syncope in the absence of pituitary apoplexy, pulmonary embolus or myocardial infarction. The trigemino-cardiac reflex (TCR) causing bradycardia and hypotension has been described in patients undergoing pituitary surgery, thought to be due to stimulation of the trigeminal nerve when removing adenomas near the cavernous sinus. It is unclear if a pituitary macroadenoma can trigger the TCR but this could be a possible explanation of syncope in our patient.

Conclusion: This case illustrates 1) syncope is a possible presenting symptom of pituitary macroadenomas without pituitary apoplexy; 2) it is important to consider pituitary adenomas in patients with intractable headache; and 3) head CT lacks sensitivity for detection of pituitary pathology.

Abstract #854

A REVIEW OF THE CARDIAC MANIFESTATIONS/COMPLICATIONS OF ACROMEGALY, THEIR MANAGEMENT AND OUTCOMES.

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Case Presentation: A 27 year old Bangladeshi female with a past medical history of GH secreting pituitary adenoma s/p surgery and radiation is admitted three times within a span of two months; for complaints of recurrent nausea, vomiting and headaches. Hormonal assay was consistent with panhypopituitarism and increased IGF-1. An oral glucose tolerance test showed a markedly elevated GH response: >5ng/ml consistent with the diagnosis of Acromegaly. MRI showed an empty appearance of the pituitary fossa. Patient was treated with a trial of cabergoline and other hormones were replaced accordingly. However, patient was lost to follow up: she had traveled to Bangladesh and missed several appointments, and she also could not afford her medications due to lack of health insurance. She then showed up at the clinic, 17 months later with complaints of dyspnea. She was found to have elevated JVD, bibasal crackles, S3 gallop, and a grade 2 bilateral pitting pedal edema. Systolic blood pressure was 150, hemoglobin A1C was 8.5, and ECHO showed EF of 20%, severe global hypokinesis involving all segments of the left ventricle, severe enlargement of the LV cavity size, severe LV systolic dysfunction, stage 3 diastolic dysfunction, moderate mitral regurgitation and left atrial enlargement. A diagnosis of Congestive heart failure was made and she was aggressively managed with furosemide, lisinopril, metformin, Life vest and later carvedilol. At this time, octreotide injections were also started. Repeat ECHO done 4 months later showed marked improvement in LV function with normal LV size, normal LV thickness, no regional wall motion abnormalities, EF of 45 % and stage 1 diastolic dysfunction. IGF -1 and A1C has been trending down, patient has been asymptomatic and is being closely followed in the clinic.

Discussion: Acromegaly is a disorder characterized by Growth hormone (GH) hyperssecretion, most commonly GH –secreting pituitary adenoma. Patients with
Acromegaly have an increased risk of Type 2 Diabetes mellitus, cardiovascular disease (CVS), hypertension, hypertrophic cardiomyopathy and atherosclerotic disease. They have a higher mortality rate, with CVS disease accounting for 60% of deaths.

**Conclusion:** GH and IGF-1 both have regulatory roles in the cardiovascular system and when in excess, can lead to myocyte hypertrophy, interstitial fibrosis and both systolic and diastolic dysfunction. We emphasize the importance of early control of GH and IGF-1 excess; in ameliorating cardiac abnormalities and leading to a significant reduction of left ventricular hypertrophy with improvement in cardiac performance. Radiation and medical therapy can also be used as an adjunct to surgery in patients with residual disease.
REPRODUCTIVE ENDOCRINOLOGY

Abstract #900

TRANSIENT MALE HYPOGONADISM

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Objective: To describe a case of hypogonadism in a young male patient which resolved without medical intervention who had biochemical evidence of secondary hypogonadism.

Methods: A 42 year old male presented with a one year history of loss of libido with difficulty achieving and maintaining erections satisfactory for successful intercourse. He admitted to fatigue, and inability to play soccer though he is an avid player. No history of traumatic brain injury. He has two children.

He was shaving less than before. He denied salt craving, nausea or abdominal pain nor cold intolerance. No personal history of hemochromatosis, no bronze skin discoloration, no arthritis. He binges on alcohol on weekends and holidays, no marijuana, tobacco, opiate or androgen abuse.

On examination, vitals were within normal limits. He had decreased male distribution of hair, normal testicular volume bilaterally and a normal phallus.

Case Presentation: In his laboratory studies, he had normal complete metabolic profile and normal complete blood count. He had a low IGF 1, low normal FSH and LH, low normal total am testosterone twice. He also had normal cortisol and estradiol levels. His prolactin level was mildly elevated three times first 15.5 ng/ml then 30 ng/ml then 19.9 ng/ml.

Pituitary MRI suggested a non specific 4 mm hypoenhancing lesion in left lateral pituitary which could represent a microadenoma.

Patient’s symptoms resolved on follow up 4 weeks later, an improvement which was sustained for 2 subsequent visits. Dopamine agonist therapy was therefore not indicated.

MRI study is to be repeated 6 months after his last visit to document microadenoma growth. Patient is to be monitored for headache and visual symptoms.

Discussion: Transient hypogonadism in males is a recognized phenomenon. The causes are varied and may be due to anabolic steroid use, multiple concussions in contact sports, infection, alcohol abuse among others. These cause secondary hypogonadism.

Hyperprolactinemia also causes secondary hypogonadism. The degree to which fluctuations in this patient’s mildly increased prolactin levels contributed to transient hypogonadism in addition to his other risk factors is not clear.

Close follow up of his clinical progress may provide further clues.

Conclusion: Transient hypogonadism is increasingly being recognized in young male patients. These patients usually require extensive endocrinology work up initially and close follow up as deemed necessary. Many resolve over time with supportive treatments or without treatment.

Abstract #901

LEYDIG CELL OVARIAN TUMOR

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Objective: Leydig cell tumors are quite rare in the general population representing less than 1% of ovarian neoplasms; also referred to as sex-cord stromal tumors. The majority of patients with one of these tumors presents with both hirsutism and virilization.

Case Presentation: The patient is a 79-year-old woman who presented for evaluation of hirsutism and deepening of her voice. For 15-years, she has had dark hair diffusely present on her body, especially her face and breasts which have required shaving. In contrast, she also noticed increased thinning of scalp hair. Her voice has deepened significantly over the past few years.

Her gynecologic history included menarche at age 11 with regular monthly menses until she underwent a partial hysterectomy in 1982 for abnormal uterine bleeding; both ovaries were left intact. Fertility was never an issue with 6 total pregnancies. She was never on estrogen replacement therapy or over the counter supplements.

Physical examination included significant terminal hair present on her cheeks, chin, neck, upper lip, breasts bilaterally, and abdomen. There was hair thinning and male pattern balding on her head. Clitoromegaly was present. Hormonal evaluation revealed an elevated testosterone level at 298 ng/dL, highest of 320 ng/dl, LH 19 IU/L, FSH 52 IU/L, estradiol 20.7 pg/mL, estrone 33.5 pg/mL & total estrogen 54.2 pg/mL.

CT Scan of the pelvis displayed a 3.7 x 1.7 cm slight prominence of left adnexa.

Discussion: The findings were concerning for an ovarian tumor causing hirsutism and virilization. After an adrenal etiology was ruled out, given the elevated estradiol and testosterone levels, the possibility of a germ cell or sex cord-stromal tumor of the ovary was considered. Due to the slow growing, indolent nature of ovarian cancer with progressive symptoms; surgical removal of the lesion was recommended for definitive diagnosis. The pathology of the right fallopian tube and ovary was positive for a 1.1 cm Leydig Cell tumor confined to the ovary staining positive for inhibin. Post-operatively the hyperandrogenism resolved. Her testosterone levels normalized to 26 ng/dL and she began having mild symptoms of estrogen deficiency including hot flashes.

Conclusion: This case was presented to increase awareness
of Leydig Cell tumors of the ovary that may present with hyperandrogenism. The majority are unilateral, benign and present with symptoms of virilization, hirsutism, amenorrhea/oligomenorrhea, irregular menses and infertility. Following surgical removal of the tumor, significant reductions in testosterone levels are anticipated in addition to partial or complete reversal of some of the presenting clinical features.

Abstract #902

THE WIDE SPECTRUM OF ANDROGEN INSENSITIVITY SYNDROME

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Case Presentation: 21 year old male attended for evaluation of an eight month history of painless bilateral breast enlargement. Past history included type 1 DM since the age of 12 treated with insulin. Pubic and axillary hair development had occurred by age 16. One sister with diabetes, all other siblings without any known medical problems. He had no prior exposure to hormonal medications nor was he on medications associated with gynecomastia. Examination revealed a phenotypic male with short stature with severe bilateral gynecomastia. He had normal axillary hair, male pattern pubic and abdominal hair, scant chest hair, normal sized testes with no hypospadias. Laboratory tests revealed very high testosterone levels of 1836 ng/dl (250-1100 ng/ml), slightly elevated estradiol of 45 pg/ml (normal male < 39 pg/ml), FSH of 3.1 mIU/ml (1.6-8 mIU/ml), LH of 9 mIU/ml (1.5-9.3 mIU/ml), DHEAS 436 mcg/dl (110-510 mcg/ml), 17-hydroxyprogesterone 172 ng/dl (32-307 ng/ml), prolactin 5.5 ng/ml (2-18 ng/ml), normal thyroid functions, ACTH 12 pg/ml (6-50 pg/ml). CT abdomen & pelvis without contrast did not show any testicular mass or adrenal pathology. Genetic testing for AR mutation was not done due to financial constraints. The clinical presentation and biochemical data were consistent with mild AIS and he was referred to plastic surgery for bilateral mastectomy.

Discussion: Androgen Insensitivity Syndrome (AIS) is caused by mutation in the androgen receptor gene which is X-linked recessive. Karyotype is 46, XY. A large number of mutations are reported in AR gene. The degree of loss of androgen function directly determines the phenotypic features. Complete AIS- Born as phenotypic females who present with primary amenorrhea with normal breast development and absence of terminal axillary and pubic hair. Mullerian derivatives namely uterus and tubes are absent secondary to production of antimullerian hormone by the testes while inutero resulting in a blind vaginal pouch. Here the gonads may be felt in the groin.

Partial AIS: A Spectrum of phenotypes may be seen varying from females with clitorormegaly to males with varying degrees of masculinization encompassing hypospadias, micropenis, bifid scrotum and descended testes. The mildest variants may present with gynecomastia, as in this case report, or simply with male factor infertility.

Conclusion: AIS occurs in up to 2-5:100,000 live births. It is important to appreciate that a phenotypic spectrum exists. The history, physical examination and discordant lab findings of very high serum testosterone in the face of absolute (female phenotype) or relative under masculinization are key to correct diagnosis.

Abstract #903

PATTERNS OF SEMINAL FLUID ANALYSIS IN MALE PARTNERS OF INFERTILE COUPLES ATTENDING GYNECOLOGICAL CLINIC AT FEDERAL MEDICAL CENTRE ABEOKUTA

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Objective: The contribution of male factors as cause of infertility is increasingly being noted in the recent times and has become a source of concern to the affected couples with its attendant social and psychological effects and the potential of threatening relationships. This study was to assess the seminal fluid analysis parameters in male partners of infertile couples presenting at gynecological clinic in Federal Medical Centre, Abeokuta and to determine the patterns of seminal fluid abnormalities in the seminalysis results.

Methods: The study is a 3 year retrospective review (2011-2013) of seminal fluid analysis results of male partners in infertility cases at the Federal Medical Centre, Abeokuta. Seminal analysis was done using the WHO 2010 laboratory manual for the examination and processing of human semen revised fifth edition.

Case Presentation: During this study period, a total of 214 semen samples were analysed for semen quality over the 3 year period. Among the men examined, Sixty four (30%) had normal semen parameters, while one hundred and fifty (70%) had abnormal semen parameters. The abnormal semen parameters consists of low volume (12.6%), prolonged liquefaction time (9.8%), oligozoospermia (28%), azoospermia...
(8%), asthenozoospermia (25%), teratozoospermia (9%),
combined defects of oligo-asthenozoospermia (23.8%), oligo-
teratozoospermia (9.8%), astheno-teratozoospermia (12.60%) and
oligoasthenoteratozoospermia (11.20%) . The microbiological
culture isolated various microbes in 24.8% of the samples while 21% have abused various substances comprising of alcohol, tobacco, marijuana. This could have negative impact on their fertility potential.

**Conclusion:** This study reveals that the contribution of abnormal seminal parameters to infertility is significant in our environment. Efforts should be made in enlightening men on the common aetiologies of abnormal semen and options of treatment of the likely causes.

**Abstract #904**

**QUALITY OF TESTOSTERONE REPLACEMENT PRESCRIBING AND MONITORING AT VETERANS AFFAIRS MEDICAL CENTER**

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**Objective:** Providers are replacing Testosterone (T) in men 50+ years of age due to ill-defined conditions. We noted men in the private sector and at our facility were started on T replacement without recommended labs and screening. We also found dosing and laboratory follow up was not appropriate. We sought to enable providers to appropriately identify patients for T replacement and ensure it was done safely under current guidelines.

**Methods:** We developed a template to educate and assist in prescribing and monitoring of T replacement using the Endocrine Society’s guidelines. Retrospectively, one hundred pre-template patients have been compared to nineteen post-template patients thus far for quality of prescribing and monitoring.

**Results:** Pre-template data is as follows: 31% had 2 separate AM testosterone levels drawn prior to treatment. 3% had LH, FSH, and Prolactin levels drawn. 75% had a prostate specific antigen lab within one year. 20% had a digital rectal exam (DRE) before treatment. 43% had the correct dosage of injectable T prescribed. 2% patients had positive history of prostate cancer. 0% patients had discussion of fertility issues before treatment. Voiding issues were discussed with 4% patients before the treatment. 48% patients had T levels checked post initiation of T replacement. Overall, pre-template evaluation showed lack of compliance to guidelines before initiating T replacement. Post-template chart reviews showed improvement. Nineteen new patients started on testosterone were reviewed. 68% of patients had 2 separate AM T levels checked prior to treatment. 63% of patients had LH, FSH, and prolactin drawn prior to treatment. 84% had PSA level checked within one year. 58% had prostate exam within one year. 100% had correct dosing of injectable T. None of the patients had prostate cancer. Fertility issues and voiding issues were discussed with 100% patients before the T treatment. Data to verify appropriate prescribing and monitoring post T replacement is in progress.

**Discussion:** Testosterone replacement promises the “fountain of youth”. T replacement has become ubiquitous worldwide. Risks remain unknown in the over 50 year old population. We believe that we need to closely adhere to guidelines to not only correctly identify men that will benefit from T replacement but also prevent untoward events.

**Conclusion:** We have found that the quality of prescribing is enhanced by a prescribing template.

**Abstract #905**

**SPONTANEOUS RECOVERY OF THE GONADOTROPIC FUNCTION AFTER PREGNANCY IN A CASE OF IDIOPATHIC HYPOPITUITARISM**

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**Objective:** Humans with hypopituitarism are less likely to be fertile and are more prone to experience high-risk pregnancies, with full-term viable births observed in only 61% of cases and spontaneous lactation in 14.3% of cases (Ganie, et al, 2010). The following case study reviews a panhypopituitarism patient who gained spontaneous gonadotropin pituitary function following an in vitro fertilization (IVF) pregnancy.

**Methods:** The patient’s medical records and personal
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account were utilized as data for this analysis.

Case Presentation: The patient was diagnosed with adrenal insufficiency at age five. Stimulation testing at age seven revealed non-existent or decreased ACTH, TSH and GnRH levels and MRI testing revealed an “empty sella.” These findings led to the diagnosis of idiopathic panhypopituitarism. Subsequently, the patient was started on supplemental cortisol, levothyroxine, and human growth hormone therapy.

At age 27, the patient wished to become pregnant and was therefore treated with high-dose injectable FSH/LH for ovary stimulation. IVF was prompted following failed intrauterine insemination. IVF was successful and the patient experienced spontaneous labor at 36 weeks gestation with milk-let down and lactation. The patient continued to breastfeed over the following 16 months. One month post-breastfeeding, the patient experienced her first menses, which lasted for six days. The patient spontaneously experienced menses four times on an irregular 30-35 day cycle. Menses ceased after she became pregnant a second time without medical intervention. At 36 weeks gestation during the second pregnancy, the patient went into spontaneous labor, which stalled and required low dose pitocin to progress. The patient vaginally delivered her second child with spontaneous milk let-down and lactation. The patient was maintained on levothyroxine and cortisol throughout both pregnancies and while breastfeeding.

As the patient is currently breastfeeding, she has not undergone hormone testing. Upon cessation, her levels will be investigated, though the patient has clearly exhibited sufficient levels for impregnation.

Conclusion: We present a patient with idiopathic hypopituitarism who exhibited spontaneous and continuous production of endogenous prolactin, FSH and LH after a successful IVF-induced pregnancy. The recovery of the pituitary gonadotrophic function (FSH and LH) resulted in a natural second pregnancy. A spontaneous vaginal delivery associated with normal prolactin secretion was experienced, which led to lactogenic and galactopoetic activities. This further emphasizes the uniqueness of the panhypopituitarism patient’s recovery of limited pituitary function.

Abstract #906

AN UNUSUAL COMPLICATION OF HORMONE THERAPY IN A TRANSGENDER PATIENT

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Upstate Medical University

Case Presentation: Estrogen therapy is a known cause of hypertriglyceridemia. This case encompasses an interesting presentation of severe hypertriglyceridemia in a patient on estrogen therapy.

A 35 year old male-to-female transgender on estrogen therapy with a past medical history of diabetes mellitus type 2 and hypertriglyceridemia presented to the hospital with progressively worsening abdominal pain radiating to her back. On initial work up, she was found to have an elevated triglycerides level of 28,173 mg/dl. Lipase and amylase were within normal limits. She was admitted to the ICU and placed on a continuous insulin infusion for treatment of severe hypertriglyceridemia. She was monitored closely for signs or symptoms suggestive of the development of pancreatitis, which has been reported to be life threatening in patients with similar presentations. In addition, hematology was informed of the possible need for initiation of plasmapheresis, should the patient develop pancreatitis. The patient’s triglycerides slowly trended down with continued management, and no further interventions were required.

Discussion: This patient’s history of estrogen replacement therapy is the most likely etiology of her hypertriglyceridemia. A recent study demonstrated that in patients with elevated triglycerides at baseline (>750 mg/dl), there was a significant increase in triglycerides with estrogen replacement therapy (mean 1665 mg/dl on follow-up). This patient did have a previous diagnosis of hypertriglyceridemia, however, the dramatically high triglyceride level of over 28,000 mg/dl is very rare. The vast majority of cases of triglyceride induced pancreatitis demonstrate triglyceride levels of only a several thousand. It is even more impressive that this patient did not have evidence of pancreatitis, with these significantly elevated levels present in the plasma.

Conclusion: The combination of estrogen therapy with multiple other risk factors for hypertriglyceridemia can result in a dramatic increase in triglyceride levels. In patients with hypertriglyceridemia at baseline, estrogen therapy should be used with caution to avoid serious complications such as pancreatitis. In addition, these cases should to be managed in a setting with a high level of care, as the risk for life threatening acute pancreatitis is high.
Abstract #907

BARIATRIC SURGERY A PROMISING OPTION FOR TREATING HAIR-AN SYNDROME

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Objective: HAIR-AN syndrome (HyperAndrogenism (HA), Insulin Resistance (IR) and Acanthosis Nigricans (AN)) is a rare multi-system disorder in women. Despite available medical therapies like metformin and TZD among others, severe forms may be refractory. Bariatric surgery may have a promising effect in such instances. We report herein a case of HAIR-AN managed by Roux-en-Y gastric bypass surgery with significant improvement.

Case Presentation: A 40 year old lady known to have polycystic ovarian syndrome, infertility, hirsutism, obesity, hypertriglyceridemia and carpal tunnel syndrome and recently diagnosed with HAIR-AN syndrome, presented with a history of severe oligomenorrhea since menarche at age 13 with about 10 menstrual cycles in the last 16 years, a long standing history of facial hirsutism and acne, increased tongue size, spacing of teeth, enlargement of her hands and feet and 59 lbs weight gain in the last 8 years. She underwent supervised weight loss programs without success and has been on metformin for the last 14 years, then pioglitazone was added to no avail. She was also taking spironolactone and was on monthly vaginal Etonogestrel/Ethinyl Estradiol. Her physical exam was pertinent for a weight of 207 lbs, height 5’4”, with a BMI of 35.5 kg/m2, BP 135/77 mm Hg and HR 78/min, severe acanthosis nigricans in her flexural areas, facial hirsutism and acral growth with macroglossia suggestive of acromegaly. The rest of her exam was unremarkable. Her lab results were significant for extremely elevated fasting insulin at 652.53 uIU/ml commensurate with a fasting glucose of 121 mg/dl. Her HbA1c was 6.7%. IGF-1 was adequate at 125 ng/ml, AM cortisol and prolactin were normal at 10.6 mcg/dl and 15 ng/ml respectively, a 24-hour urine collection for Cortisol/Creatinine ratio was within normal at 8.8 mcg/gm. Testosterone level was elevated at 127.1 ng/dl and Sex hormone binding globulins was low at 8.5 nmol/L. She underwent laparoscopic Roux-en-Y gastric bypass after which her fasting insulin level dropped to 73.9 uIU/ml and testosterone level to 8 ng/dl on day 2 postoperatively. Upon subsequent follow up visits she had significant improvement in her symptoms.

Conclusion: HAIR-AN syndrome is caused by abnormal insulin signaling resulting in multisystem manifestations secondary to the severe insulin resistance, hyperinsulinemia and hyperandrogenism. At the extreme it can lead to pseudo-acromegaly features as in our patient. Bariatric surgery is yet another effective option that leads to rapid significant improvement of the components of the HAIR-AN syndrome by improving insulin resistance.

Abstract #908

INTRAVENOUS INTRALIPID THERAPY IS NOT BENEFICIAL IN HAVING A LIVE DELIVERY IN WOMEN AGED 40-42 WITH A PREVIOUS HISTORY OF MISCARRIAGE OR FAILURE TO CONCEIVE DESPITE EMBRYO TRANSFER UNDERGOING IN VITRO FERTILIZATION-EMBRYO TRANSFER

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Objective: A previous uncontrolled observational study at another reproductive center found a high pregnancy rate in women with previous failure to conceive despite in vitro fertilization-embryo transfer (IVF-ET) or previous miscarriage treated by intravenous intralipid therapy. However, though the numbers were small (n=4) there were no pregnancies in the women > age 40. The present study evaluated the efficacy of intralipid in a larger series to determine if the lack of pregnancies in this older reproductive group was merely fortuitous related to small numbers or could intralipid therapy have a negative effect in this age group.

Methods: A matched control was performed. Women aged 40-42 with a previous history of miscarriage or who failed to conceive despite previous embryo transfer who entered an IVF program were offered intravenous intralipid therapy (4 mL of 20% Liposyn II in 100 mL normal saline over 1 hour) during the mid-follicular phase. Clinical pregnancy rates (8 weeks with viable gestation) and live delivered pregnancy rates were then determined and compared.

Case Presentation: The results were evaluated after 10 matched cycles. There were no clinical pregnancies in those receiving intralipid vs. a 40% clinical and a 30% live delivered pregnancy rate in the untreated controls (p=0.087, Fishers exact test). The study was terminated because of these preliminary data.

Discussion: In the test tube adding intralipid to natural killer cells can inhibit their cytolytic action. However, the use of intravenous intralipid to suppress natural killer cell activity does not seem to improve the chance of a live delivery in women 40-42 with a previous history of miscarriage. In fact this therapy may actually be detrimental in this age group.

Conclusion: Since efficacy of this therapy was not found
in a group of advanced reproductive age it is not clear why this should be effective for a younger population. A controlled study for the younger group is needed. Perhaps such a study could be limited to only those with miscarriage rather than also concluding failure to conceive despite embryo transfer.

Abstract #909

THE EFFECT OF CONTINUOUS USE OF ORAL CONTRACEPTIVES ON SERUM LEVELS OF ANTI-MÜLLERIAN HORMONE AND IMPLICATIONS FOR PRESERVING OVARIAN RESERVE FROM DAMAGE FROM CHEMOTHERAPY

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Objective: To determine how fast and to what degree do oral contraceptives suppress active follicle growth as determined by interval testing of serum AMH.

Methods: A prospective study of one woman where a baseline serum AMH was obtained followed by subsequent measurements of serum AMH at various intervals over several months while on a continuous oral contraceptive (Quartette) was performed.

Case Presentation: A baseline serum AMH obtained prior to starting oral contraceptives was 4.44 ng/mL. The serum AMH levels according to the number of weeks on continuous oral contraceptives were as follows (ng/mL): Baseline before oral contraceptives 4.44, week 3 – 3.62, 5- 4.07, 7 – 3.99, 9 – 4.39, 11 – 3.53, 17 – 1.58, 21 – 2.59, and 29 – 1.60.

Discussion: The anti-Müllerian hormone (AMH) is made by actively growing pre-antral follicles. Many chemotherapy agents will damage actively growing cells. Serum AMH will give an estimate of the degree of the number of actively growing follicles, which is representative of the ovarian oocyte reserve. One method to mitigate the adverse effect of certain chemotherapeutic drugs, e.g., alkylating agents is to try to suppress the levels of actively growing follicles. Most frequently gonadotropin releasing hormone agonists are used to suppress follicle stimulating hormone (FSH). Some studies suggest efficacy of oral contraceptives in preserving ovarian function while others fail to corroborate these findings. Speedy suppression is needed to prevent delay in treatment.

Conclusion: The use of oral contraceptives does not appear to be a quick and efficient method to suppress pre-antral follicular growth as determined by its ability to suppress serum AMH. The same study will be repeated shortly, only this time with a gonadotropin releasing hormone agonist.

Abstract #910

BIRTH OF A GENETICALLY NORMAL BABY FOLLOWING TRANSFER OF A SINGLE EMBRYO INTO A WOMAN WITH DIMINISHED OOCYTE RESERVE DESPITE SELECTIVE REDUCTION OF 1 OF 2 DICHORIONIC DIAMNIOTIC TWINS WITH TRISOMY 21

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Objective: To present a rare occurrence to prevent the possible mistake of terminating a perfectly normal fetus.

Methods: A cell free DNA test was performed on a woman with diminished oocyte reserve who conceived twins following the transfer of a single embryo following the transfer of a single embryo following mild ovarian hyperstimulation and oocyte retrieval then oocyte fertilization.

Case Presentation: The cell free DNA test indicated trisomy 21. Since the fetuses were considered as identical twins with a late cleavage, a perinatologist recommended a D&E. Because of the preciousness of this pregnancy we suggested an alternative possibility, i.e., the natural conception from an oocyte released later, and thus the possibility of a normal fraternal twin along with one with trisomy 21. Thus, we suggested amniocentesis at 16 weeks (was too late for chorionic villus sampling). At 16 weeks the ultrasound showed obvious cardiac abnormalities of one fetus but the other appeared normal. Selective reduction was performed on the fetus with the cardiac defect. Amniocentesis confirmed trisomy 21. Though the fetal karyotype of the remaining fetus showed 46 XY, the perinatologist still favored mosaicism in an identical twin and suggested termination. The patient chanced the alternative hypothesis and was rewarded with a normal healthy full-term baby.

Discussion: In the much less common circumstance of dichorionic diamniotic “identical twins” one must consider the possibility of the circumstance of a singleton from the IVF-embryo transfer and natural conception of the second. This can be very important where one of the twins is chromosomally abnormal to prevent the wrongful termination of a precious normal conceptus. The principles of mild stimulation were applied because of marked decreased oocyte reserve which may have helped to achieve this pregnancy despite marked diminished oocyte reserve.

Conclusion: The case supports the retrieval of only 1 oocyte and transfer of a single embryo since a live pregnancy may be achieved even in women with
diminished ovarian reserve as determined by low antral follicle count, elevated day 3 serum follicle stimulating hormone levels and/or low anti-mullerian hormone levels. The very poor outcome that many IVF centers claim in women with poor egg reserve is probably related to the excessive use of gonadotropin stimulation in this group which leads to meiosis II errors and thus aneuploidy.

Abstract #911

MARKED IMPROVEMENT OF THE AROMATASE INDUCED ARTHRALGIA SYNDROME FOLLOWING TREATMENT WITH THE SYMPATHOMIMETIC AMINE DEXTROAMPHETAMINE SULFATE

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Objective: Post-menopausal women with breast cancer taking the aromatase enzyme inhibitor letrozole have been shown to increase their life span and decrease the frequency of local recurrence and distal metastasis. Unfortunately a side effect known as the aromatase induced arthralgia (AIA) syndrome will develop at some point in about 50% of the women taking aromatase inhibitors and it is so severe that 20% of the women stop therapy before the prescribed 5 years. The objective of the present study was to determine if treatment with sympathomimetic amines, e.g., dextroamphetamine sulfate, can relieve the pain of AIA similar to its effect on arthritis, fibromyalgia, and chronic regional pain syndrome.

Methods: A 53 year old woman developed stage I breast cancer and elected to have simple mastectomy plus letrozole 2.5mg daily post-operatively. After 1 ½ years she developed severe right shoulder pain which was so severe it precluded sleep. An orthopedist diagnosed her with frozen shoulder syndrome and recommended physical therapy. Unfortunately, physical therapy seemed to make it worse. Analgesics did not help. An injection of steroids into the shoulder was suggested by the orthopedist but instead she re-consulted our group since we had helped her with severe deep thigh pain that she developed after initiating exercise by prescribing dextroamphetamine sulfate 30 mg/day. This pain had remained under control for 25 years as did her possible multiple sclerosis (presumed diagnosis for unexplained loss of bladder control). Her dosage of dextroamphetamine sulfate was increased to 45mg.

Case Presentation: Within a short time her shoulder pain (which had extended to her left shoulder) gradually improved and after a couple of months it completely disappeared.

Discussion: The AIA syndrome can be added to the long list of various chronic pain syndromes generally resistant to standard therapy that dramatically improves following therapy with certain sympathomimetic amines especially dextroamphetamine sulfate. The syndrome has been termed the sympathetic neural hyperalgesia edema syndrome. The hypothesized mechanism is that related to diminished sympathetic tone certain specific tissues absorb foreign chemicals and materials that would normally be precluded and thus these foreign elements induce inflammation (the sympathetic nervous system controls cellular permeability).

Conclusion: Severe estrogen deficiency may further compromise sympathetic tone.

Abstract #912

SUCCESSFUL LIVE DELIVERY DESPITE AN INAPPROPRIATE RISE IN THE SERIAL HUMAN CHORIONIC GONADOTROPIN LEVEL

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Objective: To report a successful delivery of a normal baby from a pregnancy that at one point failed to show a normal rise of the serum beta human chorionic gonadotropin (hCG) level.

Methods: For the past 10 years our practice has been looking to find any exception to the general rule that if at any time up to a level of 10,000 mIU/mL the serum hCG fails to double in a 2 to 3 day interval the woman will have a miscarriage even if at one point a heart beat is demonstrated. Over 10,000 pregnancies where serial serum hCG levels were obtained from early conception to 10,000 mIU/mL were evaluated. Any pregnancy successfully completing the first trimester with inappropriate rise of beta hCG would be reported and observed for any anomalies at birth.

Case Presentation: A 32 year old woman with secondary infertility conceived while observing follicular maturation and treating with vaginal progesterone once oocyte release was documented. Her first serum beta-hCG level was 484 mIU/mL taken 17 days from conception. She was not able to return for another serum beta-hCG until 11 days later when she should have had a beta hCG level of 10,000 mIU/mL, but her level was only 4844 mIU/mL. Three days later her beta-hCG level only doubled to 9585 mIU/mL. This level of 9585 occurred 31 days after conception when it should have been achieved 3 days earlier. Nevertheless the woman delivered a full-term perfectly normal baby.
**Discussion:** A previous publication from our infertility practice found no live fetuses at 12 weeks even if one serum level of serum hCG level failed to double in 2 or 3 days up to 10,000 mIU/mL. The study period was 5 years. There were 16 who did show a heart beat at mid first trimester but all had a miscarriage by 12 weeks. Increasing the time span to 10 years with 9000 pregnancies evaluated one case of fetal viability completed the first trimester despite inappropriate rise of the serum beta hCG levels and her case was published. She has successfully delivered a healthy baby subsequent to the publication. The case reported herein is thus the second case found of a healthy delivery despite an early inappropriate rise of the serum hCG level.

**Conclusion:** Two successful cases provide more hope than just one case which could encourage physicians and patients to continue therapy even if inappropriate rise of hCG is found which in this case was the use of vaginal progesterone. Of course one needs to carefully exclude ectopic pregnancy.

**Abstract #913**

**A SECOND CASE OF SUCCESSFUL CONCEPTION IN A NATURAL CYCLE DESPITE A MAXIMUM ENDOMETRIAL THICKNESS IN THE LATE FOLLICULAR PHASE OF 4MM**

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**Objective:** To determine if a successful conception is possible in a natural cycle despite a maximum endometrial thickness in the late luteal phase of only 4mm (since there is only one case report in the literature where this feat was achieved).

**Methods:** A 31 year old woman who had failed to conceive after 4 months sought help in getting pregnant. She was evaluated with serial pelvic sonography and serial hormonal levels for estradiol, progesterone, and LH. Endometrial thickness was also measured throughout the follicular phase until oocyte release.

**Case Presentation:** In two cycles of evaluating follicular maturation she was found to have a long follicular phase but she did attain a mature follicle both times (average diameter follicle >18mm and a serum estradiol >200 pg/mL) and oocyte release was also documented as was a normal post-coital test. In both cycles her early follicular phase endometrial thickness was 2mm and only reached a peak of 4mm in the late follicular phase. She was treated with vaginal progesterone, and conceived in her second cycle. She is currently entering her last trimester.

**Discussion:** There is only one documented case report in the literature describing a successful pregnancy in a natural cycle with a maximum endometrial thickness of 4mm. Similarly there are very few successful reports of pregnancies with a 4mm maximum endometrial thickness in cycles of in vitro fertilization-embryo transfer (IVF-ET). Thus most reproductive endocrinologists faced with this circumstance would have advised IVF-ET with transfer of the embryos to a gestational carrier. This suggestion could cost as much as $100,000.

**Conclusion:** The reporting of a second case of successful pregnancy in a natural cycle makes it less likely that the first case was merely a miracle. The treating physician should seek other causes of infertility (in this case a luteal phase defect) and correct these infertility factors and give the woman a fair chance of conceiving before recommending such an expensive option as a gestational carrier.

**Abstract #914**

**ESTABLISHED RISK FACTORS AND NOT TESTOSTERONE THERAPY IN ITSELF IS ASSOCIATED WITH INCREASED MYOCARDIAL INFARCTION IN HEALTHY YOUNGER MEN: THE LOW T EXPERIENCE**

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Low T Center

**Objective:** Of those that had MI at the Low T Centers, we wanted to assess if there were risk factors that resulted in MI. The community based specialized centers treats younger, relatively healthier men have strict protocols requiring regular 1-2 week monitoring in the office for efficacy and safety.

**Methods:** We conducted a retrospective analysis of patients that had MI pre and post testosterone therapy. IRB approval was obtained. Data was extracted from our electronic health record (Advance MD) of the multi site Low T Centers across the United States. Altogether 40 Centers were examined. Prior to extraction of data; we held 3 nationwide conference calls with providers to ensure that all ICD-9 were updated, with particular attention to MI and strokes. We also interviewed patients & families of patients that had MI. Data was entered into Excel and comparative statistics was performed using Graph Pad®.

**Case Presentation:** 39,937 patients were seen between years July 2009- July 2014 and approximately 50% met criteria for treatment. 80.8% of patients are below 55 years. Of the treated patients, there were 6 cases of MI (36-53 years); and rate of new MI was 30 per 100,000. Our MI rates are very low in comparison to a managed care (Kaiser
Permanente) rate, which were 208 per 100,000. Of the 9 patients, all had risk factors except one. The prevalence of risk factors in those that had MI was compared with those with that did not have MI. We found for higher rates of smoking (44% vs. 3.5%, p=0.0001); hypertension (44% vs. 15%, p=0.0001); DM (22% vs. 4%, p=0.0001).

