2016 AACE ANNUAL SCIENTIFIC & CLINICAL CONGRESS ABSTRACTS

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# ABSTRACTS

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ADRENAL DISORDERS

Abstract #100

UNTREATED CONGENITAL ADRENAL HYPERPLASIA (CAH) PRESENTING WITH A LARGE UTERINE LEIOMYOMATA AND PARARENAL MASS: CASE REPORT AND REVIEW OF LITERATURE

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Objective: CYP21 A2 deficiency is the most prevalent cause of CAH. If left untreated, female patients may develop severe virilization, adrenal hyperplasia and adrenal rest tumors. We present a case of CAH diagnosed in infancy with noncompliance to treatment who presented with a large uterine fibroid and a pararenal adrenal rest tumor.

Case Presentation: A female born with an enlarged clitoris was diagnosed with classic CAH at age 8 months. In spite of the diagnosis, she felt well off all glucocorticoid therapy and only took medication during illness. She had menarche at age 7, early menopause at age 35. At age 43, she presented with abdominal distention, constipation and menorrhagia. Physical examination was notable for short stature (4’ 8”), a markedly distended abdomen, increased muscle mass, severe alopecia and hirsutism. Labs were notable for ACTH 440 pg/ml (nl <46), 17-OH Progesterone 11,000 ng/dL (n <206), androstenedione 15.6ng/mL ( nl- 0.13-0.82 ), PM cortisol 3.6 mcg/dL, testosterone 618 ng/dL (10-75), DHEA-S 390 mcg/dL (35-430), DHEA 3.810 ng/mL (0.63-4.7), estradiol 162 pg/mL, LH 2.7 mIU/ml, FSH 0.2 mIU/ml, Prolactin 15.1 ng/mL, aldosterone 12.5 ng/dL, renin 2.3 ng/mL/h, sodium 141 mEq/L and potassium 3.5 mEq/L. Abdominal CT revealed a very large uterine fibroid (30 x 30 x18 cm), bilaterally enlarged adrenals and a 5.3 x 4.2 x 5.4 cm left pararenal mass. The patient underwent total abdominal hysterectomy with removal of a 10 kilogram leiomyoma along with resection of the pararenal mass, originally read as metastatic adrenal cortical carcinoma but revised to ectopic adrenal rest tumor given her clinical history.

Discussion: Untreated CAH patients may have severe sequelae secondary to elevated ACTH, androgens and low glucocorticoids with or without mineralocorticoid deficiency. This patient demonstrates some additional, less common, sequela of untreated severe CAH in adulthood. Excess androgens in females with CAH may be aromatized to estrogens resulting in estrogen-dependent tumors such as the massive fibroid noted in this case. Chronic ACTH stimulation resulting from untreated CAH can produce adrenal rest tumors, most commonly noted in the testes of male patients. However, ectopic adrenocortical cells have also been reported in the retroperitoneum, broad ligaments, ovaries, and inguinal regions. This patient had a rarely reported pararenal adrenal rest tumor, initially read as a metastatic adrenal cell carcinoma by the pathologist because of the unusual location of adrenal cortical tissue.

Conclusion: This case illustrates the untoward effects of untreated CAH in females and the need for thorough clinical history when evaluating pathologic specimens in these patients.

Abstract #101

A CASE OF RAPIDLY GROWING ADRENAL MASS AND HYPERPIGMENTATION CAUSED BY DISSEMINATED TUBERCULOSIS

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Case Presentation: A 51 year old Bolivian woman presented to clinic with 100 pound weight loss and hyperpigmentation over the past few months. Seven months prior, she had a right nephrectomy for necrotizing granulomatous nephritis. CT Abdomen at that time showed hyperplasia of the adrenal glands without a discrete mass. Four months after nephrectomy, she presented with nausea, vomiting and hypotension diagnosed with adrenal insufficiency and started on hydrocortisone and fludrocortisone. Her a.m. cortisol was 1.4 ug/dL with ACTH >2000 pg/mL. CT imaging of the abdomen/pelvis was repeated (6 months after initial CT) showing an enlarging right upper quadrant mass measuring 6.5 x 3.5 x 5.6 cm, partially calcified with lymphadenopathy in the portal, retroperitoneal and paraaortic region, with left adrenal gland thickening and nodularity with calcification. Significant labs drawn at our institution two months later revealed Cortisol 1.1 (10 am), ACTH >2000 pg/mL, 11-deoxycortisol 19 ug/dl, Aldosterone < 1 ng/dL, DHEA-Sulfate 1 ug/dL, 24-hour urine metanephrines < 20 ug/24 hr, FSH 20.4 mIU/mL, LH 27.2 mIU/mL, TSH 3.770 mIU/mL. Physical exam showed diffuse hyperpigmentation of skin, palmar creases, tongue and oral mucosa. Causes for primary adrenal insufficiency including sarcoidosis, coccidioidomycosis, histoplasmosis, HIV, and...
autoimmune etiologies were negative. A Quantiferon gold test was positive. Subsequent CT chest revealed a right apical lung mass 2 cm with two additional lung nodules. Open lung biopsy cultures isolated mycobacterium tuberculosis, with a pathology of focally necrotizing granulomatous pneumonitis. Acid fast bacilli (AFB) stains were negative. The patient was given a regimen of rifampin and isoniazid. Two biopsies of the right adrenal mass were non-diagnostic, with negative AFB stain. Based on CT findings of bilateral adrenal enlargement with calcification, and identification of pulmonary tuberculosis, the patient was diagnosed with adrenal insufficiency due to tuberculosis. She continues to be on hydrocortisone and fludrocortisone replacement therapy. A repeat CT 10 months after initiation of TB treatment showed a decreased interval size of left adrenal mass with no clear visualization of the prior right adrenal mass.

Conclusion: Adrenal tuberculosis is a rare but life threatening cause of Addison’s disease. Diagnosis of adrenal tuberculosis can be challenging because percutaneous adrenal biopsy is non-diagnostic in up to 37% of cases. Therefore, we relied on systemic findings, positive quantiferon gold assay, clinical imaging and response to treatment for the diagnosis and to guide therapy.

Abstract #102

CUSHING’S SYNDROME DUE TO ECTOPIC ACTH PRODUCING METASTATIC MUCOEPIDERMOID CARCINOMA TO THE LUNGS

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Objective: To present a case of Cushing’s syndrome caused by ectopic ACTH secretion (EAS) from mucoepidermoid carcinoma (MEC) metastatic to the lungs.

Case Presentation: A 52 year old male with a prior history of mucoepidermoid carcinoma status-post total laryngectomy with metastasis to the lungs, post chemotherapy and radiation treatment, presented with a 3 month history of facial plethora and Cushingoid facies. He also had symptoms of easy bruising, fatigue, and polyuria. Initial laboratory revealed a serum cortisol of 30 mcg/dL, ACTH 73 pg/ml, and 24 hour urinary free cortisol of 1516 mcg/d. Pituitary MRI showed no abnormalities. High dose dexamethasone did not suppress ACTH production. CT scan showed a mass in the right lung apex, a solid lesion in the left hilum representing pulmonary metastases, normal adrenals, and no metastatic disease in the abdomen or pelvis. He was diagnosed with EAS caused by metastatic MEC. He was started ketoconazole and the dose was titrated to 1200 mg daily. His signs and symptoms of Cushing’s syndrome, most notably the facial plethora, resolved. The urinary free cortisol normalized to 26.4 mcg/d.

Discussion: ACTH-dependent Cushing’s represents 80% of the cases of endogenous Cushing’s. EAS accounts for 20% of ACTH dependent Cushing’s syndrome. Of these, small cell lung carcinoma is the leading cause. There is one other reported case of MEC causing EAS to our knowledge. MECs originate from glandular tissue identical with salivary glands. These tumors are rare and compose 0.1-0.2% of all lung cancers. Currently accepted treatment for MEC is complete resection of the primary tumor and postoperative radiation therapy. The first line treatment of EAS is surgical removal of the primary tumor or bilateral adrenalectomy, or a combination of both. In cases of metastatic disease, the surgical approach may not be possible. For those non resectable tumors, medical therapy should be introduced. Steroidogenesis inhibitors such as ketoconazole, metyrapone, and mitotane are used. Occasionally, combination therapies are used as an alternative to bilateral adrenalectomy.

Conclusion: Conclusion: EAS caused by MEC is rare. Treatment of the EAS is challenging. Surgical excision is the treatment of choice, followed by medical therapy to block glucocorticoid production.

Abstract #103

PRIMARY ADRENAL LYMPHOMA PRESENTING AS FATIGUE AND BILATERAL ADRENAL ENLARGEMENT

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Case Presentation: 78 year old Hispanic woman presented to the emergency room with generalized weakness and fatigue for 4 weeks. Her fatigue was progressive and was associated with anorexia, weight loss, intermittent fever and night sweats. Her local doctor obtained a CT scan of the abdomen which revealed bilateral adrenal masses, with the right-sided mass of 10.2 cm with 40 Hounsfield Units (HU) and the left adrenal gland measuring 7.3 cm in greatest dimension with 41 HU. Patient was referred to our institution. Past medical history was remarkable for renal cell carcinoma (RCC) for which she had had a right nephrectomy 8 years ago. She had not had recurrence since then. She had no travel history outside of the United States. Physical exam showed an ill-appearing patient, and mild tenderness to palpation over the abdomen. Based on history of RCC, differential was metastasis from RCC, and an adrenal biopsy was planned. Work up for adrenal dysfunction revealed plasma aldosterone concentration...
of < 1 ng/dL and plasma renin activity of 3.24 ng/ml/hr, normal urinary metanephrines of <19 ug/hr (45-290 ug/hr) and normal urinary normetanephrines of 371 ug/24 hrs. Cosyntropin stimulation test showed suboptimal response, with cortisol rising to 10.2 mcg/dL at 60 min, consistent with adrenal insufficiency, and hydrocortisone and fludrocortisone replacement was started. Fine needle aspiration of patient’s left adrenal mass revealed diffuse large B-cell lymphoma.

Discussion: Even though secondary involvement of adrenal glands by lymphoma occurs in a quarter of the patients with the disease, primary adrenal lymphoma is rare, and to our knowledge, less than 200 cases have been reported. PAL usually affects people with average age of 68 years and there appears to be a preponderance for men. Majority of the cases are bilateral, which holds true for our patient. Interestingly, while secondary involvement of adrenal glands with lymphoma and other malignancies is usually not associated with adrenal insufficiency, almost 40% of the cases of primary adrenal lymphoma had adrenal dysfunction. This is thought to be due to the fact that adrenal lymphomas are aggressive tumors and have been shown to replace almost all of the adrenal medulla and cortex on autopsy studies.

Conclusion: Primary adrenal lymphoma is a rare cause of adrenal masses, and should be considered in the differential diagnosis, especially in the setting of bilateral involvement and suggestive clinical presentation.

Abstract #104

IS THERE UTILITY FOR OCTREOTIDE TREATMENT IN PHEOCHROMOCYTOMA?

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Objective: Pheochromocytoma (PCC) and paragangliomas (PGL) have limited treatment options when they exhibit metastatic behavior. We present a challenging case in the diagnosis and treatment of metastatic PCC.

Case Presentation: 68-year-old male with uncontrolled hypertension presented with progressive left lower quadrant pain and unintentional weight loss. Evaluation revealed a left, heterogeneous adrenal mass on CT scan measuring 9.5cm in the greatest dimension with regional lymphadenopathy. Biochemical studies were consistent with PCC: total urine catecholamines 193 ug/24hr (ref <100), norepinephrine 187 ug/24hr (ref <80), dopamine 779 ug/24hr (ref <500), plasma normetanephrines 363 pg/mL (ref <205) and plasma chromogranin A 780 ng/mL (ref 1.9-15). Octreoscan showed abnormal uptake in the left lower neck, left upper quadrant, chest/mediastinum and lungs; thus he was started on Octreotide treatment with improved pain and appetite. An MRI neck was obtained for further evaluation of the abnormal uptake in the neck, demonstrating a left supraclavicular mass, abnormal signal intensities in the second rib and a possible left thyroid or parathyroid mass. Calcitonin, PTH and thyroid labs were normal.

Our patient underwent debulking surgery after adequate alpha blockade and was noted to have extensive tumor involvement, requiring distal pancreatectomy, splenectomy, radical nephrectomy with lymph node dissection and adrenalectomy. Pathology confirmed PCC (11.5cm) arising from the left adrenal gland that extensively invaded into the pancreas, renal and retroperitoneal soft tissues with metastasis to regional lymph nodes.

Discussion: Surgical debulking is helpful for controlling symptoms related to metastatic PCC/PGL to reduce hormonal secretion and improve symptoms. In our patient, surgery was combined with Octreotide, which provided symptomatic relief, although the utility of octreotide therapy on PCC/PGL control remains unclear. While the patient is currently continuing octreotide, a metaiodobenzylguanidine (MIBG) scan is scheduled to determine if he would benefit from high dose 131I-MIBG therapy, systemic chemotherapy, or perhaps DOTA-octreotate therapy.

Conclusion: Although it is uncommon for patients to get an octreoscan for PCC/PGL tumors, it may be helpful clinically for symptomatic management. Surgery, high dose MIBG (if positive), and systemic chemotherapy are the limited mainstay treatment options for patients with metastatic PCC/PGL. Possible new therapies with DOTA-octreotate may prove to be an option in the future.
Abstract #105

A CASE OF ADRENAL CRISIS (A MIMICKER OF ACUTE ABDOMEN) RESULTING FROM MEDICAL ADHERENCE: BALANCING RISK AND BENEFIT.!!

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Objective: Autoimmune Polyglandular Syndrome (APS) type II consists of Hashimoto’s thyroiditis associated with other autoimmune disorders, such as T1DM or Addison’s disease. Furthermore, Celiac disease, another not uncommon autoimmune disease, may co-exist with APS. Clinicians must cautiously alter management of patients with APS to maintain their delicate hormonal balances. The objective is to present a challenging case, featuring interacting endocrine pathophysiologic derangement.