**Conclusion:** Our study showed that carefully monitored testosterone treated younger patients was safe and did not cause MI. Established risk factors such as smoking, hypertension and diabetes are associated with higher rates of MI in our testosterone treated patients. Testosterone therapy is not causal of MI.

**Abstract #915**

**EFFECT OF ONE-YEAR TESTOSTERONE REPLACEMENT WITH AN ORAL TESTOSTERONE (T) FORMULATION (REXTORO) OR A T-GEL (ANDROGEL) PREPARATION ON THE CARDIOVASCULAR BIOMARKERS C REACTIVE PROTEIN (HSCR) AND LIPOPROTEIN-ASSOCIATED PHOSPHOLIPASE A2 (LPPLA2)**

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**Objective:** To explore the effects of an investigational oral testosterone replacement therapy (TRT)(REXTORO\(^\text{TM}\)) or T-gel (AndroGel\(^\circ\)) on hsCRP and LpPLA2.

**Methods:** Study CLAR-09007 was an open-label, 2-arm, 1 year study in hypogonadal men who were randomized to either daily REXTORO (oral testosterone undecanoate) (n=88) or AndroGel (n=94). Both REXTORO and AndroGel were dose adjusted based on serum testosterone (T) levels. hsCRP and LpPLA2 serum samples were drawn on Days 0 (pre-dose), 90 or 105, 180 and 365. LpPLA2 (mass) was assayed using an ELISA and hsCRP was assayed using an immunoturbidimetric method (Pacific Biomarkers). In addition to comparisons between treatment groups using ANOVA, a non-inferiority analysis was predefined.

**Results:** The mean baseline LpPLA2 was similar for the REXTORO and T-gel groups. At Day 365, the mean change for the REXTORO group was -39.6 mg/mL compared to the T gel group mean change of -37.6 mg/mL. Differences between the REXTORO and T-gel groups were not statistically significant in a repeated measures analysis (p = 0.45). The non-inferiority analysis showed that the difference between point estimates (LpPLA2 and hsCRP), for REXTORO and T-gel and its 95% CI was 0.049 (-0.07 to 0.17). Thus, it can be concluded that there was non-inferiority for REXTORO compared to T-gel in the prediction of cardiovascular risk based on the composite classification of hsCRP and LpPLA2.

**Discussion:** hsCRP is a strong independent predictor of cardiovascular disease risk. LpPLA2, an inflammatory enzyme secreted by macrophages and found in atherosclerotic plaque, is involved in lipid peroxidation and the formation of rupture prone plaque. Epidemiologic studies have demonstrated that LpPLA2 is an independent risk factor of coronary or cerebrovascular events.

**Conclusion:** In summary, the biomarker analyses suggests that TRT, with either oral TU (REXTORO) or transdermal T did not substantially change the CV risk based on the biomarker analysis. However, a larger CV outcome trial is necessary to determine the impact of TRT on CV risk.

**Abstract #916**

**PURPOSEFUL CRYOPRESERVATION OF SPERM PRIOR TO INTRAUTERINE INSEMINATION TO OVERCOME THE EMBRYO IMPLANTATION DEFECT ASSOCIATED WITH SPERM WITH A SUBNORMAL HYPOOSMOTIC SWELLING TEST**

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**Objective:** To determine if the toxic protein causing sperm to have low hypoosmotic swelling (HOS) test score and subsequent embryo implantation defects caused by this abnormality is cryolabile and thus purposeful cryopreservation followed by intrauterine insemination (IUI) could result in a pregnancy.

**Methods:** The etiologic factor for a 2 year history of infertility failing to respond to IUI and 2 cycles of in vitro fertilization-embryo transfer (IVF-ET) using conventional insemination was found secondary to a very low HOS test (32% with abnormal <50%). With IVF-ET with intracytoplasmic sperm injection (ICSI) she conceived.
Case Presentation: A viable pregnancy was achieved following the first IUI cycle with frozen thawed sperm. Unfortunately there was fetal demise found to be secondary to trisomy 14.

Discussion: Low HOS tests usually result in failure to conceive following sex, IUI or conventional IVF. However it does not inhibit fertilization but instead causes embryo implantation defects hypothesized to be related to the supernumerary sperm attached to the zona pellucida which hypothetically causes a functional impairment of the embryo membrane by transferring the toxic protein to the embryo membrane. Males with low HOS tests rarely achieve any pregnancy but rarely a pregnancy is achieved but ends in miscarriage. The one exception is that transfer of frozen thawed embryos have been reported to allow pregnancies despite conventional insemination suggesting that the toxic factor may be cryolabile.

Conclusion: This is the first reported case of a pregnancy achieved by IUI using cryopreserved sperm with low HOS scores. The miscarriage was probably related to the trisomy 14. Nevertheless, one cannot exclude the possibility that a miscarriage would have occurred even if chromosomes were normal.

Abstract #917

INJECTION OF HUMAN CHORIONIC GONADOTROPIN (HCG) CAN CAUSE THE LUTEINIZED UNRUPTURED FOLLICLE SYNDROME

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Objective: To demonstrate that the injection of human chorionic gonadotropin (hCG) intramuscularly for purpose of timing of an intrauterine insemination (IUI) can cause an oocyte to fail to rupture from the follicle.

Methods: A 33 year old woman sought help for infertility that seemed related to a male factor problem. The office performed IUI’s morning and evenings on weekdays but only in the morning on weekends. The timing of IUI was generally 40 to 48 hours after the initiation of the luteinizing hormone (LH) surge. She was monitored with ultrasound for follicular size and with a.m. serum LH, estradiol (E2) and progesterone (P) levels. When a follicle reached a minimum E2 of 200pg/mL and an ultrasound with at least one follicle of an average of 20mm an injection of hCG 10,000 units I.M. was given in the evening on a Thursday or Friday, for an IUI on Saturday or Sunday. Weekday IUI’s were based on endogenous LH surge. Ultrasounds were performed on the day of IUI and the next day if no oocyte release. Release was considered to have occurred if shrinkage of the follicle by >5mm took place.

Case Presentation: In 6 natural cycles where IUI was performed Monday-Friday the peak sera E2 levels reached 368, 334, 337, 465, 365, and 355pg/mL. Oocyte release was confirmed in all 6 cycles. There were 2 cycles where hCG was given for weekend IUI’s. In the first cycle a serum E2 of 211 was reached with a 20mm follicle. The hCG was given the next day but the follicle on the day of IUI measured 23.3mm and the serum P was 3.3 ng/mL. In the second cycle the hCG was given with a follicle size of 20.6mm and a serum E2 of 288pg/mL. The LH level on the day of hCG was 7 and 6 mIU/mL. The luteinized unruptured follicle (LUF) syndrome was confirmed with serum P exceeding 2ng/mL. In one cycle for a weekend IUI leuprolide acetate 1mg every 12 hours x 3 also failed to release an oocyte when given with a 335pg/mL serum E2 and a follicle size of 22.6mm.

Discussion: Failure of oocyte release in multiple consecutive natural cycles is known as the LUF syndrome. One corrective treatment is giving 10,000 units hCG. However, frequently hCG fails to enable oocyte release, and interestingly using the gonadotropin releasing hormone (GnRH) agonist leuprolide acetate frequently enables oocyte release even in cases where hCG fails. It is common practice by most reproductive endocrinologists to automatically time all IUI cycles with hCG injections. Unfortunately many physicians fail to check for oocyte release and just assume that the hCG injection ensures egg release.

Conclusion: Though hCG injection and GnRH agonists can correct LUF syndrome, in some instances hCG and GnRH agonists it can actually cause LUF syndrome.
Abstract #918

**RARE VARIANT OF KLINEFELTER SYNDROME IN A MAN PRESENTING WITH SUSPECTED HYPERTHYROIDISM**

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**Objective:** Kleinfelter syndrome (47, XXY) is the second most common aneuploidy after Turner’s syndrome, diagnosed in about 1 out of 500 male births. Although much less common, aneuploidies 48,XXYY, 48,XXXY and 49,XXXXY are considered variants of Klinefelter syndrome because of their similar features.

**Case Presentation:** 42-year-old male with medical history of Type 2 Diabetes Mellitus (T2DM) and Cognitive Impairment presented with unexplained 26lb weight loss over a 5-month period. Examination revealed a tall male (Height 70in, BMI 21.8 kg/m2) with hypertelorism, epicanthal folds and diffusely enlarged thyroid without palpable nodules. Patient had prominent elbows, arm span of 173cm, bilateral gynecomastia, micro phallus and micro orchidism. Laboratory studies showed subclinical hyperthyroidism with a TSH: 0.49 (0.55–4.78 mIU/mL); Free T4: 1.18 (0.8–1.76 ng/dL), and Free T3: 2.9 (2.3–4.2 pg/mL). Thyroid ultrasound showed mild diffuse thyroid enlargement without nodules. Serum Testosterone was <20 (262–1593 ng/dL), Free Testosterone: 3 (50–350 pg/mL), SHBG: 39.8 (13–71 nmol/L), FSH: 23.8 (1.0–1.8 mU/mL), and LH: 17.12 (1-9 mIU/mL); all consistent with hypergonadotrophic hypogonadism. Karyotype analysis revealed a 48, XXXY chromosome pattern, with two extra copies of the X chromosome observed in all metaphases. Hemoglobin A1c was 5.3%.

**Discussion:** The rare 48,XXXY syndrome is diagnosed in about 1:50,000 male births. It is considered a variant of Klinefelter Syndrome due to their shared phenotypic characteristics. Compared to KS, in 48, XXXY Syndrome the presence of two extra X chromosomes increases the likelihood of endocrinopathies, autoimmune disorders and malignancies. Patients benefit from early diagnosis of these syndromes as some of these associated medical problems are potentially treatable. This patient shows unexplained weight loss in the setting of normal thyroid function, well controlled T2DM, which by itself warrants further investigation. Underlying malignancy should be excluded given that Leukemia, Lymphoma and Germ Cell Tumors among others are common in variants of KS. If after further investigation, it is determined that there is no contraindication for testosterone therapy, this treatment should be considered since it poses a potential medical and psychological benefit for the patient.

**Conclusion:** We propose that although rare, there must be higher awareness of these chromosomal aneuploidies. They should be diagnosed early in life to minimize long-term complications and to potentially provide these patients with a better quality of life.

Abstract #919

**THE USE OF SYMPATHOMIMETIC AMINES TO ERADICATE PREMENSTRUAL URTICARIA AND ANAPHYLAXIS**

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**Objective:** To determine if treatment with dextroamphetamine sulfate, which has been shown in the past to be highly effective in helping chronic treatment resistant urticaria, can ameliorate severe premenstrual urticaria and anaphylaxis in the luteal phase despite prior resistance to improve following standard therapy.

**Methods:** Treatment with low dose dextroamphetamine sulfate to gain relief of symptoms was given to one young woman whose urticria only occurred premenstrually but was also associated with life threatening anaphylaxis. Patient 2 had chronic daily urticaria which was exacerbated premenstrually.

**Case Presentation:** Both patients showed prompt 100% improvement in the urticaria. Patient 2 after 20 years of therapy ran out of medication for 1 month. Her severe urticaria quickly returned only to dissipate when dextroamphetamine sulfate was started again.

**Discussion:** Use of dextroamphetamine sulfate was successful in treating the anaphylaxis and severe luteal phase hives in patient 1 as well as treating chronic hives with a premenstrual exacerbation in patient 2. These cases are both consistent with the proposed mechanism of the sympathetic neural hyperalgesia edema syndrome, i.e., these various pathological disorders are all linked by having increased cellular permeability related to sympathetic nervous system hypofunction. In these cases, the hypothesis is that there was an increased permeability related to sympathetic nervous system hypofunction. Since this part of the menstrual cycle, possibly related to progesterone secretion, is associated with a mild decrease in sympathetic tone. The hypothesis is that there was a
general defect in sympathetic tone but it was not quite severe enough to allow increased permeability of the vesicles containing histamines during the follicular phase. However, with an added insult by the hypothesized diminished sympathetic tone occurring premenstrually adding to the generalized disorder sympathetic nervous system hypofunction the sympathetic tone became low enough to allow increase permeability of the vesicles containing histamines.
THYROID DISEASE

Abstract #1000

DIAGNOSIS OF THYROID LYMPHOMA MAY BE SUGGESTED BY USE OF DEXAMETHASONE

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Objective: A rapidly enlarging thyroid mass warrants an immediate and thorough investigation to determine whether it represents thyroid lymphoma or anaplastic thyroid cancer, and although cytology or pathology can reveal the definite diagnosis, other modalities can be utilized to establish the diagnosis.

Case Presentation: A 76 year old female with a history of Hashimoto’s thyroiditis for 20 years, presented to the Emergency Room in respiratory distress. She reported a mass over her right neck which had rapidly enlarged over the past 4 months. Accompanying this large neck mass was a sense of dysphagia and hoarseness, and for these reasons she presented to an outside hospital for a fine needle aspiration, which revealed a benign result. In the days following the FNA, she noticed that the mass had enlarged at an even faster rate, and she began to have respiratory trouble. On initial evaluation, it was found that she had a significant neck mass which was encompassing the entire right side, as well as most of the left side of the neck, and was associated with a positive Pemberton sign and a rubbery left neck lymph node. ENT preformed a laryngoscopy which could not identify the vocal cords, but identified circumferential fullness of the supraglottis and a paralyzed right vocal cord. She was euthyroid, with a TSH of 6.59 mIU/L, free T4 1.04 and a positive anti TPO. A CT of the neck revealed a large mass measuring 10.5 x 6.5 x 11.7 cm, which invaded the right internal jugular vein, and narrowed the airway to 4 mm. High dose dexamethasone was initiated at that time and the patient was transferred to the ICU for close monitoring of her respiratory status. The patient noted substantial decrease in size of the mass and increased ease of work with breathing. ENT performed an incisional biopsy, revealing thyroid lymphoma. The patient subsequently received treatment with RCHOP, and had a significant further reduction in size of her neck mass.

Conclusion: This case illustrates that the classic teaching that a rapidly enlarging thyroid mass eludes to anaplastic thyroid cancer may not always be the case; rather this presentation warrants further workup to identify whether the mass could represent a thyroid lymphoma. To help differentiate between an anaplastic thyroid cancer and thyroid lymphoma, ENT typically implores use of dexamethasone, with the belief that a significant response to steroids suggests a lymphoma diagnosis rather than anaplastic thyroid cancer. As physicians asked to aid in the diagnosis and treatment of these diseases, endocrinologists should be well aware of the methods used to differentiate these two diseases, so that timely and proper treatment may be offered.

Abstract #1001

MULTIPLE DISTANT METASTASIS OF PAPILLARY THYROID CANCER TO SKELETAL MUSCLES

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Objective: Papillary thyroid cancer (PTC) is the most common differentiated thyroid carcinoma. Metastases usually occur in regional lymph nodes, lungs or to the bone. Distant metastases to skeletal muscle are rare. Here, we report a patient with multiple skeletal muscle metastasis secondary to PTC.

Case Presentation: A 78-year-old woman who underwent near total thyroidectomy for multinodular goiter in 2003 and was found to have PTC on surgical histopathology. She underwent whole body scan that showed residual thyroid tissue within the thyroid bed and received radioactive iodine (153.3 mCi of I-131). The patient had normal follow up and negative whole body scans for 4 years post-surgery until she was found with local recurrence in the thyroid bed and paratracheal lymph nodes and underwent neck dissection followed by radioactive iodine (150 mCi of I-131) in 2007. Another dose of radioactive iodine was given in 2010 for local recurrence (208.7 mCi of I-131) and after that neck ultrasound and whole body scans were negative. Patient also had negative thyroglobulin. In 2013 patient presented with left arm pain and mass and CT showed an enhancing lesion within the left triceps muscle without bone involvement, biopsies showed metastatic papillary thyroid cancer. Patient underwent radiation therapy then surgical resection of that lesion in March 2014 confirming the diagnosis. Patient also was found to have posterior neck and paraspinous muscle metastasis confirmed to be papillary thyroid skeletal muscle lesions on surgical resection in May 2014. Most recent follow up showed hypermetabolic lesions on PET scans involving left Masseter and right Gluteal muscles suggestive of further skeletal muscle metastasis.

Discussion: We report an elderly woman who was diagnosed with PTC after total thyroidectomy for nodular goiter. Over a 10 years follow up patient had two episodes of local recurrence treated with surgical resection and radioactive iodine, but within the last year she had multiple skeletal muscle metastatic lesions without evidence of thyroid cancer metastasis elsewhere. This is an unusual pattern of metastasis for PTC.

Conclusion: Distant skeletal metastasis in PTC are very rare but can occur in combination with metastasis elsewhere or in isolation.
Abstract #1002

THYROTOXICOSIS DUE TO ACUTE SUPPURATIVE THYROIDITIS IN A POSTPARTUM WOMAN

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Case Presentation: A 24 year old female, 5 months postpartum, presented to the emergency room with severe throat pain, palpitations, and intermittent fevers for two weeks; failed outpatient antibiotics for strep throat and steroid treatment. She was hypertensive and tachycardic on presentation. Labs revealed a low TSH of 0.13 mcU/mL, elevated FT4 of 2.04 ng/dL, thyroglobulin of 588 ng/mL, WBC of 17 k/ul. TSI, thyroid antibodies were not elevated. Thyroid ultrasound revealed a 3.4x1.8x2.1cm left cystic nodule, which was hypofunctioning on technetium scan. CT neck confirmed the thyroid lesion and an adjacent soft tissue abscess. She was treated with broad spectrum antibiotics and underwent FNA with drainage of the thyroid lesion and adjacent abscess. Both bacterial cultures grew Strep constellatus and abscess cultures also grew Eikenella corrodens. Cytopathology was benign. She was discharged on Augmentin for 14 days. At 4 week follow-up, her thyroid function tests had normalized.

Discussion: Thyroidal infections are rare, in part due to the rich blood supply and lymphatic drainage of the gland, the high iodine content, and the protective capsule. They typically occur in individuals with pre-existing thyroid disease, and are most often due to bacterial infection; though fungal, mycobacterial, and parasitic organisms have all been reported. Suppurative thyroiditis tends to occur in immunocompromised adults or in children with piriiform sinus fistulas. Patients usually present with acute onset neck pain, fever, and tender thyromegaly. Fluctuance and cervical lymphadenopathy may also be present. Thyroid function is typically normal, though both destructive hypothyroidism or thyrotoxicosis may occur, which usually spontaneously resolves in 2-3 months. Leukocytosis and elevated inflammatory markers may also be present. Empiric antibiotics should be started rapidly, and ultrasound may help differentiate between subacute thyroiditis and acute suppurative thyroiditis. FNA is the best diagnostic test. Urgent surgical drainage or thyroidectomy may be needed in cases of airway compromise, clinical deterioration, or persistent abscesses. There is a current trend towards less invasive management when possible.

Conclusion: Acute suppurative thyroiditis is a rare, potentially fatal condition which must be recognized and treated quickly. How to best approach these patients remains controversial. There is a current trend for less invasive management, but surgery may be necessary. More study is needed to determine the best diagnostic approach, duration of antibiotics, and if/when to consider surgical intervention.

Abstract #1003

SONOGRAPHIC PATTERN STRATIFIES THE RISK OF MALIGNANCY OF THYROID NODULES WITH INDETERMINATE CYTOLOGY

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Objective: Currently, the management of thyroid nodules relies on the cytological diagnosis. However cytology is indeterminate in around 25% of the specimens and most of these patients end up with a diagnostic surgery. To better select nodules that need to be biopsied, the provisional 2014 revised ATA guidelines for the management of thyroid nodules recommends using a classification based on the sonographic appearance of the nodules. Each pattern is associated with an estimated risk of malignancy (ROM) and a different size threshold for biopsy. We hypothesize that the same sonographic patterns could stratify the ROM of cytologically indeterminate nodules.

Methods: In this IRB-approved study, we reviewed the charts of all patients with cytological evaluation at our institution between October 2008 and May 2014. Only those nodules with indeterminate cytology (Bethesda categories III and IV) and histological confirmation that had ultrasound images available for review were included in this analysis.

Results: During the study period 367 (85%) of 432 thyroid nodules with indeterminate cytology and histological confirmation, had ultrasound images available for review. The overall ROM in this cohort was 30.8%. Cytology was classified as Atypia of Undetermined Significance (AUS) in 147 nodules (40%) and Follicular Neoplasm (FN) in 220 (60%). The overall ROM in these categories was 28.6% and 32.3% respectively. According to the new ATA classification the sonographic suspicion pattern was “very low” in 27 nodules (7.4%), “low” in 170 (46.3%), “intermediate” in 36 (9.8%) and “high” in 134 (36.5%). The ROM observed in these categories was 3.7%, 25.3%, 22.2% and 45.5% respectively. No significant differences were observed in the ROM of nodules with cytological diagnosis of AUS or FN in each category. Differences in the ROM between the “low” and “intermediate” suspicion groups were observed in the different size threshold for biopsy as recommended by the new guidelines.

Conclusion: The new 2014 ATA guidelines for the management of thyroid nodules recommend using sonographic pattern and morphology to stratify the risk of malignancy of thyroid nodules. However, a larger study population is needed to confirm the results from this study.
patterns were not significant, and were grouped for other comparisons. Differences in the ROM were statistically significant (p<0.01) when the “low-intermediate” suspicion pattern was compared to the “very low” suspicion pattern and to the “high” suspicion pattern.

**Discussion:** The sonographic pattern effectively stratifies the ROM of nodules with indeterminate cytology. Surgery could be avoided in nodules with a “very low” suspicion sonographic pattern, with a negative predictive value of 96%. Hypoechogenicity alone does not seem to improve risk stratification for thyroid nodules with indeterminate cytology. However, any other suspicious sonographic feature significantly increases the ROM.

**Conclusion:** Sonographic pattern should be used to set the threshold for biopsy of thyroid nodules, and may also stratify the ROM to guide management after the biopsy.

**Abstract #1004**

**THE SONOGRAPHIC PATTERNS PROPOSED IN THE PROVISIONAL 2014 ATA GUIDELINES FOR THE MANAGEMENT OF THYROID NODULES PERFORMS WELL IN MEDULLARY THYROID CARCINOMA AND AGREEMENT IS GOOD AMONG DIFFERENT OBSERVERS**

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**Objective:** The 2014 provisional ATA guidelines for the management of thyroid nodules provide a classification based on the sonographic pattern. Each pattern is associated with an estimated risk of malignancy and a size threshold for biopsy. These were developed based on the appearance of papillary and follicular thyroid carcinoma, but the performance on medullary thyroid carcinoma (MTC) is unknown. This study aims to evaluate how MTC would be classified by this system and to measure the agreement between different observers.

**Methods:** In this IRB-approved retrospective study, we included all patients with MTC evaluated at our institution between 1998 and 2014 whose ultrasound images were available for review. Five independent reviewers with expertise in ultrasound (4 endocrinologists and 1 radiologist) reviewed the images. Each investigator assessed information regarding echogenicity, margins, calcifications, extrathyroidal extension and presence of suspicious lymph nodes. The shape “taller than wider” in the transverse view was considered positive when there was a difference ≥2mm in the measurements given to identify the nodule (common to all observers). Hetero-echogenic nodules in the absence of other suspicious features were considered “low-suspicion”. Iso-, hyper- or hetero-echogenic nodules with at least one suspicious feature were considered “high-suspicion”. For all other situations, the suspicion pattern was specified by the ATA classification and was followed. Percentage of overall agreement and free marginal kappa were calculated using an online kappa calculator (http://justus.randolph.name/kappa).

**Results:** Images were available for review in 30 MTC and 90-100% were classified as “intermediate” or “high-suspicion” by all raters. The percentage of overall agreement for all categories was 77% with a Kappa coefficient of 0.72 (good agreement). The agreement was moderate for the individual features and the kappa coefficient ranged from 0.44 for irregular margins to 0.56 for extrathyroidal extension and for presence of suspicious lymph nodes. Six of the 30 nodules evaluated were classified as “low-suspicion” by at least one of the observers. However, biopsy would have been warranted in 5 due to size >1.5 cm (n=3) or clinical history (known MEN2 and elevated plasma calcitonin, n=2). Biopsy could have been delayed in one nodule (1.3 cm) by one of the observers.

**Discussion:** Most MTC have an “intermediate” or “high-suspicion” sonographic pattern and therefore are unlikely to be missed by the new classification.

**Conclusion:** The new sonographic patterns proposed in the provisional 2014 ATA guidelines perform well for MTC and interobserver agreement is good overall.

**Abstract #1005**

**CLINICAL CHARACTERISTICS OF THYROID NODULES WITH INDETERMINATE CYTOLOGY**

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**Objective:** To evaluate patient demographics, TSH values, radioactive iodide scan (I-scan) results, and ultrasound (US) characteristics of indeterminate thyroid nodules.

**Methods:** A retrospective chart review was conducted at a Midwest academic medical center. Over two years, 883 ultrasound-guided fine needle aspiration (UGFNA) biopsies of thyroid nodules were performed. Results of 200 biopsies were randomly selected for evaluation, and of those, 34 patients had indeterminate findings. We evaluated multiple clinical measures for each indeterminate result, including family history, TSH values, I-scan results, and US features.

**Results:** Of the 200 biopsies that underwent UGFNA, there were 37 indeterminate nodules. The majority of these patients were female (82%), Caucasian (74%), and
had no significant co-morbidities. TSH was documented in 28 nodules (82%) and was <5.0. Characteristics and echogenicity were documented in about half of US reports. Of those, 16 (84%) of the nodules were solid while 3 (15%) were of mixed character. In addition, 10 (56%) were hypoechoic, 5 (28%) were isoechoic, and 3 (17%) were hyperechoic. Nine cases (47%) had infiltrative margins, and no abnormal lymph nodes were noted. Surgical excision was performed for 23 nodules (62%). Of those, 9 (39%) were malignant and 14 (61%) were benign.

Discussion: According to current guidelines, evaluation of thyroid nodules starts with TSH values. A normal or high TSH prompts US evaluation. UGFNA is indicated for any nodule >1cm in diameter that is solid and hypoechoic or for any nodule >2cm that is mixed cystic-solid without worrisome US findings. If UGFNA result is indeterminate, an increased risk of malignancy is implied, but controversy remains regarding the next step in management among these patients. In our study, 28 (90%) had normal TSH values and US evaluation was performed in 19 (51%). US characteristics of thyroid nodules were documented in half of the US reports, and of these, 56% of the patients had hypoechoic nodules and 47% had infiltrative margins. Of the 23 surgical excisions, less than half of the nodules were malignant, indicating surgery could have been avoided in more than half of the cases.

Conclusion: It appears there is a disparity between current patient care and the clinical guidelines for the evaluation of thyroid nodules. Thorough descriptions of thyroid nodules are important in US evaluation, as certain features can suggest malignancy. Our findings show inconsistencies from guidelines due to lack of US documentation and incomplete description of important characteristics. Further studies are needed to examine adherence to current practice guidelines for the management of thyroid nodules.

Abstract #1006

TRENDS IN DEMOGRAPHICS AND AGGRESSIVENESS OF PRIMARY THYROID CANCER AT THE COMMUNITY MEDICAL CENTERS IN CALIFORNIA’S CENTRAL VALLEY

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Objective: To determine the trends in demographics and aggressiveness of thyroid cancer at the Community Medical Centers in Fresno, California over 10- year period.

Methods: This is a retrospective, cross-sectional study. Patients were identified from the cancer registry of community medical centers, and we reviewed the electronic medical records of all patients with primary thyroid cancer. They were included in the study if there was demographic data and detailed pathology report of thyroid cancer in the electronic medical records. Demographic data, pathology results and outcome of these patients (cancer recurrence and mortality rate) were collected. The study period was from 2001 to 2011. Patients were assigned to 2 periods based on the year of diagnosis: period 1 (first 5 years from 2001 to 2005) and period 2 (second 5 years from 2006 to 2011).

Results: Of 463 patients with thyroid cancer in the cancer registry from 2001 to 2012, 403 patients with primary thyroid cancer met the inclusion criteria. The cases with primary thyroid cancer were twice as high in period 2 as in period 1 (135 vs 268). Patients at period 2 were slightly older (45.3 vs 47.95 years), and 23.5% of patients in period 2 were aged 60 or above compared with only 14.1% in period 1 (p= 0.037). 84% of patients were women in period 2 compared with 76.5% in period 1 (p= 0.037). There was no difference in thyroid cancer rates among different ethnicities, cancer types and tumor stages between the 2 periods. Also there was no significant difference in mean tumor size, patients with multifocal tumors (3 or more tumors), number of thyroid lobes involved and cervical lymph node metastasis between the 2 periods. However, period 2 had fewer cases with tumor capsular invasion (48.9 vs 37.1%; p=0.09) and lympho-vascular invasion (34.1 vs 18.6%; p= 0.010). There was no statistically significant difference in cancer recurrence (6.7 vs 4.1%; P = 0.39) and mortality rate (9.6 vs 4.30%; P = 0.07) between the 2 periods.

Conclusion: The cases with primary thyroid cancer were twice as high in period 2 as in period 1. Patients were slightly older and there were more women in period 2 than
in period 1. There was no change in cancer rates among different ethnicities. It appeared that thyroid cancer was no more aggressive in period 2 than in period 1.

Abstract #1007

PATIENTS CHARACTERISTICS AND SONOGRAPHIC FEATURES IN THYROID NODULES WITH INDETERMINATE CYTOPATHOLOGY

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Objective: The Bethesda System (TBS) for thyroid cytopathology recommend limiting the use of indeterminate cytology or atypia of undetermined significance/follicular lesion of undetermined significance (AFLUS) to less than 7% of fine needle aspiration (FNA) cases as such finding represents diagnostic dilemma. None of the available biomarkers or gene mutation studies have accurate estimate of malignancy risk in this group making management plan to be dictated by the overall clinical impression. This study evaluated the rate of reporting AFLUS in a tertiary thyroid center and evaluated patients’ characteristics and sonographic features for thyroid nodules with AFLUS cytopathology to see if these findings can assist in management planning.

Methods: Retrospective study. An 833 ultrasound-guided FNA cases were performed at a tertiary center from January 2010 to January 2012. We randomly selected 200 patients which reflected 273 FNA cases. Documented patient characteristics included: age, gender, race, comorbidities, radiation exposure, and family history of thyroid cancer. Cytology findings were classified per TBS: benign, AFLUS, suspicious, malignant, and nondiagnostic. Sonographic features included solid or cystic component, size, echogenicity, microcalcifications, vascularity, margins, and length to width ratio. Mann-Whitney, chi-square and exact fisher tests were used in statistical analysis.

Results: A 273 thyroid nodules were evaluated in 200 patients (51 Males, 149 Females), median age 54 years (47-67). FNA results included: Benign 221 (80.9%), AFLUS (13.6%), malignant 5 (1.8%), and non-diagnostic 10 (3.7%). No significant difference in patients’ characteristics comparing benign nodule group to AFLUS group. In comparison to benign nodules, AFLUS nodules were not significantly different in size, hypoechoigenicity [18% vs. 27%, p=0.9], microcalcifications [56% vs. 33%, p=0.2], vascularity [25.7% vs. 255, p=0.96], infiltrative margins [42.4% vs. 42.8%, p=0.58], or having taller than wide dimensions [32% vs. 29%, p=0.46]. AFLUS nodules were more likely to be solid or have solid component [AFLUS 43.2% vs. benign 21.6%, p=0.002].

Conclusion: Study reflects the difficulty in achieving recommended rate of reporting AFLUS even in tertiary center. Application of quality control measures and consultation with expert cytopathologist are some options to ensure meeting guidelines requirements. No patient characteristic or sonographic feature helped in differentiating AFLUS cases from those with benign nodules except for the presence of solid nodule component. Clinical judgment is the ultimate factor in formulating management plan in such cases.

Abstract #1008

PATTERN AND DEGREE OF LYMPHOCYTIC INFILTRATION IN PATIENTS WITH PAPILLARY THYROID CARCINOMA WITH OR WITHOUT HASHIMOTO’S THYROIDITIS

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Objective: To study the association between pattern and degree of lymphocytic infiltration (LI) and specific clinical, histological and immunological findings in patients with papillary thyroid carcinoma (PTC).

Methods: Medical records of patients who underwent surgery for PTC between 2001 and 2006 were retrospectively reviewed. Patients whose histological slides were available and had at least 5-year follow up were included. We looked at severity, distribution and volume of LI. We studied the relationship between pattern and degree of LI with each of the following: known history of Hashimoto’s thyroiditis (HT), history of hypothyroidism, presence of thyroglobulin (Tg) antibodies (Ab), tumor size and number of tumor foci. To measure the association between the different factors and the degree of LI Wilcoxon rank sum tests were performed. Spearman correlations were used to compare associations between number of foci and tumor size with LI pattern and severity.

Results: A total of 267 records was analyzed. There were 15 patients (5.7%) with known HT; 24 (9.7%) with known hypothyroidism; 63 (24.1%) with positive Tg Ab. Patients with known hypothyroidism or history of HT were more likely to have more severe LI, while patients without hypothyroidism or HT were more likely to have only peri-lesional or non-lesional Lc distribution (p<0.001). Positive Tg Ab status was more likely associated with HL-Lc distribution and with germinal centers (p<0.001). The
LI severity and volume were not associated with Tg Ab status. There was no correlation between the severity of LI and tumor size or number of tumor foci.

**Discussion:** Literature has suggested that PTC with co-existent HT is associated with less aggressive disease. However, differentiation between HT and tumor associated LI is often not made. In this study by further classifying the pattern and degree of LI, we did not show an association between the degree or volume of LI and tumor size or number of tumor foci.

**Conclusion:** Distribution, severity and volume of LI do not seem to be clinically significant in patients without HT compared to patients with HT. We suggest that a more accurate description of LI and distribution is needed when reporting thyroid cancer histology. Further correlation with outcomes is needed.

Abstract #1009

**SPINAL COMPRESSION FRACTURE AND WIDESPREAD METASTATIC LESIONS: A RARE PRESENTATION OF FOLLICULAR THYROID CARCINOMA**

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University of Connecticut

**Objective:** Follicular Thyroid Carcinoma is a condition most commonly limited to the thyroid. Initial presentation of this condition as widespread metastatic disease is a rare phenomenon.

**Case Presentation:** A 73 year old Jamaican female with history significant for multinodular goiter and left hemi thyroidectomy 8 years ago for an atypical follicular adenoma, presented with a 2 month history of 15 lb weight loss, progressive left leg weakness, back pain and a new-onset gait disturbance. On exam she had an unsteady gait and a positive Babinski sign on the left lower extremity. MRI of the spine showed multiple lesions concerning for metastatic disease as well as a 3.6x3.3x2.8 cm enhancing mass on T1 causing severe spinal stenosis with cord compression at the level of T8. She was treated with intravenous steroids and decompression and stabilization of her spine. Pathology of the spinal mass showed follicular thyroid carcinoma. Further staging revealed multiple areas of skeletal metastatic disease. Ultrasound demonstrated vascular nodules bilaterally, with largest nodules in the right and left lobes measuring 3.4x2.4x2.1cm and 3.4x1.9x2.5cm, respectively. She was euthyroid on levothyroxine. No family hx of thyroid cancer or personal hx of head or neck radiation noted. 1st FNA of the spinal lesion was positive for NRAS, PIK3CA, KIT and TP53 mutations. Further management included treatment with levothyroxine and radioactive iodine.

**Discussion:** This case illustrates the potential for extensive metastases from follicular thyroid carcinoma (FTC), a common thyroid cancer in which extra-nodal metastases are uncommon. Vascular invasion with skeletal metastases has been reported in only approximately 10% of FTCs. Studies have shown that some thyroid nodules, such as the excised atypical thyroid adenoma in this patient, may have malignant potential. Through genetic fine-tuning, driving somatic gene mutations may regulate fundamental characteristics of FTCs, such as differentiation, invasion and metastasis. Mutations of the RAS and TP53 genes are some mutations that have been associated with rare aggressive and invasive forms of disease, such as the metastatic follicular thyroid carcinoma seen in this patient.

**Conclusion:** Distribution, severity and volume of LI do not seem to be clinically significant in patients without HT compared to patients with HT. We suggest that a more accurate description of LI and distribution is needed when reporting thyroid cancer histology. Further correlation with outcomes is needed.

Abstract #1010

**UVEAL MELANOMA MASQUERADING AS A NON-TOXIC MULTINODULAR GOITER**

Rokshana Thanadar, MS, MD, Uzma Siddiqui, MD, Marie Lithgow, MD, Runhua Hou, MD

University of Massachusetts

**Objective:** Describe a rare case of uveal melanoma metastasizing to the thyroid and the challenge of making a correct diagnosis.

**Methods:** Thyroid nodules are commonly seen and often benign; however, 5-10% are malignant with <2% due to metastases. Metastases to the thyroid is generally associated with RCC, but also seen with breast, lung, GI, hematologic cancers, melanoma and sarcoma. We describe an elderly ♀ with a unique presentation of malignant uveal melanoma in thyroid nodules.

**Case Presentation:** 86 yo W♀ with a hx of hypothyroidism, mild cognitive impairment, and osteoporosis was found, on eye exam, to have a retinal detachment 2○ to choroidal melanoma. She had no any visual complaints and was treated with γ-knife radiosurgery. During evaluation for metastasis, CT neck demonstrated thyroid nodules. Ultrasound demonstrated vascular nodules bilaterally, with largest nodules in the right and left lobes measuring 3.4x2.4x2.1cm and 3.4x1.9x2.5cm, respectively. She was euthyroid on levothyroxine. No family hx of thyroid cancer or personal hx of head or neck radiation noted. 1st FNA of the R dominant nodule was non-diagnostic. Repeat
FNA on nodule was again non-diagnostic, but FNA of the L dominant nodule showed large atypical epitheloid cells requiring repeat FNA. 3rd FNA on R nodule demonstrated malignant cells and FNA of L nodule showed rare but similar appearing cells. Immunohistochemistry staining was + for melaninA, Mart-1, MSA, SOX10 and (-) for S100, pankeratin, TIF-1, calcitonin-a profile consistent with malignant melanoma. FDG PET showed areas of intense uptake in the brain, thyroid, liver, axial and appendicular skeleton supporting diffuse metastatic disease. 

**Discussion:** Malignant melanomas account for ~ 4% of thyroid metastases. More unusual are uveal melanomas with incidence between 0.75 – 3%. Metastasis is typically to the liver. Search of the English literature reported only four cases of metastasis to the thyroid. Metastatic melanoma is an ominous sign carrying a grim prognosis, with time between diagnosis and death 6-12 months. Metastases to the thyroid may occur at the same time as other areas or years after original diagnosis. Patients with metastatic melanoma typically have normal thyroid function with metastases discovered incidentally during screening or surveillance. In this case, diagnosis was challenging as repeated FNA had to be done before a diagnosis was made. Immunohistochemistry staining helped to confirm the diagnosis.

**Conclusion:** This case demonstrates the need to consider metastasis in the differential dx of patients with thyroid nodules and history of cancer. Immunohistochemical staining at the time of FNA for markers associated with a patient’s known malignancy can facilitate diagnosis.

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**Abstract #1012**

**DISCORDANT THYROID FUNCTION TESTS – A ROOT CAUSE ANALYSIS**

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TTUHSC School of Medicine at Permian Basin

**Objective:** Free Thyroxine (FT4) and thyroid stimulating hormone (TSH) are measured in patients to assess thyroid function. At one of our teaching hospitals we observed a pattern of discordance, abnormal elevation in FT4 and a normal TSH—a pattern that is very unusual. Some of the possible
CAUSES OF HYPERTHYROIDISM

1. Thyroiditis
2. Graves’ Disease
3. Excessive TSH due to pituitary tumor

Discussion:

- The frequency of discordance in different clinically euthyroid patients separated over time was puzzling. This led us to investigate the assay being used to measure FT4 and the reported reference ranges for this particular assay.

- Apply the root cause analysis (RCA) method to:
  1. Ascertain that in fact there is a high prevalence of false positive high FT4
  2. Determine if the reported reference range was accurate
  3. Calibrate the reference range and measure how it affects the FT4 values and discordance with TSH

Methods:

- RCA revealed the euthyroid reference interval for FT4 (0.54-1.24 ng/dL) suggested by the VITROS 5600 integrated system was incorrect. The recommended (and widely used) reference range is 0.8-1.8 ng/dL. TSH and FT4 concentrations of 78 randomly selected patients were tabulated by laboratory personnel. We evaluated the frequency of patients with normal TSH and FT4 after application of old and new FT4 reference ranges. Chi-square test was used to compare the data.

Results:

- Twelve patients had subnormal TSH. These were presumed to be hypothyroid and excluded from further analysis. Out of the remaining 66 patients, 65 (98%) had FT4 higher than 1.24 ng/dL and 14 (21%) had FT4 higher than 1.8 ng/dL (p<0.001 by chi-square).

- Nine patients had high TSH concentrations, 4 of these patients had normal or low FT4 and were presumed to be hypothyroid. The other 5 patients had inappropriately elevated FT4 (all were >1.8 ng/dL).

Discussion:

- We ascertained that there was a high prevalence of false positive high FT4 values. Correction of the laboratory reference range dramatically reduced the number of patients with discordant thyroid function tests. However, there is still a group of patients (21%) that would need clinical follow-up to determine if their FT4 concentrations are falsely or truly elevated.

Conclusion:

- Unexpectedly abnormal or discordant thyroid function tests (Normal or elevated TSH with high FT4) may be seen with some rare, but clinically significant conditions such as TSH-secreting pituitary tumors, or the presence of heterophilic antibodies (HAMA). False high FT4 results might thus burden patients to be subjected to further testing and sometimes harmful interventions.

Abstract #1013

A CASE OF MICRO-MEDULLARY THYROID CARCINOMA PRESENTING WITH BONE METASTASIS

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1. Cleveland Clinic Foundation, 2. Ohio State University, 3. Robert J Tomsich Pathology & Laboratory Medicine Institute

Objective:

- To describe a case of sporadic micro-medullary thyroid cancer (mMTC) presenting with bone metastases.

Methods:

- We present the initial clinical manifestations, pathology results, laboratory findings and management of a patient with mMTC. A review of the literature related to mMTC and its presentation was done.

Case Presentation:

- Thirty-five year old female patient presented with a neck mass and was found to have a left level IV lymphadenopathy. She had a fine needle aspiration (FNA) that revealed benign lymphoid tissue. She was kept under observation but a repeat FNA of the same persistent lymph node one year later revealed low grade neuroendocrine tumor. Thyrotropin was 1.27 mlU/L (reference range 0.4-5.5) and serum calcitonin was 1996 pg/mL (reference range 0.0-5.1). Computerized tomography (CT) demonstrated multiple small sclerotic lesions in the spine, ribs and pelvis that were suspicious for metastatic lesions. A neck ultrasound revealed one subcentimeter, hypoechoic thyroid nodule in the lower isthmus and suspicious neck lymph nodes. Fluorodeoxyglucose positron emitting tomography (FDG-PET) revealed hypermetabolic cervical lymph nodes and multiple sclerotic skeletal lesions. The patient underwent total thyroidectomy with bilateral modified radical neck dissection. Tumor stage was pT1a pN1b M1 based on the identification of a 2-mm mMTC in the left lobe with lymphovascular space invasion and metastatic MTC involving 17 left side neck lymph nodes. Repeat CT revealed multiple lesions throughout the spine, iliac bones, sacrum and ribs suspicious for osteoblastic metastases. A biopsy of her right iliac bone lesion was consistent with metastatic MTC. She was negative for germline mutations. She underwent adjuvant radiation therapy to neck.

Discussion:

- Thirteen to forty-three percent of mMTC patients present with lymph node metastases. Distant metastases have been seen in 1-5% of cases. Overall, 10-year survival of patients with distant disease is 50%. Two cases of mMTC have been described in the literature so far that presented with bone metastasis.

Conclusion:

- Sporadic mMTC can rarely present with distant metastasis and be associated with poor prognosis.
Abstract #1014

DIAGNOSIS OF CLEAR CELL CARCINOMA IS NOT SO “CLEAR”

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**Objective:** Metastatic renal cell carcinoma to the thyroid is a rare condition that was nearly missed as the fine needle aspiration (FNA) biopsy of a thyroid nodule was negative for thyroid malignancy. Due to persistent hoarseness, the patient had a right hemi thyroidectomy which led to the incidental discovery of clear cell renal carcinoma that was in a 77 years old man with a history of clear cell renal carcinoma 18 years in remission.

**Case Presentation:** A 77 year-old male with a history of renal clear cell carcinoma, status post left nephrectomy in 1996 who was admitted to the hospital for shortness of breath in March 2014. A CT scan revealed an incidental finding of enlargement right thyroid lobe compared with a CT scan from March 2011. A follow up thyroid ultrasound revealed a large solid slightly heterogeneous nodule to right thyroid lobe, measuring 3.4 x 3.3 x 3 cm. A fine needle aspiration showed a benign cytology result with follicular cells, lymphocytes and blood. TSH was 3.11uIU/ml and Free T4 was 1 ng/dl, Free T3 was 3.9pg/ml. Thyroglobulin Ab was <1 IU/ml, thyroid peroxidase Ab was 2 IU/ml which are all negative. The patient had persistent hoarseness. A diagnostic right hemi-thyroidectomy was done in August 2014. Pathology result revealed that there was a clear cell neoplasm with rich vasculature. Immunostatins showed positive cells for CD10, negative for thyroid transcription factor 1 (TTF-1) and synaptophysin. The patient eventually required low dose of synthroid treatment.

**Discussion:** A nodular goiter is a common sign in clinical practice but it is rarely due to metastatic neoplasm. The initial thyroid FNA showed benign cytology. Current guideline recommends repeating the ultrasound in 6 to 18 months. The key differentiator was the patient’s symptom of persistent hoarseness and the medical history of renal malignancy. This prompted the hemi-thyroidectomy which found a clear cell neoplasm conflicting with the results of the thyroid FNA. Invasive tests and procedures are not typically recommended when searching for rare conditions but keep in mind that thyroid FNA can rarely have false negative. This case provides a clear example where further procedures were warranted due to the previous history of malignancy.

Abstract #1015

ABSTRACT WITHDRAWN

Abstract #1016

A RARE CASE OF LITHIUM INDUCED HASHITOXICOSIS WITH NEGATIVE AUTO-IMMUNE SEROLOGY.

Helen Anaedo, MBBS, Hassan Shawa, MD
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**Objective:** Hashimoto thyrotoxicosis (Hashitoxicosis) is a term used to describe rare cases of autoimmune thyroid disease that is associated with high titers of TSH-receptors and thyroid peroxidase (TPO) antibodies. Lithium use has been associated with goiter, hypothyroidism and to less extent with hyperthyroidism. The latter is usually due to silent thyroiditis (4%) or Graves’ disease (1%). We present a rare case of surgically proven lithium-induced hashitoxicosis with negative autoimmune serology and low radioactive uptake scan during the active hyperthyroid state.

**Case Presentation:** A 36-year-old woman with medical history of bipolar disease which was treated with lithium for many years. She presented with palpitations, heat intolerance, tremor and weight loss. Biochemical work up was consistent with overt hyperthyroidism. Thyrotropic immunoglobulin and thyroid peroxidase antibodies were normal. Thyroid uptake was only 1.2%. Preliminary diagnosis of sub-acute thyroiditis was made and a beta blockers was prescribed. Six months later, she remained symptomatic and biochemical work up revealed persistent overt hyperthyroidism. Repeat thyroid uptake was low again (1.4%) despite low iodine diet for one week prior to the study and a normal 24-hour urine collection for iodine. She was started on methimazole 10 mg daily. After 3 months, she required increase in dose of methimazole to 15 mg daily as TSH remained suppressed. Within 6 months of therapy, she became hypothyroid on methimazole which was discontinued. Thyroidectomy as a definitive therapy was pursued. Mixed picture of hashimoto’s thyroiditis (fibrotic changes) and Graves (diffuse hyperplasia) were identified on final pathology making hashimoto’s thyrotoxicosis a plausible explanation for her clinical picture.

**Conclusion:** Lithium-induced hashitoxicosis may not be necessarily associated with elevated autoimmunity titers. Thyroid radioactive iodine uptake may be very low even if done during the active hyperthyroid status.
UNEXPLAINED WEIGHT LOSS IN A PATIENT WITH SUBCLINICAL HYPOTHYROIDISM DUE TO COBALT TOXICITY AFTER PROSTHETIC HIP REPLACEMENT

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Mount Sinai Beth Israel

Case Presentation: A 66-year old female presented with unexplained weight loss (eight pounds over the last three years). She denied any cognitive impairment, cough, fever, chest pain, shortness of breath, palpitations, fatigue, nausea, vomiting, change in bowel habits or decrease in appetite. Past medical history was significant for subclinical hypothyroidism, severe osteoarthritis s/p bilateral hip replacements in 2009 and 2011, hypertension, vitamin d deficiency, and osteopenia. Physical examination was unremarkable. Laboratory work-up showed elevated TSH 5.7 (n 0.4-4.5 mIU/L) with normal FT4 1.1 (n 0.8-1.8 ng/dL), ESR 1 mm/hr, ANA negative, A1c 5.4, morning cortisol 16.7 (n 4-22 mcg/dL). Colonoscopy and mammography were normal. Patient had comprehensive evaluation and no pathological cause of weight loss was identified. On routine follow up with orthopedist her serum cobalt concentration was found to be elevated at 13.4 mcg/L (n < 1). MRI of the hip revealed bony erosion and surrounding soft tissue edema. It was concluded that her weight loss is related to systemic cobalt toxicity. Patient is scheduled for removal of the cobalt-containing prosthetic implant due to the systemic and local complications.

Discussion: Cobalt-containing hip prosthesis may cause increased local and systemic cobalt concentrations due to abrasion between bearing surfaces and corrosion of non-moving parts. The commonly reported systemic effects include hypothyroidism, neuro-ocular and cardiac toxicities. There are only few case reports on cobalt toxicity associated with weight loss. In our patient, unintentional weight loss was attributed to the elevated serum cobalt concentration as other etiologies were ruled out. Subclinical hypothyroidism was diagnosed before the hip replacement and is unlikely to be related to the cobalt toxicity.

Conclusion: We report an unusual case of weight loss most likely related to cobalt toxicity. It is important to suspect and recognize cobalt toxicity due to a large number of patients with cobalt-containing prosthesis. There are no laboratory criteria to guide physicians when evaluating an individual hip implant patient’s risk of developing systemic health effects. The UK Medicines and Healthcare Products Regulatory Agency, as well as the Mayo clinic have proposed a blood cobalt guidance value of 7 and 10 mcg/L, respectively. The most common treatment is removal of the metal-containing prosthesis.

DISSEMINATED INTRAVASCULAR COAGULATION SECONDARY TO THYROTOXICOSIS

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Case Presentation: A 67 year old woman with a medical history of ischemic cardiomyopathy, coronary artery disease, and atrial fibrillation was admitted with symptoms of acute shortness of breath and bilateral lower extremity swelling. She was treated for decompensated heart failure, however, additional work-up revealed evidence of hyperthyroidism: TSH 0.03mIU/L, free T4 5.20ng/dL, and total T3 224ng/dL. TPO and TSI antibodies were negative. Thyroid ultrasound demonstrated a multinodular goiter with normal Doppler flow. A thyroid uptake scan could not be performed as the patient was exposed to a contrast enhanced CT scan on admission. The patient denied history of thyroid disease or amiodarone exposure, and clinically did not meet criteria for thyroid storm. After endocrinology consultation, methimazole and dexamethasone were initiated. Subsequently, the patient’s clinical condition acutely deteriorated. It was characterized by worsening hepatic function, rising free T4, total T3, thrombocytopenia, elevated INR, PT, PTT, low fibrinogen, and increased D-dimer levels. She developed diffuse purpura and digital gangrene on her bilateral upper and lower extremities. Hematology confirmed the diagnosis of disseminated intravascular coagulation (DIC) and attributed it to acute thyrotoxicosis, as alternative etiologies were excluded. Potassium iodide was added to her treatment schedule, which was followed by gradual normalization of her total T3 and free T4. Concurrently, fibrinogen levels normalized with the PT and INR remaining mildly elevated. Despite biochemical improvement of her thyroid function and DIC parameters, the patient experienced progressive multi-organ failure and ultimately passed away.

Discussion: DIC as sequela of thyroid dysfunction has previously been reported in 2 cases of thyroid storm; however this is the first description of its occurrence secondary to thyrotoxicosis. The known major precipitating factors for DIC are sepsis, obstetrical or surgical complications, trauma, cancer, amphetamine overdose, heat stroke, burns and fulminant hepatic failure. The phenomenon of simultaneous systemic thrombosis and hemorrhage occurs as clotting factors and platelets are consumed in conjunction with intravascular fibrin deposition. Management is targeted at treating the
underlying cause and despite improved recognition of multiple inciting causes, morbidity and mortality remains significant. This underscores the importance of increasing awareness of the potential for thyroid disorders to drive this devastating complication.

**Conclusion:** This case demonstrates that DIC can be associated with thyrotoxicosis without evidence of thyroid storm.

**Abstract #1019**

**PREDICTIVE VALUE OF IDEAL BODY WEIGHT FOR LEVOTHYROXINE REPLACEMENT IN OBESE HYPOTHYROID PATIENTS AFTER TOTAL THYROIDECTOMY.**

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**Objective:** Recommendations for levothyroxine (LT4) replacement in patients with hypothyroidism are based on the evidence from studies in non-obese subjects. The aim of our study was to compare LT4 regimens required to achieve euthyroidism between obese and non-obese hypothyroid patients.

**Methods:** We retrospectively identified consecutive female patients in endocrinology clinic between November 2010 and October 2014 who had total thyroidectomy for benign goiter or stage I thyroid cancer and who achieved euthyroid state on LT4 therapy after surgery. Obesity was defined as body mass index (BMI) of >30 kg/m2. Clinical and biochemical characteristics and LT4 requirement were analyzed using Student’s t-tests and Fisher’s exact tests.

**Results:** We identified 30 hypothyroid females (14 non-obese/16 obese, 17 whites/13 blacks, age 48.7±15.2 years and thyroid-stimulating hormone (TSH) 1.1±0.8mIU/L), who achieved euthyroid state on the steady LT4 dose. There was no difference between the groups in age, TSH, and ideal body weight (IBW); as expected obese patients had higher total body weight (TBW) (105.1±22.9 vs 65.3±10.3kg, P<0.001) and BMI (38.8±8.3 vs 24.6±2.8, P<0.001). Compared with non-obese, obese women required higher LT4 dose (148±38 vs 102±13mcg, P=0.0002). There was no difference in LT4 per TBW (1.43±0.39 vs 1.60±0.30 mcg/kg, P=0.21), however, LT4 per IBW was higher in obese than in non-obese females (2.65±0.69 vs 1.89±0.29 mcg/kg, P=0.0006) and this difference persisted after adjustments for age and race (P<0.05). There was a marked variability in LT4 dose in obese patients. When we categorized obese patients who became euthyroid on LT4 dose of <150mcg (n=10) vs >150mcg (n=6), age, weight, and BMI were not different between the subgroups; however, the latter group of patients was more likely to have postoperative hypoparathyroidism (50% vs 0%, P=0.04) and had a higher dose of LT4 per TBW (1.73±0.47 vs 1.26±0.20 mcg/kg, P=0.06) and IBW (3.27±0.44 vs 2.27±0.52 mcg/kg, P=0.002), respectively.

**Conclusion:** Compared with non-obese, obese females after total thyroidectomy require higher LT4 dose per IBW but not per TBW. Among obese women, there was a significant heterogeneity in final LT4 dosage. To prevent iatrogenic hyperthyroidism, we recommend using the IBW as opposed to the TBW as a more accurate initial approach for therapy of hypothyroidism in a majority of obese females.

**Abstract #1020**

**HYPERTHYROIDISM WITH NODULES: A CHALLENGING TREATMENT DILEMMA IN SAFETY NET PATIENTS**

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Baylor College of Medicine

**Objective:** The most popular definitive treatment for hyperthyroidism in the US is radioactive iodine (RAI), with thyroidectomy utilized in patients who fail or are not candidates for RAI. In treating hyperthyroid patients with nodules, the risk of surgical complication must be balanced with a missed malignancy or failure of non-surgical treatment. Patient socioeconomic status (SES) has been shown to impact outcomes in thyroid disease; in this study, we review treatment utilization and outcomes of hyperthyroid patients with nodules in a safety net public hospital system.

**Methods:** We reviewed all hyperthyroid patients with nodules who received RAI or surgery in 2012 and 2013 in our hospital with >1 year of follow up. Patients had Graves’ Disease (GD) with nodules or Toxic Multinodular Goiter (MNG). Healthcare utilization included surgical procedures, RAI diagnostics/treatments, clinic appointments, imaging, fine needle aspirations, laboratory tests and medications. Costs from the health care system were estimated using 2013 Medicare charges. Provider and Diagnosis–related group payments were excluded in this unfunded safety net population. Pathology, complications, and thyroid status at 12 months post treatment were assessed.

**Results:** We reviewed all hyperthyroid patients with nodules who received RAI or surgery in 2012 and 2013 in our hospital with >1 year of follow up. Patients had Graves’ Disease (GD) with nodules or Toxic Multinodular Goiter (MNG). Healthcare utilization included surgical procedures, RAI diagnostics/treatments, clinic appointments, imaging, fine needle aspirations, laboratory tests and medications. Costs from the health care system were estimated using 2013 Medicare charges. Provider and Diagnosis–related group payments were excluded in this unfunded safety net population. Pathology, complications, and thyroid status at 12 months post treatment were assessed.

**Conclusion:** Compared with non-obese, obese females after total thyroidectomy require higher LT4 dose per IBW but not per TBW. Among obese women, there was a significant heterogeneity in final LT4 dosage. To prevent iatrogenic hyperthyroidism, we recommend using the IBW as opposed to the TBW as a more accurate initial approach for therapy of hypothyroidism in a majority of obese females.
by mean total cost of treatments provided for the RAI cohort (GD = $491, MNG = $505) and the surgery cohort (GD = $2068, MNG = $1923) at 1 year. Surgical cohort average gland size was 74gm (GD) and 59gm (MNG). Surgical complications included permanent hypocalcemia (n=1) and nerve injury (n=1); both had concomitant lymphocytic thyroiditis. RAI complications included worsening ophthalmopathy (n=2). No incidental cancers were found on pathology.

**Conclusion:** Hyperthyroidism with nodular thyroid disease represents a challenging therapeutic dilemma in safety net patients with limited access to care. At 1 year, RAI cost is cheaper, but treatment failure and potential need for further nodule workup add to long-term additional cost. Both RAI and surgical treatment of hyperthyroid patients with co-existing thyroid nodules can be successful even in resource-limited settings; RAI may be a better option for select patients with concomitant thyroiditis to avoid thyroidectomy complications. Developing treatment pathways utilizing this information can further improve cost efficiency of care in a resource limited public hospital system.

**Abstract #1021**

**ABNORMAL THYROID ULTRASOUND FINDINGS IN PEDIATRIC PATIENTS WITH PTEN MUTATION DURING ENDOCRINOLOGY SURVEILLANCE**

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Miami Children's Hospital

**Objective:** The study aims to identify abnormal thyroid pathology in pediatric patients with PTEN mutation during yearly endocrinology evaluation.

**Methods:** A retrospective case series study, containing seven pediatric PTEN mutation cases were evaluated from the files of Miami Children's Hospital. A search was conducted in the database of the hospital, between the months of January to November of 2014. In order to meet criteria, selected cases needed to include: Genetic confirmation for PTEN mutation, evaluation by endocrinology and genetics, and thyroid ultrasound (US) study.

**Case Presentation:** The population was predominantly male (5 patients, 62.5%), with a mean age of 9 years. All patients had baseline thyroid function studies, and 100% had at least one thyroid ultrasound study performed to screen for anomalies. 57% of patients had thyroid US changes. Half of those abnormal images (50%) had left thyroid lobe nodule representing the most common finding. Radiological image of the nodules were suggestive of follicular adenoma and one case required hemithyroidectomy as fine needle aspiration was suggestive for possible malignancy.

Other associated findings were developmental delay (100%) and gastrointestinal polyps (37%). Interestingly, two siblings also had Von Willebrand disease, Growth Hormone deficiency, and hypoglycemic episodes which are not classical findings of Bannayan Riley Ruvalcaba syndrome.

**Discussion:** Phosphatase and tensin homolog (PTEN) gene is an essential regulator of cell cycle, by creating an enzyme with phosphatase activity. Mutations of these tumor suppressor, prevent the phosphorylation of PIP3, leading to activation of AKT signaling pathway, and thus uncontrollable cell proliferation and tumor growth. Pediatric PTEN mutation has diverse phenotypic features ranging from neurodevelopmental delay/autism, PTEN Hamartoma-Tumor Syndrome (PHTS), an increase lifetime risks of malignancies (more commonly thyroid and germ cell neoplasia). Our case series, reflects common reported findings including developmental delay, and significant thyroid abnormalities, with an overall 28% association with follicular adenoma.

**Conclusion:** Appropriate PTEN activity is crucial to control cell proliferation. For this reason, pediatric patients diagnosed with mutation in this tumor suppressor gene, should have a multidisciplinary healthcare team, with endocrinologist playing a key role in thyroid surveillance, as previous studies have reported a 30% thyroid involvement. In our case series, ultrasound was a perfect non-invasive and painless screening study for pediatric cases, with high sensitivity in early diagnosis of thyroid adenomas.

**Abstract #1022**

**AGRAULUCYTOSIS SECONDARY TO METHIMAZOLE COMPLICATED BY ACALCULOUS CHOLECYSTITIS AND ACUTE PANCREATITIS**

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Makati Medical Center

**Objective:** To present a non surgical management of acalculous cholecystitis and pancreatitis in a hyperthyroid patient complicated by agranulocytosis secondary to methimazole intake

To illustrate dose administration of lithium carbonate in a patient with multiple history of drug allergy

**Case Presentation:** 30 year old female, known hyperthyroid maintained on methimazole 5 mg/tablet OD, came in for fever with sore throat. Vital signs: Blood pressure: 120/70mmHg, Heart rate: 107 bpm Temperature 38.4, icteric sclera, exophthalmos, hyperemic tonsils, thyroid gland enlarged, right upper quadrant tenderness.
Laboratories showed WBC 1.10 with ANC 22, TSH 0.01 uIU/ml, FT4 43pmol/L, total bilirubin 5.26 mgdl, direct bilirubin 4.43mgdl. MRCP showed gallbladder wall thickening and pericholecystic fluid. Started on propranolol 40mg every 6 hours, dexamethasone 2 mg IV every 6 hours. Referred to hematology, started on GCSF 300mcg subcutaneously OD; surgery service placed on nothing per orem, given parenteral feeding, hydration with 0.9 PNSS was increased. Second hospital day, WBC was noted at 1.13, no identifiable segmenters, referred to interventional radiology for fluoroscopy guided cholecystostomy tube insertion. Fifth hospital day, lipase was elevated at 355 U/L from 40 U/L. Octreotide drip started. Seventh hospital day, WBC increased to 2.87 with segmenter 18. Lipase improved to 109 U/L. Diet resumed to clear liquids then slowly progressed. She was given nystatin swish and swallow due to oral thrush however noted anaphylaxis. Tenth hospital day, cholecystogram was done which revealed patent cystic duct. While injecting the contrast dye, patient again had anaphylaxis. Repeat FT4 32 from 25. With history of multiple allergic reaction (methimazole, nystatin, contrast dye), patient was referred to allergology service prior to starting lithium carbonate. Allergology started Desloratadine 5mg/tablet OD at breakfast, Levocetirizine 5mg/tablet 1 tablet ODHS both for one week, Lithium carbonate 450 mg 1/4 tablet for 4 days then 1/2 tablet OD. Patient tolerated the trial therapy hence dose was increased to 450 mg/tablet 1/2 tablet BID. Repeat MRCP noo evidence of calculus in the biliary tree, gallbladder contracted with cholecystostomy tube, pancreas normal in size, pancreatic duct not dilated. Repeat laboratory: FT4 at 22.294. She was discharged stable with Lithium carbonate 450mg/tablet 1/2 tablet BID, propranolol 10mg/tablet 1 tablet TID

**Conclusion:** This case report elucidated a non surgical option for a patient with agranulocytosis and acalculous cholecystitis. In the course of management, it has shown a method of introducing a new drug in a patient with multiple history of allergy.

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**Abstract #1023**

**ASSOCIATION BETWEEN BMI AND TSH IN TREATED HYPOTHYROID PATIENTS AND EUTHYROID CONTROLS**

Bert Bieler, MD, Maliha Khan, MD, Girish Rao, MD, Krystal Hunter, MBA, John Gaughan, Farah Morgan, MD

Cooper University Hospital

**Objective:** The standard of care for treatment of patients with autoimmune thyroiditis is repletion with levothyroxine to within the “normal” range. This is known to prevent serious complications of hypothyroidism including weight gain, and at the extreme, myxedema coma. While the normal TSH range includes the 95% confidence intervals, it is not known if there is an association between weight and TSH when the TSH is within this interval. Although patients often associate even treated hypothyroidism with difficulty losing weight, our hypothesis is that there is no difference in BMI between healthy controls versus those with treated hypothyroidism with similar TSH. We did speculate that patients with treated hypothyroidism with a TSH in the upper half of normal would have a BMI greater than those with treated hypothyroidism and a TSH in the lower half of the normal range.

**Methods:** We conducted a chart review of patients seen within the Cooper Health System from January 1 to August 31, 2014. The initial group of 878 treated hypothyroid patients and 386 euthyroid controls was culled to 250 treated hypothyroid patients and 163 euthyroid controls, after exclusions. Data collected included age (18-60 years-old included in the study), gender, race, height, weight, diabetes history, smoking history, and for those on treatment, type and dose of thyroid hormone. The data was analyzed for significance using Welch-Satterthwaite analysis, pooled analysis, and Fisher’s exact test.

**Results:** Hypothyroid and control groups were similar in height, weight, BMI, and number of diabetic patients. There were more females, Caucasians, and non-smokers in the hypothyroid group. The average TSH was slightly higher in the treated hypothyroid patients versus the non-hypothyroid controls (2.06 v. 1.73, P < 0.01). There was no significant relationship between TSH and BMI in the treated hypothyroid patients or the euthyroid controls (BMI did not increase with increasing TSH within the normal range).

**Conclusion:** The fact that there is no significant relationship between BMI and TSH in patients with treated hypothyroidism suggests that there may not be a benefit in terms of weight reduction in keeping the TSH in hypothyroid patients in the lower half of the normal range. In addition, patients should be counseled that hypothyroidism, if properly treated, is unlikely to significantly contribute to weight gain. Other factors, such as nutrition and exercise counseling, should be offered to these patients.
RIEDEL’S THYROIDITIS IN THE SPECTRUM OF IGG4-RELATED SYSTEMIC DISEASE

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Objective: Riedel’s thyroiditis (RT) is an extremely rare chronic fibrosing disorder of unknown etiology is often associated with multiple organ involvement and systemically described as multifocal fibrosclerosis (MFS). IgG4–related sclerosing disease (IgG4-RSD), a new clinico-pathological entity also associated with MFS, is characterized by IgG4 + plasma cell infiltration and fibrosis in one or more organs. Although very recently the association of RT and IgG4-RSD has been suggested, it has seldom been studied or reported. We report a classic case of RT with immunohistochemical (IHC) assessment demonstrating increased IgG4 suggestive of underlying IgG4-RSD.

Methods: A 53-year-old Asian female presented with chronic enlarging right thyroid mass and associated weak voice, globus sensation and compressive symptoms. Previous medical history was significant for left thyroid lobectomy for presumed benign condition. Physical examination revealed a non-tender right thyroid mass with vocal cord paralysis. CT neck demonstrated a 6 cm right thyroid mass with extension to the mediastinum, trachea, and carotid artery. FNA was non-diagnostic, and the patient underwent right completion thyroidectomy for obstructive symptoms. Histopathological examination revealed all the morphological features of RT and IgG4-RSD, including extensively fibrosing thyroiditis with entrapped thyroid parenchyma and keloid-like fibrosis infiltrated by prominent lymphocytes and plasma cells and extension into adjacent skeletal muscle, vasculitis, and obliterative phlebitis. Immunohistochemical (IHC) examination demonstrated increase number of IgG4 supporting an IgG4-related disease. There was no evidence of involvement of other organs at the time of RT diagnosis.

Case Presentation: Histopathological examination revealed all the morphological features of RT and IgG4-RSD, including extensively fibrosing thyroiditis with entrapped thyroid parenchyma and keloid-like fibrosis infiltrated by prominent lymphocytes and plasma cells and extension into adjacent skeletal muscle, vasculitis, and obliterative phlebitis. Immunohistochemical (IHC) examination demonstrated increase number of IgG4 supporting an IgG4-related disease. There was no evidence of involvement of other organs at the time of RT diagnosis.

Discussion: Historically RT has been thought to be an isolated disorder of the thyroid or part of a systemic process termed MFS. Very new clinico-pathological criteria suggest RT and MFS are likely part of a broader clinical disease spectrum of IgG4-RSD due to the similarities between these entities. Therefore, RT with increased IgG4 + plasma cells may in fact represent the first clinical manifestation of an underlying IgG4-RSD, which clinically may indicate the need for future monitoring in these patients. However, due to the extreme rarity of both conditions, recent establishment of diagnostic criteria, and limited sensitivity of IHC in the diagnosis of IgG4-RSD, further studies are needed to definitively confirm this association.

Abstract #1025

ACUTE FLARE OF PRETIBIAL MYXEDEMA AFTER RADIOACTIVE IODINE ABLATION IN PATIENT OF GRAVE’S DISEASE

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University at Buffalo

Objective: Progression of Grave’s ophthalmopathy with radioactive iodine(RAI) treatment for hyperthyroidism is well known. Acute exacerbation of pretibial myxedema following RAI has not been reported. We hereby report a case of worsening of pretibial myxedema and ophthalmopathy in a patient with Grave’s disease who was given RAI ablation for multifocal papillary thyroid cancer (PTC).

Case Presentation: 55 year old Caucasian male with PMH of COPD, chronic smoking presented with symptoms of unintentional weight loss of 100 pounds, palpitations and tremors. Physical exam showed normal ocular findings, diffusely enlarged thyroid with bruit and fine tremors of hands. He also had hyperpigmented thick skin with nodules on legs. Hyperthyroidism was confirmed with TSH of <0.010, elevated Free T4 of 5.4, and total T3 of 398. He had positive thyroid stimulating immunoglobulins(TSI) of 367 % and increased diffuse uptake of 51% on RAI scan. Patient was treated with Methimazole and beta blocker with good control of symptoms. Two years later, patient underwent thyroidectomy for obstructive symptoms related to goiter. He was found to have multifocal PTC with largest focus of 1.4 cm with no lymph node involvement. He had RAI after surgery as adjuvant treatment for thyroid cancer. On follow up, he was noted to have worsening of skin changes with hyperkeratosis and marked nodule formation. Skin biopsy was consistent with pretibial myxedema. A trial of topical steroid therapy had no noticeable improvement. Coincidentally, he also developed new eye symptoms of exophthalmos, double vision which on CT evaluation were found to be related to severe ophthalmopathy, requiring surgical decompression and high doses of systemic steroids. Patient had marked improvement of his eye and skin symptoms.

Discussion: Of all extra thyroidal manifestations, there is evidence that RAI therapy worsens ophthalmopathy. However, progression of dermopathy following RAI
for thyroid cancer is not reported. These patients characteristically have higher serum concentrations of TSI. The implicated pathogenesis is due to expression of TSH receptor antigen in skin fibroblasts; triggering autoimmune response.

**Conclusion:** This case provides clear evidence for potential of RAI not only to worsen eye disease but also pretibial myxedema. Also, skin changes improved significantly with systemic steroids given for ophthalmopathy. We also suggest that subjects with history of Graves’ disease who are subsequently found to have thyroid cancer should be made aware of the possibility of worsening ophthalmopathy with adjuvant RAI treatment.