Case Presentation: A 19 year-old female with Addison’s disease and Hashimoto’s thyroiditis, maintained on stable levothyroxine and hydrocortisone replacement, was recently started on a gluten free diet for celiac disease. Few weeks later, she presented to the emergency department with abdominal pain and vomiting. Imaging of the abdomen, blood glucose, and infectious work up were normal and acute abdomen was ruled out. Further investigation supported the diagnosis of acute adrenal crisis. She responded quickly to corticosteroid and mineralocorticoid therapy, and appropriate adjustment of her levothyroxine dose was made.

Discussion: This case exemplifies the complex interactions between endocrine systems. Villous atrophy associated with celiac disease impairs medication absorption; the atrophy quickly improves with cessation of gluten, resulting in physiologic need for lower doses of levothyroxine. These changes may occur more quickly than the six weeks needed for thyroid stimulating hormone to stabilize. In turn, supraphysiologic levothyroxine therapy can precipitate adrenal crises, by rapid metabolism of exogenous corticosteroids. Furthermore, for reasons not clearly understood, adrenal crisis may present with abdominal pain mimicking acute abdomen. This case illustrates the complex interactions of these pathophysiologic processes, and serves to raise awareness amongst treating physicians.

Conclusion: Clinicians should be vigilant in managing patients with multiple autoimmune disorders, where interplaying disease processes may alter therapeutic intervention. This applies in particular to patients on both levothyroxine and glucocorticoid therapy. The improved absorption of levothyroxine upon implementing gluten-free diet in this patient with Addison disease and hypothyroidism (who developed celiac disease) resulted in adrenal crisis, as explained above. This should always be kept in mind amongst endocrinologists.

Abstract #106

PERIOPERATIVE HYPERTENSIVE CRISIS IN BIOCHEMICALLY SILENT PHEOCHROMOCYTOMA

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Objective: We present a patient with unsuspected pheochromocytoma, who encountered hypertensive crisis during adrenalectomy.

Case Presentation: 67-year-old female with a 2.3 cm right adrenal nodule which had increased in size, from 1.7 cm in 2 years. She had no history of palpitations, sweating or diaphoresis. Past medical history included ovarian cancer status post TAH-BSO and chemotherapy with no recurrence and primary hyperparathyroidism status post parathyroidectomy. Vital signs were normal. Labs: normal plasma metanephrines (MN) 34 pg/mL (0-57), slightly elevated normetanephrines (NMN) 329 pg/mL (0-148), normal 24-hour urine MN 175 mcg (90-315) and NMN 661 mcg (122-676). Biochemical studies showed no evidence of Cushing’s syndrome or hyperaldosteronism. CT scan showed a 2.3 cm right adrenal nodule, density of 6 Hounsfield units. The left adrenal gland was normal. PET CT showed adrenal nodule with hypermetabolism, maximum standardized uptake values of 6.7, suspicious for malignancy. Because of the increasing size of the nodule and PET findings, she was referred for adrenalectomy.

During adrenalectomy, blood pressure fluctuated to a maximum of 230/140 mmHg, requiring intravenous medications for control. Following surgery, she became hypotensive and required intravenous fluid administration. Postoperative troponin level was slightly elevated and peaked at 0.17. Cardiac evaluation was consistent with demand ischemia. Subsequently blood pressure returned to normal on second day. No other complications were noted. Pathology was consistent with pheochromocytoma. Given history of hyperparathyroidism, she was referred to genetic counseling for MEN.

Discussion: Asymptomatic pheochromocytoma has been reported in up to 20% of all pheochromocytoma, but biochemically silent pheochromocytoma has rarely been reported. Some tumors with low or intermittent secretory activity, or rarely, non-functioning tumors may have false negative biochemical tests. Duration of progression from silent pheochromocytoma to symptomatic stage is unknown. In most cases of biochemically silent...
pheochromocytoma, the diagnosis is usually made after surgery by tissue pathology.

**Conclusion:** Our case illustrates a challenge in diagnosis and management of pheochromocytoma in the setting of normal biochemical tests and atypical imaging. Resection of unrecognized pheochromocytoma can precipitate life-threatening hypertension. Preoperative preparation with alpha-blocker in such patients remains controversial. This case emphasizes that hemodynamic variables must be monitored closely despite low clinical suspicion, and all precautions should be taken for managing hypertensive crisis.

**Abstract #107**

**TOO MUCH OF A GOOD THING – A RARE CASE OF LICORICE TOXICITY CAUSED BY COMMON HERBAL TEA DRINK**

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**Objective:** Licorice extract is a sweet ingredient found in many popular herbal tea products. When consumed in large quantities, licorice extract creates a dangerous state of non-aldosterone mineralocorticoid excess causing life-threatening electrolyte abnormalities. We present a rare case of apparent mineralocorticoid excess from consumption of a popular herbal tea containing licorice root extract.

**Case Presentation:** A 42-year-old woman was hospitalized for further evaluation of newly diagnosed hypertension and severe hypokalemia. She denied any recent illnesses, vomiting or diarrhea. She took no medications. There was no family history of hypertension or endocrine disorders. She denied using tobacco, alcohol or drugs. But, she drank a popular herbal tea daily because she enjoyed its taste. She used roughly 8 tea bags per day (suggested servings: 3-12 bags per day). One of the tea’s primary ingredients was licorice root extract. Physical exam was unremarkable, except for blood pressure 177/109. Pertinent laboratory results included potassium 1.8 mmol/L, bicarbonate 44 mmol/L, aldosterone <1.6 ng/dL, and renin 0.1 ng/dL. EKG showed U waves. The patient was started on antihypertensive medications. She required 300 meq of potassium daily during hospitalization. Endocrine consult was obtained. Other laboratory results included sodium 144 meq/L, TSH 1.2 mU/L, and random cortisol 12.8 mcg/dL. Further work-up revealed normal 17-OH progesterone (30 ng/dL) and elevated urine cortisol-to-cortisone ratio of 0.87 (normal ratio <0.5). She was diagnosed with chronic licorice ingestion causing apparent mineralocorticoid excess. She was instructed to stop drinking the herbal tea and was discharged on antihypertensive medications and potassium supplementation. Eight weeks later, medications were no longer needed and repeat 24 hour urine free cortisol improved from 53 ug/d to 32 ug/d.

**Discussion:** Licorice root can cause a syndrome of apparent mineralocorticoid excess. Both cortisol and aldosterone bind with similar affinity to mineralocorticoid receptors. Its active metabolite, glycyrrhetic acid, inhibits the enzyme 11-beta-hydroxysteroid dehydrogenase 2, which converts cortisol to its inactive form, cortisone. The resulting elevated cortisol levels cause excessive mineralocorticoid activity. Cessation of the herbal tea led to symptom resolution. It is noted that potential adverse effects of licorice extract are not labeled on product packaging.

**Conclusion:** This case illustrates that daily consumption of popular herbal teas containing licorice extract can lead to life-threatening apparent mineralocorticoid excess state. We suggest the use of warning labels to prevent toxicity.

**Abstract #108**

**ADRENOCORTICAL CARCINOMA WITH DELAYED ISOLATED OVARIAN METASTASIS: A CASE REPORT**

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**Objective:** Adrenocortical carcinoma (ACC) has a high recurrence rate that often occur within the first 2-3 years after initial resection. Ovarian metastases in ACC are rare and usually part of a widely metastatic disease. In this report, we summarized a rare case of isolated ovarian metastasis that occurred 7 years after resection of ACC and initially presumed to represent primary ovarian tumor. Methods: We describe clinical details of a patient with ACC and subsequent metastatic disease in the ovary. Available images, surgical pathology slides and proliferative activity (Ki-67) are reviewed.

**Case Presentation:** A 34 year-old Caucasian woman presented with hirsutism associated with right sided ACC. She underwent open adrenalectomy with R0 resection margins, received 2 years of adjuvant mitotane and followed without any evidence of recurrence. Seven years later, she had noticed repeated hirsutism and acne; found to have large left ovarian mass (20 cm) that was initially presumed to represent a primary ovarian tumor. After complete resection, pathological features were compatible
with recurrent ACC. Staging studies did not reveal any evidence of disease elsewhere.

**Conclusion:** This case is the first report of ACC with delayed isolated ovarian metastasis. Clinicians managing patients with ACC should be aware of the possibility of uncommon site metastasis even with many years of surveillance. Surgical resection is the preferred treatment for isolated and delayed ACC metastasis.

Abstract #109

**MAX (MYC ASSOCIATED FACTOR X) GENE ASSOCIATED WITH PHEOCHROMOCYTOMA.**

Adnan Haider, MD, Sandeep Dhindsa, MD

Texas Tech University

**Objective:** To present a case of bilateral pheochromocytomas due to a rare germline mutation.

**Case Presentation:** A 44 year old Hispanic woman was incidentally noted to have bilateral adrenal nodules (3.6 cm on right with central necrosis and 2 cm multilobulated nodule on left) on abdominal imaging performed for uterine fibroids. She had a 4 year history of hypertension which was not under good control in spite of therapy with three anti-hypertensives. She also reported episodic palpitations and sweating over the last 10 years. She had recently developed mild type 2 diabetes that was controlled with metformin. Family history was negative except for meningiomas in mother. Lab studies showed normal electrolytes, calcium and hemoglobin. Serum norepinephrine was >10 times the upper limit of normal while serum epinephrine and dopamine were minimally elevated. Urine metanephrine and normetanephrine were elevated 2 -5 fold higher than the upper limit of normal. MIBG showed increased uptake only in the adrenal nodules. Laparoscopic bilateral adrenalectomy was uneventful and pathology confirmed the presence of bilateral encapsulated pheochromocytomas, which had high cellularity and vascular invasion (PASS score 4/20). Synaptophysin was highly positive, S100 stain highlighted sustentacular cells and Ki67 index was 2%. Post operatively, she was started on hydrocortisone and flornifene. Plasma/urine metanephrines/normetanephrines and chromogranin A levels have remained normal on follow up biannual visits for the last 2 years following the surgery. She continues to be normotensive and euglycemic without any medications. Her age at diagnosis and bilateral involvement of adrenals prompted genetic work up following her recovery. She was found to be heterozygous for a p.R75* (c223C>T) pathogenic mutation that creates a premature stop codon in the MAX gene (14p23.3).

**Discussion:** MAX gene mutations were first reported in conjunction with pheochromocytomas/paragangliomas (PPGL) in 2011. MAX gene is a tumor suppressor gene that undergoes paternal transmission with maternal imprinting. MAX gene mutations usually cause bilateral adrenal tumors that predominantly produce norepinephrine and carry a moderate risk of extra adrenal metastasis. Less than 30 cases of MAX gene mutation associated PPGL have been reported in literature.

**Conclusion:** Our case is the 7th patient (the oldest) described in the literature with c223C>T mutation in the MAX gene. All these 7 patients had bilateral pheochromocytomas without extra-adrenal metastasis. While a third of all PPGL harbor a germline mutation, MAX gene mutations are a rare cause (<1% of all PPGL) of this rare disease.

Abstract #110

**PRIMARY ALDOSTERONISM AND SUBCLINICAL CUSHING’S FROM THE SAME ADENOMA: AN UNCOMMON VARIANT**

Jared Dendy, MD, Susana Dipp, MD, Alan Burshell, MD

Ochsner Medical Center

**Objective:** We present a case of a patient with presumed primary aldosteronism with subclinical hypercortisolism arising from the same adrenal adenoma. Knowledge of and recognition of this entity could have important diagnostic and therapeutic implications.

**Case Presentation:** A 64-year-old female with a medical history significant for diabetes mellitus type 2, hypertension, hyperlipidemia, and obesity was referred to endocrine clinic for evaluation of endocrine causes of secondary hypertension. She had hypertension for nearly 3 decades that had become resistant to therapy over the past year. She was on 5 anti-hypertensive agents with 2 having been added in the past year. She was noted to have hypokalemia requiring daily potassium replacement. This prompted her primary care physician to obtain adrenal magnetic resonance imaging (MRI). MRI revealed a 1.9 cm mass of the left adrenal gland demonstrating central high T2 signal and low T1 signal. No significant signal loss was noted on out-of-phase images. On history she denied easy bruising, muscle weakness, or depression. Physical examination showed some mild supraclavicular/dorsocervical fullness but did not exhibit violaceous abdominal striae, facial plethora, facial fullness, or central obesity. Labs were as follows: aldosterone 16.1 ng/dL, plasma renin activity 0.7 ng/mL/h, 8 AM cortisol after 1mg overnight dexamethasone suppression 2.7 ug/dL, late-night salivary cortisol 150 ng/dL (nml <100ng/dL), DHEA-SO4 19.9 ug/dL (nml 29.7-182.2 ug/dL), ACTH 13 pg/mL, hemoglobin...
Abstract #111

ENDOCRINE TOXICITIES OF MITOTANE THERAPY

Charisse Hanne Te, MD, Karen Herbst, MD, PhD

University of Arizona

Objective: Adrenocortical cancer (ACC) is a rare and aggressive disease treated with surgery and the adrenocorticolytic drug, mitotane, as adjuvant therapy. Common side effects of mitotane include fatigue, nausea, vomiting, and anorexia. The goal of presenting this case is to review the endocrine toxicities of mitotane that were overlooked.