**Abstract #1026**

**BEXAROTENE INDUCED CENTRAL HYPOTHYROIDISM**

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**Case Presentation:** A 71-year-old woman was diagnosed with mycosis fungoides by skin biopsy about 10 years ago. She had received several treatments including topical tacrolimus, psoralen plus UVA (PUVA), clobetasol gel, topical bexarotene and radiation therapy. Six years after the initial diagnosis, oral bexarotene 150 mg daily was initiated and was gradually increased to 300 mg daily for progression of the disease. The patient was euthyroid before initiation of oral bexarotene, but repeat evaluation one month after the treatment showed TSH 0.04 μIU/mL (0.34-5.60) and free T4 0.6 ng/dl (0.58-1.64), suggestive of central hypothyroidism, and the patient was commenced on levothyroxine 25 mcg. At two year follow up, TSH was within the reference range. At three year follow up, TSH was significantly suppressed at 0.028 μIU/mL, and the patient reported significant hair loss and muscle cramps. Her primary care provider thought of over-replacement and stopped levothyroxine. Repeat thyroid function tests off the levothyroxine showed, suppressed TSH of 0.317 μIU/mL and low free T4 of less than 0.25 ng/dl, consistent with the central hypothyroidism. She was started on 50 mcg of levothyroxine, which was later advanced to 100 mcg (1.6 mcg/kg body weight) based on the follow up TSH results. After three months of the therapy, the patient reported improved energy levels, and free T4 values increased to the upper half of normal range. The patient continues bexarotene therapy with levothyroxine replacement and remains euthyroid.

**Discussion:** Bexarotene is a synthetic retinoid X receptor (RXR)-selective retinoid approved for treatment of cutaneous T-cell lymphoma. In clinical trials, central hypothyroidism is common affecting 40-80% of the patients treated with bexarotene and the degree of suppression of TSH secretion tended to be greater in patients treated with higher doses. Several animal and human studies showed direct suppression of TSH synthesis, decreased TSH secretion, and altered peripheral metabolism of thyroxine through altered type 1 deiodinase activity or by the induction of hepatic enzymes as a plausible mechanism for hypothyroidism. As Bexarotene causes secondary hypothyroidism, TSH values are unreliable in gauging thyroid status and levothyroxine dose adjustments should be based upon the results of free T4.

**Conclusion:** Oral bexarotene therapy may cause central hypothyroidism. Patients who are treated with this agent should have periodic thyroid function tests and hypothyroidism should be appropriately treated.

**Abstract #1027**

**RECURRENT RHABDOMYOLYSIS UNMASKING SEVERE HYPOTHYROIDISM**

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**Objective:** Hypothyroid myopathy with muscle stiffness and varying degrees of myalgia is a known entity, but rhabdomyolysis as the presenting feature in undiagnosed hypothyroidism is rare. Rhabdomyolysis is a potentially life threatening condition if not detected and treated promptly. Hypothyroidism should always be considered as a differential diagnosis since treatment with Levothyroxine rapidly brings down creatinine kinase (CK) levels.

**Case Presentation:** A 34 year old gentleman with type 1 diabetes mellitus, presented with worsening pain in both arms and legs limiting physical activity since four months. He denied statin use, exercise, or alcohol use. On examination he was obese, with pulse of 100 beats/min and significant nonpitting generalized edema. Labs; creatinine- 2.17(0.40-1.40 mg/dl), CK-5172(0-180units/L), urine-large blood and nephrotic range proteinuria of 3.9gm(1-14 mg/dl). He was admitted with a diagnosis acute kidney injury(AKI) with proteinuria, likely secondary to rhabdomyolysis of unclear etiology and underlying kidney disease from diabetic nephropathy. He was hydrated to treat rhabdomyolysis and diuretics for edema. Renal ultrasound did not show hydronephrosis. Echocardiogram was normal. Complement levels, ANA, ANCA, were normal. Generalized edema improved, CK
decreased to 3000 units and he was discharged. Followup with PCP in 5 days revealed rising CPK of 6559, worsening creatinine-2.62, persisting myopathy and hoarseness of voice. He was readmitted with AKI and rhabdomyolysis. This time, thyroid functions were checked revealing TSH 90.85 (0.4 -5.0 mc/unit/ml) with undetectable FT4, Thyroglobulin antibodies>30000 units, Antithyroid microsomal antibodies–62176units/ml. Treatment with Levothyroxine 100mcg was initiated and his CK levels fell to 190, TSH to 30 and creatinine to 1.46 in 8 weeks. **Discussion:** Rhabdomyolysis without an inciting cause such as statin use, exercise or alcohol, should prompt investigations to rule out hypothyroidism. Elevated muscle enzyme levels are commonly found in overt hypothyroidism, but rarely seen in acute hypothyroidism. Pathophysiology of rhabdomyolysis in hypothyroidism is postulated to be secondary to biochemical abnormalities like glycogen accumulation and reduced mitochondrial oxidative metabolism. Additionally, reduction in myosin ATPase caused by reduced glycolysis and oxidative phosphorylation may cause alteration in the sarcolemmal membranes allowing leak of CK from cells. Treatment with Thyroxine results in remarkable lowering of CK as early as 3 weeks, even before normalization of TSH. **Conclusion:** Work up for rhabdomyolysis of obscure origin should include hypothyroidism since this can be easily reversed with initiation of Thyroxine, thus avoiding complications like AKI.

**Abstract #1028**

**SUNITINIB INDUCED THYROTOXICOSIS**

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**Objective:** Sunitinib is an oral tyrosine kinase inhibitor (TKI) used for treatment of renal cell carcinoma and other tumors. It has been known to cause thyroid dysfunction mainly in the form of hypothyroidism. There are fewer cases reported regarding the incidence of TKI induced thyrotoxicosis. We present a case of Sunitinib related overt thyrotoxicosis caused by thyroiditis.

**Case Presentation:** A 36 year old woman with advanced renal cell carcinoma received 2 cycles of Sunitinib. The TSH prior to Sunitinib treatment was 0.73 µIU/ml (0.3 -5.6). Two months after the second cycle she presented with palpitations, heat intolerance, diarrhea and weight loss. She has no prior personal or family history of thyroid illnesses. She had a normal thyroid exam. The TSH was found to be 0.06 (0.34-5.60 µIU/ml), with Free T4 of 3.74 ng/dl (0.58-1.64) and Free T3 at 8.0 (0.7-2.0). The Thyroglobulin level was elevated at 604 ng/ml (1.6-50). The anti-thyroglobulin antibodies, antithyroid peroxidase antibodies and TSH receptor antibodies were negative. The vascularity was normal on thyroid ultrasound. The diagnostic uptake and scan showed low uptake of 0.7 % at 4 hours. Sunitinib was held and the patient was treated symptomatically with propranolol. Thyroid parameters normalized within 3 months after this episode with no recurrence of thyroid dysfunction.

**Discussion:** Hypothyroidism is the cause of thyroid dysfunction in majority of the patients treated with Sunitinib. Several mechanisms of TKI induced thyroid dysfunction have been proposed including atrophy of the thyroid gland by inhibition of the vascularization by suppressing angiogenic growth factors inducing thyroid ischemia. Thyrotoxicosis caused by thyroiditis is a self-limited process and results from a subacute release of preformed thyroid hormones. It is observed as a side effect of many drugs like Lithium and Amiodarone. The mechanism by which Sunitinib causes thyroiditis remains unclear. Thyroid antibodies have been implicated in a few cases of Sunitinib induced thyrotoxicosis which indicate an autoimmune process. Our patient, however, was tested negative for thyroid related antibodies, suggesting that Sunitinib related thyroiditis can occur in the absence of background autoimmunity. In our patient, there was spontaneous resolution of hyperthyroidism within 3 months of discontinuing Sunitinib, which indicates that a rapidly resolving self-limiting condition is associated with this agent.

**Conclusion:** It is well know that TKI mainly cause hypothyroidism. Self-limiting transient thyroiditis can occur in the absence of an autoimmune process in patients receiving tyrosine kinase inhibitors. Periodic surveillance of thyroid function during Sunitinib therapy is mandatory.
A CASE OF HYPERTHYROIDISM WITH HYPOGLYCAEMIA AND HYPOKALAEMIA

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Objective: To report a case of repeated hypoglycemia and hypokalaemia leading to a diagnosis of thyrotoxicosis.

Case Presentation: A 39 years old Bangladeshi woman presented with two years history of repeated hypoglycemic symptoms like palpitations, sweating, craving for food, drowsiness, which are relieved by taking oral rehydration salt. She gives history of repeated hospital admissions earlier for this symptoms. There she was found to be hypoglycemic and hypokalemic. She was advised to take ORS and green coconut water for relief of symptoms. In the recent year, she developed weight loss and increased frequency of bowel with formed stool but no heat intolerance. On query she had irregular menstruation for the last three years. She is on anti hypertensive medication since 2011, which was uncontrolled for last 6months. She had no eye signs, coarse tremor was present, jerks were exaggerated. There was thyromegaly with no bruit. CBC shows ESR-100, Hb 10.9 g/dl. USG revealed- Both lobes and the isthmus of thyroid gland enlarged, parenchymal echotexture is heterogeneous. Thyroid Scan- high early radio iodine uptake that turned over by 24hours. T3-312.5ng/dl ,FT4-7.74ng/dl, TSH <0.004iu/ml, SGPT-40, FBS-6.0 mol/L, 2h after 75g glucose 6.8 mmol/L, s.Cr.0.6mg/dl. Anti thyroglobulin Ab <20.0 iu/ml, Anti thyroid peroxidase An 409.0iu/ml. She was started with carbimazole 30 mg and propranonol 60 mg. She is better now, her bowel habit normal, tremor decreased, no hypoglycemic symptoms. On query she had irregular menstruation for the last three years. She is on anti hypertensive medication since 2011, which was uncontrolled for last 6months. She had no eye signs, coarse tremor was present, jerks were exaggerated. There was thyromegaly with no bruit. CBC shows ESR-100, Hb 10.9 g/dl. USG revealed- Both lobes and the isthmus of thyroid gland enlarged, parenchymal echotexture is heterogeneous. Thyroid Scan- high early radio iodine uptake that turned over by 24hours. T3-312.5ng/dl ,FT4-7.74ng/dl, TSH <0.004iu/ml, SGPT-40, FBS-6.0 mol/L, 2h after 75g glucose 6.8 mmol/L, s.Cr.0.6mg/dl. Anti thyroglobulin Ab <20.0 iu/ml, Anti thyroid peroxidase An 409.0iu/ml. She was started with carbimazole 30 mg and propranonol 60 mg. She is better now, her bowel habit normal, tremor decreased, no hypoglycemic symptoms. No hypokalaemia. After 1 month her SGPT-41 ,Hb-12.4mg/dl, ESR-11, no leucopenia, TSH - 0.015iu/ml, FT4-1.82 ng/dl. Thyroid receptor antibody was not done due to lack of fund.

Discussion: This patient presented to different clinicians with similar symptoms. Differential diagnosis of intestinal TB and pancreatic islet cell tumor were suggested but subsequent investigations like CT abdomen and endoscopy and colonoscopy revealed normal findings. At last thyroid function test was advised and it was fruitful. Therefore every altered bowel habit and hypoglycemic patient should undergo thyroid function test.

Conclusion: In the English literature, there was 3 case reports of hypoglycemia accompanied by hyperthyroidism. The first was caused by anorexia, the second was caused by liver dysfunction and lactic acidosis and the third was not clear. In the present case, anorexia nervosa was rejected because of her past history and symptoms, adrenal insufficiency was also excluded. Probably increased bowel movement caused hypoglycemia and hypokalaemia.
Abstract #1031

PAINLESS THYROIDITIS CAUSING PARALYSIS

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Objective: Hypokalemic periodic paralysis (HPP) is a medical emergency and leads to acute flaccid muscle paralysis. In severe cases acute respiratory failure and cardiac arrhythmias can occur. It is a genetic disorder with autosomal dominant inheritance. However, up to 43.3% of the patients have a secondary cause with 16.6-32% showing thyrotoxicosis. It is usually associated with Graves Disease with most cases reported in Asian males and rarely in other ethnic groups. We report a rare case of hyperthyroidism due to painless thyroiditis presenting as HPP in a Caucasian patient.

Case Presentation: 28-year-old Caucasian gentleman with no past medical history presented to the Emergency Room with inability to ambulate due to severe leg weakness and no history suggestive of other neurological dysfunction. On examination he was afebrile with BP of 134/78mm Hg and heart rate of 98/min. His physical exam was normal except for flaccid weakness of both upper and lower limbs, mainly proximal, with 3/5 power, depressed deep tendon reflexes and intact sensory examination.

Blood tests showed normal CBC, potassium 1.9mEq/L and phosphate 1.2mg/dL. Other electrolytes, renal and liver functions were normal.

Thyroid function tests (TFT’s) revealed TSH 0.002mU/ml, and elevated free T3 - 8.1pg/ml [1.7 to 3.7], total T3 - 254ng/dl [75 to 165], free T4 - 2.22ng/dl [0.8 to 1.8], Total T4 - 14.1mcg/dl [4.9 to 11.7] and normal T3 uptake 35.2% [24 to 37]. Thyroid peroxide antibodies were elevated at 209units/ml with normal thyroglobulin antibody. Radio Active Iodine uptake scan showed low uptake of 2% consistent with thyroiditis.

His hypokalemia and weakness resolved with potassium replacement. He had no symptoms suggestive of hyperthyroidism. He denied exposure to exogenous thyroid hormones, iodine or other drugs.

Patient remained asymptomatic during hospitalization and was discharged home on propranolol. 4 weeks follow up TFT’s showed normal T4 - 6.9mcg/dl, T3 Uptake - 27.2%, free T4 - 1.11ng/dl but still suppressed TSH at 0.010mcUnit/ml. His Potassium levels remained normal.

Conclusion: Our case highlights a rare presentation of painless autoimmune thyroiditis with hypokalemic paralysis. HPP may be a rare presenting feature of hyperthyroidism of any cause with most cases associated with Grave’s disease. TFT should be considered in unexplained muscle weakness in patients of all ethnic groups. It is hypothesized that hypokalemia is due to intracellular shift of extracellular potassium because of increased Na/K ATPase activity from increased thyroid hormones. Nonspecific beta-blockers may alter Na/K ATPase activity and help in resolving hypokalemia. Restoring euthyroidism may prevent recurrent paralysis episodes.

Abstract #1032

THYROID FINE NEEDLE ASPIRATION BIOPSY: CLINICAL EXPERIENCE AT THE ENDOCRINOLOGY CLINICS OF THE UNIVERSITY HOSPITAL OF PUERTO RICO

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Objective: This study aimed to establish a profile of the ultrasound-guided thyroid fine needle aspiration biopsies (FNABs) performed at the endocrinology clinics of the University Hospital of Puerto Rico in terms of the most common cytological diagnosis, patients’ risk factors and nodules’ sonographic characteristics.

Methods: A retrospective study was conducted in all thyroid FNABs performed from July 1, 2011 to December 31, 2013. Data on socio-demographic, FNAB cytology, surgery, and histopathology was collected from medical records. Chi-square test was used to assess associations between predictors (i.e., risk factors, sonographic characteristics) and outcome (i.e., FNAB cytology results). McNemar’s test was used to compare FNAB cytology and histopathology results.

Results: A total of 240 FNABs were performed in 192 patients. The cytological diagnosis distribution was: 181 (75.4%) Benign; 39 (16.3%) Non-Diagnostic (ND); 15 (6.3%) Indeterminate; and 5 (2.1%) Malignant. In our study, 91.2% were female; patients with malignant cytology were more likely to be less than 45y/o (100% vs 33%, p=0.01) and smokers (75% vs. 17.5%, p=0.02) than those with benign nodules. Benign nodules were more likely to be > 1cm than those malignant (88.2% vs 25%, p=0.01). Histopathology results were available for 38 nodules; there was no statistically significant difference between cytology and histopathology results (p>0.05). The sensitivity and specificity for FNAB cytology was
75% and 100%, respectively. About 47% of nodules with an initial indeterminate cytology underwent surgical resection; 71% had a final benign histopathology.

Discussion: In our study, most FNABs performed had a benign cytology. A malignant cytology was associated with those patients younger than 45y/o, even though several studies have found higher rates of malignancy associated with extreme of ages. A high concordance was shown between cytology and histology. For those with indeterminate cytology, the majority of cases had a final benign histopathology result. These data suggest the need to implement other approaches such as molecular markers to improve our diagnostic and therapeutic strategies according to our population based disease prevalence.

Conclusion: Most thyroid FNABs performed at our Institution yielded a benign cytology, with a low rate of malignancy. Although molecular testing is not performed in our Institution, these data support the need for larger studies to promote application of molecular markers to predict those at lower risk for malignancy.

Abstract #1033

SERENDIPITY IN TESTING THE THYROID

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Objective: A study conducted by Freeman, et. al. in 1986 demonstrated a higher incidence of post-partum thyroiditis (PPT) among Orthodox Jews as compared to other ethnicities. The original purpose of this study was to identify possible risk factors and environmental factors that might be involved in the development of PPT in this specific population.

Methods: Patients include a subset of ultra-Orthodox Jews seen at the Center for Health Education Medicine and Dentistry (CHEMED) in Lakewood, New Jersey, USA. This is observational study which involves collection of data, between February 2013 to April 2013, from medical records of Orthodox Jews diagnosed with PPT. A flow sheet with relevant data was designed and filled out by the observers. Exclusion criteria of the study include non-Jewish women, previous thyroid surgery, and a history of radioactive-iodine ablation.

Results: After reviewing 35 charts, we found that 15 patients had abnormal thyroid function tests by the obstetrician/gynecologists during pregnancy, 12 after pregnancy and 8 at a time uncertain with respect to the pregnancy. Of the 35 patients, 10 were asymptomatic and presented with hypothyroidism during pregnancy, 8 had abnormal studies post-partum (6 hypothyroid and 2 hyperthyroid), and 5 were found to have subclinical hypothyroidism at a time unspecified in relation to pregnancy. These patients presented with no symptoms that could be attributed specifically to the thyroid and not to the pregnancy or its subsequent effects.

Discussion: PPT is characterized by transient hyperthyroidism followed by transient hypothyroidism within the first year postpartum. The prevalence of PPT varies widely geographically, from 1.1% to 18%. The exact pathophysiology is incompletely understood. In 2002, the American College of Obstetrics and Gynecology (ACOG) published a clinical practice guideline on the management of PPT. They found that PPT occurs in 5% of women who do not have a history of thyroid disease. The diagnosis of PPT is made by documenting new-onset abnormal levels of TSH or free T4 or both.

Conclusion: On October 1, 2007, ACOG stated TSH screening is not part of routine prenatal care except for those who have relevant symptoms or medical history. However, we’ve observed that early detection through TSH testing will detect thyroid disease early in its course. Adverse outcomes of thyroid disease in pregnancy include preterm delivery, pre-eclampsia, low birth weight, and placental abruption. It is our conviction that TSH level determination should be part of routine prenatal care for pregnant females when they are seen before, during or soon after pregnancy. A large-scale research similar to this study is recommended to strengthen this conviction.

Abstract #1034

AGGRESSIVE PAPILLARY THYROID CARCINOMA ASSOCIATED WITH PROLONG GRAVE’S DISEASE (GD)

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Rutgers Robert Wood Johnson

Objective: The finding of differentiated thyroid cancer (DTC) in GD is not uncommon when GD is treated with total thyroidectomy (TT). We present an case in which delay in definitive treatment of GD was associated with an apparent transformation of a follicular nodule to an aggressive carcinoma.

Case Presentation: A 20 years old female presented with weight loss and anxiety. Patient denied any history of head or neck radiation or family history of thyroid disease or
cancer. Physical examination was positive for tachycardia and a palpable painless left sided thyroid nodule. TSH was <0.050, FT4 1.89, thyroid US showed a vascular nodule with calcifications (15mmx11mmx15mm). Follow up one year later showed a TSH <0.005, FT4 6.14, T3 455, TSH receptor antibodies (TSHR Ab) 11 u/L, thyroid US showed a dominant, heterogeneous nodule with internal vascularity and microcalcifications (17mmx14mmx17mm). Thyroid scan showed uptake significantly elevated at 6 and 24 hours consistent with hyperthyroidism, a cold nodule protruded off the inferior left lobe. Diagnosis of GD was made and patient started on methimazole. FNA showed atypical follicular cells, a second pathology opinion described follicular cells, hurthle cells and colloid. Thyroid US reevaluation 12 months later demonstrated an enlarge heterogeneous mass with microcalcifications replacing much of the left lower pole, highly suspicious for carcinoma, as well as a small right lower pole nodule with microcalcifications. Cervical lymphadenopathy with scattered left sided (levels II, III, IV) lymph nodes, highly concerning for abnormal process. She underwent US guided FNA of suspicious lymph nodes which showed atypical follicular cells in lymph nodes levels lII and VII. Patient underwent TT with left modified radical neck dissection. Pathology showed papillary thyroid carcinoma, classical and follicular variant with capsule, lymphovascular and perineural invasion.

Conclusion: The increased prevalence of thyroid nodules in GD is well known, but the clinical risk and circumstance of indolent follicular nodules evolving into aggressive DTC has not been generally recognized. This case demonstrated a rapid transformation of a follicular nodule into an aggressive DTC during a continuing and prolonged period of inflammation within the thyroid. This case is consistent with the postulation that the natural history of an otherwise indolent metaplastic process might be significantly altered by a state of chronic inflammation and stimulation by TSHR Ab. Prompt medical therapy of GD is known to attenuate this inflammatory state. But definitive therapies which either ablate or remove the gland, preclude the risk of an adverse outcome from an coincidental thyroid nodule.

Abstract #1035

SARCOIDOSIS PRESENTING AS GRAVES’ OPHTHALMOPATHY AND THYROIDITIS

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UAMS

Objective: We describe a rare case of patient presenting with ophthalmopathy concerning for Graves’ disease and thyroiditis with evaluation revealing neurosarcoidosis and thyroid granulomas.

Case Presentation: A 49 year old woman presented with headache, double vision, dizziness, puffiness around the eyes for two months. She was evaluated by ophthalmologist who noted exotropia and hypertropia. She complained of heat intolerance, insomnia, fatigue, headaches and numbness on the right side. She denied recent iodinated contrast exposure or neck pain. The thyroid gland was mildly enlarged with asymmetric nodular texture. There was no palpable cervical adenopathy. The eye examination showed erythema, proptosis, periorbital puffiness and diplopia more prominent in left field of vision both vertical and horizontal. The TSH was 5.11 u IU/ml (0.450 - 4.500 uIU/mL), free T4 0.88 ng/dl (0.82 - 1.77 ng/dL), TPO antibodies 356 IU/ml (0 - 34 IU/mL), TSH Receptor antibody < 0.51 IU/L (0.00 - 1.75 IU/L) and TSI was 51 % (0 - 139 %). Thyroid ultrasound showed multinodular goiter with right thyroid lobe enlargement. The CT of the orbits revealed bilateral exophthalmos with asymmetric enlargement of extraocular muscles. The MRI of the orbits showed marked enlargement of extraocular muscles, largest in bilateral lateral rectus, left medial rectus and left inferior rectus with lacrimal gland involvement. Leptomeningeal enhancement of the surface of brain and spinal canal and thickened infundibulum was noted concerning for sarcoidosis. Serum angiotensin converting enzyme was 28 U/L (9 - 67 U/L). The thyroid biopsy showed granulomatous changes consistent with sarcoidosis.

Discussion: Sarcoidosis is a multi-system granulomatous disease. Ocular disease may be seen in 30% of the cases most commonly as uveitis, chorioretinitis and eyelid granulomas. Rarely, extraocular orbital tissues may be affected, lacrimal gland being most common. Extraocular muscle involvement is very rare but has been reported. Granuloma infiltration of thyroid is extremely rare, with a prevalence of 4% in autopsied patients with systemic sarcoidosis. Autoimmune thyroid disease in patients with sarcoidosis, ranging from 2.9% to 10.2% has been reported. In a study clinical hypothyroidism was seen in 5.3% and Graves’ disease in 4% of the female sarcoidosis patients. Unilateral or bilateral proptosis may occur due to retro-orbital infiltration by sarcoid tissue. If untreated,
ocular disease can cause permanent visual impairment.

**Conclusion:** Orbital sarcoidosis may be the presenting manifestation of the disease and may be confused with Graves’ ophthalmopathy. Thyroid involvement may be seen with granuloma infiltration and presence of anti-thyroid antibodies.

**Abstract #1036**

**IMPACT OF HYPOTHYROIDISM ON OVERALL SURVIVAL (OS) OF ADULT PATIENTS WITH ACUTE MYELOGENOUS LEUKEMIA (AML).**

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**Objective:** The overall survival relationship between Acute Myelogenous Leukemia (AML) and Hypothyroidism in adult patients is unclear in the literature. This study aims to identify the impact of hypothyroidism on clinical outcomes in terms of survival in adult patients with AML.

**Methods:** This is a retrospective study that includes AML patients from Akron General Medical Center, Akron OH enrolled between 2002-2011. The data included basic demographics, overall survival (OS) in weeks after the diagnosis and cytogenetic complete remissions (CR). Patients with TSH value of >3.740 (uIU/mL) was defined as hypothyroid while TSH values from 0.358 to 3.740 (uIU/mL) were considered as euthyroid. The Kaplan-Meier test was applied for OS estimation using JMP Software version 9.0. Chi square was used to analyze the two groups (hypothyroid and euthyroid) and a *p*-value of <0.05 was taken as statistically significant. Institutional Review Board (IRB) approval was obtained according to Helsinki Declaration.

**Results:** A total of 187 patients were included in the study with AML with the median age was 70 years and 98 (52%) were males. A total of 92 patients had TSH checked and of them, 17 (18.5%) were identified as hypothyroid while 75 (81%) were included in euthyroid group. Median OS was 131 weeks in hypothyroid group while 322 weeks in the euthyroid group. Overall survival in both groups combined was 221 weeks. Although the OS was lower in the hypothyroid patients however it was not translated into statistical significant difference (*p* = 0.220).

**Conclusion:** Our results show that the overall survival was lower in the hypothyroid group. However the results were not statistically significant as the sample size was small. Its important to treat hypothyroid in AML patients as it will improve their quality of life and we recommend that it be checked in AML patients especially if they have been exposed to radiotherapy. Further studies are recommended in order to better identify the effect of hypothyroidism on survival of AML patients.

**Abstract #1037**

**ABSTRACT WITHDRAWN**

**Abstract #1038**

**FAMILIAL DYSALBUMINEMIC HYPERTHYROXINEMIA: A CASE REPORT AND REVIEW OF THE LITERATURE**

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Danbury Hospital

**Objective:** To describe a rare case of Familial Dysalbuminemic Hyperthyroxinemia (FDH) diagnosed during work up for an incidental thyroid nodule.

**Methods:** Case presentation and review of literature.

Case Presentation: A 55-year-old female was found to have an incidental thyroid nodule on CT scan of the head and neck during the work up for a fall. She did not have any signs or symptoms of thyroid disease. She stated that her family members had some kind of thyroid problem. She had an elevated free thyroxine (FT4) and a normal thyroid stimulating hormone (TSH). T3 resin uptake, thyroglobulin autoantibody level, and thyroglobulin level were within normal range. Fine needle aspiration of the nodule revealed clusters of benign follicular epithelial cells and colloid consistent with benign hyperplastic nodule. We also found that her siblings and some other family members had abnormal thyroid function tests and were not on any therapy. She was then reassured about the diagnosis of FDH.

**Discussion:** FDH is an autosomal dominant disorder, associated with elevated total thyroxine (TT4), normal TSH, and the absence of signs or symptoms of thyroid disorder. It is a common cause of increase in serum TT4 in Caucasian population. It is characterized by the presence of mutant albumin molecules, which have greater affinity for TT4 than for triiodothyronine (T3) in clinically euthyroid individuals. The affected individuals have consistently elevated TT4 and elevated or normal FT4 values with normal TSH levels. FDH may be confused with hyperthyroidism or thyroid hormone resistance syndromes, prompting unnecessary laboratory tests and treatment. The diagnosis of FDH is made by performing a resin (or charcoal) uptake test using radiolabeled T4, rather than T3. In patients with FDH, this test will show increased binding of T4. The diagnosis can also be made by electrophoresis of binding proteins in the presence of radio labeled T4, which will show increased T4 binding in the albumin zone. Detailed family history should be...
obtained to reveal the characteristic pattern of autosomal dominant inheritance. After diagnosis of FDH, the patients should be reassured that they do not need any treatment. **Conclusion:** FDH is a rare genetic disorder that is detected during work up for elevated TT4 in asymptomatic patients. Typically, these patients are referred to endocrinologists. Affected subjects may be missed if only free hormone levels are tested. But, a newly found instance of FDH can initiate a family investigation. However, clinicians need to be aware that autoimmune thyroid dysfunctions such as Graves disease or Hashimotos thyroiditis can occur unrelated to the binding aberration and appropriate follow up initiated.

**Abstract #1039**

**THYMOMA AND DIFFUSE ADENOPATHY IN GRAVES’ DISEASE**

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University of Arkansas or Medical Sciences

**Objective:** Thymic hyperplasia is often associated with Graves’ disease and reverts with treatment. Thymoma with diffuse adenopathy has rarely been reported in Graves’ disease. We report a case of Graves’ associated with diffuse adenopathy and B1 thymoma.

**Case Presentation:** A 50 year old woman presented with weight loss and dyspnea. She had a small goiter. The TSH was 0.020 uIU/mL (0.35-5.5), Free T4 4.22 ng/dL (0.58-1.64) and TSH Receptor antibodies (TRAb) were 86 % (< 10) which were consistent with Graves’ disease. She was treated with propylthiouracil. The CT chest for evaluation for dyspnea revealed anterior mediastinum 5 cm x 2 cm mass, numerous enlarged lymph nodes within the axilla, mediastinum and diffusely enlarged thyroid gland containing multiple nodules. She received 30 mCi of I131 radioiodine. The follow up CT chest after 6 months showed interval improvement in size of axillary lymphadenopathy but no significant change was noted in the mediastinal mass. The biopsy was considered but in light of a large goiter and concern for thymoma, she underwent a total thyroidectomy and thymectomy. The pathology showed B1 thymoma. She had annual surveillance and there was no recurrence of thymoma after 4 years of follow up.

**Discussion:** Thymic enlargement is a common feature in hyperthyroidism and seen in approximately 38% cases of thyrotoxicosis. This is mostly due to thymic hyperplasia which regresses after treatment of hyperthyroidism. In our case, the thymic mass did not regress despite achieving euthyroid status and was later found to be a thymoma. The mechanism of enlargement is thought to be due to excess stimulation of thyrotropin receptors by thyroid hormones and TSH receptor antibodies. It is important to know the association between thyrotoxicosis and thymic hyperplasia as it can mimic a malignancy. The time span between achieving euthyroid state and regression of thymic enlargement is unclear. In one case series, regression was seen around 16 weeks after achieving euthyroid state, but there is no standardization as to how frequently the tumor was assessed. The thymic enlargement in Graves’ should be followed closely due to instances of malignant thymoma. Biopsy of anterior mediastinal mass is recommended when regression fails to occur after achieving euthyroid state.

**Conclusion:** Thymic hyperplasia and lymphadenopathy in Graves’ disease may be part of a generalized lymphoid hyperplasia that characterizes a systemic autoimmune process. Although thymic hyperplasia is common but the possibility of other malignant processes should be considered in patients with thymic enlargement depending upon the clinical circumstance as the management and outcome are completely different.

**Abstract #1040**

**SEVERE THYROTOXICOSIS COMPLICATING A TWIN PREGNANCY CONSISTING OF COMPLETE HYDATIDIFORM MOLE AND CO-EXISTENT FETUS**

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**Objective:** We report a case of severe thyrotoxicosis in a woman with complete hydatidiform mole and coexistent fetus (CHMCF).

**Case Presentation:** A 22 year old African-American woman presented at 12 weeks gestation for vaginal bleeding. Ultrasound revealed intrauterine twin pregnancy, with one normal fetus and the other with features suggestive of hydatidiform mole. Vital signs were normal and she did not have clinical signs of thyrotoxicosis. Hormonal analysis revealed serum beta human chorionic gonadotropin (hCG) of 2,990,568 mIU/mL (12 weeks normal range: 25,700-288,000), and thyroid function tests (TFTs) consistent with thyrotoxicosis: TSH 0.005 mIU/mL (0.4-1.8) and free T4 4.21 ng/dL (0.83-1.76). Due to 2,990,568 mIU/mL, free T4 was 3.07 ng/dL and triiodothyronine (T3) was 5.17 ng/mL (0.6-1.81). She was treated with propylthiouracil, hydrocortisone and propranolol and
discharged 2 days later with resolution of symptoms on propranolol and methimazole. The pathology report confirmed CHMCF. Two weeks later, TSH was 0.663 mIU/mL, free T4 was 0.84 ng/dL and hCG had risen to 50,978 mIU/mL. She underwent repeat D&C and chemotherapy with methotrexate and actinomycin D and achieved remission 5 months after delivery, with hCG <5 mIU/mL.

**Discussion:** CHMCF is a rare event with an estimated incidence of 1 in 22,000 to 100,000 pregnancies, of which 6% of cases have laboratory evidence of thyrotoxicosis. Thyrotoxic patients with trophoblastic tumors often lack clinical features of thyrotoxicosis because of the relatively brief duration of the excess hormone. Most have higher serum T4/T3 ratios than patients with Graves’ hyperthyroidism. They rarely require any treatment for thyrotoxicosis and TFTs normalize as the serum hCG falls following resection of the tumor. The effect on the thyroid is believed to occur due to molecular mimicry between hCG subunits and TSH. Due to low potency of hCG for TSH receptors, extremely high levels of hCG are usually required to produce an effect on the thyroid gland.

**Conclusion:** This case highlights the rare occurrence of thyrotoxicosis in CHMCF. The ability to diagnose thyrotoxicosis in an ongoing pregnancy with hydatidiform mole may be clinically challenging. Physicians should be cognizant of this complication in CHMCF patients and undertake timely evaluation and careful management of the thyrotoxicosis.

**Abstract #1041**

**RARE CASE OF POORLY DIFFERENTIATED THYROID CARCINOMA PRESENTING AS UNILATERAL EXOPHTHALMOS**

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Hofstra North Shore-LIJ School of Medicine

**Objective:** To report an unusual presentation of poorly-differentiated thyroid cancer.

**Case Presentation:** A 55-year-old African-American woman with a history of morbid obesity presented to an outside hospital complaining of headache, blurred vision, and a left eye that was “bulging out” for several weeks. She was told she had a brain mass and underwent endoscopic CT-guided excisional biopsy of the left orbital mass. Pathology revealed poorly differentiated thyroid carcinoma (PDT) consistent with thyroid follicular cell origin and Ki-67 proliferation index 5-10%. The patient was started on dexamethasone and levetiracetam and was discharged with a plan for outpatient whole body iodine (WBI) scan. One day before getting the scan, she presented to our tertiary center in DKA. Physical exam was significant for left exophthalmos and an unremarkable thyroid gland. Brain MRI showed an exophytic mass centered on the left sphenoid wing measuring 2.4 x 4.6 cm with intracranial and intraorbital extension. WBI scan was positive only for uptake in the thyroid, but in the setting of CT scans done days earlier. A thyroid ultrasound done revealed a dominant 2.5 cm hypoechic nodule with possible punctuate microcalcifications. FNA of this nodule concurred with biopsy of the orbital mass. Neurosurgery was recommended but patient refused. Discharge plan was for radiotherapy and thyroidectomy. Following five sessions of radiation to the left orbit, she was readmitted for dyspnea on exertion due to new bilateral pulmonary emboli. Repeat brain MRI revealed interval increased size of the mass. The patient was not deemed a surgical candidate for thyroidectomy and was referred to hospice due to poor prognosis.

**Discussion:** Well-differentiated follicular thyroid carcinoma (FTC) is known to metastasize to lymph nodes, lung and bone; case reports have documented eye involvement. Metastasis patterns are less clear for PDT, a relatively new diagnostic entity viewed histologically and prognostically between well-differentiated FTC and anaplastic carcinoma. PDTs are associated with extrathyroidal extension and distant metastases present at diagnosis. Patients will typically have recurrences, poorer prognosis, and significantly lower survival rates than those of well-differentiated carcinomas. Due to the aggressive nature of this entity, a multimodality treatment approach should be employed, including thyroidectomy, radioactive iodine ablation post-op, and external beam radiation therapy. Unfortunately in the case of our patient, her disease was already advanced at the time of diagnosis.

**Conclusion:** We present a rare case of PDT with metastasis to the orbit initially presenting as unilateral exophthalmos.
Abstract #1042

CORRELATION OF THYROID HISTOPATHOLOGY WITH FINE NEEDLE ASPIRATION OF THYROID NODULES

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Objective: We studied the correlation of thyroid histopathology with fine needle aspiration cytology (FNAC) to determine its efficacy in diagnosing thyroid pathology.

Methods: Data was retrospectively collected in 142 patients (predominantly African Americans) with thyroid nodules in an urban hospital over a period of 8 years. The study included only patients who had both FNAC and histopathology results. The Bethesda System for Reporting Thyroid Cytopathology (BSRTC) was used to classify FNAC results. Patients who had multiple biopsies and who had samples from both sides of the thyroid were excluded. Study data also included patient demographics, clinical thyroid status and nodule characteristics. The FNAC results were compared with the histopathology results to determine the sensitivity of FNAC in predicting thyroid histopathology.

Results: Our study analysis showed that FNAC predicted benign lesions with a sensitivity of 89.5% and specificity of 57.1%. The positive predictive value was 96.3%. Diagnostic accuracy was 87.1%. Atypia of undetermined significance (AUS) on FNAC correlated with benign histopathology in 63% of the patients. 76% of patients with follicular neoplasm on FNAC were later found to have benign histopathology. Interestingly, 4 of the 5 patients who had Hürthle cell tumor (HCT) on FNAC were found to have malignant lesions.

Discussion: Our study showed that FNAC predicted benign thyroid histopathology with a high sensitivity but low specificity. 7% of our patients had AUS on FNAC, of which two-third had benign histopathology. FNAC is traditionally associated with a low efficacy in predicting follicular malignancy. Of the 25 patients in our study with follicular neoplasm on FNAC, 19 were benign on histopathology. HCT was seen only in 5 patients, of which 4 were malignant. This rate of malignancy is higher than that commonly seen with HCT. Among the 4 patients, one had Hürthle cell carcinoma and the other three had other malignancies. Hence, the findings on FNAC are not a reliable method to differentiate between true follicular neoplasms and HCT and between the benign and malignant types of HCT.

Conclusion: Our study concludes that FNAC has a strong correlation with histopathology in predicting benign thyroid nodules. Also, Hürthle cell neoplasm on FNAC is strongly associated with malignant rather than benign histopathology. However, our sample size of Hürthle cell neoplasm was insufficient to make a decisive conclusion.

Abstract #1043

LITHIUM ASSOCIATED THYROTOXICOSIS: A RARE PRESENTATION WITH LONG TERM LITHIUM THERAPY

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Objective: Since the turn of the last century, Lithium has been the drug of choice for the treatment of bipolar disorder. The incidence of lithium toxicity is only 5.4 cases in 100,000 per year with a mean toxic level of 2.16 mmol/L. We report a case of a rare side effect associated with lithium therapy.

Case Presentation: A 52 year old woman with a history of bipolar disorder was admitted for altered mental status. She was disoriented, agitated and appeared to suffer from visual and auditory hallucinations. The physical examination was significant for tachycardia but muscle strength, deep tendon reflexes and thyroid exam were normal. On admission, laboratory tests revealed a lithium level of 3.15 mmol/L and TSH of < 0.008 mIU/L but normal thyroxine and triiodothyronine levels. Repeat testing a week later revealed a thyroxine of 5.1 ng/dl and triiodothyronine of 347.8 mg/dl. Thyroid stimulating immunoglobulin was 333% and a subsequent thyroid scan showed uniform tracer distribution in both lobes consistent with graves’ disease (figure.1). Later, she developed a deep venous thrombus extending from the popliteal vein to the common iliac, despite prophylactic anticoagulation.

Discussion: The most common thyroid abnormality associated with lithium therapy is hypothyroidism. Only case reports demonstrate Lithium associated thyrotoxicosis (LiAT). The mechanism for LiAT is unknown but may be mediated by either a lithium triggered autoimmune process, Jod-Basedow like phenomenon or direct toxicity of thyroid follicles. One study reported 14 cases of LiAT, the incidence of which was 3 times more than the local reported prevalence of thyrotoxicosis alone. Assessment of thyroid function prior to starting lithium therapy can be considered due to variable effects of lithium on the thyroid gland and the easy availability of thyroid function tests. As for the thromboembolic disease, a review of
the literature revealed that thyrotoxicosis may shift the hemostatic balance towards a hypercoagulable state. In fact, the MEGA study found a gradually increasing risk of venous thrombosis with increasing free T4 levels.

**Conclusion:** This report presents a rare presentation of lithium therapy associated thyrotoxicosis. Though a definitive causal relationship cannot be established between lithium therapy and the clinical presentation, we are of the opinion that lithium significantly contributed to the underlying autoimmune process that precipitated the sequence of events.

**Abstract #1044**

**MANAGEMENT OF THYROTOXICOSIS IN THE SETTING OF PTU-INDUCED LIVER INJURY**

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**Objective:** Graves’ disease (GD) is one of the most common causes of thyrotoxicosis. Hepatic injury in this setting has been observed and can be due to underlying disease or other factors. Liver toxicity due to thionamides is estimated to occur in less than 0.5% of patients and is more common with propylthiouracil (PTU) than with methimazole (MMI). Liver dysfunction sets limitations on therapeutic options in patients with thyrotoxicosis. Evidence has highlighted treatment strategies such as steroids, beta-blockers, potassium iodide, and plasmapheresis in the setting of severe thyrotoxicosis refractory to thionamides or in cases of liver injury. Our case notes the dilemma of treating thyrotoxicosis with goiter in the setting of PTU-induced liver toxicity.

**Case Presentation:** A 26 year old female presented to the emergency room with complaints of weakness, tremors, 20 lbs weight loss, palpitations, hair loss, and bulging eyes. She had dysphagia to solids and shortness of breath while supine. She had been diagnosed with GD in 2013, treated with PTU, and discharged on MMI. She developed a diffuse rash to MMI and was changed to PTU 50 mg/day. On Methimazole 5 mg and 10 mg alternate day, she complained of neck pain made worse by swallowing and yawning. On examination, she was afebrile, though she complained of mild fever at home. Her heart rate was 95/min and BP 124/76 mm Hg. Her thyroid was mildly enlarged and very tender on palpation. Ibuprofen was started and PTU was increased to 200 mg every 8 hours, as was propranolol at 60mg every 8 hours. The patient had an obvious improvement in sinus tachycardia and diaphoresis. TSH was <0.0015. Free T4 was >8 ng/dL (0.82-1.77). She also had positive TSI. Ultrasound of the thyroid revealed diffusely enlarged thyroid gland with increased vascularity. She underwent thyroid uptake and scan which was 47% at 24 hours. She had 19 miCu of 131I induced radiation thyroiditis is a potential complication to know about. She underwent thyroid uptake and scan which was 47% at 24 hours. She had 19 miCu of 131I induced radiation thyroiditis is a potential but rare complication of treatment of Graves’ disease. In this case report we describe one such case. Case Presentation: We evaluated a 24 year old Caucasian female for hyperthyroidism. Her other medical conditions included Polycystic ovarian syndrome for which she was on oral contraceptives. She was on methimazole for possible Graves’ disease for 2 years. She complained of persistent palpitations and heat intolerance. She opted for radioactive iodine ablation treatment. On initial evaluation, she had mildly enlarged thyroid gland- about 1.5 – 2 times normal. She felt warm with a heart rate of 108/min. She did not have any stigmata of Graves’ ophthalmopathy. She was started on metoprolol 75 mg/day. On Methimazole 5 mg and 10 mg alternate day, her TSH was 0.75 uIU/ml (0.45-4.50) and Free T4 was 0.99 ng/dl (0.82-1.77). She also had positive TSI. Ultrasound of the thyroid revealed diffusely enlarged thyroid gland with increased vascularity. She underwent thyroid uptake and scan which was 47% at 24 hours. She had 19 miCu of 131I after being on iodine free diet and off methimazole. On the third day post radioactive iodine ablation, she complained of neck pain made worse by swallowing and yawning. On examination, she was afebrile, though she complained of mild fever at home. Her heart rate was 95/min and BP 124/76 mm Hg. Her thyroid was mildly enlarged and very tender on palpation. Ibuprofen

**Abstract #1045**

**A CASE OF 131I INDUCED THYROIDITIS – A COMPLICATION TO KNOW ABOUT**

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**Objective:** 131I induced radiation thyroiditis is a potential but rare complication of treatment of Graves’ disease. In fact, the MEGA study found a gradually increasing risk of venous thrombosis with increasing free T4 levels. Treatment continued with hydrocortisone 50 mg every eight hours, propranolol 80 mg every 8 hours, SSKI 150 mg every eight hours, and cholestyramine 4 g twice daily with lowering in heart rate and improvement of her status. General Surgery was consulted for thyroidectomy, but declined to do surgery, noting that her thyrotoxicosis should be stable prior to the procedure. After being stable for several days, thyroidectomy was performed.

**Conclusion:** The mechanism of PTU-induced hepatic injury is not clear, but is thought to be multifactorial. Severe toxicity is noted to be dose related. Cessation of PTU is critical and initiation of alternative medications for management can lead to resolution of thyrotoxicosis. Definitive therapy, thyroidectomy or radioactive iodide ablation, should be pursued as soon as possible in such patients.
did not provide pain relief. Repeat ultrasound revealed enlarged heterogeneous thyroid gland. She was started on prednisone 40 mg/day with a plan to taper over 4 weeks. Repeat thyroid function revealed Free T4 of 2.13 ng/dL (0.82-1.77). Her symptoms improved with steroids. 

**Discussion:** Radiation induced thyroiditis is a potential complication of 131I treatment for hyperthyroidism. The reported incidence is about 1%. Radiation induced thyroid follicular cells destruction results in inflammation and release of thyroid hormone reserves. It is relatively seen more often in thyroid cancer patients who receive higher dose of radiation treatment. Usually the symptoms develop within 5-10 days after radiation treatment. Symptoms usually consist of mild pain in the neck. It resolves with NSAIDs frequently and can last up to 2-3 weeks. Occasional severe cases need high dose prednisone for 4-6 weeks. 

**Conclusion:** Radioactive iodine treatment is one of the effective modality of treatment of Graves’ disease. However patient should be counselled about the potential complication of radiation induced thyroiditis. In severe cases not controlled by NSAIDs, high dose prednisone should be started early in the course. 

**Abstract #1046**

**SUBCLINICAL HYPERTHYROIDISM AND AMIODARONE: A CAUTIONARY TALE**

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Montefiore Medical Center

**Objective:** Multiple adverse effects of Amiodarone have been documented but careful monitoring of non-cardiac parameters remains suboptimal to date. We present a case of a patient with a history of subclinical hyperthyroidism that was started on amiodarone therapy which led to thyrotoxicosis.

**Case Presentation:** 71-year-old man with a history of atrial fibrillation presented with shortness of breath and dizziness for 3 days. The patient had been rate controlled on amiodarone for three years. Physical exam revealed thyroid nodules and an irregularly irregular pulse of 150 bpm. Carotid doppler and ECHO were unrevealing. Bloodwork showed abnormal TSH of 0.03 uU/mL (0.5–6.0 μU/ml) and free T4 of 1.73 ng/dL (0.7–1.7 ng/dL) suggestive of hyperthyroidism. Amiodarone was stopped for suspected Type-1 amiodarone-associated hyperthyroidism causing decompensation of rate-controlled atrial fibrillation. Methimazole 10mg orally bid was initiated and later doubled to 20mg. Thyroid ultrasound showed thryomegaly and two large nodules with hypervascularity. He was discharged on pradaxa, digoxin and metoprolol after rate control was achieved. One month later, the patient was readmitted for postural hypotension, increased sweating, diarrhea and a 10 lb. unintentional weight loss. Repeat thyroid panel showed free-T4 of 1.42 ng/dL, slightly improved from the previous 1.73 ng/dL and a TSH of 0.02 uU/mL. A retrospective review of thyroid panels over four years showed the evidence of subclinical hyperthyroidism with TSH 0.135 uU/mL and free T4 of 1.04 ng/dL. This was not taken into consideration before starting amiodarone. 

**Discussion:** Amiodarone is a lipophilic drug rich in iodine that has been associated with thyroid disorders. 2-12% of patients on chronic amiodarone therapy eventually develop amiodarone-induced thyrotoxicosis (AIT). While there is general agreement on following thyroid panels for patients with overt disease, no clear guidelines exist on management of subclinical disease in patients being considered for amiodarone therapy. Subclinical hyperthyroidism has independently been associated with worse cardiovascular outcomes. It also increases the risk of amiodarone-induced thyrotoxicosis (AIT), which could further worsen the cardiac problems being treated. 

**Conclusion:** Full assessment of baseline thyroid function tests is warranted in subclinical cases. Patients with serological evidence of subclinical hyperthyroidism should be fully evaluated to determine the etiology of thyroid condition and closely monitored. AIT should be considered when treated patients develop clinical signs of thyrotoxicosis or decompensation of previously rate controlled atrial fibrillation.

**Abstract #1047**

ABSTRACT WITHDRAWN

**Abstract #1048**

TECHNETIUM 99–SESTAMIBI THYROID SCAN AS AN IMAGING MODALITY IN THE DIFFERENTIAL DIAGNOSIS AND MANAGEMENT OF AMIODARONE INDUCE THYROTOXICOSIS

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**Objective:** Thyroid disorders are well-recognized side effects of amiodarone therapy. Amiodarone is an iodine rich drug that may cause 2 types of thyrotoxicosis (AIT). Type 1 AIT is a state of thyroid Harmon overproduction resulting from exposure of an abnormal thyroid gland to excess iodide from the drug itself. This form of AIT response to thionamides. Type 2 AIT results from amiodarone induced destructive thyroiditis and glucocorticoids are the therapy
of choice. The differentiation between AIT 1 and AIT 2 is essential for appropriate therapeutic choice.

Case Presentation: A 66-year old male was referred with abnormal thyroid function. He was treated with amiodarone after coronary artery bypass surgery. Three months after amiodarone treatment, he was found to have suppressed TSH of < 0.02 (0.34-5.60). 6 months later he again had low TSH of 0.27 with normal free T3 of 2.65 (2.50-3.90) and elevated free T4 of 1.53 (0.61-1.12). He denied chest pain, palpitation, dizziness, sweating, mood swings, and loss of appetite, nausea, vomiting or diarrhea. Physical exam was normal without the evidence of ophthalmopathy, dermopathy or proximal muscle weakness. There was no enlargement of thyroid gland.

Repeat Thyroid function test (TFT) showed suppressed TSH of 0.45 (0.47-4.6) with high normal Free T3 of 4.3 (2.8-5.3) and free T4 of 2.00 (0.78-2.1) with elevated thyroid stimulating immunoglobulin of 145. Because Radioactive iodine uptake imaging would be uninformative in the setting of iodide load from amiodarone, he underwent Tc99-sestamibi scan which showed increased uptake in the right lobe, most consistent with type 1 AIT. Amiodarone therapy was discontinued.

Conclusion: This case provides the evidence that MIBI scintigraphy can be employed to differentiate AIT 1 and AIT 2. Type 1 AIT is characterized by diffuse or nodular goiter with positive MIBI uptake. Whereas type 2 AIT is consistent with normal or slightly enlarged thyroid gland with either decreased or normal uptake on the TC-99 MIBI scan. This differentiation between 2 types is important clinically as the treatment for both condition are entirely different. Imaging modalities such as thyroid color flow Doppler sonography or thyroid radioactive iodine uptake cannot always effectively identify the type of AIT and hence are usually not very helpful to make the correct diagnosis. Recent literature shows that Tc 99-sestamibi scan could potentially be an easy and highly effective tool for differentiating between the two types of AIT and hence aid in the appropriate therapeutic choice.

Abstract #1049

THE CALM BEFORE THE STORM: A FATAL CASE OF SILENT NSTEMI MASQUERADING THYROID STORM

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Objective: Thyroid storm is a diagnostic and therapeutic challenge. We present a case of non-ST elevation myocardial infarction (NSTEMI) concealing thyroid storm resulting in a delay in treatment and leading to rapid clinical deterioration with a fatal outcome.

Case Presentation: A 76 year old female with a history of hypertension, Alzheimer’s dementia, and toxic multinodular goiter presented to the emergency department complaining of “chest pain”. Her son at the bedside stated she had nausea, decreased appetite and worsening confusion. Two months prior to this admission, outpatient labs indicated a TSH of 30.8 mIU/mL and free T4 of 0.30 ng/dl and methimazole was discontinued. She failed to follow up in clinic for reevaluation. Her home medications were Propanolol and Enalapril. Initial vital signs were blood pressure of 83/54, heart rate of 112, respiratory rate of 20, oxygen saturation of 95% on room air and a temperature of 96.9F. Pertinent physical examinations were notable for a comfortable appearing female, alert and oriented to person, non-palpable thyroid gland and tachycardia. An electrocardiogram showed sinus tachycardia with ST depressions in leads V3 and V4. Relevant labs were a troponin of 1.650 ng/mL, CKMB 1.5 ng/mL and treatment for NSTEMI was initiated. A late laboratory finding of TSH 0.03 mIU/mL, free T4 7.77 ng/dl, and free T3 >20pg/ml led to a diagnosis of thyroid storm. The Burch and Wartofsky score was 50, highly suggestive of thyroid storm. Propanolol and Methimazole were immediately ordered, however the patient rapidly deteriorated with the cardiac monitor showing pulseless ventricular tachycardia leading to a fatal outcome.

Discussion: Thyroid storm is a life-threatening condition with various manifestations making the diagnosis difficult to discern. This elderly patient with baseline dementia was a poor historian; furthermore, she did not present with the typical hyperkinetic symptoms. The apathetic presentation along with the diagnosis of NSTEMI masked the underlying thyroid storm. This caused a delay in her diagnosis and treatment, leading to a fatal outcome. Despite the diagnostic dilemma of identifying two life-threatening conditions with one disguising another, the Burch and Wartofsky scoring system proves to be a reliable clinical criteria for diagnosing thyroid storm in this case. Clinical suspicion of thyroid storm should remain high in the differential amongst patients with cardiovascular manifestations such as acute coronary syndrome in the setting of underlying thyroid disorder.

Conclusion: To our knowledge, after a literature review over the last 30 years, this is the first reported case of NSTEMI concealing a thyroid storm causing a fatal outcome.
Abstract #1050

AGRAVLANYCOTOSIS SECONDARY TO METHIMAZOLE COMPLICATED BY ACALCULOUS CHOLECYSTITIS AND ACUTE PANCREATITIS

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Makati Medical Center

Objective: To present a non surgical management of acalculous cholecystitis and pancreatitis in a hyperthyroid patient complicated by agranulocytosis secondary to methimazole intake. To illustrate dose administration of lithium carbonate in a patient with multiple history of drug allergy.

Case Presentation: 30 year old female, known hyperthyroid maintained on methimazole 5 mg/tablet OD, came in for fever with sore throat. Vital signs: Blood pressure: 120/70mmHg, Heart rate: 107 bpm Temperature 38.4, icteric sclera, exophthalmos, hyperemic tonsils, thyroid gland enlarged, right upper quadrant tenderness. Laboratories showed WBC 1.10 with ANC 22, TSH 0.01 uIU/ml FT4 43pmol/L, total bilirubin 5.26 mgdl direct bilirubin 4.43mgdl. MRCP showed gallbladder wall thickening and pericholecystic fluid. Started on propranolol 40mg every 6 hours, dexamethasone 2 mg IV every 6 hours. Referred to radiology for fluoroscopy guided cholecystostomy tube insertion. Fifth hospital day, lipase was elevated at 355 U/L from 40 U/L. Octreotide drip started. Seventh hospital day, WBC increased to 2.87 with segmenter 18. Lipase improved to 109 U/L. Diet resumed to clear liquids then slowly progressed. She was given nystatin swish and swallow due to oral thrush however noted anaphylaxis. Tenth hospital day, cholecystogram was done which revealed patent cystic duct. While injecting the contrast dye, patient again had anaphylaxis. Repeat FT4 32 from 25. With history of multiple allergic reaction(methimazole, nystatin, contrast dye), patient was referred to allergology service prior to starting lithium carbonate. Allergology started Desloratadine 5mg/tablet OD, Levocetirizine 5mg/tablet TID. Repeat FT4 at 22.294. She was discharged stable with Lithium carbonate 450mg/tablet ½ tablet BID, propranolol 10mg/tablet 1 tablet TID.

Conclusion: This case report elucidated a non surgical option for a patient with agranulocytosis and acalculous cholecystitis. In the course of management, it has shown a method of introducing a new drug in a patient with multiple history of allergy.

Abstract #1051

TRIIODOTHYRONINE THYROTOXICOSIS - A CASE REPORT

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Jos University Teaching Hospital

Objective: To present a case of triiodothyronine thyrotoxicosis.

Methods: A 67 year old man who presented with symptoms and signs of thyrotoxicosis and his management.

Case Presentation: A 67 year old man presented with palpitations, easy fatiguability, dyspnoea on exertion, heat intolerance, increased appetite, weight loss and increased frequency of normal bowel motions. There were no other significant symptoms. He had been diagnosed hypertensive ten years prior to presentation. Examination revealed an elderly man with bilateral proptosis, lid retraction, positive Von Graefe’s sign and Kocher’s sign, digital clubbing, moist palms but no neck mass. Pulse was 124/min and irregularly irregular, BP 160/100mmHg, heart sounds were normal. Examination of other systems was essentially normal, except for hyperreflexia. Investigations were normal except T3 9.7nmol/l, T4 68nmol/l with undetectable TSH. Electrocardiogram showed fibrillary waves, a rate of 110 per minute with normal axis and chambers. Echocardiogram showed normal chambers with irregularly irregular tachycardia, uniform cardiac contractility, normal wall thickness and chamber size. A diagnosis of triiodothyronine (T3) thyrotoxicosis was made. He was commenced on oral propranolol, carbimazole, digoxin, lisinopril, bendroflumethiazide and aspirin. Sixteen months later, thyroid function test results showed low T3 and T4 levels with elevated TSH. Carbimazole and Propranolol were therefore discontinued. Palpitations recurred after 19 months off thionamide and beta blocker. Thyroid function test showed elevated T4 and T3 with normal TSH level. Medications were recommenced and he has been clinically and biochemically stable since.

Discussion: Triiodothyronine(T3) thyrotoxicosis typically presents with symptoms and signs of thyrotoxicosis, it occurs in up to 10% of elderly patients, atrial fibrillation is a common presentation as was the case in this patient.
It may be the initial manifestation of Graves disease with thyroxine (T4) levels initially normal and later increasing in the course of the disease as occurred in this patient. Other causes of hyperthyroidism may present with T3 thyrotoxicosis. Treatment is with thionamides and beta blockers as required.

**Conclusion:** T3 thyrotoxicosis should be borne in mind in patients with typical features of thyrotoxicosis who have normal T4 and suppressed TSH levels.

**Abstract #1052**

**STARE**

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**Case Presentation:** A 60 year-old African-American male was admitted for elective coronary artery bypass graft, mitral valve repair, and tricuspid valve repair after a recent hospitalization for atrial fibrillation and non-ST elevation MI. On his sixth post-operative day, he was transferred to the intensive care unit for altered mental status, fever, and respiratory distress and was subsequently intubated. He underwent a computed tomography (CT) scan of the chest, abdomen, and pelvis with contrast which revealed no pulmonary embolism but with dilated small bowel loops. Two days later after receiving iodinated contrast from the CT scan, he was noted to have a suppressed TSH (<0.005 mIU/L) and a highly increased free, with levels ranging from 3.92 to 6.22 ng/dL (reference range: 0.76-1.46 ng/dL). He was clinically diagnosed to have thyroid storm and was treated with Propylthiouracil, Hydrocortisone, Lugol’s solution, and Metoprolol. He was subsequently extubated, transitioned to oral Methimazole, with resolution of his symptoms.

The patient is known to have Graves’ disease which was diagnosed a year prior to his hospital admission after he presented with unintentional weight loss of 30 pounds in a span of a year. His symptomatology, thyroid function tests (TFTs), thyroid ultrasound, and thyroid uptake and scan were consistent with Graves’ disease. His course was complicated by Graves’ orbitopathy and atrial fibrillation. His TFTs were fluctuating between hyper- and hypothyroid levels for which he was treated to and fro with Methimazole and Levothyroxine. Immediately prior to his most recent hospitalization, he was on Levothyroxine.

**Discussion:** Thyroid storm is manifested clinically with symptoms of thyrotoxicosis and occurs 0.2 per 100,000 per year in hospitalized patients. It has a high mortality rate of 10-30%. It is known to have been precipitated by acute events, including surgery, acute iodine load, trauma, and infection.

**Conclusion:** The cause of thyroid storm in this case is likely multifactorial - a combination of improper dosing of Methimazole and Levothyroxine during his outpatient course, stress from his surgery, and iodine load from the contrast he received from his CT scans. It is important to diagnose thyroid storm clinically early in its course as to prevent mortality among patients.

**Abstract #1053**

**STEROID-RESISTANT AND IVIG-RESPONSIVE RELAPSING HASHIMOTO’S ENCEPHALOPATHY: A CASE REPORT**

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**Objective:** Hashimoto’s Encephalopathy, an autoimmune, rare and underdiagnosed encephalitis, is steroid responsive and associated with autoimmune thyroiditis. It has a relapsing and remitting course, characterized by stroke like symptoms, seizures and slow progressive cognitive decline. Diagnosis is based on elevated levels of anti-thyroid peroxidase antibodies and exclusion of infectious, toxic and metabolic etiologies. We report a case of relapsing Hashimoto’s encephalopathy while being maintained on oral steroids.

**Case Presentation:** A 46 year old Caucasian male with history of seizure disorder, hypothyroidism and Hashimoto’s encephalopathy presented with postural instability, confusion, jerky movements of extremities and episodes of psychosis described as auditory hallucination. He was maintained on tapered oral prednisone for Hashimoto’s encephalopathy, initially diagnosed through CSF examination and elevated TPO antibodies. He was also on levothyroxine for hypothyroidism and levetiracetam for seizure prevention. On work-up, the patient was noted to have elevated thyroid peroxidase antibody at 945 IU/ml (0-60 IU/ml) and thyroglobulin antibody at 758 IU/ml (0-60 IU/ml), normal TSH at 3.7 uIU/ml (0.358-3.740 uIU/ml), free T3 at 2.8 pg/ml (2.2-4.0 pg/ml), free T4 at 0.86 ng/dl (0.76-1.46 ng/dl). CSF analysis did not show any signs of infection. The 24 hour screen for heavy metals was negative. Neuroendocrine syndrome and other paraneoplastic encephalopathies were ruled out, with normal levels of urine catecholamines, metanephrines and 5-HIAA, serum immunoglobulin A and glutamyl decarboxylase, voltage-gated calcium, anti-Ma1, anti-Ma2, VGKC and neuronal nuclear antibodies. No epileptiform discharges were recorded on EEG. Head CT and brain MRI did not show any acute intracranial abnormalities. Given the clinical and laboratory findings,
the patient was treated for relapsing Hashimoto’s encephalopathy with intravenous immunoglobulin (IVIG) for five days. There was notable improvement in the mental status, gait and balance during the course of treatment. The patient was discharged with improved neurological function.

**Conclusion:** Hashimoto’s Encephalopathy typically responds to steroids. Many patients remain disease free after discontinuation of steroids but those who relapse require either additional course, continuous treatment with steroids or immunomodulatory therapy to maintain remission. Although steroid therapy provides a favorable long-term prognosis, immunoglobulin therapy should be considered as an alternative treatment approach or rescue therapy, as it has been reported to be effective, safe and convenient in established cases of steroid-resistant Hashimoto’s encephalopathy.

**Abstract #1054**

**AMIODARONE-INDUCED HYPOTHYROIDISM PRESENTED WITH SEVERE DEPRESSION**

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**Case Presentation:** A 95-year-old Caucasian male was brought to the emergency department after a suicide attempt. Prior to presentation he had no documented history of depression. He continued to express suicidal thoughts during the interview with the psychiatrist. Initial vital signs were within normal limits. His TSH level was 73.7 IU/mL and FT4 was 0.2 ng/dL. 5 months earlier he was started on amiodarone for atrial fibrillation, at the time his TSH level was 3.2 IU/mL. After 10 hours from presentation, he was found to be obtunded with a temperature of 92.1 °F and heart rate of 40/min. Levothyroxine 150 mcg IV with hydrocortisone 50 mg IV were given to patient for the treatment of myxedema coma. 9-hours after the initiation of treatment the his temperature improved to 95.1 °F, his HR increased to 60/min, and his mental status was returned to baseline.

**Discussion:** Amiodarone is a di-iodinated benzofuran derivative, an effective antiarrhythmic drug. A common side effect of amiodarone is thyroid dysfunction which is due to its high iodine content and direct toxicity on the thyroid gland. Patients with underlying autoimmune thyroid disease are more likely to develop amiodarone-induced hypothyroidism (AIH). AIH typically occurs between 6-12 months after initiation of amiodarone. Patients with thyroid autoantibodies and elevated baseline TSH are at risk for developing AIH. Amiodarone is highly lipophilic, it accumulates in adipose tissue, muscle, and thyroid gland. Therefore, thyroid function should be monitored for at least a year after the drug is discontinued. Clinical manifestations of AIH are not different compared to those with hypothyroidism from any other cause. Less commonly, patients present with neuropsychological symptoms including confusion, depression and psychosis. As in any form of hypothyroidism, levothyroxine is the treatment of choice. Amiodarone is usually not discontinued unless it fails to control the underlying arrhythmia. However, if amiodarone is stopped, AIH in patients with no apparent preexisting thyroid disease often resolves. In contrast, it may persist in patients who have anti-TPO antibody.

**Conclusion:** This case highlights neuropsychiatric symptoms of hypothyroidism and emphasizes a cautious use of amiodarone is required in patients with a history of depression or in the elderly who are more susceptible to side effects. The North American Society of Pacing and Electrophysiology recommends TSH and T4 tests at baseline and then every 6 months. We suggest to include thyroid autoantibodies prior to initiation of amiodarone and to perform more frequent follow-up thyroid function test if they are at risk of developing AIH.

**Abstract #1055**

**IODINE-INDUCED HYPERTHYROIDISM AFTER CORONARY ANGIOGRAPHY: A CASE REPORT AND REVIEW OF LITERATURE**

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**Objective:** To describe a case of iodine induced hyperthyroidism in a previously euthyroid elderly patient with cardiovascular disease following coronary angiography.

**Methods:** Clinical case presentation and review of literature.

**Case Presentation:** A 69-year-old male with history of aortic stenosis presented to the hospital 10 days after coronary angiography due to shortness of breath and chest pain that interfered with his activity. He was found to have new atrial fibrillation with rapid ventricular rate. Thyroid function tests were: thyroid stimulating hormone (TSH) at 0.02mIU/L, free thyroxine (FT4) at 2.0ng/dL, and free triiodothyronine (FT3) at 6.0pg/dL. Thyroid stimulating immunoglobulin (TSI) was elevated at 4.8 and thyrotropin binding inhibitory immunoglobulin (TBI) was elevated at 3.89IU/L. Technetium 99 scan revealed rapid and homogenous uptake of tracer throughout the gland without nodularity consistent with diffuse toxic goiter, likely Grave’s disease.

**Discussion:** Iodinated contrast used for various radiologic
procedures including coronary angiography results in massive iodine exposure to thyroid gland that may be liberated as free iodide in the body. A typical dose of iodinated contrast medium contains about 13,500 μg of free iodide and 15–60 g of bound iodine. This represents an iodide load of 90 times to several hundred thousand times the recommended daily intake in an adult that can overwhelm thyroid hormone regulation. Administration of iodine to an individual with thyroid autonomy may lead to hypersecretion of thyroid hormone, known as Jod-Basedow phenomenon, first described by Coindet in 1821. Until 1972, it was thought that iodine induced hyperthyroidism occurred only in individuals living in iodine deficient regions. The prevalence was reported to be about 1.7% in iodine deficient areas. In 1974, Blum et al described a case with nontoxic nodular goiter from an iodine sufficient region. The risk is also higher in elderly population and individuals with underlying thyroid diseases and cardiovascular diseases. Our patient did not have any clinical signs or symptoms of thyroid disease prior to coronary angiography. He had high TSI and TBII, and Tc 99 uptake scan was suggestive of Grave’s disease. Our patient most likely had Jod Basedow phenomenon in the setting of previously unrecognized Grave’s disease.

**Conclusion:** Thyroid dysfunction is an independent risk factor for mortality and major cardiovascular events. Iodinated contrast medium used in various radiological and interventional procedures may further compromise the thyroid function in susceptible population. It is important for clinicians to be aware of iodine-induced hyperthyroidism to avoid life-threatening complications.

**Abstract #1056**

**ADENORCARCINOMA OF THE LUNG IN A PATIENT WITH RADIOIODINE REFRACTORY METASTATIC PAPILLARY THYROID CARCINOMA.**

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**Objective:** This is the case of a 66 year-old woman with known history of papillary thyroid cancer (PTC) with metastases to the lungs, who was later found to have a primary lung adenocarcinoma. It serves to illustrate challenges in diagnosing these patients.

**Case Presentation:** The patient, a former smoker, was initially treated for a pT2 pN0 M0 PTC with total thyroideotomy and 100millicuries (mCi) of I-131. Post-treatment whole body scan (WBS) was negative for distant iodide avid metastases. A recombinant human thyrotropin (rh-TSH)-stimulated WBS a year later was negative and the patient was maintained on a suppressive dose of levothyroxine. After a year of observation, her thyroglobulin (Tg) increased to 2.0 ng/mL (negative Tg antibodies). Her Tg increased to 4.5 ng/mL after rh-TSH, while the WBS remained negative. During the following year she was monitored with periodic neck ultrasound exams, one of which revealed enlarged lymph nodes in the right level IIa. She was advised to undergo biopsy and possible neck dissection but the patient opted for observation. She subsequently had a computerized tomography (CT) of the chest that revealed bilateral pulmonary nodules, the largest in the left lower lobe measuring 12x9mm. These findings were suspicious for pulmonary metastases from her known PTC. At that point, the decision was to treat with 175mCi of I-131 to attempt to treat or stabilize the lung. Post-treatment scan showed no uptake in lung nodules. A CT chest revealed that none of the nodules had changed in size and the largest nodule increased to 30x26 mm. The nodule was resected and found to be a stage IIIA primary adenocarcinoma of the lung. The tumor cells stained positive for TTF-1 and negative for thyroglobulin and calcitonin. The tumor was described as poorly differentiated, not resembling a thyroid cancer morphologically. The patient received adjuvant chemotherapy and external beam radiation.

**Discussion:** Only 2 to 10% of patients with PTC have metastases beyond the neck. Two-thirds have pulmonary metastases. It is even less common to find another primary cancer in conjunction with PTC. Since the lung is the most common site of metastasis, lung nodules are frequently thought to be thyroid of origin. However it is important to look at the whole picture. In our case, the patient had lung nodules with rising Tg, negative iodine uptake on WBS and progression of a single lung lesion after I-131. Lung biopsy was thus indicated at this point.

**Conclusion:** This case emphasizes the need to use cross sectional imaging in patients with negative radiiodine scan and elevated Tg. If a lesion does not respond to I-131, the possibility of a primary of the lung should be considered and addressed accordingly.
Abstract #1057

TIMING OF POSTOPERATIVE RADIOACTIVE IODINE ABLATION DOES NOT IMPACT OVERALL SURVIVAL IN HIGH RISK AND METASTATIC PAPILLARY THYROID CARCINOMA

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Objective: Postoperative radioactive (RAI) ablation is recommended in papillary thyroid carcinoma (PTC) with high-risk features and metastases. There is variability in the timing of RAI treatment with no consensus. Recent literature has recommended early RAI ablation after thyroidectomy. We herein report the largest retrospective analysis of the impact of the timing of RAI ablation on overall survival (OS) in PTC.