Case Presentation: 62-year old male with ACC for 4 years, s/p left adrenalectomy, was admitted for generalized weakness, progressive fatigue since beginning mitotane therapy, excessive sleeping, poor oral intake and a 35-lb weight loss despite being in remission. Medications: mitotane 3500 mg/day, hydrocortisone 40 mg/day, and ondansetron. Blood pressure was normal; heart rate 102 beats/minute. He was slow to respond and drowsy, otherwise the physical exam was unremarkable. Sodium was low at 132 (136-145 mmol/L), potassium at 6.4 (3.5-5.1 mmol/L) and BUN/creatinine were elevated at 85 (9-26 mg/dl) /2.7 (0.7-1.3 mg/dl). Thyroid-stimulating hormone (TSH) was suppressed at <0.02 (0.35-4.0 uIU/ml) and free thyroxine was inappropriately low normal at 0.9 (0.7-1.5 ng/dl). Cortisol and adrenocorticotropic hormone were normal. Aldosterone was 4 ng/dl, but plasma renin activity (PRA) was elevated at 31 (0.2-1.6 ng/ml/hr supine). He was hypogonadal with an elevated luteinizing hormone of 39.7 (1.7-8.6 IU/L), a normal testosterone (T) at 610 (240-950 ng/dl) but high sex hormone-binding globulin (SHBG) at 437 (10-37 mmol/L), so free T was low at 15.6 (35-155 pg/dl). Computed tomography scan of the head, chest, abdomen and pelvis showed no abnormalities.

Discussion: Endocrine toxicities of mitotane include adrenal atrophy requiring glucocorticoid replacement, aldosterone deficiency, hypogonadism, and hypothyroidism. Mitotane increases levels of corticosteroid-binding globulin, thyroid hormone-binding globulin and SHBG, making the diagnosis of hormone dysfunction complicated. Increased SHBG levels can lower free T levels, as in this case. Metabolism of cortisol is increased by mitotane, requiring higher doses of glucocorticoids. This patient exhibited hyponatremia, hyperkalemia and high PRA, consistent with mineralocorticoid deficiency. Some studies suggest a direct inhibitory effect of mitotane on TSH secretion, as illustrated in this case. After increasing hydrocortisone and starting levothyroxine and fludrocortisone, the patient improved clinically and was discharged.

Conclusion: Multiple mitotane-induced toxicities were initially overlooked in this case and instead recurrence was sought by imaging. Endocrinologists should be familiar with the potential endocrine side effects of mitotane to recognize and treat them early on, and avoid unnecessary testing and radiation exposure.

Abstract #112

PATIENTS WITH ARMC5 MUTATIONS: THE NIH CLINICAL EXPERIENCE

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Objective: 1. To present the different phenotypical characteristics of patients with ARMC5 MUTATIONS. 2. To report the largest US cohort of ARMC5 MUTATIONS

Methods: We identified 20 patients with ARMC5 mutations (germline and/or somatic) that enrolled in our protocol at the NIH. Sociodemographic, clinical, laboratory and radiological information were extracted from all the subjects.

Results: Three families (with a total of 8 patients) were identified with ARMC5 germline mutations; the rest of the subjects (13/20) had sporadic mutations. Male to female ratio was 1.2:1. The cohort mean age was 48 yo and 60% were African American. CS was diagnosed in 40%, subclinical CS in 20%, hyperaldosteronism in 30% and...
no diagnosis in 10%. The mean serum cortisol (8 am) and Urinary Free Cortisol were 13.1 mcg/dl and 77 mcg/24hr, respectively. Bilateral adrenal enlargement (CT or MRI) was found in 95% of the subjects. Bilateral adrenalectomy was performed in 45%, unilateral adrenalectomy in 25%, medical treatment in 20% and no treatment in 10%.

Discussion: Armadillo repeat containing 5 (ARMC5) mutations have been shown to be associated with Primary Macronodular Adrenal Hyperplasia (PMAH) and are also observed in patients with primary hyperaldosteronism (PA) especially in African Americans. ARMC5 is located in 16p11.2 and is likely to be a tumor-suppressor gene. PMAH is a rare type of Cushing’s syndrome (CS) that results in increased cortisol production and bilateral enlargement of the adrenal glands.

Conclusion: ARMC5 mutations present a broad spectrum of clinical phenotypes including no symptomatology, subclinical CS, CS, PA, and PA with glucocorticoid secretion. The analysis of this cohort demonstrated that patients with bilateral adrenal enlargement on imaging and suggestive symptomatology may be screened for ARMC5 mutations. Further studies are needed for a genotype-phenotype correlation.

Abstract #113

BILATERAL ADRENAL LYMPHOMA WITH ACUTE ADRENAL INSUFFICIENCY PRESENTING AS ADRENAL HEMORRHAGE- A DIAGNOSTIC CHALLENGE

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Objective: Primary adrenal lymphoma constitutes 3% of extranodal lymphomas. Approximately 70% of patients present with bilateral disease and may have adrenal insufficiency. Many times adrenal lymphoma mimics adrenal hemorrhage on initial presentation, and therefore should be considered in the differential of an unresolving adrenal hemorrhage on serial imaging.

Case Presentation: 80 year old Caucasian female with a distant history of mastectomy for left breast cancer, paroxysmal atrial fibrillation on Apixaban, type 2 diabetes, and obstructive sleep apnea presented with right sided flank pain. CT abdomen was reported as bilateral adrenal hemorrhage most likely from anticoagulation, thus it was discontinued. Random serum total cortisol AM 12.7 mcg/dl and repeat was 22.1 (Ref 16-20 mcg/dl) not clearly suggesting primary adrenal insufficiency. However, she was empirically started on treatment with hydrocortisone and stable when discharged home.

Three weeks later on readmission for persistent flank pain, CT abdomen revealed increasing size of the adrenal lesions (7.5cm to 9 cm on the right and 2.3cm to 6.6 cm on the left), now reviewed by radiologist as bilateral neoplastic disease. The patient had sudden drop and wide fluctuations in blood pressure raising concern for pheochromocytoma. Markers for pheochromocytoma were negative: Plasma Metanephrine <25pg/ml (Ref <= 57 pg/ml), Normetanephrine 97 pg/ml (Ref <=148 pg/ml); 24 hour urine total metanephrine 385 mcg/24hr (Ref 224-832 mcg/24hr) and normetanephrine 385 mcg/24hr (Ref 122-676 mcg/24hr), Plasma Epinephrine <20pg/ml (Ref <20 pg/ml), Plasma Dopamine <30 pg/ml (Ref <30 pg/ml). Considering she was obese and had high normal cortisol levels on initial presentation, a concern for cushing’s disease arose and her levels were in favor of primary adrenal insufficiency off hydrocortisone for 1 week: Serum cortisol AM 1.7 mcg/dl (Ref 16-20 mcg/dl), Serum ACTH 224 pg/ml (Ref 9-46 pg/ml), Plasma renin activity 19.35 ng/ml/hr (Ref 0.25-5.82 ng/ml/hr), Aldosterone <1 ng/dl (Ref 3-16 ng/dl), with normal electrolytes. CT guided biopsy confirmed a diffuse large B cell Non Hodgkin lymphoma

Discussion: We present a case of an elderly female on anticoagulation, presenting as a diagnostic dilemma what was initially radiologically interpreted as bilateral adrenal hemorrhage with normal random plasma cortisol. Subsequently CT adrenals read as bilateral adrenal neoplastic disease confirmed as B cell lymphoma on biopsy. She developed primary adrenal insufficiency and responded well to hydrocortisone.

Conclusion: PAL is a difficult diagnosis and should be considered in patients with unresolved bilateral adrenal hemorrhage or increase in size of adrenal lesion on serial imaging.

Abstract #114

ADRENAL INSUFFICIENCY PRESENTING AS SEVERE HYPERCALCEMIA DURING IMMobilIZATION

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TTUHSC

Objective: Immobilization and adrenal insufficiency are both causes of mild hypercalcemia. We present a report of adrenal insufficiency which manifested as severe and prolonged hypercalcemia in an immobilized man.

Case Presentation: 26 year old man with history of paraplegia after a motor vehicle accident in March 2015 was admitted with urosepsis in June 2015. His medications prior to admission were levothyroxine 100 mcg daily and seroquel 150mg twice a day. Physical exam was
significant for hypotension and tachycardia (86/46 mmHg and 144 beats/minute; both improved with fluid bolus), paraplegia, tracheostomy, G-tube in stomach, indwelling foley catheter and a small decubitus ulcer on right heel. Lab studies showed corrected calcium of 14.5mg/dl and ionized calcium of 2.0mmol/L(1.1-1.3), phosphorous 2.8 mg/dl(2.5-4.7), magnesium 1.7 mg/dl(1.7-2.3), creatinine 1.2mg/dl, TSH 2.4mIU/L, PTH 5.7pg/ml(18-88), undetectable PTHrP, 25-OH vitamin D 43 ng/ml, 1.25(OH)2 D 5pg/ml(20-79), and 24 hour urine calcium of 1.07g. Aggressive intravenous fluid therapy improved hypercalcemia to 12.5 mg/dl over the next 10 days. AM cortisol was checked after endocrinology consultation and found to be low, 4.2 µg/dl(6-28) along with a high ACTH of 406 pg/ml(7-69). Cortisol did not stimulate after 250 mcg intravenous ACTH (4.9, 5.1 and 4.9µg/dl at 0, 30 and 60 minutes). Anti-adrenal antibodies were negative and imaging of adrenals was normal. He did not have hyperpigmentation. Patient was started on hydrocortisone 50mg every 8 hours which improved his hypercalcemia further to 11.5 mg/dl. However, he subsequently required two doses to pamidronate to normalize his calcemia. The patient was discharged on 10mg twice a day of hydrocortisone and fludrocortisone 0.1 mg once a day. He has remained eucalcemic for the last 5 months.

**Discussion:** Immobilization leads to an increase in sclerostin and the accompanying bone resportion causes mild hypercalcemia that usually responds to fluid therapy. Hypercalcemia in our patient was persistent and severe probably due to underlying adrenal insufficiency. In one study, patients with endogenous hypercortisolism were found to have diminished sclerostin concentrations in serum which increased after treatment of hypercortisolism. While the mechanism of adrenal insufficiency induced hypercalcemia is not well understood, it is tempting to postulate that an increase in sclerostin underlies the hypercalcemia of adrenal insufficiency.

**Conclusion:** To our knowledge, this is the first reported case of severe hypercalcemia due to combined adrenal insufficiency and immobilization.

**Abstract #116**

**CASE REPORT: SYMPTOMATIC SMALL-SIZED ADRENAL PHEOCHROMOCYTOMA**

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**Case Presentation:** A 56 year old female, known hypertensive for 10 years on amlodipine, irbesartan and hydrochlorothiazide which was non-compliant presenting with elevated blood pressure ranging SBP of 160-200mmHg, intermittent nape pain, palpitations, anxiety, diaphoresis, restlessness and body malaise occurring 4 times a week. Initial lab work ups showed urine metanephrine 7.126 mg/24 hr (normal 0-1 mg/24hr) and urine VMA 17.4 mg/24 hr (normal <13.5 mg/24 hr). CT scan of adrenal was negative however MRI of adrenal showed 0.6cm suspicious nodular focus right adrenal gland. Other work ups such as aldosterone, renin, potassium and cortisol levels were all normal, as well as ionized calcium, intact PTH and calcitonin. The relative small size of the adrenal nodule made the patient hesitant on advised surgery. She was requested urine metanephrines twice in span of 3 months which showed 28.675 umol (normal 0-5.5 umol/24 hr) and 22.2 umol. CT scan of brain and chest were also done to rule out any extra-adrenal tumor that may appear showing nonspecific pulmo nodules and small meningioma which was advised only watchful monitoring. Patient decided then to do adrenalectomy due to persistence of her symptoms. Post-operative findings: right adrenal gland with 1x1cm yellowish, well-circumscribed mass. Histopathology showed tumor cells with characteristics typical of pheochromocytoma. Patient was followed-up 2 weeks post procedure and claimed to have resolution of symptoms. Blood pressure was controlled with a range of SBP 110-130 maintained on one antihypertensive medication.

**Conclusion:** Pheochromocytomas and paragangliomas are catecholamine producing tumors derived from the sympathetic or parasympathetic nervous system that rarely to be biologically silent. These disease entities may appear with symptoms of excess hormone production which presented in our patient (nape pain, palpitations, anxiety, diaphoresis, restlessness and body malaise) posted a unique challenged to our practitioners on developing and convincing the patient on therapeutic plans due to the relative small size of the mass. It therefore reminds us to be keen in these rare situations that the clinical presentation of a patient still takes precedence even on a minute difference in imaging studies.

**Abstract #117**

**PSEUDOTUMOR OF THYMUS OCCURING AFTER HYPERCORTISOLISM RECOVERY: CASE REPORT**

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**Objective:** Cushing syndrome is due to an ectopic secreting adrenocorticotropic hormone (ACTH) in 10% to 20% of cases. Among them, thymic tumors represent almost half...
of cases. It has been described that patients sometimes develop benign hyperplasia after hypercortisolism correction. This enlargement of the thymus present a misleading tumoral appearance that can lead to an unnecessary diagnostic thoracotomy. We represent a case of a thymic tumor to enhance the awareness of this entity in order to avert diagnostic thoracotomy.

Case Presentation: A 45-y.o man was admitted in our department to manage a severe cushing’s syndrome. The results of endocrine work-up were consistent with an ectopic cushing syndrome. Morphologic investigations, a computed tomography body scan and an octreoscan, has shown a 1/1.5 cm pulmonary tumor. The patient underwent a thoracic surgery. The histology revealed a carcinoid tumor with positive immunostaining for ACTH. This surgery led to a rapid remission of the hypercortisolism. However, 6 months later, a follow-up CT scan showed a triangular nodular mediastinal enlargement. Based on the fact that the cortisol and ACTH levels were normal, we have decided to not operate the patient and follow the thymic tumor progression by CT scan. 6 months later, the CT scan has shown a significant reduction in the thymic enlargement.

Conclusion: The mechanism of thymic hyperplasia is thought to be thymic depletion resulting for high plasmatic cortisol concentrations followed by the thymic enlargement when cortisol levels are normal again. It must be known to avoid unnecessary thoracotomy during follow-up of patients with ectopic cushing’s syndrome.

Abstract #118

ASSOCIATION BETWEEN LATE ONSET TYPE 1 DIABETES MELLITUS AND METASTATIC ADRENOCORTICAL CARCINOMA: WHAT ARE THE CHANCES?

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Advocate Illinois Masonic Medical Center

Objective: We describe a unique case of a patient with Adrenal myelolipoma (AML) who was found to have Adrenocortical carcinoma (ACC), presenting with diabetes mellitus type 1 (DMT1) instead of the usual diabetes mellitus type 2.

Case Presentation: A 66-year-old female with newly diagnosed DMT1 and hypertension was evaluated for severe hypokalemia on routine labs. Associated symptoms included generalized fatigue, muscle cramps and bilateral leg swelling. Physical exam was remarkable for moon face, bibasilar crackles and lower extremity edema. Initial workup showed sodium of 151 mEq/L, potassium of 1.7 mEq/L, bicarbonate of 42 mg/dL and creatinine of 1.38 mg/dL. Bilateral pleural effusions and innumerable round lung masses were seen on chest radiograph. CT imaging revealed innumerable soft tissue pulmonary nodules suspicious for hematogenous metastases and a heterogeneous mass in the left adrenal gland with few calcifications, highly suspicious for ACC. CT guided lung biopsy was not diagnostic, but ultrasound guided fine needle aspiration of a liver lesion was positive for metastatic malignancy. Serum ACTH, AM cortisol, Dexamethasone suppression test, DHEA-S and 11-deoxycortisol values were consistent with a cortisol secreting tumor. Review of a 2012 CT abdomen and pelvis revealed a heterogenous fat containing mass in the left adrenal gland, highly suggestive of AML. Unfortunately, follow-up imaging was not done although the patient’s niece had died from metastatic adrenal cancer at age 39. Ultimately, the patient was diagnosed with metastatic ACC associated with new onset DMT1 and enrolled in hospice as she was not deemed a surgical candidate.

Discussion: ACC is a rare malignancy with poor prognosis that occurs in 1-2/million, mainly in females during the 4-5th decade of life with evidence of adrenal steroid hormone excess. In our patient, the incidental left sided AML found on CT abdomen 3 years prior could have coexisted with an underlying adrenocortical tumor or represented a malignant transformation not found on time due to lack of follow-up. Furthermore, the patient’s family history of ACC might have indicated a familial form although genetic evaluation was not pursued. The negative antibody panel was compatible with idiopathic diabetes, which is the first case described of new onset DMT1 in a patient with ACC. Overall, there have only been 4 cases reported of ACC and AML coexistence according to literature. Thus, physicians should be aware of the importance of close follow-up imaging of AML and the possibility of their coexistence.

Conclusion: This case demonstrates the interesting association between DMT1, AML and ACC. It is paramount that physicians be aware of the existence of such an association.

Abstract #119

ADVANCED CUSHING’S DISEASE MASKED BY OBESITY IN A 28 YEAR OLD WOMAN

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1. GRMEP, 2. Spectrum Health Medical Group

Objective: Cushing’s disease is caused by excessive secretion of ACTH from the pituitary gland which leads to an increase in the cortisol levels. Excess of cortisol can
cause central obesity, muscle atrophy, muscle weakness, hypertension, diabetes, osteoporosis and fractures. Many signs and symptoms of Cushing’s disease and obesity overlap with each other as a result of which most patients with obesity are not screened for hypercortisolism and there is a delay in the diagnosis and treatment of hypercortisolism. **Case Presentation:** We present a case of a 28-year-old woman with morbid obesity, recent diagnosis of osteoporosis, difficult to control diabetes requiring insulin since 3 years, resistant hypertension and hypothyroidism who was admitted to the hospital with a vertebral compression fracture of T6, T7 and T8 vertebral bodies. She also had history of multiple falls in the last couple of months from imbalance and proximal muscle weakness. During her admission she was screened for hypercortisolism. Her free urine 24-hour cortisol level as well as her blood ACTH level were elevated at 46 and 112 respectively. Renin and angiotensin levels were within normal limits. Low-dose dexamethasone suppression test was negative. MRI of her brain showed a macroadenoma of the pituitary gland involving the right side of the pituitary fossa with invasion of the superior surface of the right cavernous sinus. High-dose dexamethasone suppression test suppressed the ACTH levels. She underwent transsphenoidal resection however, the whole tumor could not be resected because part of the tumor was extending into the cavernous sinus. After the surgery, patient continued to have persistent disease based on her post-operative cortisol level which remained elevated. She was initiated on Ketoconazole and received fractionated pituitary irradiation one month later. After radiation, ketoconazole was stopped. Her cortisol and ACTH levels normalized. Her blood glucose level was well controlled with metformin monotherapy. Blood pressure improved as well. **Conclusion:** Obese patient especially with diabetes, difficult to control hypertension or muscle weakness should be screened for hypercortisolism. Early diagnosis and treatment prevents the tumor from extending into the surrounding structures and makes management easier. It also reduces complications of long standing diabetes, hypertension and osteoporosis as they improve once the hypercortisolism resolves.
ABSTRACTS – Adrenal Disorders

Abstract #115

RADIOFREQUENCY ABLATION: AN INNOVATIVE TREATMENT FOR ADRENAL NEOPLASMS

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Objective: Metastatic or primary adrenal neoplasms, including non-functional adenomas, adrenal cortical carcinomas, cortisol producing adenomas, pheochromocytomas and aldosteronomas, affect 1% of the population. The definitive treatment is adrenalectomy, however when not feasible, radiofrequency ablation (RFA) has shown to be effective. We present a patient with an adrenal cortisol-producing tumor successfully treated with radiofrequency ablation.

Case Presentation: A 65 year old woman presented with weight gain, decreased energy and proximal muscle weakness. She had a history of type 2 diabetes mellitus, uncontrolled hypertension and low-grade ovarian cancer post total hysterectomy and omentectomy. She had a 0.9 cm right-sided adrenal mass that had increased in size over 5 years to 3.6 cm x 3.5 cm x 3.3 cm with an attenuation of 30.2 Hounsfield Units (HU). Physical exam revealed a hypertensive, anxious, obese woman with prominent supraclavicular fat pads and proximal muscle weakness. Laboratory evaluation included normal serum metanephrines, cortisol of 14.1 mcg/dL (3.0-23.0 mcg/dL), normal urinary 24 hour free cortisol of 15.2 ug/d (3.0-23.0 mcg/dL), normal serum creatinine, glucose of 88 mg/dL (60-100 mg/dL), normal liver function tests, and normal electrolytes. An abdominal CT-guided RFA of the adrenal mass demonstrated a decrease in size of the adrenal mass to 3.3 cm x 3.2 cm x 3.2 cm with a marked decreased attenuation to 22 HU. A seven month evaluation revealed a stable lesion of 3.2 cm x 3.1 cm x 3.2 cm with attenuation of 21.7 HU with drastic clinical improvement.

Discussion: Increasing evidence is emerging demonstrating the efficacy of percutaneous RFA for treatment of both adrenal metastases and functional adrenal tumors as an alternative for patients unable to undergo surgical intervention. Mendiratta-Lala et al. retrospectively studied the effect of RFA as primary treatment in 13 patients with symptomatic primary functional adrenal neoplasms over a 7 year period and concluded that all patients had resolution of abnormal biochemical markers and clinical symptoms. Conclusion: RFA is an effective, alternative method for the treatment of unresectable adrenal tumors. Our case highlights the use of RFA in a patient with hormonally functioning adrenal tumor. We hope to raise awareness about the utility of RFA in select patients.

Abstract #121

ADDISONIAN CRISIS BROUGHT ON BY A CELIA FLAREUP

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Objective: Addison’s disease is a fairly prevalent malady in the United States. Treatment requires a delicate balance and replacement of corticoids to prevent symptoms and potentially fatal crisis. Central to this is the absorption of exogenous replacement hormones. We present a case of Addisonian Crisis brought on by flare of Celiac disease

Case Presentation: A 56 year old woman with known history of Addison’s disease and Celiac disease presented to the hospital for 2 weeks of increasing nausea, diarrhea with progression to vomiting to 2 days prior. Patient was found to be in crisis with hyponatremia, hyperkalemia and hypotension. Patient reports that she was taking her exogenous replacement until 2 days prior because of intolerable vomiting. She reports that her food was being prepared by others and had been unknowingly eating gluten during this time period. She was started on IV hydrocortisone and florinef and placed on gluten free diet. Her electrolytes stabilized and blood pressures normalized. She was discharged home in stable condition with instructions to strictly avoid gluten.

Discussion: Addison’s disease is one in which deficiencies of cortisol and mineralocorticoid exists and treatment is their replacement to maintain physiologic function. Inadequate replacement can lead to crisis as deficiencies can lead to hyponatremia, hyperkalemia, and shock. Early
recognition is key and treatment should be initiated, if suspicious for, prior to confirmatory lab results. Treatment includes adequate resuscitation for hypotension, electrolyte replacement and corticoid deficiency replacement to avoid significant morbidity and mortality. Celiac disease is one that presents with gastrointestinal symptoms related to insensitivity to gluten triggering Ig-A activity and causing villous atrophy. This leads to symptoms of malabsorption causing diarrhea and nausea directly related to the presence of gluten. By unknowingly eating gluten, our patient was placed in a situation where her previously adequately dosed corticoid replacement was no longer being absorbed precipitating her crisis to the point where she was vomiting up her medication.

**Conclusion:** This case presents an expected outcome for one who is not able to absorb corticoid replacement therapy. It highlights the need to be diligent in educating patients in regards to the important and necessary role replacement plays. Central to this is educating patients to avoid gluten or other substances that can decrease absorption and lead to symptoms even while on replacement therapy. With diligent education and discussion with their provider patients can maximize the effectiveness of their replacement therapy

**Abstract #122**

**ATYPICAL PRESENTATION OF CUSHING’S DISEASE**

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**Objective:** Cushing’s syndrome is a state of excess glucocorticoids due to ACTH dependent or ACTH independent causes. Dexamethasone suppression test can be used to differentiate between pituitary and adrenal sources of hypercortisolism.

**Case Presentation:** We present a rare case of Cushing disease with an unusual presentation and paradoxical elevation of cortisol on high dose dexamethasone suppression test. A 57-year-old male presented with fatigue, weight gain and behavioral changes of several months duration. Physical exam revealed central obesity, multiple bruises and uncontrolled hypertension. Labs revealed severe hypokalemia of 2.0 meq/liter. CT head and MRI brain revealed pituitary macro adenoma of 2.9 x 2.4 cm. Elevated serum cortisol and low serum ACTH levels prompted high dose dexamethasone suppression test, which resulted in paradoxical elevation of serum cortisol levels. CT chest, abdomen and pelvis did not reveal any adrenal or ectopic source of hypercortisolism. Repeat testing in the outpatient setting revealed highly elevated ACTH levels consistent with diagnosis of Cushing’s disease. Patient was started on ketoconazole and underwent trans-sphenoidal removal of pituitary macroadenoma. Post-op serum cortisol was within normal limits.

**Conclusion:** Cushing’s Disease is a state of hypercortisolism commonly caused by pituitary microadenomas. These adenomas are usually seen in young females and are characterized by cortisol suppression upon administration of dexamethasone. Paradoxical elevation of serum cortisol levels upon dexamethasone suppression test should prompt diagnostic imaging to rule out adrenal and ectopic etiologies. If work up for non-pituitary sources of hypercortisolism is negative repeat ACTH testing with appropriate techniques and atypical presentation should be considered.

**Abstract #124**

**PHEOCHROMOCYTOMATOSIS FROM SEEDING OF THE PERITONEUM WITH PHEOCHROMOCYTOMA CELLS DURING NEPHRECTOMY**

Nashmia Riaz, MD¹, Syed-Azhar Hassan, MD¹, Roger Harty, MS¹, Jody Banister, MD²

1. GRMEP, 2. Mercy Health Saint Mary’s

**Objective:** Pheochromocytomas and paragangliomas (PGLs) are tumors of the adrenal medulla or non-adrenal sympathetic paraganglia respectively that secrete catecholamines. The most common presentation in symptomatic patients is hypertension, headache, perspiration, anxiety or tachycardia. Rarely these tumors can seed into the peritoneum either spontaneously or iatrogenically during surgery leading to recurrent tumors in the abdomen known as pheochromocytomatosis.

**Case Presentation:** We report the case of a 36 year old woman who wanted to to donate her left kidney to a family member with end stage renal disease. She underwent imaging studies that revealed a 2 cm mass in the left adrenal gland. It was thought to be a myelolipoma and she underwent laparoscopic-assisted left donor nephrectomy and partial resection of the adrenal mass. Surgical pathology of the mass was consistent with pheochromocytoma, with focal extension into the inked margin. Postoperatively, she developed classic symptoms of adrenal medullary hyper function, difficult to control blood pressure, anxiety and palpitations. Biochemistries revealed normal plasma fractionated metanephrines as well as 24 hour urine catecholamines/methanephrines, and imaging revealed non-specific fullness in the left adrenal gland. She continued to have worsening symptoms.
so she underwent re-exploration. Intraoperatively she was noted to have a soft tissue mass in the sympathetic chain. Pathology findings were consistent with multiple ganglioneuroma/paraganglioma. Remaining adrenal mass was also resected. Patient does not have a family history of paraganglioma/pheochromocytoma/MEN syndrome or neurofibromatosis. She underwent genetic screening revealing no mutation for SDH (B, C, or D), RET or VHL. Post-operatively she continued to complain of significant anxiety and palpitations. Further investigation again showed normal 24 hour urine catecholamines/metanephrines, suggesting periodic secretion of catecholamines rather than continuous secretion. MIBG scan was normal. Patient is planned for repeat exploratory laparotomy for evaluation of a recurrence.

Conclusion: Even though pheochromocytomas are rare tumors and benign adenomas are more common care should be taken during surgery with adrenal masses as partial resection during surgery can cause seeding in the abdomen and be difficult to control.