Methods: The National Cancer Data Base (NCDB) was queried for PTC from 1998-2006. Patients treated with near, subtotal or total thyroidectomy and had adjuvant RAI ablation were included. Patients were categorized as high-risk based on American Thyroid Association (ATA) criteria including tumor size (>4 cm), cervical lymph node involvement or grossly positive margins. Patients with distant metastatic disease were analyzed separately. Median, 5, and 10 year OS were calculated and Kaplan-Meier (KM) survival curves plotted. Univariate and multivariate Cox survival analyses were performed, adjusting for patient, socioeconomic, and tumor-related variables. Data analysis was performed with SPSS v. 22.

Results: There were 9727 patients in the high-risk group without metastatic cancer. Median and OS were similar regardless of the timing of RAI ablation. Median survival was calculated in relation to the timing of RAI for weekly and monthly time intervals over one year. This failed to demonstrate any survival difference at any time point (weekly P=0.208, monthly P=0.049). At a 3 month time point, there was no survival difference on KM (5 years OS 94.5% vs. 92.9%, 10 years OS 84.1% vs. 82.9%, P=0.045) or Cox multivariate analysis (HR 1.23, 95% CI 0.99-1.53, P=0.059). Delay in RAI ablation beyond 3 months did not affect OS in males (HR 1.20, 95% CI 0.96-1.50, P=0.117) or patients >45 years of age (HR 1.09, 95% CI 0.93-1.26, P=0.245). There were 205 patients with distant metastatic PTC who received postoperative RAI. In these patients timing of RAI ablation did not affect median and OS treated within or beyond 3 months (HR 0.96, 95% CI 0.40-2.28, P=0.918).

Discussion: ATA guidelines recommend adjuvant RAI ablation in high-risk and metastatic PTC. Early RAI administration within 3 months is considered important in these patients although no conclusive evidence supports such a cutoff. Higashi et al. showed a decreased disease specific survival in metastatic PTC patients with delay in RAI ablation beyond 6 months. In this large retrospective analysis based on NCDB, there was no survival benefit of the timing of adjuvant RAI in high risk and metastatic PTC patients.

Conclusion: The timing of postoperative RAI ablation does not seem to influence OS in patients with high-risk or distant metastatic PTC.

Abstract #1058

EIGHT YEAR FOLLOW-UP OF 378 CONSECUTIVE LOW-INTERMEDIATE RISK DIFFERENTIATED THYROID CANCER PATIENTS WITHOUT I131 ABLATION IN A COMMUNITY BASED SETTING.

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UTHSCSA

Objectives: There is significant controversy surrounding use of I131 ablation in low risk patients with differentiated thyroid cancer (DTC). Although ATA guidelines recommend judicial use of I131 in low-risk patients, most low-risk patients continue to receive I131. The object of this study is to demonstrate the utility of two week post-operative non-suppressed thyroglobulin (2wPONSTg) to determine observation instead of I131 use in low risk patients.

Methods: From 2005-2012, 451 patients with DTC were stratified into low, intermediate and high risk categories of recurrence. After outliers were removed, the remaining 378 patients: F/M-268/110, ages 18-79, age 18 to 79, tumor size 0.8mm-4.0cm. 21 patients <45y had lymph node metastasis <5mm, and 34% were multifocal. Careful central neck inspection or dissection was recommended for prognostication selectively based on pre-op ultrasound, BRAF positive status or age >45 years. If the 2wPONSTg was <2ng/ml, LT4 was started and I131 deferred. If Tg >2 but <5 patients were evaluated for possible residual disease. Suppressed Tg was performed at 3, 6, 9 months, then at 6 month intervals. Neck surveillance ultrasound (US) was performed at six months post-op and not again unless Tg elevated. TSH was suppressed to <0.5 year one, then relaxed to <2 for low risk patients.

Results: 378 patients had Tg <2 and opted for no I131 ablation. Surgical complications were 1.9% transient RLN effect and <2% transient hypoparathyroidism. During eight years follow up from 2006 to 2013 no patients requested I131 ablation and 72% of cases developed undetectable Tg over a period of two years. Those who
have remained detectable have remained stable with the thyroglobulin velocity <10% increase over five years. No recurrence has been observed.

**Discussion:** A 2wPONSTg <2 ng/ml, in low-intermediate risk patients, increases confidence in conservative use of I 131 per ATA guidelines. This reduces the morbidity associated with I131 without increasing mortality or recurrence. There was low morbidity associated with no LT4 use two weeks post-op and a non-suppressed Tg allows for prognostication regarding residual thyroid remnant as well as possible micro metastasis. Using a 2wPONSTg cut off of <2, allows one to safe avoidance of immediate I131 and allow for natural Tg decline over time. Excellent surgical dissection remains the most important variable in treating DTC.

**Conclusion:** In a community setting, low and intermediate, stage I and II patients, can be managed safely and effectively without I131 using a 2wPONSTg <2ng/ml. This further supports the conservative management set forth in the ATA guidelines.

**Abstract #1059**

**TIMING OF LEVOTHYROXINE IN THE TREATMENT OF PRIMARY HYPOTHYROIDISM**

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**Objective:** In patients with hypothyroidism a proper timing of levothyroxine administration could have a beneficial effect in early obtaining euthyroid state. This approach to treatment is based on the fact that thyrotropin (TSH) is one of the biological substances that is subjected to circadian rhythm. This study aimed at investigating the best time for levothyroxine administration to patients with primary hypothyroidism that can achieve earlier normalization of TSH and free thyroxine (FT 4).

**Methods:** From November 2012 to July 2013 one hundred and eight patients with primary hypothyroidism were enrolled for this prospective, randomized study from Al-Faiha Diabetes Endocrine and Metabolism Center in Basrah (FDEMC), Southern Iraq. Patients were divided in to two groups; the first group (morning group), were instructed to take levothyroxine one hour before breakfast. The second group (evening group), patients took the dose of levothyroxine at bedtime, 2 hours after the last meal. The blood pressure, body mass index, TSH, FT 4, lipid profile, were measured before starting the study, and at each month over three month (the study period).

**Results:** Eighty two patients had completed the study. The mean difference of reduction in TSH from baseline for the two groups was compared (11.3±22.5 mIU/l for the morning group vs 13.6±22.2 mIU/l for evening group). Although, it was higher for the evening group but it was not statistically significantly different from that of the morning group( P=0.63, df =80, 95% CI: -12.17- 7.5). Comparing the difference of increase in FT 4 for morning and that of the evening group (7.6±6 pmol/l for morning vs 5.7±4.9 pmol/l for evening ) pmol/l revealed no significant differences between the two( P=0.12, df=80, 95% CI: - 0.5-4.3).

**Conclusion:** We concluded that there was no difference between the morning and evening levotyroxine intake in regards to earlier normalization of TSH and FT 4.

**Abstract #1060**

**PRIMARY HYPOTHYROIDISM IN A PATIENT WITH IRRITABLE BOWEL SYNDROME (IBS): A CASE REPORT**

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**Objective:** To present a patient with irritable bowel syndrome (IBS) in whom thyroid function tests revealed primary hypothyroidism.

**Methods:** Clinical features and laboratory data are presented followed by a discussion of the pertinent findings.

**Case Presentation:** A 38-year-old Bangladeshi male presented with a 10-year history of intermittent, alternating episodes of non-bloody diarrhea and constipation that were associated with nausea, bloating, dyspepsia and cramping in the lower abdomen that was relieved after defecation. He denied having melaena, hematemesis or nocturnal bowel movements. There was no association between the bowel pattern and diet. Despite these symptoms his weight remained stable. Thyroid gland was not enlarged/ palpable & tendon reflex was not delayed. Colonoscopy and upper GI endoscopy revealed no sign of inflammation. Routine blood tests including CBC, renal function, electrolytes, calcium, albumin, Vitamin D, Vitamin B12, anti-transglutaminase, blood glucose and liver function were normal. Stool R/E & Occult blood test were normal. Given the patient’s stooling pattern, thyroid function tests were measured in order to exclude hyperthyroidism, but paradoxically revealed primary hypothyroidism: TSH 13 mIU/L [0.4-4.5], FT4 7.2 pmol/L [11.8-24.6] and FT3 2.16 pmol/L [2.8-7.1]. TSH was repeated and was persistently elevated at 15.5mIU/L. The patient started oral levothyroxine 50 μg daily. Follow up
visit after 12 weeks revealed improvement of both clinical (e.g. hyperdefecation, nausea, bloating) and biochemical variables, with a TSH of 5.3mIU/L.

**Discussion:** Symptoms related to IBS, including hyperdefecation, warrant an evaluation for hyperthyroidism. Our patient was found, surprisingly, to have primary hypothyroidism. To date no literature found describing association between IBS and hypothyroidism. His clinical symptoms improved with levothyroxine replacement therapy.

**Conclusion:** Primary hypothyroidism may co-exist with irritable bowel syndrome.

**Abstract #1061**

**CRIBRIFORM-MORULAR VARIANT THYROID CANCER(C-MV TC): CLINICAL, HISTOPATHOLOGICAL AND GENETIC FEATURES.**

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King Faisal Specialist Hospital & Research Center

**Objective:** Herein are presented 2 cases of C-MV TC; a sporadic case, & another one harboring genetic mutation in familial adenomatous polyposis (FAP) gene. The latter case presented a unique & first indication to work up for an underlying FAP syndrome. .

**Methods:** C-MV was diagnosed using histopathology and immunostaining of resected thyroid tumor for beta-catenin. Genetic analysis for APC gene was done, & colonoscopy was done/planned.

**Case Presentation:** Pt A: 34 yrs. old female had total thyroidectomy (TT). The resected tumor was 6.5 cm lt. lobe C-MV variant PTC, w/ focal lympho-vascular invasion (PTNM: PT3N0Mx). Immunostain was positive for beta-catenin. She received I 131 for thyroid remnant, had no evidence of extrathyroidal metastases. She had mutation in APC gene. It involved exon 15 deletion at C.3202-3205 del TCAA. She is scheduled for colonoscopy & family counselling.

Pt B: A 54 yrs. old lady had TT. Tumor was large 9 cm lt. lobe C-MVPTC, w/ lympho-vascular invasion, & large multiple bilateral metastatic lymph nodes (PT3, N1b, Mx). Immunostain was negative for beta catenin. She had I131 for thyroid remnant & pulmonary metastases. She is in remission at 42 months FU. She had no mutation in APC gene, & had resection of a sporadic tubular adenoma of low grade atypia.

**Discussion:** C-MV of PTC exhibits striking female prevalence & indolent course. It carries a better prognosis than other variants of PTC.

FAP harbor germline mutation in APC gene. APC gene encodes tumor-suppressor protein. Defects in this gene predisposes to FAP, a pre-malignant condition that usually progresses to malignancy. CMV-PTC may present before colonic manifestations are apparent. Conversely, screening for TC must be done in all patients w/ FAP & in those w/ a FAP proband in family. 

**Conclusion:** C-MV of PTC is a rare morphologic entity, is usually associated with FAP, & may provide first indication of an underlying FAP syndrome. Mutation in APC gene & family counselling should be undertaken.

**Abstract #1062**

**SICKER THAN A DOG: ACCIDENTAL THYROTOXICOSIS FROM INGESTING PET’S MEDICATIONS.**

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**Objective:** A 66-year old Caucasian female with Hashimoto’s thyroiditis and hypothyroidism, stable with a levothyroxine replacement dosage of 100 mcg/d underwent meningioma resection referred from psychiatrist’s office for severely depressed TSH levels. She presented with new symptoms of weight loss of 20 lbs, anxiety, lower extremity edema since her surgery.

**Case Presentation:** Repeat thyroid stimulating hormone was undetectable. Her vitals on admission were normal. On physical exam, no exophthalmos, or enlarged goiter or tenderness of thyroid gland. Upon admission, TSH was < 0.01 (normal 0.45-4.5), T4 7.5 (normal 0.8-1.7), T3 393 (normal 80-200), free T3 19.6 (normal 2-4.8), TSI < 89, thyroglobulin level 22, thyroglobulin ab < 20, antimicrosomal antibody < 10. Also, of note she had leucopenia with WBC of 2.5 (normal 4-11) on admission. Patient also underwent imaging with CT angio for her
moodiness of hyperthyroidism including palpitations, anxiety and tremors. The TSH was 0.07 uIU/mL (0.34-5.60 uIU/mL), free T4 of 3.30 ng/dl (0.60-1.10 ng/dl), free T3 of 9.80 ng/dl (2.50-3.90 ng/dl), thyroglobulin Ab of 448.3 U/Ml (0.0-4.1 U/Ml), TPO (microsomal Ab) >1000.0 IU/Ml (0.0-5.6 IU/ Ml). A markedly decreased thyroid uptake of 0.2% (normal range 10 to 30%) on a nuclear medicine scan was suggestive of the diagnosis of subacute thyroiditis. Several months later, his labs revealed TSH of 5.73, free T4 of 0.80, free T3 of 3.30, thyroglobulin Ab of 521.1, TPO of >1000.0 consistent with the hypothyroid phase of thyroiditis. Three years later, following the birth of his daughter, the patient presented with a similar clinical presentation and a suppressed TSH (0.08), elevated free T4 (2.04), elevated free T3 (6.0), thyroglobulin Ab (333.1), TPO of >1000. These TFTs were consistent with recurrent, post-partum, thyroiditis.

**Discussion:** The diagnosis of thyroiditis was confirmed by low radioactive iodine uptake scan, elevated TFTs, positive anti-thyroid antibodies and all three episodes occurring within one year of his wife’s late termination of pregnancy and subsequent two normal deliveries. In addition, the illness followed the typical time course of subacute thyroiditis: hyperthyroidism, followed by euthyroidism, a late hypothyroid phase and then a complete resolution of symptoms and normalization of thyroid function tests over a several month period. Previous reports have demonstrated evidence of a strong correlation between hormonal, physical or symptomatic changes in males and females post-partum although none have specifically addressed thyroid hormones. Literature reviewed demonstrates change of various hormones in paternal males that appear to make evolutionary sense as they increase bonding and paternal responsiveness.

**Conclusion:** To our knowledge, this is the first case report of a recurrent, possibly sympathetic post-partum thyroiditis in a male. Anxiety, palpitations, weight loss and tremors in new fathers should prompt a workup for sympathetic thyroiditis.

**Abstract #1064**

**THE CONFOUNING EFFECT OF MULTIPLE CO-EXISTING ENDOCRINOPATHIES THAT MAY EFFECT FREE WATER CLEARANCE ON WEIGHT FLUCTUATION**

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**Objective:** To describe the effect on weight gain or loss of idiopathic orthostatic edema and/or thyrotoxicosis in a female with panhypopituitarism and diabetes insipidus that followed...
surgery and subsequent radiotherapy for an optic glioma. 

**Methods:** A 29 year old girl taking hydrocortisone 10mg 2x/day and levo-thyroxin 50 mcg/day noticed a weight gain from 110 pounds to 168 pounds despite no change in eating habits, increased exercise and serum thyroid and cortisol levels that were in the normal range. Her mild diabetes insipitus had been controlled with intermittent use of low dosage DD arginine vasopressin. An increase in capillary permeability leading to movement of fluid from intravascular to extravascular space related to decreased sympathetic tone was suspected. Thus she was started on the sympathomimetic amine dextroamphetamine sulfate. At the age of 56 she developed Grave’s disease and became hyperthyroid.

**Case Presentation:** On 10mg extended release capsules of dextroamphetamine sulfate over 8 months she returned to her weight of 110 pounds. She remained stable on 20mg dextroamphetamine sulfate until age 55 when she gained 18 pounds in one weeks. She had gradually gained some weight over the years so her total was now 150 pounds. Her dosage of dextroamphetamine sulfate was increased to 30mg and she lost weight to 125 pounds over 2 months. Eventually her weight was maintained despite reducing the dosage of amphetamine to 15mg. More than a year later her weight decreased suddenly down to 102 pounds. Her dextroamphetamine sulfate was reduced to 10mg extended release capsules but her weight did not increase. She was found to have increased serum free thyroxin levels with decreased thyroid stimulating hormone levels (checked three times on different days). Treatment with methimazole returned her weight to 114 pounds. She remains on dextroamphetamine sulfate and her thyroid is now in remission and she no longer takes methimazole.

**Discussion:** This woman had developed the syndrome now called the sympathetic neural hyperalgesia edema syndrome which generally responds very well to dextroamphetamine sulfate. She only had the edema part and no pain syndromes. It is unusual to show such rapid weight loss with only mild thyrotoxiosis.

**Conclusion:** Possibly deficiency of the arginine vasopressin hormone allows a more profound effect of sympathomimetic amines in free water clearance explaining the quick weight loss of water with dextroamphetamine treatment or exposure to mild thyrotoxiosis.

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**Abstract #1065**

**TECHNETIUM 99M SESTAMIBI SCINTIGRAPHY STEAL: “PARATHYROID STEAL” BY PAPILLARY THYROID CANCER .

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**Objective:** We present a case of coexisting parathyroid adenoma (PA) and papillary thyroid cancer (PTC) wherein preferential uptake of sestamibi was evident in PTC only; following resection of PTC uptake of radiotracer by PA was unmasked. The case highlights false positive findings with diagnostic and therapeutic implications.

**Methods:** Sestamibi scan, serum ca++, PTH, Vitamin D, US & FNA thyroid, thyroidectomy, resection of PA, and histopathogy.

**Case Presentation:** A 76-yr. old female was diagnosed as a case of primary hyperparathyroidism based on the following lab findings: serum Calcium (Ca) 2.6 mmol/L (RR: 2.1-2.6 mmol/L) ,Phosphorus 1.0 mmo/L (0.9-1.5 mmol/L), PTH 355 ng/L (15-65 ng/L) and vitamin D 80 nmol/L ( optimal level 62-199 nmol/L). Sestamibi scan showed localized avid uptake in Lt. lower neck that was thought to represent Lt. inferior PA. Thyroid US & FNA both showed Lt. thyroid nodule suspicious of malignancy. Pt. underwent total thyroidectomy in addition to resection of 2Lt. parathyroid glands. Intra-operatively PTH did not drop. Histology confirmed Lt. thyroid PTC, & normal parathyroid glands. Post operatively hypercalcemia ( ca 4.0 mmol/l) & high PTH (165 ng/L) persisted. Follow up sestamibi scan revealed new focus of radiotracer in RT. lower neck that was removed & was confirmed histologically as PA. FU data: remission of PA; serum Ca 2.1 mmol/l, PTH 71 ng/ & vitamin D was 51 nmol/l.

**Discussion:** Preoperative imaging localization of parathyroid adenoma is mandatory. Of the available imaging modalities Sestamibi scintigraphy has highest positive predictive value. However, our case highlights important false positive findings in a pt. with concomitant PTC. 99mTc-sestamibi is taken up by the mitochondria in both thyroid & parathyroid tissue; however, radiotracer is taken up & retained preferentially by mitochondria-rich oxyphil cells in parathyroid glands. These features are applied to advantage in planar imaging protocol. The findings in our case indicated that radiolabelled technetium was shunted and pooled into PTC, thus depriving PA from concentrating radiotracer. We would consider this phenomenon as “sestamibi scan steal phenomenon”. Since thyroid tissue also takes up sestamibi, it can set up potential competition against parathyroid gland for
radiotracer uptake. Indeed, although rare, sestamibi uptake by thyroid adenoma and PTC with coexisting PA has been described. Furthermore, non-competitive uptake of sestamibi by both PA and PTC with “lightening” of both glands was also reported.

**Conclusion:** Thyroid cancer can masquerade as parathyroid adenoma on technetium 99m sestamibi scintigraphy. Recognition of this false positive finding has implications in diagnosis and management of parathyroid adenoma.

**Abstract #1066**

**HYPERTHYROIDISM WITH HEPATITIS IN THE SETTING OF UNDIAGNOSED ADRENAL INSUFFICIENCY**

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**Objective:** We report two cases of hyperthyroidism and hepatitis in which adrenal insufficiency was diagnosed and treated with resolution of transaminase elevation and improvement of thyroid disease.

**Case Presentation:** Case One: 35-year old woman presented with fatigue. Vitals: P 138, RR 25, BP 105/71, and T of 36.6 C. She was alert, oriented and in no distress. Exam showed icterus, and brisk tendon reflexes. TSH undetectable, FreeT4>7ng/dL (0.78-2.20), T3:643 (97-170) and LFTs>2000 U/L (AST <40; ALT<51). CT body with contrast showed thymus hyperplasia and no adrenal masses. Metoprolol was started; thionamides were initially held because of elevated transaminases. Thyroid scan/uptake were deferred due to recent study with iodinated dye. Adrenal reserve was assessed: cortisol level 1-hour after 250 mcg ACTH was 13.3ug/dL (≥ 20), confirming adrenal insufficiency. High dose hydrocortisone was started with quick improvement of mental status and hemodynamics. Free T 4 had decreased to 2.16 ng/dL (0.78-2.2) prior to discharge.

**Discussion:** Hypocortisolemia may precipitate hyperimmunity causing severe decompensation of autoimmune thyroid disease and concomitant elevation of hepatic transaminases. Treatment of adrenal insufficiency led to clinical improvement and, by improving liver function, facilitated treatment with thionamides.

**Conclusion:** It is important to evaluate adrenal reserve in patients with hyperthyroidism, particularly in the presence of liver enzyme elevation. Treatment of adrenal insufficiency helps achieve clinical stability and facilitates the implementation of appropriate treatment of hyperthyroidism.

**Abstract #1067**

**MUSCLE PARALYSIS IN THYROTOXICOSIS – A CASE REPORT**

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**Objective:** Thyrotoxic periodic paralysis (TPP) is a condition characterized by muscle paralysis due to hypokalemia secondary to thyrotoxicosis. We want to disseminate the knowledge amongst medical community for TPP where definitive treatment is possible.

**Methods:** We describe a case of young Pakistani man who was already under treatment for thyrotoxicosis and developed TPP.

**Case Presentation:** 31 year old male with no known comorbs presented in Endocrine Clinic with complaint of difficulty in breathing, palpitations and weight loss for last one month. On examination there was a small diffuse goiter and there were tremors on outstretched hands. His TSH was <0.005 uIU/mL (0.4-4.2 uIU/mL) and FT4 was 6.46 ng/dl (0.93-1.7 ng/dl). Initial provisional diagnosis of Graves’ Hyperthyroidism was made. Carbimazole 30mg per day along with propranolol 10mg three times daily was started. Three months after initial presentation, patient presented in the emergency room (ER) with complaint of severe muscle pain and inability to stand. Lab results revealed hypokalemia {Serum Potassium 1.8 mmol/L (3.5-5.1 mmol/L)}. All the symptoms reverted back on administration of IV potassium in next few hours. A diagnosis of Graves’ Hyperthyroidism was made. Carbimazole 30mg per day along with propranolol 10mg three times daily was started. Three months after initial presentation, patient presented in the emergency room (ER) with complaint of severe muscle pain and inability to stand. Lab results revealed hypokalemia {Serum Potassium 1.8 mmol/L (3.5-5.1 mmol/L)}. All the symptoms reverted back on administration of IV potassium in next few hours. A diagnosis of Hypokalemic Periodic Paralysis was made in the ER. A week later he came for follow-up at Endocrine clinic with complaint of pain in legs. Diagnosis of Thyrotoxic Periodic Paralysis due to Graves’ Disease was made. Dose of Propranolol was increased to...
40mg three times daily and Carbimazole was continued. He did not experience further attacks of paralysis. Once euthyroid, RAI-131 ablation therapy (15 mci) was done as definitive therapy after patient’s agreement. Patient developed Post RAI ablation hypothyroidism and is doing well on levothyroxine replacement.

**Discussion:** TPP usually affects males of Asian origin. Dysfunction of Na/K-ATPase pump causes hypokalemia and is responsible for the muscle symptoms. It needs to be distinguished from other forms of periodic paralysis. In our case the absence of a family history of muscle paralysis, predominance of male sex and deranged thyroid function tests strongly favored a diagnosis of TPP. Proximal muscles are affected more than distal muscles. Most commonly attack is triggered by a carbohydrate rich meal or while resting after exercise. Potassium supplementation and nonselective beta-blockade can help revert muscle symptoms and prevent cardiac arrhythmias. Definitive treatment of Graves’s Disease prevents further attacks of TPP.

**Conclusion:** TPP can easily be misdiagnosed because of its rare prevalence if competent clinical correlation is not made. To prevent further attacks of TPP, definitive therapy of Graves’ disease by either surgery or radioactive iodine is needed.

**Abstract #1068**

PAPILLARY THYROID CANCER ASSOCIATED WITH AN INSULAR CARCINOMA IN A WOMAN OF 67 YEARS WITH HIP FRACTURE

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**Objective:** To report a case of Poorly Differentiated thyroid carcinoma (PDTC, insular carcinoma) associated with papillary thyroid carcinoma (PTC).

**Methods:** We report the clinical and paraclinical characteristics of a patient with coexistence of PTC and PDCT debuting with a pathological hip fracture.

**Case Presentation:** Female, 67 years old. Refer to 01 years before admission condition starts with local pain in right hip, not associated with trauma; also has tumor 2x2cm scalp. Diagnosed “pathologic fracture”; node biopsy pathology scalp: metastases of unknown primary; Body CT: multiple metastases (lung, liver, brain, kidney, adrenal), then loses contact with health services; 05 months after entering emergency back pain and dysphagia, pathology review: moderately differentiated adenocarcinoma metastatic TTF-1 (+), thyroid ultrasound: RTL 40x17x14mm, 14x9mm nodule with irregular borders circular calcification hypoechoic nodule 5x4mm and 8x7mm; LTL: 57x31x42mm, 43x27mm heterogeneous nodule with irregular borders partially calcified; 7mm isthmus; FNA: suggestive of insular thyroid carcinoma; Tg> 300ng / dl, Calcitonin <2 pg / ml. She received cranial radiation and right femur. Total thyroidectomy was performed, pathology: RTL: PCT follicular variety (90%) and classical (10%), lymphatic tumor microemboli, infiltrates the capsule and extending into the soft tissues. LTL: PDCT (island pattern), infiltrates the capsule, extends to adjacent tissue. She received 150mCi of radioiodine therapy, her the TBS post was positive only in neck.

**Discussion:** Thyroid cancer is the most common endocrine malignancy. The PCT represents 80% of all thyroid cancers, whereas the PDCT represents <5%, both more common in women. The PDCT occur at older ages (54 vs. 36a); are d emayor size at diagnosis, and more frequently and have metastases (26 vs. 2%). PDCT was histologically defined by grouping cells that form islet follicular and usually exhibit central necrosis foci. PDCT cells are uniformly small in both nuclear and cytoplasmic size, with prominent nucleoli and finely granular chromatin. Mitosis are scarce.

**Conclusion:** PDCT treatment is similar to the DCT: surgery, radioiodine and LT4 suppression therapy; should be emphasized that have lower response to radioiodine that the PCT. The patients suffering PDCT have a worse prognosis than those with DCT, due to a higher rate of recurrence and increased mortality.

**Abstract #1069**

COEXISTENCE OF PAPILLARY THYROID CARCINOMA AND MEDULLARY THYROID CARCINOMA IN A WOMAN OF 56 YEARS

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**Objective:** To report a rare case of association of papillary thyroid carcinoma (PTC) and medullary thyroid carcinoma (MTC).

**Methods:** We report the clinical and paraclinical characteristics of a patient with coexistence of PTC and PDCT debuting with a pathological hip fracture.

**Case Presentation:** Female, 58 yo, attended the clinic of Endocrinology, with a time of 12 months disease, referring anterior cervical volume increase associated with dysphagia and dysphonia. History of thyroid cancer sister and father. Analysis: TSH: 1.66uUI / ml; AbTPO / TgAb (-) Calcitonin: 23.8pg / ml (VN: <11). Thyroid ultrasound: RTL 42.2x16.2x13.3 mm hypoechoic nodule with
10.7x9.6 mm in the middle third. LTL 41.7x12.2x12.4 mm volume decreased slightly heterogeneous echogenicity with 6.7x4.6 mm nodule in the upper pole. FNA of nodule RTL: PTC. She underwent total thyroidectomy whose pathological evaluation reported: RTL: PTC classic variant with dystrophic calcification, diameter: 11mm, partially encapsulated, absence of vascular, lymphatic and perineural embolism. thyroid capsule: no infiltration. LTL: MTC of 7x5 mm, nodular pattern. IHC: Calcitonin(+). RET mutational study: not available.

Discussion: PTC is the most common type of thyroid cancers, constituting about 70% to 80% of all cases. Tends to grow slowly and spread to lymph nodes in the neck, usually has a favorable prognosis. On the other hand, MTC, is responsible for 5% to 10% of thyroid cancers, can be sporadic or often part of multiple endocrine neoplasia type 2, are worse prognosis due to their great potential for hematogenous metastases. Recent studies have shown that the RET protooncogene would be involved in oncogenesis carcinomas both the enzyme tyrosine kinase activation either by point mutations of its receptor (medullary thyroid carcinoma associated to MEN2) or gene rearrangement (PTC).

Conclusion: The association of PTC and MTC is not common; in literature describing more than 20 cases.

Abstract #1071

MALIGNANT CARDIAC SALVOES IN A CASE OF SUBCLINICAL HYPERTHYROIDISM UNRAVELLED BY A THERAPEUTIC FIASCO; THE NEED FOR THE ENDOCRINOLOGIST CARE

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Objective: Clinical Case Report.

Methods: A 25 year lady with hypothyroidism since 2004 was admitted to hospital with a history of worsening palpitations following minor accidental overdose of thyroxine tablets. She was normally on 125 mcg/day. She had taken tablets of 100 mcg on three successive days instead of 25 mcg. Initial ECG was suggestive of SVT but cardiac monitoring showed further arrhythmia with a more malignant appearance, suggestive of Ventricular Tachycardia. She was treated conservatively with beta blockers, thyroxine was omitted for one week.
Echocardiography was normal. On reviewing her TFT series over the preceding years she showed evidence of subclinical hyperthyroidism.

**Case Presentation:** Malignant dysrhythmias subsided following omission of thyroxine for one week and remained symptom free. Thyroxine was recommenced at a reduced dose of 50 mcg and patient was followed up at short intervals in clinic and the dose was adjusted. Subsequent cardiac electrophysiological studies confirmed an aberrant cardiac conduction pathway. Patient was booked for radiofrequency ablation. She remained euthyroid and symptom free.

**Discussion:** Subclinical thyrotoxicosis is well known to be associated with increased risk of severe morbidity, including risk for cardiac dysrhythmia. Occult aberrant cardiac conduction pathway may prove to be fatal if triggered by hyperthyroxinaemia. Our patient had a chronic history of cardiac symptoms which were undoubtedly brought on the surface by her subclinical hyperthyroidism. The accidental minor overdose brought her problem to the fore for the medical attention. Her case argues for better management of cases of primary hypothyroidism by primary care physician and the need for early referral for cases which are poorly controlled especially those with symptoms.

**Conclusion:** Patients with iatrogenic subclinical hyperthyroidism should be referred early for the endocrinologist care especially if they have florid symptoms of ongoing morbidity and failure to achieve this may result in unnecessary mortality.

**Abstract #1072**

**CLINICAL AND BIOCHEMICAL CHARACTERISTICS OF PATIENTS WITH THYROTOXIC PERIODIC PARALYSIS IN A NATIONAL HOSPITAL OF LIMA-PERU FROM 2011 TO 2014**

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**Objective:** To describe the clinical and biochemical features of PPT in patients treated at the HNERM-Lima-Peru in the period 2011-2014.

**Methods:** In patients with thyrotoxicosis treated at the Department of Endocrinology (HNERM) in the period July 2011-June 2014, we selected those who had the triad: flaccid paralysis, signs of thyrotoxicosis and hypokalemia during paralytic crisis. The study design was descriptive, cross-sectional, retrospective review of medical records by. Clinical and paraclinical characteristics of these patients are described.

**Case Presentation:** In 410 patients with hyperthyroidism, 8 patients with PPT were detected (2 cases/100 patient throughput). The mean age at diagnosis was 38.4 yo (range: 31-47), 100% were male, 25% were born in departments known iodine deficiency and 50% had a family history of thyroid disease. As precipitating factors, 75% had food (copious consumption of high calorie foods or high sugar content) and 50% had physical (strenuous physical activity). The average time from the start occurrence of hyperthyroidism was 2.8 mo (range 0.1-8.0 mo). The predominant motor pattern was paraplegia (63%), followed by tetraparesis (25%) and paraparesis (12%), and one case was presented cardiopulmonary arrest, without further consequences. The mean duration of episodes was 2.7hs (range 0.5-8 hs); 50% occurred in the early hours of the morning and the rest overnight. The average was kalemia 2.5mEq/L (range: 1.4-3.5mEq/L). Finally thyrotoxicosis etiology was 87.5% due to Graves disease whose degree of intensity was severe in 62.5%, moderate and mild in 25% in 12.5%.

**Discussion:** The PPT could be related to mutations in the potassium channel Kir 2.6; It is a pathological entity that requires rapid diagnosis, because although it is reversible, calls for emergency treatment the mortality risk associated with cardiac complications. Although it is rare that the paralysis is revealed as an initial symptom of hyperthyroidism should be suspected in any patient PPT young male presented with symptoms of paralysis associated with low serum potassium levels, even without symptoms or nasal mucus of hyperthyroidism. The experience of the physician to detect subtle signs of hyperthyroidism, such as anxiety, tremor and tachycardia, will be essential to guide the diagnosis.

**Conclusion:** Two out of every 100 patients treated with hyperthyroidism presented PPT. Occurring in men between 30 and 50 years within the first eight months of diagnosis of hyperthyroidism, occurring predominantly as paraplegia less than 8 hours.

**Abstract #1073**

**PAPILLARY THYROID CARCINOMA WITH PULMONARY METASTASIS IN A WOMAN WITH SYSTEMIC AMYLOIDOSIS AND AMYLOID GOITER**

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**Objective:** To report a case of papillary thyroid carcinoma (PTC) in the context of amyloid goiter (AG) in a patient with systemic amyloidosis (SA).

**Methods:** Clinical and paraclinical characteristics of a patient with SA and PTC are presented.

**Case Presentation:** Women, 43 yo, admitted for emergency, by accentuating clinical picture 8 mo of...
evolution characterized by foamy urine and anasarca.
Analysis: Proteinuria 24h: 7.33g/d. Albumin: 1.36g/dl.
Hb: 13.3. Creatinine: 1.29mg%. Bence Jones in urine (+).
BMA: 16% plasma cells. Hematology: Multiple Myeloma + amyloidosis, initiating chemotherapy with partial response evidenced by decreased levels of proteinuria but with renal impairment (creatinine clearance: 33ml/min) and heart checked (Echocardiogram: restrictive filling pattern moderate concentric hypertrophy LV with areas suggestive septum level of infiltration). CT: reported as moderate bilateral pleural effusion. Diffuse interstitial thickening with bilateral pulmonary nodular opacities less than 1cm. Thyroid ultrasound: LTL: 33x17x11mm, RTL: 45x39x31mm isoechogenic nodular formations 24, 17, 13 and 7mm; scattered microcalcifications, 3mm isthmus. Superior cervical ganglia chain morphology preserved and bilateral 14x4mm 16x4mm. FNA: Positive malignancy. She underwent total thyroidectomy plus neck dissection whose pathological evaluation concluded: PTC 100% follicular variety unencapsulated infiltrating the thyroid capsule without evidence of lymphatic emboli which measures 10mm located in LTL. Amyloid goiter thyroid remnant. IHC: Tg (+) Congo red (+). Referred to the Department of Endocrinology for ablative treatment. Pre- ablative Profile: TSH> 75; Tg: 83; TgAb: (-). She received 70 mCi of radioiodine dose adjusted for renal function whose subsequent TBS was positive in neck and lungs.

Abstract #1074

PAPILLARY THYROID CARCINOMA: 18 YEARS LONG EVOLUTION OF UNTREATED LUNG METASTASES

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Objective: Papillary thyroid carcinoma (PTC) is the least aggressive form of thyroid carcinoma. Distant metastases are rare but are associated with an unfavorable prognosis. Our aim was to present a case of metastatic PTC with an indolent, very long evolution without any treatment.