Abstract #123

PHEOCHROMOCYTOMA PRESENTING WITH HEMATURIA

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1. Grand Rapids Medical Education Partners, 2. Spectrum Health Hospital

Objective: Pheochromocytoma is a catecholamine-secreting tumor that arises from chromaffin cells of the adrenal medulla. We report a case of pheochromocytoma presenting with hematuria without involvement of the urinary bladder. Hematuria has been reported in the past with pheochromocytoma of the urinary bladder but not with pheochromocytoma localized to the adrenal glands.

Case Presentation: A 53 years old woman presented to PCP office with vague abdominal pain, recurrent headaches and palpitations. Urinanalysis was done to evaluate for the abdominal pain which was positive for hematuria. CT abdomen and pelvis was done which showed a right suprarenal mass measuring 4.1 cm x 5.8 cm x 4.9 cm. Urinary Metanephrines, Normetanephrine, Total Metanephrines, Norepinephrine and Epinephrine were ordered to evaluate for pheochromocytoma all of which were elevated more than three times the upper limit of normal. The patient’s dopamine UR, Cortisol, ACTH, DHEAS, estradiol, progesterone, testosterone, renin and aldosterone levels were normal. MRI of the abdomen and pelvis were also done which again showed the adrenal mass but no involvement of the renal parenchyma or the urinary bladder. Patient developed hypertension within a few days of the diagnosis and was started on doxazosin followed by propranolol for a total of 4-5 weeks after which the blood pressures stabilized and she was scheduled for adrenalectomy. During laparoscopic adrenalectomy, the patient’s blood pressure escalated to 310 systolic with MAPs in the 200s. Surgery was aborted. Intra-op, the patient was started on a nitroglycerin drip which stabilized her blood pressure. She was started on phenytoin/phenazone and Propranolol prior to attempting surgery the second time. She had open adrenalectomy after 5 weeks without any complications.

Conclusion: Pheochromocytoma is a rare disorder and can present in an atypical manner. Suspicion should remain high in young patients who come in with vague symptoms of headaches, palpitations and new onset hypertension, if these findings are present with hematuria and there is no other explanation for the hematuria then pheochromocytoma should be in the differentials. Patients with hematuria and pheochromocytoma should be followed closely for recurrence and bladder involvement. There have been case reports of bladder pheochromocytoma presenting with hematuria, these patients might have microscopic invasion of the bladder with the pheochromocytoma cells which does not show up in the scan at an early stage but might be causing hematuria.

Abstract #125

ADRENAL INSUFFICIENCY SECONDARY TO TOPICAL STEROID USE - A CASE REPORT

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Objective: Topical steroids are like wonder drugs especially in dermatology and their use has increased over time. Prolonged use of these can cause adrenal insufficiency because of suppression of the Hypothalamic-pituitary-adrenal axis. Factors contributing to this include the strength of the corticosteroid, duration of usage and location of use.

Case Presentation: A 53 years old woman presented to PCP office with vague abdominal pain, recurrent headaches and palpitations. Urinanalysis was done to evaluate for the abdominal pain which was positive for hematuria. CT abdomen and pelvis was done which showed a right suprarenal mass measuring 4.1 cm x 5.8 cm x 4.9 cm. Urinary Metanephrines, Normetanephrine, Total Metanephrines, Norepinephrine and Epinephrine were ordered to evaluate for pheochromocytoma all of which were elevated more than three times the upper limit of normal. The patient’s dopamine UR, Cortisol, ACTH, DHEAS, estradiol, progesterone, testosterone, renin and aldosterone levels were normal. MRI of the abdomen and pelvis were also done which again showed the adrenal mass but no involvement of the renal parenchyma or the urinary bladder. Patient developed hypertension within a few days of the diagnosis and was started on doxazosin followed by propranolol for a total of 4-5 weeks after which the blood pressures stabilized and she was scheduled for adrenalectomy. During laparoscopic adrenalectomy, the patient’s blood pressure escalated to 310 systolic with MAPs in the 200s. Surgery was aborted. Intra-op, the patient was started on a nitroglycerin drip which stabilized her blood pressure. She was started on phenytoin/phenazone and Propranolol prior to attempting surgery the second time. She had open adrenalectomy after 5 weeks without any complications.

Conclusion: Pheochromocytoma is a rare disorder and can present in an atypical manner. Suspicion should remain high in young patients who come in with vague symptoms of headaches, palpitations and new onset hypertension, if these findings are present with hematuria and there is no other explanation for the hematuria then pheochromocytoma should be in the differentials. Patients with hematuria and pheochromocytoma should be followed closely for recurrence and bladder involvement. There have been case reports of bladder pheochromocytoma presenting with hematuria, these patients might have microscopic invasion of the bladder with the pheochromocytoma cells which does not show up in the scan at an early stage but might be causing hematuria.
at 0.1 mcg/dL. His FSH was 6.8 mIU/mL, LH - 2 mIU/mL and prolactin was 8.5 ng/mL. All other labs were normal. He was started on IVF and thyroid hormone replacement. The patient had been using topical fluocinolone cream on his entire back daily for eczema over the past year. The patient was as such diagnosed with hypothyroidism-secondary to hashimoto’s, adrenal insufficiency secondary to chronic topical steroid use and hyponatremia secondary to both adrenal insufficiency as well as hypothyroidism. He was started on hydrocortisone 20mg in AM and 10mg in PM. The patient’s condition slowly improved and his serum sodium levels normalized.

Discussion: Topical steroids are commonly prescribed for skin conditions as they have lesser side effects than systemic steroids. The availability of these as over the counter medication has lead to increase in usage. In our case the cause of adrenal insufficiency rooted down to the topical steroid use. Exogenous steroid is the most common cause of secondary adrenal insufficiency. Factors effecting the suppression of adrenals by topical steroids are the type & strength of steroid, duration & frequency of use, area of use, thickness of the skin and condition used for. In our case the steroid ointment was applied to the whole of the back daily for over a year. Slowly the skin thins so increasing systemic absorption more. Lab tests that measure adrenal function include measurement of plasma total cortisol, 24-hour steroid, adrenocorticotrophin hormone stimulation & insulin tolerance.

Conclusion: Topical steroids should be used cautiously & awareness has to be made about the over the counter formulations. The patients often present with subtle symptoms so history is important. All the patient as well as medication parameters should be considered when prescribing steroids.

Abstract #126

STERIOD INDUCED PHEOCHROMOCYTOMA MULTISYSTEM CRISIS IN A PATIENT WITH UNDIAGNOSED PHEOCHROMOCYTOMA

Nashmia Riaz1, Roger Harty, MD1, Syed-Azhar Hassan, MD1, Terrance W Barnes, MD2

1. GRMEP, 2. Spectrum Health

Objective: Pheochromocytoma multisystem crisis (PMC) is a rare and fatal entity that was first described in 1988. Enormous release of catecholamines from the adrenal glands in PMC can rapidly lead to circulatory collapse and multiple organ failure mimicking septic shock. Fever can also be part of the presentation. PMC can occur spontaneously or can be triggered by surgery, vaginal delivery, stress, exercise or steroid use in patients with underlying pheochromocytoma. The patient was as such diagnosed with hypothyroidism-secondary to hashimoto’s, adrenal insufficiency secondary to chronic topical steroid use and hyponatremia secondary to both adrenal insufficiency as well as hypothyroidism. He was started on hydrocortisone 20mg in AM and 10mg in PM. The patient’s condition slowly improved and his serum sodium levels normalized.

Discussion: Topical steroids are commonly prescribed for skin conditions as they have lesser side effects than systemic steroids. The availability of these as over the counter medication has lead to increase in usage. In our case the cause of adrenal insufficiency rooted down to the topical steroid use. Exogenous steroid is the most common cause of secondary adrenal insufficiency. Factors effecting the suppression of adrenals by topical steroids are the type & strength of steroid, duration & frequency of use, area of use, thickness of the skin and condition used for. In our case the steroid ointment was applied to the whole of the back daily for over a year. Slowly the skin thins so increasing systemic absorption more. Lab tests that measure adrenal function include measurement of plasma total cortisol, 24-hour steroid, adrenocorticotrophin hormone stimulation & insulin tolerance.

Conclusion: Topical steroids should be used cautiously & awareness has to be made about the over the counter formulations. The patients often present with subtle symptoms so history is important. All the patient as well as medication parameters should be considered when prescribing steroids.

Abstract #127

WHEN EMOTIONS LEAD THE WAY: A CASE OF METASTATIC ADRENOCORTICAL CARCINOMA

Denise Sese, MD1, Irtsam Shahid, MD1, Hyo Young Seo, MS III2, Michael Morocco, MD1

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

Case Presentation: We report a case of a previously healthy 28-year-old woman who presented to the hospital with abdominal pain, nausea and vomiting of 1 day duration. Two days prior to her presentation she was started on oral prednisone for a rash on her lower extremities due to poison Ivy. On presentation the patient was hypoxic, tachycardic, tachypneic and hypotensive. CT scan of the abdomen without contrast did not show any abnormalities. She was fluid resuscitated but deteriorated rapidly. She had to be intubated and required presser support. For presumed septic shock she was started on broad spectrum antibiotics empirically. Her condition continued to worsen and she had to be placed on VA-ECMO. Echocardiogram showed significant systolic dysfunction with EF of 10%-15%. On the second day of admission she developed bilateral lower extremity compartment syndrome requiring lower extremity fasciotomies. Patient’s hemodynamic and neurological status deteriorated even with aggressive supportive measures. Supportive care was withdrawn after two days since the time of admission and the patient expired. Autopsy report did not show evidence of any infectious process. She was found to have a 4.5 cm mass within the right adrenal gland and the histopathology confirmed it as pheochromocytoma. Other findings on autopsy included features of multisystem organ failure from PMC, including cardiomyopathy, diffuse alveolar damage, hepatocellular necrosis, and cerebral edema. She did not have a prior diagnosis of pheochromocytoma.

Conclusion: Cases have been reported of PMC induced by exogenous glucocorticoids which could have contributed to triggering the crisis in her case. PMC should be suspected in patients who have a rapidly progressive multisystem failure or those patients who have a presumed diagnosis of septic shock but are unresponsive to antibiotic therapy. Early diagnosis of PMC is crucial as it has a very high mortality. The treatment of PMC includes aggressive preoperative medical therapy and early tumor removal.

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Conclusion: Cases have been reported of PMC induced by exogenous glucocorticoids which could have contributed to triggering the crisis in her case. PMC should be suspected in patients who have a rapidly progressive multisystem failure or those patients who have a presumed diagnosis of septic shock but are unresponsive to antibiotic therapy. Early diagnosis of PMC is crucial as it has a very high mortality. The treatment of PMC includes aggressive preoperative medical therapy and early tumor removal.
and whose most common presentation is rapid virilization in the presence of hormonal excess. While clinicians recognize objective features of hormonal excess, emotional lability is often forgotten at a time when early diagnosis is critical.

A 58 year old female was at the outpatient office complaining of strong palpitations, diaphoresis, shortness of breath and occasional abdominal pain. For six months she experienced severe emotional outbursts and new onset anxiety attacks which she concealed from family. She was admitted to our institution for management of accelerated hypertension when it was noted that she had some cushingoid features including abdominal striae, posterior cervical fat deposition and hirsutism. Due to tachycardia and shortness of breath a CT pulmonary embolism protocol was initiated where a 10.7x6.7x8cm heterogeneously enhancing right adrenal mass was seen adjacent to a 3.2 cm liver lesion. A follow up CT and MRI of the abdomen confirmed the 10 cm mass and revealed multiple liver lesions. Laboratory investigations revealed an elevated PM cortisol 42.2 (3.1-16.7) μg/dL and dehydroepiandrosterone sulfate. She had mild hypokalemia of 3.4 (3.5-5.0)mmol/L, normal aldosterone 5.4(4-31)ng/dL, 24 hour urine meta/normetanephrines and urinary vanillylmandelic acid. Finally, a liver biopsy revealed mildly pleomorphic cells with eosinophilic cytoplasm and tumor cells in a trabecular pattern. Immunohistochemistry staining was positive for melanin A, inhibin and SF1, confirming the diagnosis of metastatic adrenal cortical carcinoma. Deemed a poor surgical candidate, she was discharged on Metyrapone and Spironolactone with plans of initiating Mitotane.

Discussion: Sixty percent of ACCs are heralded by symptoms of hormonal excess progressing over three to six months. These present as Cushing’s syndrome alone or a mixed Cushing’s and virilization syndrome. Germ line mutations in p53 are confirmed to cause this tumorogenesis. When ACC is suspected, phemochromocytomas must be ruled out and determination of the SF-1 tumor marker confirms the adrenocortical origin of the tumor, which was the case with our patient.

Conclusion: Emotional complaints are neglected in outpatient offices but when accompanied by rapid progression and features of cortisol or androgen excess, an organic etiology should be suspected. Earlier detection is key for ACCs as outcome is poor. Complete resection is the treatment of choice along with adjuvant chemotherapy.

Abstract #128

UNUSUAL POSTPARTUM ENDOCRINOPATHIES: POSTPARTUM THYROIDITIS FOLLOWED BY PRIMARY AUTOIMMUNE ADRENAL INSUFFICIENCY AND EUTHYROID AUTOIMMUNE THYROIDITIS

Yanjin Yang, MD, Sabita Moktan, MD, FACE, Edmund Giegerich, MD, FACP, FACE

New York Methodist Hospital

Objective: Schmidt’s Syndrome is an autoimmune disease characterized by primary adrenal insufficiency with the presence of either autoimmune thyroid disease and or Type 1 Diabetes Mellitus. The prevalence of postpartum thyroiditis (PPT) worldwide is 1 to 17% and only a few isolated case reports of postpartum adrenal insufficiency (AI). We present an unusual case of Schmidt’s Syndrome where PPT was followed by postpartum AI.

Case Presentation: 33 year old-female presented with new onset hyperthyroidism four months after an uneventful pregnancy. She reported normal menses and appeared very anxious. On examination, she had palpable non-tender goiter and mild tremor. Lab revealed, TSH: <0.005 uIU/mL (0.27-4.2 uIU/mL), Free T4: 1.67ng/dL (0.76-1.46 ng/dL), Free T3: 6.6 pg/mL (2.3-4.2 pg/mL), Thyroid Peroxidase Antibody: 533 IU/mL (0-34 IU/mL), Thyroid Stimulating Immunoglobulin 54% (1-139%) Thyroid uptake scan was 0.4% (10-30%). She was diagnosed with PPT and started on propranolol for symptom management. One month later, she complained of abdominal pain, fatigue, and dizziness. On examination, she had orthostatic hypotension and diffuse skin hyperpigmentation. Lab revealed, sodium: 122mmol/L, potassium: 5.6 mmol/L, AM cortisol level: 6.17ug/dL, ACTH: 2556 (6-50pg/mL); 21-Hydroxylase Antibodies: 853 u/mL (<1 u/mL), Anti-Adrenal Antibodies: 1:40 (<1:10). The patient refused cosyntropin stimulation test. CT abdomen revealed normal adrenal glands. She was diagnosed with primary AI and improved with hydrocortisone and fludrocortisone therapy. She had normalization of thyroid function tests with persistently high thyroid antibody titers. She was assessed to have euthyroid autoimmune thyroiditis and AI.

Discussion: This is a rare case of PPT followed by primary autoimmune AI and euthyroid autoimmune thyroiditis which is consistent with Autoimmune Polyglandular Syndrome (APS) type II, an autosomal dominant disease with incomplete penetrance and is uncommon with a prevalence of 1.4 per 100,000. This entity rarely presents in the postpartum period. Literature suggests that patient with autoimmune conditions during pregnancy may have subclinical disease with the presence of autoantibodies.
Autoimmune processes suppressed during pregnancy exacerbate in the postpartum period, due to increased T cell activation resulting in the clinical presentation noted in our case of two autoimmune diseases PPT and AI.

**Conclusion:** Long term follow up of this patient and her family will require surveillance for other entities known to occur with APS type II.

**Abstract #129**

**ADRENOCORTICAL FUNCTION IN PATIENTS WITH PULMONARY TUBERCULOSIS CO-INFECTED WITH HIV**

Ifedayo Odeniyi, MBBS, FMCP, FACE¹, Olufemi Fasanmade, MBBS, FWACP, FACE², Michael Ajala, MD, FACE², Augustine Ohwovoriole, MBBS, FMCP¹

1. College of Medicine, University of Lagos/Lagos University Teaching Hospital, 2. General Hospital

**Objective:** The adrenal gland, as studies have shown, is not spared from involvement by tuberculosis. One of the recognized causes of adrenal insufficiency is tuberculosis. Adrenal insufficiency secondary to Human Immunodeficiency Virus (HIV) infection has been well studied. Adrenocortical insufficiency, mostly at the subclinical level, is common in persons with Pulmonary Tuberculosis (PTB) infection, occurring in about 23% of patients. Co-infection with PTB and HIV may compromise adrenocortical function and produce significant adrenocortical insufficiency. The objective of this study is to determine if co-infection with tuberculosis and HIV have a compound effect on adrenocortical function in persons with HIV and PTB co-infection.

**Methods:** Persons with sputum-positive PTB, treatment naive, who met other inclusion criteria were selected. All the recruited patients were screened for HIV and those positive for HIV infection had confirmatory test. A baseline blood samples for cortisol, fasting plasma glucose (FPG), full blood count (FBC) and electrolytes were collected between 08.00 hour and 9.00 hour immediately before administration of ACTH. The subjects received an intravenous bolus injection of 1μg ACTH (Alliance Pharmaceuticals Ltd, Chippenham, Wiltshire SN15 2BB) and blood sample was drawn for cortisol level at 30 minute. The samples were separated and stored at -200C until assayed. Serum cortisol levels were determined by an Enzyme Linked Immunosorbent Assay (ELISA) technique using the Diagnostic automation Inc. cortisol assay method.

**Results:** Forty four people with PTB infection and 40 with PTB and HIV co infection met the inclusion criteria for the study. The body mass index in the participants with PTB and PTB and HIV co infection was 18.89±2.91 and 21.77±2.60 kg/m² (p<0.05) respectively. The adrenal response to 1μg ACTH stimulation in participants with PTB and PTB and HIV co infection showed the mean basal cortisol level in the 2 groups was not statistically significant; however, 30-minute post ACTH stimulation cortisol level was 630.84±372.17 and 980.36±344.82 nmol/L (p<0.001) and increment was 367.79±334.87 and 740.77±317.97 nmol/L (p<0.001) respectively. Fourteen persons (31.8%) out of 44 of those with PTB has subnormal adrenal response to ACTH stimulation while only 2 (5%) persons with PTB and HIV co infection has sub normal response. There is no significant difference in the biochemical parameters in the PTB and PTB and HIV co infection.

**Conclusion:** Adrenal insufficiency, at subclinical level, was less frequent in those with PTB and HIV co infection. This suggests that sufficient degree of infiltration of the adrenal gland to cause a clinically significant deficit does not occur.

**Abstract #130**

**A CASE OF HYPOKALAEMIA TRANSFORMED INTO A CASE OF HYPERKALAEMIA BY ADRENALECTOMY.**

Uttam Dey, MD

**Objective:** The aim of this report is to describe a case of Conn’s syndrome caused by adrenal adenoma who presented with hypokalaemia and hypertension, and adrenalectomy caused her normotensive but life threatening hyperkalaemia.

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

**Case Presentation:** Mrs.X, 53 years of age, hypertensive for last 20 years, consulted to several cardiologists and nephrologists several times for headache, palpitations, abdominal discomfort and hypertension. On examination, patient was mildly anaemic, BP was 180/100 mm Hg, pulse 100bpm, no thyromegaly, no oedema, no engorged neck vein. She was getting losartan potassium along with calcium channel blocker. Subsequent investigations revealed Hb-10.9g/dl, S.cr-1.4mg/dl, eGFR-39 ml/min, Na-141, K-2.9, Cl-99, Co2-32 mEq/L. Urine-Alb-+, E. cell 2-4/HPF and pus cell 4-6/HPF. TSH-12.5 U/L, FT4-15.72 pmol/L. ACTH-5 pg/ml, prolactin-318.97 miu/L. Cortisol at 0 min 322, at 30 min 383, at 60 min 866 nmol/L after ACTH stimulation test. Metanephrine in urine was 1521.20 nmol/day which was normal. Renin in plasma -12.29 pg/ml and aldosterone -40.05 pg/ml, both within normal range. USG of abdomen revealed a well defined hypoechoic, homogenous mass lesion which measures about 22.9*17.8mm in size seen at the region of right
adrenal gland suggestive of right adrenal mass. Contrast CT scan of abdomen confirmed the right adrenal mass. A case of Conn’s syndrome was diagnosed and patient was advised for right adrenalectomy. Before laparoscopic right adrenalectomy BP was controlled with non-dihydropyridine calcium channel blocker. The procedure was uneventful. No hypotension developed but a week later she developed weakness and palpitation. S.electrolyte revealed Na-136, K-5.7, Cl-100, Co2-30 mEq-L, Cr.-1.5 mg/dl. Management of hyperkalaemia given, after 10 days it came to normal K-3.9 mEq/L. Post operative cortisol was 430 nmol/L (normal). Histopathology of biopsy specimen: adrenocortical adenoma.

**Discussion:** Primary aldosteronism is the most common cause of secondary hypertension. Adrenalectomy is an effective treatment for adrenal tumor induced HTN. A pathophysiological consequence of unilateral aldosterone excess is suppression of contra lateral zona glomerulus (ZG) function via suppressed plasma renin level. After adrenalectomy this can lead to inadequate ZG function and hypoadosteronism impairing renal K clearance and consequent hyperkalaemia.

**Conclusion:** The case reported here highlights the importance of careful postoperative follow up with BP, electrolyte, cortisol measurement in Conn’s patient after adrenalectomy.

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**Abstract #131**

**PREVENTION OF SECONDARY ADRENAL INSUFFICIENCY WITH PRESURGICAL USE OF MIFEPRISTONE IN PATIENTS WITH AUTONOMOUS CORTISOL SECRETING ADENOMAS**

*John Parker, MD¹, James Smith, PhD²*

¹. Wilmington Health, 2. Corcept Therapeutics

**Objective:** Autonomous cortisol secretion from a functional adrenal adenoma (AA) can suppress the HPA axis and may lead to functional suppression of the normal adrenal tissue. Unilateral adrenalectomy in ~65.3% of AA patients leads to postsurgical secondary adrenal insufficiency (AI) and often requires intraoperative and postsurgical glucocorticoid replacement until the HPA axis recovers.

Herein are 2 Cushing’s Syndrome cases with cortisol secreting AA treated with mifepristone (MIFE), a competitive glucocorticoid receptor antagonist. MIFE use was associated with clinical improvements and increased ACTH and DHEA-S suggesting recovery of the hypothalamus, pituitary and normal adrenal tissue respectively. These hormonal changes represent potential biomarkers to assess recovery of the HPA axis function prior to surgery and avoiding postsurgical secondary AI.

**Case Presentation:** Pt 1: A 70yo man with a unilateral AA and poorly controlled T2DM (A1C 9.1% on Lantus, Humalog, Prandin, Glimepiride, Januvia and metformin) and hypertension (155/84 mmHg on metoprolol, eplerenone, Micardis HCT, amiloride, clonidine, spironolactone). ACTH of 17.9 pg/mL [nl:10-50], DHEA-S of 29.3 µg/dL [nl:28-175], unsuppressed 1 mg overnight DST 1.98 µg/dL. After 6 months of MIFE (600mg/d final dose), ACTH (141.4 pg/mL) and DHEA-S (69.1 µg/dL) increased, suggesting HPA axis recovery. DM greatly improved; A1C fell to 7.4% with discontinuation of all antidiabetic meds except for metformin. BP was unchanged, but all meds were discontinued and replaced with valsartan 80 mg monotherapy. After unilateral adrenalectomy, ACTH and DHEA-S normalized to 54.2 µg/mL and 37.3 µg/dL respectively. Since there was no postoperative AI (cortisol 11.7 µg/dL), he did not require steroids. Postsurgical BP and A1C remain unchanged.

Pt 2: A 44yo woman with bilateral AA, prediabetes (FBG 104 mg/dL), insulin resistance (HOMA-IR=7), hypertension (156/85 mmHg), undetectable ACTH, DHEA-S of 54.6 µg/dL [nl: 32-240], unsuppressed 1 mg overnight DST 2.66 µg/dL. Five months of MIFE (600mg/d final dose) increased ACTH (30.3 pg/mL) and DHEA-S (62 µg/dL), normalized FBG (86 mg/mL) and insulin resistance (HOMA-IR=1.4). Post partial bilateral adrenalectomy, ACTH (16.3 pg/mL) and DHEA-S (18.4 µg/dL). Postop ACTH stim test showed no AI; thus no steroid therapy provided. BP normalized to 119/82 mmHg and she is no longer prediabetic. Postoperative DST was 1.16 µg/dL, BP and A1C remain unchanged.

**Conclusion:** MIFE treatment of two patients with adrenal cortisol secreting adenoma prior to adrenal surgery improved metabolic parameters, restored HPA axis function and prevented postsurgical AI. These results suggest that response to MIFE was associated with a positive postsurgical outcome.

**Abstract #132**

**UNUSUAL CASE REPORT OF A FAMILY WITH CUHISING’S; BROTHER, SISTER AND AUNT**

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McAlester Regional Hospital

**Objective:** Exposure of unusual presentations of Cushing’s possibly a familial genetic mutation.

**Methods:** 3 patients were chosen from a private Endocrinology practice. The patients were referred for symptoms of fatigue, weight gain in the abdomen, and
mood changes. Suspected adrenal complications labs were obtained. Literature review also supports the diagnosis of Cushing’s with possible genetic mutations.

**Case Presentation:** Labs and physical exam supports the diagnosis of Cushings in all 3 patients. 63 year old female, and adolescent teen niece and nephew with sudden onset of symptoms restricting their previously active lifestyle as lifeguards. The physical exams of both siblings reveals impressive purple striae on abdominal obesity. The previously athletic 16 year old lady at 5’2” had gained 30 pounds up to 210.8 with waist of 49”. She had headaches, fatigue, depression, sharp pains in her limbs and nausea. Her blood pressure was 166/99. Although the siblings parents were heavy set more so in the abdomen, no striae were present in either parent. The aunt had left papilliedema but had no striae. Also her ACTH varies on different blood tests.

**Discussion:** The 63 year old Aunt was known to have hypothyroidism and came in to adjust her medication. Also she has dizziness and blurry vision on/off and had been gaining weight around the middle, 20 pounds, with BMI: 32.8, with increased fatigue that she attributed to thyroid and or life situations. Increased shoe size suggested a pituitary workup. It revealed her IGF1; 130 (75-263) and elevated ACTH of 69 (6-58). Both her nephew and niece who were brother and sister were athletically gifted lifeguards over the summer. both were gaining weight in the abdomen. the young man’s weight gain, depression and irritability prompted the family to refer him. History and physicals were done. Early 8am cortisols, 24 hour urine cortisols and late night(11pm) salivary cortisols were obtained on the patients. Also pituitary and thyroid laboratories were obtained.

**Conclusion:** The familial genetic mutations of Cushing’s disease is still being discovered. These 3 presentations of symptoms supported by lab values brings the unusual presentation of the disease and the research together in one paper.