Case Presentation: A 74 years old female was referred to our clinic for shortness of breath and fatigue. She had a total thyroidectomy for papillary thyroid carcinoma, follicular variant, in 1976 and was taking levothyroxine 50 μg/day until 3 weeks ago. She might have been treated with a single dose of radioiodine in the ‘80 but the history is unclear and has a tracheal canula for tracheal stenosis since 1991. In 1996 a computed tomography showed bilateral lung metastasis but she followed no treatment. 18 years later, at the present assessment (2014), the CT showed bilateral pulmonary metastasis, more numerous that on the 1996 exam. The 131I (300 μCi) whole body scan, performed without recombinant TSH administration, confirmed the uptaking of radioiodine in the pulmonary fields and thyroid bed. The neck ultrasound showed bilateral hypoechoic, ill-defined masses with microcalcifications. Thyroid function tests were normal (TSH=2.5 mU/L, fT4=17.4 pmol/L) without levothyroxine replacement therapy and the serum thyroglobulin is over 300 ng/dl. Thyroid autoimmunity tests were negative. The chemistry and hematology panels were normal.

Discussion: Although primary lung cancer can rarely take-up radioiodine, the diffuse uptake in pulmonary fields is virtually diagnostic of metastatic lesions of thyroid cancer. Metastatic struma ovarii is ruled out by the normal TSH serum level.

Conclusion: The 18 years long, indolent, evolution of pulmonary metastasis without any treatment and the radioiodine uptake even at a normal serum TSH level suggest that the thyroid metastatic cells of PTC were very well differentiated.
Abstract #1075

DOCUMENTATION OF THYROID CANCER RISK FACTORS IN PATIENTS WITH THYROID NODULES

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Objective: To examine the discrepancy between daily practice and clinical guidelines for management of thyroid nodules, based on medical record documentation and identify clinical factors associated to documentation patterns among patients with thyroid nodules.

Methods: This was a retrospective chart review study. There were 833 ultrasound-guided FNA (UGFNA) cases performed at a Midwest academic medical center from January 2010 to January 2012. We randomly selected 200 patients which reflected 273 FNA cases. The clinical measures were selected according to the clinical practice guidelines, including family history of thyroid cancer, history of neck radiation, TSH values, thyroid ultrasound, and radioactive iodide scan (I-scan). We subsequently evaluated clinical factors associated with documentation of family history of thyroid cancer and childhood neck radiation exposure using logistic regression analysis.

Results: The majority of patients were female (82%), of Caucasian race (72.5%), and had no significant comorbidities. Family history of thyroid cancer and childhood neck radiation exposure were documented in 79 subjects (40%) and 72 subjects (36%) respectively. Most subjects had TSH value and an ultrasound performed prior to biopsy (75% and 86% respectively). A radioactive iodide scan was performed in 10% of subjects. We explored the relationship of documentation of family history of thyroid cancer and childhood neck radiation exposure with sex, race, comorbidities, TSH values, utilization of ultrasound, and I-scan. Documentation of childhood neck radiation, history of malignancy, and absence of underlying HTN were found to have significant correlation with documentation of family history of thyroid cancer (p values < 0.001, 0.0421, 0.0497 respectively). Only documentation of family history of thyroid cancer was found to be significantly correlated with documentation of childhood neck radiation exposure (p values < 0.001), but not other factors.

Discussion: Documentation of clinical risk factors of thyroid cancer was lacking in 60% of USGFNA cases. Documentation of personal history of neck radiation was significantly associated with the rate of compliant with documentation of family history of thyroid cancer and vice versa, which suggested physician factors. Additional potential patients related factors included history of cancer and those without HTN.

Conclusion: It appears there is a gap between current patient care and clinical practice guidelines for management of thyroid nodules. As thyroid nodules are extremely common, improvement of physicians’ familiarity with the guidelines could be highly beneficial.

Abstract #1076

DEVELOPMENT OF A NEW MICRORNA BASED TEST FOR ACCURATE THYROID NODULE CLASSIFICATION IN FINE-NEEDLE ASPIRATE SPECIMENS

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Objective: Thyroid nodules are extremely common, yet only a small fraction of those are malignant. The identification of a nodule as benign or malignant has important surgical and therapeutic implications. Notably, in a significant number of cases, this distinction is challenging. Many of these difficult cases are classified as indeterminate and often result in unnecessary surgical procedures. MicroRNAs constitute a class of short, non-coding RNAs that play key roles in the regulation of gene expression. MicroRNA expression profiling has been shown to be a reliable method for cancer subtype classification. In the present study, we describe the development of a microRNA based test that can stratify thyroid lesions as “benign” or “malignant” in pre-operative Fine Needle Aspirate (FNA) samples.

Methods: Over two hundred thyroid FNA samples preserved as stained smears, representing various histological subtypes, were collected and used as a training set. Using proprietary protocols, high-quality RNA was extracted from the samples and the expression levels of both known and proprietary microRNAs were measured using microarray and qRT-PCR. In addition, next generation sequencing was performed on a set of thyroid resection samples in order to find novel microRNA biomarkers. A classifier for distinguishing benign from malignant thyroid nodules was developed.

Results: Differential expression of microRNAs was found between different benign lesions and malignant neoplasms in FNA samples. Importantly, a combination of a small number of microRNAs was able to successfully differentiate
benign from malignant neoplasms with accuracy exceeding 85%. In addition, microRNAs were able to distinguish between specific subtypes of thyroid tumors.

**Discussion:** Our data suggest that microRNAs expression profiling is a promising new strategy for the precise classification of thyroid nodules. Novel microRNAs were found using next generation sequencing which may further improve the classification accuracy.

**Conclusion:** These findings form the basis for the development of a simple and reliable diagnostic assay, which will offer an accurate tool for the classification of surgical and pre-operative thyroid samples, including those that presently fail cytological, as well as other methods of evaluation.

Abstract #1077

**IODINE NUTRITION STATUS IN SIMPLE DIFFUSE GOITER ATTENDING IN BSMMU**

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BSM Medical University

**Objective:** The prevalence of simple diffuse goiter (SDG) is directly related to body iodine status. Urinary iodine is a good biomarker of body iodine nutrition status. This study was aimed to determine the iodine nutrition status in subject with SDG attending in BSMMU.

**Methods:** This cross sectional study comprised of 100 subjects [age, mean±SD: 17.30±4.72yrs, sex (M: F): 21:79] with SDG. The urinary iodine (UI) content was estimated in spot urine sample using the Wet digestion method.

**Results:** Most of the studied subjects were from average socioeconomic background. On categorizing the goiter, 60% had grade-1, 31% had grade-2 and rest 9% had grade-0 (sonographically). Mean duration of goiter was 2.98±2.71 years; and 31 subjects had family history of goiter. Both mean and median urinary iodine (UI) in various age groups were comparably and statistically similar. Highest UI was observed in subjects with grade-1 goiter (41.61±4.84) followed by grade-2 (27.86±3.92) and grade-0 (16.86±5.49) which were statistically different (p=0.030). Median values also followed the same pattern accordingly (grade-1 vs. grade-2 vs. grade-0: 43.53 vs. 20.70 vs. 12.45). Frequencies of subjects with iodine deficiencies under various cut-off values showed that near cent percent fell into the group of having <100µg/L UI though there was no statistical difference between the goiter grades (p=0.858). Considering cut-off at 50µg/L, 80% fell into deficient group which was 40% at cut-off 20 µg/L. As observed, FT4:FT3 (mean±SEM) did not differ between groups divided by cut-off value of 100µg/L, 50µg/L or 20µg/L (p=NS for all). UI excretion did not correlate significantly with age, socioeconomic status, duration of goiter, TSH, FT4, FT3, family history of goiter, grade of goiter (p=NS for all).

**Discussion:** The epidemiology of endemic goiter has radically changed due to iodine prophylaxis. Nevertheless, the problem still does exist. Several endemic areas persist, especially in rural areas and in developing countries. the present study observed that very high frequency (near cent percent) of subjects with SDG suffers from iodine deficiency as assessed by the UI measurement of which 40-50% was severely deficient. Though the National Iodization Program is active, it is a great concern and should be evaluated in broad scale for correction of IDD at national level.

**Conclusion:** This study demonstrated that UI content in SDG is markedly lower than those previously reported in our country. Further studies are needed to elucidate the cause and to find out ways to correct the problem.

Abstract #1078

**PREGNANCY OUTCOME IN NEWLY DETECTED THYROID DISORDERS WITH TREATMENT**

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BSM Medical University

**Objective:** Thyroid dysfunction is not uncommonly observed during pregnancy which may affect pregnancy outcome. This study aimed to evaluate the pregnancy outcome in thyroid dysfunction among pregnant mothers.

**Methods:** This cohort study encompassed 300 pregnant mothers who were recruited on consecutive basis in their first trimester. Assay for antithyroid antibodies as well as free thyroxin and thyroid stimulating hormone (TSH) were done by chemiluminescent method. Study subjects were categorized into normal and disorder groups on the basis of American thyroid association (ATA) defined criteria and all pregnant women were followed throughout the pregnancy till delivery, to note any adverse feto-maternal outcome.

**Results:** Age of subjects was 25.68 ± 4.50 years and median gestational age: 11.0 weeks. By stratification of thyroid function on the basis of ATA criteria, 54.3% were euthyroid, 34% subclinical hypothyroid, 6.3% overt hypothyroid, 3% subclinical hyperthyroid and 2.3% overt hyperthyroid. The prevalence of goiter was more frequent among the dysfunctional group than that of euthyroid (p=0.032). Comparison among functional groups categorized by ATA criteria and conventional criteria for TSH revealed gross disparity between the two criteria, whereupon ATA criteria were stringent. Though most of the mothers were negative for antithyroid
Abstract #1079

IODINE NUTRITION STATUS AMONG SCHOOL GOING CHILDREN OF DHAKA CITY

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Objective: Iodine deficiency is a global health issue and has several important health consequences that result from inadequate thyroid hormone production causing iodine deficiency disorder (IDD). Bangladesh is one of the countries most affected by IDDs. This study aimed to determine the urinary iodine status and frequency of goiter of school-going children.

Methods: The present study observed iodine nutrition status of 530 school children of Dhaka city. The urinary iodine (UI) content was estimated in spot urine sample using the method of Dunn et al. with the modification of Sandell & Kolthoff (wet digestion method) involving colorimetric estimation of the rate of discoloration of ceric ammonium sulphate as inverse measure of organic iodine present.

Results: Among the study subjects, 201 (37.9%) children were 6-8 year of age while 216 (40.8%) and 113 (21.3%) were 9-10 year and 11-12 year respectively. Cent percent studied subjects were taking packet containing iodized salt. Mean UI (58.62±2.66; m±SEM) and median UI (39.80 µg/L) value of all school children was considered as moderately deficient. Among all the subjects more than 60% were moderately (<50mg/L) deficient while about 20% were severely (<20mg/L) deficient for iodine nutrition. The lowest mean UI level was found in 6-8 year child (49.01±4.81) in comparison to 9-10 year old child (60.16±3.81) and 11-12 year old child (72.77±5.09). However median UI value of 11-12 year child (63.99) was better than that of the 9-10 year (40.28) and 6-8 year (33.32) child. Out of 530 children 230 (43.20%) had goiter. There was no statistical difference for UI between goitrous and non-goitrous children within the study population.

Conclusion: This study demonstrated that UIIC in school children is markedly lower than those previously reported in our country. Further studies at national level are needed to elucidate the cause and find out ways to correct the problem.

Abstract #1080

EFFECT OF METFORMIN ON SERUM THYROTROPIN LEVELS IN HYPOTHYROID PATIENTS WITH DIABETES/PREDIABETES ON STABLE AND ADEQUATE LEVOTHYROXINE DOSES

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Objective: To observe the impact of metformin on serum (Thyroid Stimulating Hormone) TSH levels in hypothyroid patients who are on stable and adequate (Levothyroxine) L-T4 and found to have diabetes or prediabetes.

Methods: Total 80 patients age more than 18 years, diagnosed hypothyroid, adequate and stable L-T4 replacement therapy, type 2 diabetes or prediabetes, only on metformin along with diet and lifestyle modification for blood sugar control were studied over a period of 12 months. The subjects with uncontrolled hypothyroid, taking oral hypoglycemic agents (OHA) other than metformin, taking insulin, on metformin and other OHA and on any hormonal supplementation or medication affecting thyroid function test like oral contraceptive pill were excluded. In control group, patients received adequate and stable supplementation of L-T4 without metformin. Serum TSH values at baseline, after 3 months, 6 month and 12 months were analyzed.

Results: In study group, after 3, 6 & 12 months of on metformin, mean TSH was significantly lower than basal (Basal TSH: 4.018±0.7207, 4.018±0.7207 & 4.018±0.7207 vs. 3, 6 & 12 months after metformin, TSH: 3.72±0.6216, 2.966±0.7194 & 1.8788±0.6055microUI/ml; P < 0.0001 respectively). Mean free T4 (fT4) level changes were non-significant in 3 month, but significantly increased after 6 & 12 months of metformin administration. Mean free T4 (fT4) level changes were non-significant in 3 month, but significantly increased after 6 & 12 months of metformin administration. (Basal fT4: 1.344±0.2514, 1.344±0.2514, 1.344±0.2514 vs. 3, 6 & 12 months after metformin, fT4: 1.3405±0.2437; P=0.691, 1.372±0.238, P=0.007, 1.3848±0.2435ng/dl; P=0.001 respectively) whereas non-significant changes in mean TSH and mean fT4 in control group.

Discussion: Metformin crosses the blood-brain barrier and suppresses AMPK activity and possibly counteracts hypothalamic T3 action on TSH secretion.
Other hypotheses include changes in the affinity of TH receptors, TH binding, bioavailability and metabolism, induced constitutive activation of the TSH receptor, and interference with the TSH assay. Elevated TSH values may not necessarily reflect hypothyroidism, but could represent recovery from a nonthyroidal illness, mild resistance to TH, or obesity, as is the case in many patients with diabetes mellitus receiving metformin.

**Conclusion:** Treatment with metformin is associated with significant reduction in the serum TSH levels. TSH reduction is not associated with reciprocal changes in fT4 at 3 months but at 6 months and 12 months and is associated with significant increase of fT4 in primary hypothyroidism patients on stable and adequate levothyroxine doses who were found to have diabetes or prediabetes.

Abstract #1081

**RADIOACTIVE IODINE THERAPY FOR TREATMENT OF HYPERTHYROIDISM – OUR EXPERIENCE**

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**Objective:** Radioactive iodine (RAI) is considered as treatment of choice for hyperthyroidism. Hypothyroidism is the end result of RAI therapy. We evaluated results of 70 cases of hyperthyroidism treated with RAI over a period of 5 years, for cure rates and the incidence of hypothyroidism.

**Methods:** Hyperthyroidism was diagnosed clinically, confirmed by elevated S T3, T4 and low TSH and most of cases had high Tc99 uptakes on thyroid scintigraphy. 44 cases were on anti-thyroid drugs which were stopped 3 days prior to RAI dose. The RAI dose was calculated empirically, based on the goiter size and Tc99 uptakes. Patients were reviewed at 3 monthly intervals for 1 year, and considered euthyroid once S T3 and T4 became normal, hypothyroid when TSH>10 IU/l and low serum T4. Those with persisting hyperthyroidism were either followed-up on β blockers, given anti-thyroid drugs or subsequently provided with a second dose after 6 months.

**Results:** Of the 70 cases, 54 had Grave’s disease (GD), 10 had toxic multi-nodular goiter (TMNG), 3 had toxic adenoma and 3 had mixed disease (toxic nodular Grave’s disease). RAI doses varied from 4 mCi to 17.5 mCi. Mean ages of patients with GD, TMNG, toxic adenoma and mixed disease were 35.66 ± 14.02, 44.4 ± 10.17, 37.5 ± 7.5 years and 34.33 ± 10.8 years respectively. Mean S.T4 levels in GD and in TMNG were 301.77 ± 102.3 nmol/L and 265.44 ± 67.3 nmol/L respectively. In addition to goiter, 6 patients had AF, one had RHD and one presented with hypokalemic paralysis. Patients were divided into 4 groups as per the RAI doses, Group A (4-7 mCi), Group B (7.1-10 mCi), Group C (10.1-12 mCi) and Group D (> 12 mCi). Three patients were given 2 doses of RAI and 1 patient remained thyrotoxic in spite of 3 doses (30 mCi). Cure rate was 95.65%, 73.33%, 57.14% and 57.14% in Group A, B, C and D respectively. Hypothyroidism occurred in 52.17%, 46.66%, 42.85% and 14.28% in all the Groups respectively. Thyroid-associated orbitopathy remained stable in 77.14%, improved in 21.42% and worsened in 1.42% cases. Goiter disappeared in 41.42%; decreased in 54.28% and remained same in 4.28% cases.

**Discussion:** In this study we used a fixed-dose RAI regimen for treatment of hyperthyroidism, as it has a higher convenience coupled with an economic cost. Our results confirmed the effectiveness of this regimen, with 95% patients becoming euthyroid or hypothyroid within a year following a single dose.

**Conclusion:** RAI therapy is an effective definitive treatment modality for hyperthyroidism, with long-term cure rate approaching 95%. Its safety, efficacy and low-cost has made it the preferred therapeutic regime. Patients should be regularly followed up for the advent of hypothyroidism and to be treated accordingly.

Abstract #1082

**THE RARE CASE OF A MALE WITH GROWTH FAILURE AND PRECOCIOUS PUBERTY**

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**Case Presentation:** An 8 year 2 month old male was referred for evaluation of growth failure. He had been growing along the 25th percentile on the height growth curve until 1.5 years ago when his growth velocity slowed and he deviated to the 1st percentile (-2.18 SD). He had mild constipation and long history of dry skin. Skeletal age was 6.5 years. On exam, he was at the 1st percentile for height and the 31st percentile for weight, had a palpable thyroid, Tanner 1 pubic hair, and 6 mL testicle on the left and 6 mL testicle on the right. Knowing that there is only one cause of precocious puberty associated with growth failure and delayed skeletal age, thyroid studies and antibodies were performed revealing TSH > 150 mIU/L, free T4 0.5 ng/dL, thyroid peroxidase antibodies 958 IU/mL (<35), and thyroglobulin antibodies 458 IU/mL (<20). Testosterone was 5 ng/dL, FSH 3.98 mIU/mL, and LH 0.15 mIU/mL. He was started on low dose levothyroxine 25 mcg daily and gradually increased to normalize free T4 and TSH. Constipation and dry skin resolved and he lost 3.5 pounds during the first month of treatment with family stating he looked less “swollen.”
Most recent follow up was when patient was 8 years and 6 months, height had increased to 3rd percentile (-1.84 SD) with interval growth velocity of 11.1 cm/year since diagnosis and treatment. His genital exam showed Tanner 1 pubic hair and now 4.5 mL testicles bilaterally.

**Discussion:** Van Wyk-Grumbach syndrome is characterized by primary hypothyroidism, delayed skeletal age, and pseudoprecocious puberty. The exact mechanism is debated, but one of the most accepted theories proposes that TSH and FSH share a common B subunit and the markedly elevated TSH that occurs in longstanding primary hypothyroidism is thought to directly stimulate the FSH receptor. This would explain our patient’s increased testicular volume without enlarged phallus or development of pubic hair, while having prepubertal gonadotropins and testosterone. The stimulation of Sertoli cells would cause the increase in testicular volume, but lack of stimulation of the Leydig cells would not result in testosterone production. With treatment of the long standing hypothyroidism, the TSH is reduced and subsequently testicular volume decreased without continued stimulation.

**Conclusion:** In the rare instance that a child is found to have precocious puberty with presence of growth failure and delayed skeletal age, primary hypothyroidism should be considered and thyroid function tests should be obtained. Treating the hypothyroidism with levothyroxine will prevent further progression of puberty, while restoring normal growth velocity.

**Abstract #1083**

**FUNGAL INFECTIONS MIMICKING METASTATIC DIFFERENTIATED THYROID CANCER (DTC)**

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**Objective:** DTC accounts for 95% of all thyroid malignancies. Distant metastases (DM) most commonly occur in the lung. Whole body I-131 scans (WBS) and PET/CT are modalities used for detecting DM. However, false positive cases have been reported in patients with aspergillus (ASP). We report 2 cases of young women with fungal infections mimicking metastatic papillary thyroid cancer (PTC).

**Methods:** Cases at MD Anderson (MDA) were reviewed.

**Case Presentation:**

**Case 1:** A 39 y/o woman presented 1 yr prior with abdominal pain/vomiting to a local ER. CT scan showed left lung nodules. PET/CT showed thyroid and left (L) 2.2 cm lung nodule with satellite lesions. She underwent total thyroidectomy (TT) which showed a 1.2 cm PTC with no lymphovascular invasion (LVI). She then received 2 doses of I-131 (cumulative=255 mCi), with post-tx scans showing uptake in thyroid bed and L lung. Stimulated Tg was not available, however, 2 mos s/p I131, Tg was undetectable (TSH=2.3). Biopsy of the lung showed inflammatory cells. WBS was repeated 4 mos later which showed uptake in L lung. Stimulated Tg was undetectable. CT 4 mos later showed increase in size of the lung mass. Pt was referred to MD Anderson (MDA). She then underwent wedge resection of the lesion which grew ASP and was treated with voriconazole.

**Case 2:** A 29 y/o woman was diagnosed with PTC 3 yrs prior. She underwent TT and bilateral neck dissection. Pathology showed a 5 cm PTC with LVI and multiple + nodes (T34aN1b). 100 mCi of I131 was given with no uptake on post-tx scan. Stimulated Tg not available but the patient had + Tg antibodies (≥942) on subsequent testing. PET/CT was negative. Antibodies declined but were persistent for 3 years after surgery. She was referred to MDA. An u/s neck showed a small pretracheal node. PET/CT showed a new lung nodule measuring 1.4 cm with low SUV, and her antibodies continued to decline to 156. CT 6 months later showed increase in size of the nodule with cavitation. Tg antibody=134, which was not consistent with worsening of her DTC. Core biopsy of the lung showed necrotizing granuloma and fungal stains were consistent with coccidiomycosis. She was treated for 9 mos with fluconazole.

**Discussion:** Fungal infections as well as inflammatory lung disease can capture I131 and FDG, mimicking DM. This abnormal uptake seen in fungal infections and bronchiolitis is enhanced possibly by the oxidant-antioxidant environment found in sites of inflammation. In the case of ASP it has been attributed to the endotoxins and enzymes released by the fungus.

**Conclusion:** Caution should be used when discordant results between the tumor marker and WBS or PET/CT in young patients with DTC. Biopsy of suspicious lung lesions should be considered.
Abstract #1084

DETECTION OF INCREASING NUMBERS OF POINT MUTATIONS AND FUSIONS IN BENIGN THYROID NODULES USING NEXT-GENERATION SEQUENCING DRAMATICALLY REDUCES MUTATION MARKER PANEL SPECIFICITY

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Objective: Advances in next-generation sequencing (NGS) technology enable evaluation of thyroid nodules for cancer-associated mutations and fusions. Some mutations are highly specific for detecting cancer, while less is known about the accuracy of others. The number of thyroid cancer-associated mutations and fusions can be expected to grow as more data emerges using this sensitive technology. However, the value of ever-increasing numbers of loci in the preoperative diagnosis of thyroid FNA remains unclear. Here we assess the accuracy of four point mutation and fusion panels.

Methods: We used FNA material from samples (n=77) collected preoperatively and diagnosed post-surgically by a panel of experts as malignant (PTC, mPTC, FVPTC, PTC-TCV, MTC, WDC-NOS, HCC, FC) or benign (BFN, FA, HCA, HTA, LCT). We also evaluated surgical tissues (n=41) with histopathology truth, and a consecutive series of indeterminate FNAs without histopathology truth from our CLIA lab (n=121). Samples were subjected to NGS and analyzed using panels containing 14 genes, with increasing numbers of interrogated loci (n=15, 183, 918, and 3363) plus 43 fusions. We used several stringency filters to score the data. Samples were scored negative when no fusions or point mutations were present, and scored positive if at least one fusion or point mutation was detected.

Results: Sensitivity to detect malignancy improved in all cohorts with increasing number of loci, while specificity showed the opposite trend, falling dramatically. In FNAs, the smallest panel renders a sensitivity of 18-34% and a specificity of 97%; while the largest panel renders a sensitivity of 74-100% and a specificity of less than 36%. In surgical tissues, a similar trend is observed: in the smallest panel >75% specificity is associated with <50% sensitivity; in the densest panel a sensitivity of > 81% is associated with < 25% specificity. Frequency of mutations and fusions in CLIA samples across the four panels was 3-7%, 10-26%, 46-97% and 72-100%, respectively.

Discussion: Sensitivity gained by detecting increasingly larger numbers of point mutations and fusions comes at the cost of specificity, and runs the risk of overcalling malignancy in truly benign samples.

Conclusion: A further understanding of the significance of point mutations and fusions detected in benign thyroid nodules is warranted to avoid the risk of over-utilization of surgery in benign nodules.

Abstract #1085

FT3 CONCENTRATIONS ARE SIGNIFICANTLY PREDICTED BY 25-HYDROXYVITAMIN D AND 1,25-DIHYDROXYVITAMIN D IN A LARGE PROSPECTIVE, HOSPITAL-BASED STUDY: THE LURIC STUDY (LUDWIGSHAFEN RISK AND CARDIOVASCULAR HEALTH STUDY)

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Objective: The LURIC Study is a large prospective cohort study with 3316 included patients between 1997 and 2001. Main inclusion criterium was clinical stability except for acute coronary syndrome. All patients were referred to angiography. Accumulating evidence suggests a complex interplay between thyroid hormone status and vitamin D. Previous studies showed that thyroid hormone inhibits 25-OH-D 1-alpha hydroxylase and that vitamin D suppresses TSH secretion and exerts direct effects on thyroid cells such as inhibition of iodine uptake. Clinical data on direct effects are however sparse and partially controversial. We therefore aimed to evaluate whether 25(OH)D and 1,25-(OH)2D are associated with TSH, FT4 and FT3 levels in LURIC.

Methods: We examined 2804 participants with complete data on 25(OH)D, 1,25(OH)2D, TSH, FT4 and FT3. We performed linear regression analyses with TSH, FT4 and FT3 as outcome variables and carried out adjustments for age, sex, BMI and active smokers.

Results: Mean age of participants was 62.8±10.6 years with 30% females. In linear regression analyses with thyroid hormones and TSH as the outcome variables and adjustments for age, sex, BMI, and active smokers, we found no significant association of 25(OH)D or 1,25(OH)2D with TSH and FT4. However we observed a significant association of fT3 with 25(OH)D (beta coefficient 0.04; p=0.043) and 1,25(OH)2D (beta coefficient 0.12; p<0.001).

Discussion: In our study we found a significant relationship between FT3 and 25(OH)D and 1,25(OH)2D
in LURIC. The mechanisms by which thyroid hormones influence vitamin D metabolism is still unknown. Thyroid hormones, i.e. FT3, exert their actions by binding to thyroid hormone receptors, which belong to the nuclear receptor superfamily, including the vitamin D receptors (VDR); polymorphisms in the VDR gene have been associated with autoimmune thyroid diseases. The reason for the close relationship between FT3 and vitamin D remains speculative. To our best knowledge this is the first report a correlation between FT3 and vitamin D levels. A recent study has shown that T3 administration significantly decreased 1,25(OH)2D in mice, suggesting a negative gene regulation role by T3. Further studies are needed to investigate the causal link of the relationship between FT3 and vitamin D in humans.

**Conclusion:** In patients referred for coronary angiography in LURIC there was no significant association between TSH, FT4 and vitamin D levels, but a significant association of 25(OH)D and especially with 1,25(OH)D and FT3. Further studies are required to elucidate the underlying pathophysiological mechanisms of the close relationship between the active metabolites and the clinical relevance of this finding.

**Abstract #1086**

**COMPREHENSIVE DIAGNOSTIC EVALUATION OF NEOPLASTIC THYROID LESIONS BY NEXT GENERATION SEQUENCING AND MIRNA GENE EXPRESSION**

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**Objective:** Molecular testing for oncogenic gene alterations or gene expression in fine needle aspirations (FNAs) from thyroid nodules with indeterminate cytology increases the diagnostic yield of conventional cytopathology by detecting a subset of malignant or benign nodules with high predictive value. In the present study, we evaluated a comprehensive next generation sequencing (NGS) mutation panel and a novel miRNA-based diagnostic algorithm to further improve the yield of molecular cytology.

**Methods:** Total nucleic acids from surgical specimens and preoperative FNAs were tested for over 1,500 unique mutations in 68 distinct genomic regions from 20 genes and 46 gene fusions using pooled PCR and targeted NGS, or for 17 well-known alterations in the BRAF, HRAS, KRAS, NRAS, PAX8 and RET genes detected with the miRInform Thyroid test and combined with the qualitative results of a 10-miRNA gene expression classifier. All molecular results were compared against surgical histopathology reference diagnoses.

**Results:** Among 54 resected thyroid lesions negative for mutation by miRInform, 3 out of 36 malignant cases were positive by NGS at ≥10% variant, 6 by miRNA and 8 by both methods. Four out of 18 benign lesions were also positive by NGS, none by miRNA. At 5% variant threshold, NGS detected additional mutations in 2 malignant cases (1 positive by miRNA) and in 3 benign cases. A similar pattern was observed in 42 preoperative FNAs from thyroid nodules with AUS/FLUS or FN/SFN cytology collected at 5 endocrinology centers. miRInform correctly identified 11 malignant cases, including 6 positive by miRNA. Among the mutation-negative specimens, miRNA testing identified 6 additional malignant cases while NGS detected mutations in 2 malignant cases (both positive by miRNA) and in 4 (≥5% variant) benign cases (all negative by miRNA).

**Discussion:** Both NGS and the miRNA classifier increased the diagnostic sensitivity of mutation testing which would improve its negative predictive value and the yield of true positive/malignant results. These data suggest that miRNA testing can provide clinically relevant diagnostic results in line with NGS mutational analysis. The advantages of this approach lie in its ability to phenotypically identify malignant nodules that lack oncogenic mutations and to rule out benign nodules with germline or low-level somatic mutations of unknown clinical significance.

**Conclusion:** When using FNAs truly representative of local clinical practices and blinded surgical histology review, multi-categorical testing for highly specific miRNA and validated oncogenic mutations may provide higher predictive value than broad NGS panels targeting gene mutation hotspots.

**Abstract #1087**

**RISK OF CANCER IN ENLARGING THYROID NODULES IS INFLUENCED BY THE GROWTH RATE AND CYTOLOGIC DIAGNOSIS**

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**Objective:** The risk of thyroid cancer in enlarging thyroid nodules is poorly defined. The study aim is to identify the features of enlarging thyroid nodules that are associated with malignancy.

**Methods:** We queried a prospectively maintained database of 3855 patients who had thyroidectomy from 2008-2014 and examined outcomes for all thyroid nodule that enlarged during preoperative management. Patient
Characteristics and nodule features including ultrasound findings, FNA biopsy results, and histology reports were analyzed using independent sample t-test to compare means of continuous variables and Chi-square test for associations of variables between groups.

Results: A total of 366 enlarging nodules were identified in 287 (7.4%) patients. The mean change in volume/year was 1.3-fold ± 2.4. Malignancy was diagnosed in 16.1% (59/366) of nodules. The most common histologies were follicular variant papillary thyroid cancer (PTC, 58%) and conventional PTC (24%). One enlarging nodule was anaplastic carcinoma and one was medullary thyroid cancer. Patients with malignancy were younger than patients with benign nodules (mean, 49y v. 54y, p=0.04). Malignancy was not associated with gender (p=1.0), prior head/neck radiation (p=0.1), or pre-existing hypothyroidism (p=1.0). Histologic malignant and benign nodules were equivalent in size (mean volume, 8.8 cm³ ± 13.7 v. 9.64 cm³ ± 16.1; p=0.2). However, malignant nodules enlarged more rapidly compared to benign nodules (mean volume increase/year, 1.5-fold ± 1.6 v. 1.2-fold ± 2.5; p=0.03). By receiver operating characteristic analysis, the area under the curve was 0.59 (95% confidence interval, 0.50-0.67; p=0.03), and when the change in volume/year was >1.2-fold, malignancy was predicted with 42% sensitivity and 78% specificity. Suspicious features on ultrasound were predictive of malignancy and included calcifications (OR 3.3, p=0.008), irregular border (OR 87.9, p<0.001) and hypoechogenicity (OR 3.6, p<0.001). The risks of malignancy in an enlarging nodule by FNA cytology category were 9% benign, 25% AUS/FLUS, 15% FN/SFN, and 67% suspicious.

Conclusion: The data demonstrate that nodules with a more rapid rate of growth had a higher likelihood of cancer, although no threshold reliably correlated with malignant histology. Overall, among patients selected for surgery, histologic malignancy was present in 1 of 15 enlarging thyroid nodules. Enlarging nodules with benign and AUS/FLUS cytology had a higher than expected rate of cancer (9% and 25%, respectively), and thus should be either carefully followed with short-interval ultrasound or treated surgically for definitive diagnosis.

Abstract #1088

HIGH THYROID STIMULATING HORMONE LEVEL IN DOWN’S SYNDROME A MERE RESETTING OF HYPOTHALAMOPITUITARY AXIS?: A CASE-CONTROL STUDY

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Objective: Reduced thyroid function in Down’s syndrome (DS) has been variously attributed to causes ranging from glandular dysgenesis to altered hypothalamopituitary axis, precise etiology remaining elusive. In present study, we have compared hypothyroid Indian children with and without DS, with specific references to phenotypic presentations.

Methods: DS patients (≤18 years) with elevated thyroid stimulating hormone (TSH, ≥5 mIU/L) were consecutively recruited in a prospective manner in a tertiary care hospital in India. In the control arm, patients (≤18 years) with hypothyroidism without DS were recruited. Congenital hypothyroidism was excluded in both arms. Free thyroxine (FT4), anti-thyroid peroxidase (TPO) antibody, anti-thyroglubulin (TG) antibodies were measured in the cases and controls.

Results: Forty six cases [median age 9 years (IQR: 4-16.25), M:F=18:28] and 41 controls [median age 12 years (IQR: 8-14.50), M:F=15:26] were comparable in terms of age and sex. Median age of presentation with elevated TSH levels was significantly earlier in case of DS cases [7.50 years vs. 11 years, P=0.015]. Significantly greater number of positive family history was present the cases without DS [P=0.048]. Although the rates of positivity of anti-TPO antibody [34.78% of DS vs 43.90% of non DS cases, P=0.509] and anti-TG antibody [15.21% of DS vs 12.19% of non DS cases, P=0.763] are comparable between the groups, the median titer of anti-TPO antibodies was significantly lower in the cases with DS [31.00 U/ml vs 91.00 U/ml, P=0.008]. Incidence of goiter were comparable [36.95% of DS vs 34.14% of non DS cases, P=0.826].

Discussion: Important differences emerge in Indian children with hypothyroidism with or without DS. While earlier presentation, a lower incidence of traceable family history and lower antibody titers might support a possible resetting of hypothalamopituitary axis, the rates of antibody positivity and goiter are comparable. Also, an autoimmune etiology of the thyroid disorders cannot be ruled out, given the links between chromosome 21 anomaly and other immune dysfunctions.

Conclusion: Phenotypic differences exist in Indian pediatric hypothyroid patients with and without DS. A causal association of elevation of TSH levels in DS and resetting of hypothalamopituitary axis cannot be concluded.
Abstract #1089

THE CORRELATION OF THYROID STIMULATING HORMONE WITH LIPID PROFILE, BODY MASS INDEX AND OTHER BIOCHEMICAL PARAMETERS

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Objective: Obesity is an epidemic across the globe, with its overwhelming presence even in the developing countries. It is associated with derangements in the lipid profile which further aggravates the risk of coronary heart disease, diabetes mellitus (DM), stroke and malignancies like endometrial, colon, esophageal and uterine cancers. The relation between the thyroid function and weight is of utmost importance, as obesity is a crucial factor associated with increased morbidity, disability and mortality of the patient which can begin very early in life. The main aims with this study was to-
1. To establish an association between the TSH levels and obesity.
2. To study the lipid profile of the subjects.