**Abstract #133**

**EXCESS SWEATING AND AN ADRENAL NODULE, WHAT IS THE CONNECTION?**

Vijay Eranki

Swedish American Hospital

**Objective:** Excess sweating is a common symptom encountered in endocrinology. In this case report a rare cause of excess sweating is reviewed.

**Case Presentation:** A 34 year old female presented with one year history of having night sweats. She was on medications for anxiety and depression for about 5 years. She had no change in appetite and she lost some weight when she was training for a marathon, but later had about 10 lbs weight gain. She noted nervousness, shakiness and diarrhea. She noted the blood pressure to be slightly higher lately. She also had some flushing and irregular cycles. She has history of easy bruising but no stretch marks. Physical exam was unremarkable including no excess body hair or stretch marks.

The patient had a lengthy blood and urine work up. Labs showed non suppressed cortisol with 1 mg dexamethasone (cortisol of 19.89 ug/dl and 21.8 ug/dl – done twice), very low ACTH (<5 pg/mL) and very high 24 hour urine cortisol (183.6 ug/day). Abdominal imaging was done which revealed a left adrenal nodule (2.1 X 1.7 cm with 100 HU).

She had left adrenalectomy. The final pathology report showed a benign adrenal adenoma. She was discharged on hydrocortisone taper. She is currently on hydrocortisone 10 mg in the AM and is feeling much better.

**Discussion:** This patient is of particular interest as she did not have the classic signs and symptoms of Cushing’s syndrome and work up for nonspecific symptoms led to the diagnosis. There is not much data in the literature for patients presenting with night sweats as a primary symptom of Cushing’s.

**Conclusion:** Hence the clinician should be on the lookout for Cushing’s in patients with nonspecific symptoms such as sweating and flushing.

**Abstract #134**

**IMMEDIATE AND SUSTAINED IMPROVEMENTS IN A CUSHING’S SYNDROME PATIENT WITH PRIMARY MACRONODULAR ADRENAL HYPERPLASIA TREATED WITH MIFEPRISTONE**

Honey East, MD¹, Carlton Anderson, PhD², Dat Nguyen, PharmD²

1. Baptist Premier Medical Group, 2. Corcept Therapeutics

**Objective:** Bilateral adrenalectomy is the standard treatment for bilateral macronodular adrenal hyperplasia (BMAH). It allows for rapid and permanent reversal of hypercortisolism but obliges the patient to receive lifelong glucocorticoid and mineralocorticoid replacement. Additionally, the permanent effects of mineralocorticoid and glucocorticoid deficiency expose the patient to increased risk of adrenal insufficiency as well as increased morbidity and mortality.

Medical therapies are commonly administered for a limited time prior to adrenalectomy. Herein, we present a patient receiving long-term treatment with mifepristone (MIFE, Korlym®, Corcept
Therapeutics), a glucocorticoid receptor antagonist, for the treatment of adrenal Cushing’s Syndrome (CS).

**Case Presentation:** A 54 y/o woman presented with cushingoid clinical features and extreme muscle weakness requiring a cane. Her medical history included uncontrolled diabetes (A1C 8.5%), HTN (141/88 mmHg), morbid obesity (240lbs, BMI 43 kg/m2), dyslipidemia, congestive heart failure, COPD, sleep apnea, chronic renal insufficiency, and hyperthyroidism.

Abdominal CTs revealed diffused bilateral enlargements of the adrenal glands with density ranging from 2-20HU, which have been stable compared to previous imaging studies. Hormonal testing showed suppressed ACTH (<5pg/mL), normal UFCs (18.2, 21.3 µg/24hr [nl=4-50]), abnormal overnight 1mg DST of 18.8 µg/dL, and low normal DHEA-s 36 µg/dL [nl=8-188].

Diabetic meds: Novolin sliding scale, Lantus 20U/qhs
Anti-HTN meds: amlodipine 10mg QD, carvediolol 25mg BID, furosemide 40mg QD, hydralazine 50mg TID, Lisinopril 5mg qd, clonidine 0.2mg QD

Adrenalectomy was refused by the patient. Ketoconazole was rejected due to the potential hepatic toxicity. MIFE 300mg/d was initiated and titrated to 600mg/d.

After 2 weeks of treatment, the patient’s BP and fasting blood glucose were improved, and a 3lbs weight loss was noted. At 6 months, her A1C decreased to 5.8% and a11lbs weight loss was noted. After 1 year, she had lost 28lbs (12% of her baseline weight), BP 130/84 mmHg, A1C 5.6%, and daily log revealed well controlled daily glucose levels with reduced utilization of Lantus and Novolin.

**Conclusion:** MIFE was well-tolerated and an efficacious option in this patient with CS due to BMAH when surgical intervention was not desired. GI related adverse events (nausea, vomiting) were manageable with adjustment in dose and the beneficial effects were apparent and sustained.

**Abstract #135**

**ADRENAL CRISIS RELATED TO TREATMENT OF PROSTATE CANCER**

Shirin Haddady, MD, MPH, Gianluca Toraldo, MD, PhD
Boston University

**Objective:** Abiraterone acetate is a new androgen synthesis inhibitor, approved by the FDA in 2011 after phase 3 clinical trials showed increased survival in metastatic castration-resistant prostate cancer. This medication is administered with corticosteroids to reduce its side effects. In the past several months, we were involved in the care of multiple patients on this medication admitted with signs of adrenal insufficiency to hospital. Here we present one of these cases.

**Methods:** A case and related medical literature is presented.

**Case Presentation:** 65 year old male with metastatic prostate cancer on Abiraterone 1000mg daily and Prednisone 5 mg, 2 times a day since June 2014, and other medical problems including bilateral hydronephrosis, neurogenic bladder, Type 2 Diabetes Mellitus, coronary artery disease, presented to Emergency Department with extreme weakness, nausea, vomiting and fever. He had stopped his oral medications before admission. At presentation, his blood pressure was 80/50. Laboratory was notable for leukocytosis, hyponatremia, elevated creatinine (2.39 mg/dL). He was admitted to the Intensive Care Unit, Cosyntropin Stimulation Test was performed and showed inappropriate adrenal response (Cortisol at baseline 5.6 µg/dl, 10.4 µg/dl after 1 hour). Stress dose steroid was started with a rapid improvement of hypotension and his symptoms . Urine culture grew Klebsiella Pneumoniae which was treated accordingly. The patient stated that he had no knowledge on how to manage his prednisone at the time of illness.

**Discussion:** Abiraterone acetate has been increasingly prescribed by oncologists in castration-resistant prostate cancer. It is structurally related to Pregnenolone and able to irreversibly inhibit CYP17, an enzyme present in the adrenal gland with a critical role in synthesis of androgens and cortisol. Blockade of this enzyme leads to indirect increase of ACTH and consequent increased production of precursors above the blockade. One of these precursors is Corticosterone, a mineralocorticoid that leads to fluid retention, hypokalemia and hypertension. In order to minimize these side effects, Abiraterone is administered along with corticosteroids, often Prednisone 5 mg twice daily a dose that disrupts the physiologic circadian rhythm of cortisol.

**Conclusion:** Abiraterone acetate is a promising drug in patients with metastatic castration-resistant prostate cancer. This medication is given together with steroids in order to minimize side effects. Patients should be educated about possibility of secondary adrenal insufficiency and its management.

**Abstract #136**

**AMYLOID INDUCED ADRENAL INSUFFICIENCY**

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1. Lady Hardinge Medical College, 2. AIIMS, 3. Lady Hardinge Medical College

**Objective:** To present a case of adrenal insufficiency secondary to amyloidosis.
Case Presentation: A 28 year old male presented with history of decreased urine output, edema over face and feet of two months duration. Patient received complete treatment for pulmonary tuberculosis in the past. Patient was poorly nourished, had pallor and pitting edema, vitals were stable and rest general and systemic examination was unremarkable except for presence of free fluid in abdomen. Investigation: haemoglobin 8.3g/dl (13.3-16.2), S. Cholesterol 313mg/dl (130-230), low S. albumin 2.6 g/dl (3.5-5.5), urine protein 3+ & 24 hour urine protein 4.5g/day (<0.25). Coagulation profile was normal. USG abdomen revealed ascites & bilateral medical renal disease. Renal biopsy revealed amyloid deposition in glomeruli and was positive for different stains (PAS, Congo red & methyl violet). Final diagnosis of nephrotic syndrome with renal amyloidosis probably secondary to tuberculosis was made. He was managed with salt, fluid restriction and diuretics. Patient improved. His diuretics were reduced but after one month he again presented to us with complaints of dizziness, persistent nausea and vomiting. On examination he was conscious oriented, Pulse-104/m, BP- 102/60 mm Hg in supine position and 80/50 mm Hg in standing position suggestive of postural hypotension. Systemic examination revealed no significant finding. No other signs of autonomic nervous system involvement were found. Investigation Hb. of 8.0g/dl (13-16), Blood urea 74.0mg/dl (15-45) and S. creatinine 4.2 mg/dl (0.6-1.2), S. albumin 3.0g/dl (3.5-5.5), S. sodium 129 meq/L (135-145), S. potassium 5.6 meq/dl (3.5-5.5), FT4 1.0ng/dl (0.7-1.24), FT3 3.0pg/ml (2.4-4.2), TSH 1.3µIU/ml (0.34-4.50). Basal S. cortisol < 5 µg/dl (5-25µg/dl), ACTH 200.8pg/ml (6.0-45). Post 250µg i.VACTH stimulation S. cortisol was 6.0µg/dl. CECT abdomen revealed bulky bilateral adrenal glands. Diagnosis of primary adrenal insufficiency was made & patient was put on corticosteroid. Symptomatically patient improved markedly though proteinuria persisted. Patient was discharged on deflazacort 12.0mg/day and fludrocortisone 0.1 mg/day. Initially we thought that postural hypotension is due to volume depletion secondary to diuretic usage but hypoadrenalism was actually the cause for that.

Conclusion: All patients of renal amyloidosis should be screened for concurrent adrenal insufficiency secondary to adrenal amyloidosis.

Abstract #137

COMBINED CLINICAL PRESENTATION OF ALLGROVE’S SYNDROME AND 47XXX SYNDROME IN A 14 YEAR OLD GIRL

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1. Care Hospital, 2. Nizams Institute of Medical Sciences

Objective: To evaluate the girl for the etiology of hyperpigmentation, neuromuscular weakness and delayed development of secondary sexual characters in a 14 ½ year old girl

Methods: The girl was evaluated by neurologist and found to have development delay, sensory and motor neuropathy, ataxia, amyotrophy and dysautonomia. Referred to endocrinologist for skin and mucosal hyperpigmentation. On evaluation, Serum cortisol was 125.9 nmol/L and Adreno-CorticoTrophic Hormone – 1250 pg/ml. Primary adrenal insufficiency was diagnosed and she was started on hydrocortisone and fludrocortisone replacement. Subsequent Follicle Stimulating Hormone was 38.58µ/ml and Leutinizing Hormone 17 µ/ml, with an Estradiol value of 34 pg/ml. Ultrasound revealed infantile uterus and ovaries were not visualized. A possible diagnosis of Autoimmune Polyglandular Syndrome Type 2 was entertained

Case Presentation: CT ordered by neurophysician revealed achalasia cardia and another MRI revealed alacrimia, thus leading to a diagnosis of Allgrove’s syndrome. However, this could not explain sensory motor neuropathy and delayed puberty. MRI abdomen revealed small ovaries. Karyotype was 47XXX.

Discussion: Triple X and Allgrove’s Syndrome presenting in the same girl has not yet been reported in literature, to the best of our knowledge. A combination of Triple A (Allgrove’s) syndrome and Triple X syndrome, resulted in the complex clinical findings of this disorder with development delay, sensory and motor neuropathy and delayed puberty due to 47XXX syndrome and adrenal insufficiency, achalasia, alacrimia and dysautonomia resulting from Allgrove’s syndrome. She has also been started on estrogen replacement in addition to adrenal steroid replacement.

Conclusion: Combine Triple XXX and Triple A Syndrome in this girl resulted in complex clinical findings of global neuropathy, adrenal insufficiency and delayed puberty.
Abstract #138

WOMEN WITH CUSHING’S SYNDROME FOR CORTICO-MEDULLARY ADRENAL ADENOMA WITH EXPRESSION OF ACTH.

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Objective: Present an interesting and rare case of a cortico-medullary adrenal adenoma in a woman with Cushing (CS) syndrome.

Methods: We present the characteristics and evolution of the patient.

Case Presentation: 29 year old woman. History of hypertension and pleural tuberculosis. She refers 1 year of evolution of disease with weight gain, secondary amenorrhea and cushingoid phenotype. Referred from another institution for study of CS with adrenal adenoma on CT, elevated ACTH and pituitary MRI with microadenoma. Analysis: TSH: 0.47uUI/ml; FT4: 0.49ng/dl; AbTPO (-); FSH: 13.1ng/ml; LH: 3.09mUI/ml; E2: 52.2pg/ml; PRL: 13.1ng/ml; IGF1: 234ng/ml. Circadian rhythm of ACTH 8am/ 4pm/ 11pm: 38.1 / 39.2 / 37.3pg/ml; Cortisol 8am/ 4pm/ 11pm: 30.7 / 37 / 30.9ug/dl; DHEAS: 126.5ug/dl; UFC: 1553/1836 ug/day; Cortisol Post Dexa2: 30.7ug/dl; UFC Post Dexa2: 1299.65ug/day; Cortisol Post Dexa8: 35.9ug/dl; UFC Post Dexa8: 1517.1ug/day. TEM Adrenal: solid nodule in right adrenal 27x21mm homogeneous, washout >60%; Pituitary MRI: normal; TEM chest and abdomen-pelvis (-). She underwent laparoscopic right adrenalectomy with AP: cortico-medullary adrenal adenoma of 3x2.5 cm with IHC expression of ACTH (2+/3+) in 70%.

Immediate postoperative serum cortisol <1ug/dl; DHEAS <15; Androstenedione <0.30; ACTH: <5pg/ml.