Methods: A total of 358 patients were routinely investigated in a regular diabetic and endocrine camp which constituted the levels of FBS, TSH, T3, T4, BMI, HbA1c, Triglycerides, total cholesterol, HDL, LDL, VLDL, S.creatinine and micral.

Results: It was observed that 86.04% patients had a BMI ≥23, while 33.44% belonged to obese grade I and 66.56% belonged to obese grade II. The mean cholesterol and TGs was higher among the obese group (183.09 mg/dl and 146.93 mg/dl) than the non-obese ones (174.14 mg/dl and 142.80 mg/dl respectively). Also the LDL among the obese (110.22 mg/dl) was higher than the non-obese ones (174.14 mg/dl and 146.93 mg/dl) than the non-obese ones (174.14 mg/dl and 142.80 mg/dl respectively). Also the LDL among the obese (110.22 mg/dl) was higher than the non-obese (104.93 mg/dl). While not much difference could be accounted in the levels of HDL, FBS, HbA1c, S.creatinine and TSH among both groups.

Discussion: Any alteration in the levels of lipids in body makes the individuals more prone to develop diseases like hypertension, DM, Hyperinsulinemia etc. It was noted that individuals who led a more sedentary lifestyle with less physical activity were more prone to become obese and thereafter diabetic. When the TSH levels were correlated among the obese subjects with grade I and grade II obesity, BMI values were significantly elevated highlighting the variation in TSH levels depending on the extent of obesity.

Conclusion: The co-occurrence of the common endocrine conditions in an individual modifies the clinical presentations and the laboratory results, while simultaneously influencing the screening, diagnostic and therapeutic strategies also. A higher index of suspicion should be kept in mind while dealing with thyroid dysfunction for the occurrence of diabetes, and similarly for thyroid dysfunction in a patient with diabetes. Also the lipid profile, BMI, TSH should be well correlated among the subjects presenting with obesity. With increasing levels of BMI, the lipid profile is liable to get deranged, which in turn imparts a resistance to the TSH levels in the peripheral tissues, thus, further aggravating the thyroid problem.

Abstract #1090

USE OF PERCUTANEOUS ETHANOL INJECTION (PEI) IN THE MANAGEMENT OF COMPLEX THYROID CYSTS AND RECURRENT THYROID CANCERS

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Objective: Presented are five cases of complex thyroid cysts and two recurrent thyroid cancers which were managed with percutaneous ethanol injection.

Methods: The locations of the complex thyroid cysts and the recurrent thyroid cancers were identified by neck ultrasound. The benign natures of the five complex thyroid cysts and the malignant natures of the two recurrent thyroid cancers were biopsies-proven. The volumes of the lesions were measured prior to percutaneous ethanol injections in order to calculate the amount of ethanol injected. Local anesthesia were used for the procedures. 18-22 gauge needles were used. Informed consents were obtained from the patients, explaining procedures in details along with the potential complications and needed precautions.

Case Presentation: Five patients with benign complex thyroid cysts and two patients with recurrent thyroid cancers were studied. Pre-PEI sizes were 15.3, 3.6, 35, 8.8, 16.4 cc, respectively for the complex thyroid cysts; and 0.22 and 0.29 cc, respectively for the recurrent thyroid cancers. Post-PEI sizes were 4, 0.8, 23, 4.73, and 0 cc, respectively for the complex thyroid cysts; and 0.12 and 0.22 cc, respectively for the recurrent thyroid cancers. The estimated fluid removed were 7, 3.5, 15, 8, and 5 cc, respectively from the thyroid cysts; and 0.12 and 0.22 cc, respectively for the recurrent thyroid cancers. Post-PEI sizes were 4, 0.8, 23, 4.73, and 0 cc, respectively for the complex thyroid cysts; and 0.12 and 0.22 cc, respectively for the recurrent thyroid cancers. The estimated fluid removed were 7, 3.5, 15, 8, and 5 cc, respectively from the thyroid cysts; and the estimated ethanol injected were 5, 3.5, 10, 2.5, and 0.5 cc, respectively. No fluid removed from the two recurrent thyroid cancers given their solid natures. No significant pain, voice change, dysphonia, bleeding, tingling, or bruises reported following the procedures. The patients with the complex thyroid cysts reported immediate relieves of the pressure and documented cosmetic improvements. One of the two recurrent thyroid cancers had a reduction in the lesion size as indicated above following the procedure and reduction of thyroglobulin level from 15 to 11 ng/dl.


ABSTRACTS – Thyroid Disease

That is yet to be evaluated in the second patient with the recurrent thyroid cancer.

Discussion: Percutaneous Ethanol Injection (PEI) is a therapeutic procedure which involves an injection of ethanol subcutaneously into a variety of lesions to induce sclerosing properties and achieve measurable outcomes, such as reduction in the sizes of the lesions and relieve of pressure symptoms. It can be used as a palliative procedure in patients with recurrent thyroid cancers, in which surgery and radioiodine ablation are not indicated.

Conclusion: PEI is a relatively safe outpatient procedure that can minimize the need of primary surgery or repeat surgical intervention. It is anticipated to contribute to the reduction of the costs to the health system and is particularly useful in patients who are not candidates for surgery or radioiodine ablation.

Abstract #1091

UNUSUAL PRESENTATION OF HASHIMOTO’S THYROIDITIS

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Objective: We report a case of Hashimoto’s thyroiditis (HT) with asymmetric thyroid involvement and an unusual ultrasonographic appearance.

Case Presentation: A 40-year-old Caucasian man with a history of pituitary tumor, status post resection with pan-hypopituitarism on hormone replacement therapy (thyroxine, hydrocortisone, and testosterone) presented with a one month history of persistent right upper neck lymph node enlargement. Physical exam was unremarkable except for enlarged right submandibular lymph node. Ultrasonography (US) of the neck revealed a very unusual appearing left thyroid. The entire left lobe was of an abnormal echotexture consisting of diffuse microcalcifications with a starry sky appearance. The majority of the right lobe was normal except for very small area with HT in lower lobe. The patient was recommended to have repeat FNA biopsy of left lobe but he elected thyroidectomy. Surgical pathology was consistent with chronic lymphocytic thyroiditis involving the left lobe and isthmus. Incidental occult follicular variant micropapillary carcinoma (0.4X0.4 cm) was noted in the left thyroid. Majority of right lobe was normal except very small area with HT in lower lobe.

Discussion: HT may rarely present with diffuse microcalcifications and a starry sky appearance similar to DSPTC. This case of HT is particularly unusual because the ultrasound findings were primarily confined to the left lobe and anti-TPO antibodies were negative. Papillary thyroid microcarcinoma was an incidental finding, which is not uncommon as shown in autopsy studies of the thyroid.

Conclusion: This case demonstrates an unusual presentation of HT that illustrates the diagnostic challenge in differentiating HT and DSPTC. Secondary to the stark differences in prognosis it is critical that clinicians understand the limitations of ultrasound and FNA biopsy in diagnosis of HT or DSPTC.

Abstract #1092

PRIMARY HYPOTHYROIDISM PRESENTING AS ACUTE CEREBELLAR ATAXIA IN MIDDLE AGED MAN

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Objective: To present a case of acute cerebellar ataxia as the only manifestation of Primary hypothyroidism in a middle aged man.

Case Presentation: A 45 year old male presented with slurred speech, unsteadiness of gait (tendency to fall on either side while walking), and dizziness since last 6 days. These complaints were insidious in onset; progressive over 3-4 days but were static since last 3 days. No history of weakness, fever, vomiting, trauma to head, any drug intake or seizures. There was no h/o hypertension, diabetes or CAD. Patient was non smoker & had never consumed alcohol. EXAMINATION: Patient was conscious with a Glasgow 15, right sided homonymous hemianopia, right facial weakness, ataxic gait with positive Romberg sign, dysarthria, dysdiadochokinesia and scanning speech with a wide base gait. Dysmetria and dysdiadochokinesia was present and tandem walking was impaired. Nystagmus was not present. DTR’s were normal. Cardiovascular, respiratory and abdominal
examinations were non contributory. INVESTIGATIONS: Hb: 10.9g/dl (12-16); TLC: 4200/mm3 (4000-11000); DLC P74L22E2M2; Platelets: 22000/mm3 (150000-400000); FB Glucose: 91mg/dl (70-110); Na+: 143meq/L (135-145); K+: 4.9meq/L (3.5-5.5); Ca2+: 8.8mg/dl (8.5-10.5); Phosphate: 2.7mg/dl (2.5-5.5); Albumin: 3.8gm/dl (3.5-5.5); Blood Urea: 37mg/dl (15-45); Creatinine: 1.1mg/dl (0.6-1.2); Uric Acid: 8.8mg/dl (2.5-6.0); LFTs were normal. Total Cholesterol: 161mg/dl (150-200); HDL-C: 67mg/dl (30-65); LDL-C: 75mg/dl (50-150); VLDL-C: 19mg/dl (upto40); Triglyceride: 96mg/dl (50-200). NCCT head: normal study.

Thyroid profile TSH: 138mIU/L (0.4-5.0), FT4: 0.41ng/dL (0.8-1.80), FT3: 1.17 pg/ml (2.0-4.4), Anti TPO antibody: 1280 IU/ml (<50). He was started with thyroxine 100 µg daily and patient improved within two weeks & there was complete resolution of symptoms over 3 months.

Discussion: Untreated hypothyroidism may present as acute cerebellar ataxia which is reversible with thyroid hormone replacement.

Conclusion: Cerebellar ataxia is known to be a symptom complex of hypothyroidism along with various other manifestations. In our case, it is the only manifestation of hypothyroidism which makes this case more unique.

Abstract #1094

A PATIENT S/P ROUX-EN-Y GASTRIC BYPASS WITH REFRACTORY HYPOTHYROIDISM

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Objective: Oral levothyroxine is treatment of choice in patients with hypothyroidism. Here, we report a challenging case of hypothyroidism s/p ROUX-EN-Y gastric bypass (RYGBP) surgery where patient could not be rendered euthyroid despite various oral thyroid hormone treatment regimens.

Case Presentation: A 57-year-old woman with Hashimoto’s thyroiditis presented for evaluation of refractory hypothyroidism. The patient was diagnosed with hypothyroidism in 2002 and was started on thyroxine with improvement in thyroid hormone levels to normal. Her serum thyroid stimulating hormone (TSH) was normal in 2004 on oral thyroxine. She underwent RYGBP surgery in 2005 and total thyroidectomy in 2008 for abnormal FNA biopsy of thyroid nodule. Surgical pathology was consistent with Hashimoto’s thyroiditis. Her thyroxine dose requirement substantially increased after RYGBP surgery and thyroidectomy.
TSH could not be normalized despite increasing oral levothyroxine to 500 microgram daily. There was no interfering medication. She was subsequently started on intravenous (IV) thyroxine. The patient’s physician could not normalize TSH despite increasing IV thyroxine to 500 microgram daily. She was then referred to endocrinology clinic for management. Surprisingly, first lab obtained on 500 microgram IV thyroxine showed normal TSH (3 micro IU/ml) with normal free thyroxine. Other labs including celiac panel, TSH alpha subunit were normal. She was referred to gastroenterologist for evaluation of malabsorption. Attempts were made to transition patient from IV to oral thyroid hormones. Various regimens including combination of levothyroxine and liothyronine, liquid gel thyroxine (tirosint), combination of lower dose IV thyroxine and oral thyroxine were tried but TSH could not be normalized. Serum reverse T3 was also tested and was not elevated.

Discussion: On review of literature, we found only two cases with jejuno-ileal bypass surgery where patients required a larger than normal dose of thyroxine but oral form to achieve euthyroid state. One of these patient underwent reversal of intestinal bypass leading to reduction in oral thyroxine dose from 600 micrograms to 200 micrograms daily. This patient with RYGBP surgery not only had malabsorption to thyroxine but also other medications. Despite being on high IV thyroxine dose, patient’s TSH continues to remain elevated except one time when it was normal. The patient reported compliance with her thyroid medication. The patient is currently seeing bariatric surgeon for consideration of gastric bypass reversal.

Conclusion: This case highlights extreme case of thyroid hormone malabsorption after RYGBP surgery.

Abstract #1095

ACCURATE DETECTION OF ONCOGENIC MUTATIONS IN THYROID NODULE ASPIRATES WITH THE NEXT GENERATION SEQUENCING THYGENX TEST

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Interpace Diagnostics

Objective: Fine needle aspiration (FNA) cytology and molecular testing play an important role in the preoperative management of patients with thyroid nodules. Recent advances in molecular pathogenesis and next generation sequencing (NGS) have uncovered a large number of oncogenic gene alterations that drive thyroid cancer. In this study we evaluated the accuracy of ThyGenX, a novel NGS molecular test intended for the risk-based, preoperative diagnosis of thyroid nodules with indeterminate cytology.

Methods: FNAs collected as part of routine clinical practice were tested for the presence of 17 gene alterations in the BRAF, HRAS, KRAS, NRAS, PAX8 and RET genes using target-specific, multiplex PCR and liquid bead array detection (miRInform Thyroid test). Residual total nucleic acids were then tested in duplicate for over 100 gene alterations in the same genes plus PIK3CA using pooled PCR and targeted NGS (ThyGenX test).

Results: We compared 5,576 individual mutation calls generated in 328 representative FNAs. There was 100% negative agreement between miRInform and ThyGenX (no false positive by NGS). Gene alterations were detected by ThyGenX in 111 miRInform-positive specimens, including 29 out of 29 fusion transcripts and 1 double positive BRAF/HRAS. The positive agreement was 96%, 87% and 75% using NGS cut offs at 1%, 5% and 10% variant, respectively. The overall qualitative agreement was 99.9% at the mutation level and 98.5% at the sample level. ThyGenX identified 10 additional mutations not interrogated by the miRInform panel: 2 in BRAF codon 601, 2 in HRAS codon 13, 2 in KRAS codon 61 and 1 NRAS, 1 KRAS and 2 PIK3CA in 4 samples already positive for RAS mutations by miRInform and NGS.

Discussion: The perfect negative agreement observed for 5,459 potential mutation loci demonstrates that NGS does not generate false positive results. ThyGenX is expected to provide the same high positive predictive value as molecular tests currently used in the clinical setting. The positive agreement at 5% variant cut off was consistent with the analytical sensitivity reported in the literature for these distinct technology platforms. Duplicate NGS testing may further enable robust detection of mutations at 1% variant and, when combined with expanded mutation panels, could further increase the clinical sensitivity of molecular testing.

Conclusion: ThyGenX was highly accurate when compared to a clinically validated molecular test in 328 thyroid nodule FNAs. The NGS approach provides additional genomic insights into thyroid cancer pathology and the opportunity to interrogate novel relevant markers to further improve the diagnosis of thyroid nodules with indeterminate cytology.
Abstract #1096

THYROID TUBERCULOSIS, CLINICALLY DIFFICULT TO DIFFERENTIATE WITH CARCINOMA

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Objective: Tuberculosis of the thyroid gland is a very rare disease. The incidence is low even in countries where the prevalence of tuberculosis is high. The diagnosis is often difficult as the clinical presentation has no distinct characteristics.

Methods: Retrospective analysis of records of thyroid cases of university teaching hospital done. We present five cases of primary thyroid tuberculosis.

Case Presentation: One case was diagnosed on the basis of fine-needle aspiration cytology (FNAC), as they presented with thyroid nodule. In one case tuberculous lymphadenitis was mimicking metastatic lymph nodes from papillary thyroid carcinoma. Other cases were diagnosed on histopathology as the patient underwent thyroidectomy. All patients were given antituberculous treatment for nine months.

Discussion: It is observed that certain tissues are relatively resistant to tuberculosis, tuberculosis of heart, striated muscles, thyroid and pancreas are rarely encountered. Tuberculosis of thyroid gland whether primary or secondary is an extremely rare disease. According to literature its frequency is 0.1%-0.4% in histologically diagnosed specimen. Symptoms of thyroid tuberculosis are non specific and variable. The pathology of thyroid gland may be as follows: a) Multiple lesions throughout the gland like miliary TB; b) Enlargement of gland due to caseating granulomas; c) Cold abscess formation sometimes with multiple sinuses; d) Chronic fibrosing tuberculosis, difficult to distinguish from De Quervain’s thyroiditis; e) Acute abscess formation, when there is a danger of making wrong diagnosis of carcinoma. In present series 4 cases of thyroid tuberculosis were not diagnosed preoperatively and treated on the line of thyroid carcinoma.

Conclusion: Tuberculosis apart from metastasis in thyroid carcinoma should also be considered in the etiology of enlarged lymph nodes in those with risk factors for tuberculosis. Also tuberculosis should be kept in mind in the differential diagnosis of thyroid masses, even in patient with no history and symptom of tuberculosis disease elsewhere.

Abstract #1097

ANALYSIS OF GLUTEN AND ALUMINUM CONTENT IN SYNTHROID® (LEVOTHYROXINE SODIUM TABLETS)

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AbbVie, Inc

Objective: Concerns regarding certain excipients in pharmaceutical products and their potential impact on general health has increased as patients and consumers become more exposed to medical information. AbbVie specifically has experienced an increase in inquiries from health care providers as well as patients regarding aluminum and gluten content in Synthroid®. The objective of this study was to review and quantify levels of aluminum and gluten in Synthroid® tablets.

Methods: Aluminum level estimations were based on the information from the raw material suppliers, raw material specifications, information from the literature, and scientific judgment using worst case assumptions. Gluten content was determined in multiple lots of drug substance and excipients used in the manufacture of Synthroid tablets using the US-RIDASCREEN Gliadin Test Kit at a third party laboratory.

Results: The estimated maximum aluminum levels across the various tablet strengths, ranged from 19 to 137 micrograms per tablet. This is an order of magnitude lower than the ATSDR chronic-duration oral minimal risk level (of 1 mg Al/kg/day for aluminum). All lots evaluated had gluten concentrations of less than 3.0 ppm, which is the lowest detectable limit of the method and below the < 20 ppm threshold the FDA is tentatively considering for defining “gluten-free” in foods.

Conclusion: Across the various tablet strengths, the estimated maximum aluminum levels were far below the expert determined minimal risk level of exposure to aluminum. Synthroid® tablets do not contain gluten or gluten derivatives.
Abstract #1098

STRUMA OVARII: A RARE CAUSE OF HYPER-THYROIDISM

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Case Presentation: A 41-year-old African-American woman with no significant medical history presented to the office with fatigue of 3 months duration. Her physical exam was unremarkable. Biochemical values revealed normal FT3, FT4 and suppressed TSH levels. Thyroid stimulating immunoglobulin, thyroglobulin antibody and thyroid peroxidase antibody were within normal limits. Thyroid ultrasonography revealed a heterogeneous thyroid with no discernable nodules. She was diagnosed with subclinical hyperthyroidism and was advised follow up with repeat labs in 2 months. In the ensuing time she developed abdominal pain and dysmenorrhea that did not respond to conventional treatment. A computed tomogram of the abdomen and pelvis revealed a 10cm ovarian mass and a thickened uterine wall. She underwent bilateral salpingo-oopherectomy and abdominal hysterectomy. Histopathology of the ovarian mass revealed a mature teratoma with struma ovarii with an intact capsule and no malignant cells. After the surgery her symptoms resolved, and TSH levels returned to normal.

Discussion: Struma ovarii is a teratoma of the ovary that contains thyroid tissue. It is a rare cause of hyperthyroidism and is generally noted in the fourth decade of life. Patients usually present with abdominal pain and a pelvic mass and are usually identified based on histopathology findings consistent with thyroid follicles. If the patient is hyperthyroid TSH is low and T3 and T4 are elevated. Thyroglobulin is usually elevated. Malignant struma ovarii are difficult to diagnose and exhibit tumor invasion, metastases, recurrence or features of papillary thyroid cancer. Pelvic ultrasonography is the initial imaging of choice. Radio-imaging using Iodine-131 can be used to confirm the presence of functional thyroid tissue. Treatment involves control of overt hyperthyroid state and once euthyroid, surgical removal of the teratoma is curative. Malignant struma may need more extensive surgical resection. The use of a total thyroidectomy and radio iodine therapy is controversial and is based on isolated case reports. Mutations in BRAF and RAS genes have also been noted in malignant struma ovarii.

Conclusion: We describe a case of struma ovarii presenting as subclinical hyperthyroidism and review diagnosis and treatment options for these patients.

Abstract #1099

A CASE OF MYXEDEMA MADNESS

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Case Presentation: A 49-year-old man with unknown past medical history was brought into the Emergency Department after being found talking to himself incoherently. Upon initial evaluation, he was found hostile, uncooperative and disorganized. He was given Haldol, Lorazepam and Diphenhydramine for agitation. Soon after, he became obtunded, bradycardic, hypotensive, tachypneic and hypoxic, and was intubated for airway protection. Vasopressor was started to maintain blood pressure. Patient was admitted to MICU and Endocrinology was consulted. Physical exam revealed thyroidectomy scar without palpable thyroid gland. Work up showed TSH 89 mIU/mL, free T4 0.26 ng/dL, free T3 0.3 pg/mL and Creatinine 2.09 mg/dL. ECG showed prolonged QTc and T wave inversions in anterolateral leads but serial troponins were negative. CT head and CXR were normal. Patient remained afebrile and had negative urine and blood cultures. Myxedema crisis was strongly suspected; therefore Levothyroxine 400mg IV as loading dose was administered after a stress dose of Hydrocortisone IV was given, as adrenal insufficiency had not been ruled out. Plan was to give Triiodothyronine IV but it was unavailable, thus Liothyronine 10mcg was given enterally instead. Follow up labs showed improving TSH of 23 mIU/mL, free T4 0.54 ng/dL and free T3 1.1 pg/mL. Patient was successfully extubated and his mental status improved enough to provide a history of thyroidectomy with unclear compliance with Levothyroxine therapy. Once he started to tolerate oral diet, Levothyroxine was switched from IV to oral weight based maintenance dose.

Discussion: Myxedema crisis may occur with long-standing severe hypothyroidism but can also be precipitated by infection, cold exposure, cardiac event or the use of sedatives. Myxedema crisis may present with myxedema madness initially instead of the typical symptoms of confusion and lethargy. With our patient, he was afebrile, without leukocytosis or any objective signs of infection. ECG and troponins did not indicate acute coronary event. The most likely triggers include cold temperature given his social situation with concomitant administration of sedative medications for the management of agitation. After medication administration, patient began to exhibit the typical symptoms of myxedema coma such as bradycardia, hypotension and hypoventilation.
Conclusion: Myxedema madness is a less common presentation of myxedema crisis but it should be on the differential when encountering a patient with unknown medical history presenting with a possible thyroidectomy scar and psychotic features.

Abstract #1100

REPORT OF ANOTHER CASE OF A PYRAMIDAL LOBE MASQUERADING AS A THYROID NODULE

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Michigan State University

Objective: Pyramidal lobe is the accessory lobe of the thyroid that extends superiorly from the isthmus to the hyoid bone. We previously reported a case of a pyramidal lobe simulating a thyroid nodule on ultrasound, leading to a request for fine needle aspiration (FNA). We describe another case, to draw attention to this misleading sonographic finding.

Case Presentation: A 60-year-old male with hypertension, diabetes mellitus and dyslipidemia was referred for asymptomatic hypercalcemia. Vitals signs were stable and physical examination revealed a prominent thyroid gland. Laboratory evaluation demonstrated elevated serum calcium and parathyroid hormone levels, low vitamin D and a normal TSH. Neck ultrasound revealed a small diffuse goiter, with a hypoechoic ill-defined nodule in the isthmus measuring 1.63 x 1.25 x 0.59 cm which warranted a FNA. However, the biopsy was cancelled as meticulous pre-FNA real time sonography of the thyroid demonstrated that the isthmus nodule was not a real nodule, but actually it was a pyramidal lobe with benign-appearing texture similar to the rest of the gland parenchyma. This was further confirmed on further imaging with computed tomography of the neck that revealed a pyramidal lobe extending superiorly from the isthmus, more to the right than left.

Discussion: Pyramidal lobe is a morphological variation of the thyroid gland present in about 28-55% of the population. It is more common in men than in women. The presence of pyramidal lobe may be misinterpreted as an abnormality on imaging, which was demonstrated in our case.

Conclusion: Careful pre-FNA sonographic real-time scanning should be performed in the case of nodules in the midline or isthmus. Pyramidal lobe can masquerade as a nodule in this region, and should be excluded. This would avoid needless sampling of a normal thyroid tissue.

Abstract #1101

BEXAROTENE ASSOCIATED HYPOTHYROIDISM IN A PATIENT TREATED FOR CUTANEOUS T-CELL LYMPHOMA

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Objective: We present a case of hypothyroidism in a patient with Cutaneous T-Cell Lymphoma (CTCL) treated with the retinoid X receptor-selective agonist Bexarotene (Targretin).

Case Presentation: A 63 year old, Black man with no past medical or surgical history presented with fever and chills for 1 week. He reported weakness, shortness of breath, lack of appetite, diffuse muscle aches and patchy rashes over his elbows for >10 years, which progressed to cover his entire body in past 2 months and didn’t improve with moisturizers and triamcinolone. He denied smoking, alcohol or illicit drug use, had no allergies and no relevant family history. Examination was significant for sinus tachycardia at 137bpm, diffuse discolorated patches, with areas of peeling, excoriated and open wounds with purulent discharge and a foul odor covering the patient’s entire body. Open sores over the right hip revealed areas of necrotic, fungating tissue.

Labs were significant for leukocytosis, macrocytic anemia, elevated glucose, alkaline phosphatase and venous lactate, and low total protein, albumin, and calcium. Treatment with IV saline and Piperacillin/Tazobactam, topical mupirocin and silvadine was started. Skin biopsy was consistent with mycosis fungoides and immunophenotypic features favored T-cell lymphoma. Peripheral smear and flow cytometry showed no evidence of sezary cells. CT scan showed bilateral axillary lymphadenopathy, small pleural effusions, and hepatomegaly with fatty infiltration. Stage IV Mycosis fungoides with anaplastic large cell transformation was diagnosed and systemic Bexarotene at 300mg/m2/day (450mg daily) was started, to be followed by external beam radiation to the lower extremities lesions. Baseline thyroid function tests (TFTs) were normal. Repeat TFTs in 1 week showed decreased TSH and free T4 (FT4), 0.35 and <0.04 respectively. The patient had no symptoms or exam findings suggestive of hypothyroidism. A random cortisol level >20 excluded adrenal insufficiency and the patient was treated with PO LT4 100mcg/day. One week after starting LT4, TSH and FT4 increased to 0.74 and 0.04 respectively.

Conclusion: This patient’s hypothyroidism was due to...
Bexarotene’s central and peripheral effects (decreased TSH secretion and increased degradation of circulating thyroid hormones). Based on this experience, we conclude that higher replacement doses of LT4, relative to other hypothyroid states, are needed in Bexarotene-induced hypothyroidism to achieve and maintain euthyroidism. Frequent measurements of thyroid function, TSH and FT4, should start as early as 1 week after Bexarotene therapy.

Abstract #1102

A PUZZLING CASE OF POSTURAL ARRHYTHMIA IN THE SETTING OF HYPERTHYROIDISM POSING A DIAGNOSTIC CHALLENGE

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Michigan State University

Objective: Postural tachycardia syndrome is a heterogeneous group of disorders, the cause of which is multifactorial. We present a case of postural atrial fibrillation (AF) in a patient with hyperthyroidism, which presented a diagnostic challenge in the endocrinology clinic.

Case Presentation: A 57-year-old female presented to the endocrinology clinic for evaluation of hyperthyroidism. She reported weight loss of two months duration. Vital signs taken by the medical assistant (MA) were reported as normal, with heart rate of 84/minute and blood pressure of 126/70. Physical examination did not reveal a gross goiter or nodules, but a bruit was appreciated. Forwarded laboratory evaluation demonstrated thyroid-stimulating hormone (TSH) of <0.01 uIU/ml (0.38-7.0 UIU/ml), free thyroxine (FT4) of 2.4 ng/dl (0.7-1.8 ng/dl) and free triiodothyronine of 5.5 pg/ml (2.3-4.2 pg/ml). Thyroid ultrasound demonstrated a heterogeneous hyperemic gland without nodules.

Of interest, a rapid irregular heart rhythm was noted. An EKG showed a normal sinus rhythm. A repeated physical exam again showed irregular rapid rhythm. A consultation with cardiology was obtained onsite, who ordered a repeat EKG in the upright position, which then captured AF with a rate of 112/minute. However on recumbent position, EKG showed a return to sinus rhythm.

She had no prior history of arrhythmias, but in retrospect, she reported frequent palpitations. Following the recommendations of the cardiologist, she was treated with Metoprolol and Eliquis (a new anti-coagulant). Echocardiogram was normal with no valvular disease. Subsequent labs showed thyroid stimulating immunoglobulin of 38% (<140%) and thyrotropin receptor antibody of 47% (<17%), confirming Grave’s disease. She was started on methimazole. On subsequent visits, she was found to be in sinus rhythm while she became biochemically euthyroid. Due to disturbing rash and pruritus, methimazole was discontinued and she underwent thyroidectomy, following which the arrhythmia completely resolved, and Eliquis was stopped. Currently she is on levothyroxine and low dose metoprolol, which is being slowly tapered off.

Discussion: Postural tachycardia syndrome is a diverse group of disorders characterized by paroxysmal tachycardia due to hypovolemia or autonomic dysfunction or hyper dynamic beta-adrenergic function. Hyperthyroidism is associated with increased sympathetic activity which could probably cause positional arrhythmia as seen in our patient, which resolved after complete thyroidectomy.

Conclusion: Increased sympathetic tone in upright position results in acceleration of the heart rate and possibly AF in the setting of heightened sympathetic activity as seen in hyperthyroidism.

Abstract #1103

HYPOTHYROID ASSOCIATED MYOPATHY PRESENTING AS RHABDOMYOLYSIS AND ACUTE KIDNEY INJURY

Anatoliy Tsirlin, MD1, Silda James, MD2, Sadia Hussain, MD2

1. NewYork-Presbyterian Lawrence Hospital, 2. SUNY Downstate Medical Center

Objective: We report a case of hypothyroid myopathy in a man with acute lower extremity weakness, found to have Hashimoto’s hypothyroidism, rhabdomyolysis and acute kidney injury.

Case Presentation: A 49 year old man with no significant medical or surgical history, presented with lightheadedness, thigh pain, weakness and difficulty walking up stairs for one day. Review of systems revealed nausea and emesis 2 days prior, day time somnolence, fatigue, cold intolerance, and new onset snoring with periods of apnea. He reported using various sleeping aids (chamomile, passion flower, valerian root, skullcap extract and melatonin) with no improvement, social alcohol use, current cigarette and marijuana use, and no family history of thyroid disease. He denied vigorous exercise, trauma or illness prior to presentation. Physical exam was remarkable for bradycardia with a heart rate in the 40s, yet no other stigmata of hypothyroidism were observed (i.e., no thyroid eye disease, lid edema, goiter, neck scar, pericardial friction rub, jaundice, delayed relaxation of deep tendon reflexes, muscle tenderness, non-pitting edema, or thyroid dermopathy). Initial labs were significant for acute kidney injury with an elevated creatinine of 1.73mg/dL (0.8-1.4mg/dL), mild transaminitis with AST and ALT of 63U/L and 60U/L (0-35 and 3-36U/L respectively), CK of 2,648U/L (5-130U/L) and TSH of 199.8mcU/L.
(0.55-4.78 mcU/L). EKG showed sinus bradycardia in the range of 40 bpm. The preliminary diagnosis was Hashimoto’s hypothyroidism with hypothyroid myopathy, rhabdomyolysis and acute kidney injury. Additional tests revealed a random cortisol of 12.5 mcg/dL (3.1-16.7 mcg/dL), Free T4 (FT4) 0.44 ng/dL (0.89-1.76 ng/dL), thyroxine (T4) 0.7 mcg/dL (4.5-10.9 mcg/dL), T3 uptake 27.5%, thyroid peroxidase antibody titer of 4,895 (<60), and undetectable anti-thyroglobulin antibodies. He was treated with IV normal saline hydration, LT4 100 mcg IV x 1 dose, and continued on LT4 100 mcg PO q am, with interval improvement in symptoms and laboratory measures of CK, liver function tests, creatinine, TSH and FT4.

**Conclusion:** Mild musculoskeletal symptoms are common in hypothyroidism, while rhabdomyolysis and acute kidney injury are rarely reported manifestations. Although the exact mechanism is unknown, potential etiologies include thyroxine mediated, reversible defects in glycogenolysis and impaired mitochondrial oxidative metabolism. While myopathy is generally seen in long standing and severe hypothyroidism, a lack of overt clinical symptoms may delay prompt diagnosis and appropriate treatment. Based on our experience we propose that hypothyroidism should be considered in cases of unprovoked myopathy, rhabdomyolysis and kidney injury.

**Abstract #1104**

**DOES THE WEIGHT-BASED CALCULATION FOR THYROID HORMONE REPLACEMENT NEED TO BE REVISED?**

Malek Cheikh, MD¹, Pamela Schroeder, MD, PhD¹, Ilana Cohen, Maryann Henin, MD², Paul Sack, MD¹

1. Medstar Union Memorial Hospital, 2. University of Maryland

**Objective:** Traditionally, starting replacement doses of levothyroxine have been calculated by multiplying the patient’s total body weight by 1.6 ug/kg. However, this simple calculation does not take into account several factors like obesity, gender, sex, age, body fat percentage, hormonal state, interfering medications/ or supplements and other comorbidities. Therefore, we hypothesize that this standardized calculation may need revision.

**Methods:** A patient survey was administered to patients with hypothyroidism to better elucidate factors which affect the ideal levothyroxine dose including anthropometric patient measurements, co-morbidities, medication interactions, adherence to thyroid replacement and other factors.

**Results:** We analyzed data from 51 patients. The median age was 61, females represented 87% of the patient population.

The adherence to therapy was estimated to be 44%. We ran a bivariate analysis and the only factor that showed a meaningful relationship to normal thyroid state was adherence to medication. There was no meaningful difference of the levothyroxine dose between the traditional weight based thyroid dose, body fat percentage or body mass index.

**Conclusion:** The traditional way of calculating the thyroid replacement therapy dose is as good as using the body fat or body mass index. So far our data indicate that the only variable significantly affecting the dose is the adherence to medication. However, we are in the process of analyzing retrospective data collected from euthyroid patients on thyroid hormone replacement who underwent thyroidectomy to further clarify the ideal relationship between weight and thyroid dose.

**Abstract #1105**

**AN INTERESTING CASE OF MOLAR PREGNANCY INDUCED HYPERTHYROIDISM**

Sara Samie, MD

Kaiser Permanente

**Case Presentation:** A 22 yo woman at 13 and 3 weeks gestational period presented with a 5 day history of heavy vaginal bleeding. She complained of symptoms of heat intolerance, palpitations and tremors. On exam, she was tachycardic with a fine tremor. Admitting T3 level was 380 ng/dL, free T4 2.26 ng/dL, TSH <0.01 uIU/mL, Beta HCG 969,960 mIU/mL. Her pelvic ultrasound showed a 9.1x5.5x6.7 cm multicystic mass without fetal parts consistent with a molar pregnancy. Dilatation and curettage (D&C) was postponed for 24 hours of iodine administration to prevent release of thyroid hormone and thyroid storm during the procedure. She received Potassium Iodide (SSKI) 0.25 mL po q6hrs, Methimazole 40 mg po x1, then 20 mg po q8hrs, and was started on Propranolol 60 mg po x1 followed by Propranolol 30 mg po q6 hrs. She also received hydrocortisone 100 mg IV x1 prior to going to the OR. The patient underwent D&C on hospital day #2 and tolerated the procedure without any complications. On post op day 1, the patient’s T3 level had decreased to 155 ng/dL. Both methimazole and SSKI were stopped directly after the OR. She ran a bivariate analysis and the only factor that showed a meaningful relationship to normal thyroid state was adherence to medication. There was no meaningful difference of the levothyroxine dose between the traditional weight based thyroid dose, body fat percentage or body mass index.

**Conclusion:** In women of childbearing age presenting with hyperthyroidism, hyperthyroidism induced by gestational trophoblastic disease should be considered with consideration of treatment of the hyperthyroidism prior to D&C in order to prevent thyroid storm.
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