Discussion: Cortico-medullary adrenal tumors are a rare condition defined by histological findings with a variety of clinical conditions. Although rare, they illustrate the importance of a comprehensive biochemical assessment on each patient for coexisting functioning tumors.

Conclusion: There are about 20 reported cases of cortico-medullary adrenal tumors. Most are women who present with CS.

Abstract #139

METHYLDOPA-INDUCED HYPERALDOSTERONISM IN PATIENTS WITH CENTRAL DEMYELINATING DISEASE: COULD IT BE PARADOXICAL?

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Advocate Illinois Masonic Medical Center

Objective: Methyldopa is a psychoactive drug used as a sympatholytic or antihypertensive. We present an unusual case of methyldopa-induced hyperaldosteronism in a multiple sclerosis (MS) patient.

Case Presentation: A 35-year-old woman presented to our facility with complaints of uncontrollable hypertension and severe headache. Her history was significant for MS and hypertension. Due to her desire to conceive, she had been switched from enalapril to methyldopa, 9 months earlier. Approximately 10 days prior to presentation, she had noticed that her home blood pressure readings were trending much higher than her usual (190s/100s) along with episodic palpitations despite the increase in methyldopa dose to 500 mg twice a day. She also reported increased thirst, weakness and decreased urination despite being aggressive with fluid intake. Upon presentation, she appeared lethargic. Physical exam was unremarkable. No edema was noted. Her Blood pressure was elevated to 205/136. Her labs were significant for Hemoglobin of 11.2 g/dl, platelets of 78 x10^9/L, Potassium of 2.5 meq/L, Bicarbonate of 28 meq/L, BUN of 24 mg/dl, creatinine of 1.52 mg/dl (her baseline 0.9), and total Bilirubin of 1.3 mg/dl. Further investigation showed elevated LDH, reticulocyte count, and schistocytes on peripheral smear. More workup of her hypokalemia and hypertension was pursued, and it revealed an elevated plasma aldosterone concentration (PAC) to 52 ng/dl and a normal renin concentration of 19 (despite the possible renin suppression that can occur with methyldopa use). Her PAC-PRA (Aldosterone-Renin Ratio) ratio was close to 3. Given these values, methyldopa was discontinued. Accordingly, her blood pressure improved and Spironolactone was added to her regimen. In addition, her hemolytic anemia improved with blood pressure control.

Discussion: Hypertension in MS patients might be secondary to dysregulation of the hypothalamo-pituitary-adrenal (HPA) axis. Methyldopa impact on the blood pressure in MS patients through central sympathetic inhibition is possibly compromised given the central demyelinating effect of MS. Moreover, the alteration of the negative feedback inhibition circle of the renin-angiotensin-aldosterone system through the combined
effect of methyldopa and MS might result in a synergistic effect leading to hyperaldosteronism and ultimately paradoxical hypertension.

**Conclusion:** The hypothalamic-pituitary-adrenal axis and renin-angiotensin-aldosterone system feedback inhibition and responses are highly unpredictable even with antihypertensive medications in patients with central demyelinating disease.

**Abstract #140**

**SHOULD AN ENDOCRINOLOGY EVALUATION PREVIOUS TO BARBITIC SURGERY BE A REQUIREMENT? CASE REPORT: YOUNG MALE WITH MORBID OBESITY AND HYPOGONADISM WITH DELAY DIAGNOSE OF CUSHING DISEASE AFTER BARBITIC SURGERY**

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**Case Presentation:** 21 year old male with no medical history was admitted due to sepsis and multifocal pneumonia. He reported 100 pound gain in the previous year (BMI 45) and decrease libido. New onset diabetes, hypertension, sleep apnea and diastolic dysfunction with left ventricular hypertrophy was diagnose. Laboratory reported increase WBC 15.2, low Hb 13.6 g/dl, high A1C 7.1%, high glucose 140 mg/dl, low potassium 3.4 mEq/L, normal TSH 0.66 uIU/ML and low total testosterone 21 NG/DL (Ref 240-950). He was discharged on hypertension medications, metformin and testosterone patches without other workup for hypogonadism. Three months later preoperative clearance process for bariatric surgery was started. He was evaluated by primary care, pulmonary, gastroenterology and cardiology without further workup recommendations. Roux Y gastric bypass was done one year later. In the next 6 months patient was hospitalized with upper gastrointestinal bleed due to an anastomosis ulcer and later because of multiple lumbar and thoracic vertebral compression fractures with severe back pain. Endocrinology evaluation was requested for secondary osteoporosis. Cushing was corroborated 3 days later but ACTH dependent Cushing syndrome was diagnose 9 months after the bariatric surgery and 20 months later after the first hospital visit. Pituitary surgery was done but cortisol levels did not decrease and he had a complicated postoperative course with pulmonary embolism, acute kidney injury and sepsis. After a few months he was discharge and schedule for bilateral adrenalectomy. However patient died with cardiac arrest at home approximately 2 years after his first evaluation.

**Discussion:** Cushing syndrome diagnose is challenging and requires a high suspicion. Certain signs and symptoms suggest this syndrome but there is not a pathognomonic one and they are nonspecific including obesity, hypertension, and diabetes. When this findings are unusual for age, or severe, a more detail examination should be done to search for signs that will require further work up or endocrinology referral. The Bariatric surgery guidelines recommend a detail evaluation with further request of endocrine evaluation if required. However difficult diagnoses as Cushing requires a more specialized clinician that will balance the appropriate workup and the unnecessary screening test. It is well proven that chronic cortisol excess leads to potentially irreversible consequences and death, so the rapid recognition and treatment are fundamental.

**Conclusion:** The diagnose of secondary causes of obesity as Cushing can be difficult and delayed, so an experienced clinician is required to search for signs of endocrinopathies that will justify further workup.

**Abstract #141**

**A CASE OF PHEOCHROMOCYTOMA PRESENTING AS SIRS**

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**Objective:** To report an unusual presentation of pheochromocytoma

**Case Presentation:** 43 year old M with history of T2DM, CHF, HLD & HTN, transferred from an outside hospital (OSH) for further cardiac management and workup after being managed for atrial fibrillation with rapid ventricular rate, CHF exacerbation and sepsis secondary to pneumonia. He had originally presented with complaints of fever and cough. At the OSH, he was treated with rocephin, azithromycin, dobutamine drip, cardizem and then amiodarone drip, and digoxin. Upon arrival, intubated and sedated on versed and fentanyl, he was febrile to 103.9 F, in atrial fibrillation at a rate of 180, with a BP of 127/76. He had a leukocytosis of 19.7, lactate 0.8, TSH 0.64, HbA1C 8.8. He was continued on antibiotics for presumed sepsis. Blood cultures revealed bacillus (not anthracis) in one anaerobic bottle. Urine culture was negative. Despite this aggressive therapy, he was noted to be persistently tachycardic and febrile. TEE revealed severe AR and MR, no evidence of endocarditis. CT chest, abdomen and pelvis with contrast were performed to identify a source of infection with the only significant finding being a 4.1 x 3.9 cm heterogeneously enhancing right suprarenal mass. 24 hour urine fractionated metanephrines were 4253
mcg/24 h, and normetanephrines 1069 mcg/24 h; plasma metanephrines 1080 pg/ml and normetanephrines 747 pg/ml. He was initiated on phenoxycbenzamine 10mg po bid increased to 20mg BID after 6 days. Despite receiving rate control with addition of diltiazem, digoxin and amiodarone, his heart rate still remained over 100 until beta-blocker therapy was initiated a week later. Both his fever and leukocytosis resolved 6 days and 19 days after initiation of alpha blockade, respectively. He successfully underwent a right adrenalectomy with pathology showing a 4.5 cm moderately differentiated pheochromocytoma without capsular or vascular invasion, or necrosis. After resection of the pheochromocytoma he underwent successful replacement of aortic and mitral valves.

Discussion: The classic presentation of pheochromocytoma is well known, and includes paroxysmal hypertension, headache, diaphoresis and signs and symptoms of adrenergic excess. When a patient presents with SIRS without an identifiable source, pheochromocytoma should be considered in the differential diagnosis. The patient responded well to standard recommended therapy of alpha blockade, followed by beta blockade, and, ultimately, surgical resection. Insulin resistance - also noted to be a feature of pheochromocytoma – was noted to greatly improve subsequent to surgical resection.

Conclusion: We present a rare case of pheochromocytoma presenting as SIRS.

Abstract #142

A CASE OF A FUNCTIONING EXTRA-ADRENAL RETROPERITONEAL COMPOSITE PARAGANGLIOMA AND GANGLIONEUROMA.

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Objective: Composite paraganglioma (PG) and ganglioneuroma (GN) is a rare tumor and extra-adrenal composite PG/GN is distinctly uncommon. We present a case of an incidentally detected functional extra-adrenal PG/GN.

Case Presentation: Clinical case: A 43 year old male was found to have asymptomatic microscopic hematuria during an annual examination. Non-contrast CT demonstrated a 3.2 cm, partially necrotic, heterogeneous left adrenal mass with HU>40. He denied persistent hypertension, but had occasional systolic blood pressure of 140-150mmHg. He denied palpitations, pallor, diaphoresis, tachycardia, syncope, episodic headaches or weight gain. Vital signs and physical examination were normal. Family history was negative for adrenal disease. Hormonal evaluation (values in mcg/24 hrs) revealed elevated 24-hour urine Epinephrine (30; Ref: 2-24); Norepinephrine (154; Ref: 15-100); Total Catecholamines (184; Ref: 26-121), Normetanephrine (1075; Ref: 88-649); Metanephrine (438; Ref: 58-203); Total Metanephrines (1513; Ref: 182-739). Chromogranin A was 12.2 ng/ml (Ref: 1.9-15). One-mg dexamethasone suppression test was negative and 24-hour urine free cortisol was normal. PET-CT scan of the abdomen confirmed a 3.5x2.7 cm heterogeneous and hypermetabolic left adrenal mass. Laparoscopic left adrenalectomy was done. Pathology revealed a tumor consistent with extra-adrenal pheochromocytoma with a composite area of ganglion cells surrounded by satellite cells consistent with GN. No extracapsular or intravascular tumor extensions of this tumor were found. The final diagnosis was a retroperitoneal, extra-adrenal PG/GN. Genetic testing was performed sequentially with negative germline SDHB, SDHD and RET. His most recent urine Metanephrines were normal. He is being followed for further genetic testing as is feasible and for yearly biochemical studies.

Discussion: Literature Review: Fewer than 70 cases of composite PG/GN have been reported, with the majority located in the adrenal glands. Of the 13 cases of extra-adrenal composite PG/GN tumors, 5 were retroperitoneal, and only 1 of these was functional. In two cases the tumor showed malignant potential with local invasion and primitive neuroblastic cells, respectively. Genetic testing was not reported in any of the extra-adrenal composite PG/GN cases.

Conclusion: Composite PG/GN diagnosed via pathological specimen analysis is a rare variant of an uncommon disease. The entity can present as a typical adrenal pheochromocytoma.

Abstract #143

DEXAMETHASONE SUPPRESSION TEST UNRELIABLE IN A GASTRIC BYPASS PATIENT? - A DIAGNOSTIC DILEMMA

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Objective: Unilateral adrenal incidentalomas are detected in about 4.4 percent of patients undergoing CT abdomen and up to 10 percent in older patients. Prevalence is more common in obese, diabetic and hypertensive patients. Subclinical Cushing’s syndrome needs to be screened in these patients with adrenal incidentalomas. We report a case of adrenal nodule where dexamethasone suppression test becomes unreliable secondary to malabsorption of the medication.
Case Presentation: A 64 year old female with history of type 2 diabetes mellitus, hypertension, osteopenia, hyperlipidemia, multiple sclerosis and sleep apnea, who was seen for the evaluation of a left sided adrenal nodule found on CT abdomen. She did not report any symptoms suggestive of adrenal hormone over secretion. She had a history of gastric bypass surgery 7 years ago. Labs revealed a sodium of 142 mmol/liter, potassium of 4 mmol/liter, chloride of 108 mmol/liter, bicarbonate of 26 mmol/liter and creatinine of 0.7 mg/dl. Serum aldosterone, renin, metanephrines and normetanephrine levels were normal. A low dose dexamethasone suppression test was done to rule out subclinical Cushing’s syndrome. It revealed a morning cortisol level of 18.5 mcg/dl, indicating that cortisol level was not appropriately suppressed. Dexamethasone level concurrently tested was less than 20 ng/dl. The test was repeated after one month and showed a similar result. She reported taking the dexamethasone as prescribed. We hypothesized that the patient was not absorbing dexamethasone likely secondary to the gastric bypass surgery and the dexamethasone suppression test was unreliable. She later underwent a 24 hour urine cortisol level, which was 23 mcg/24 hrs, within normal limits. She also performed a midnight salivary cortisol, which was 0.16 mcg/dl. This test was also normal.

Conclusion: Diagnostic evaluation of adrenal incidentalomas initially involves testing for hormonal levels. Also, subclinical Cushing’s syndrome is not uncommon and appropriate patients should be screened. Low dose dexamethasone suppression test is an initial test of choice. With a history of gastric bypass surgery, this test should be interpreted with caution as these patients may have malabsorption of dexamethasone, which can lead to a false positive test. Therefore we recommend physicians to check a dexamethasone level along with the cortisol level in this subset of population to help determine if the drug is being absorbed. If dexamethasone levels are low, other modalities of testing such as 24 hour urinary cortisol or midnight salivary cortisol should be considered to screen for this condition.

Abstract #144

DIAGNOSTIC PERFORMANCE OF ADRENAL IMAGING IN A HIGH RISK POPULATION FOR ADRENAL MALIGNANCY

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Mayo Clinic

Objective: Limited evidence on diagnostic accuracy of imaging tests exists in patients at high risk for adrenal malignancy. Our objective was to determine the performance of CT and 18F-fluorodeoxyglucose-positron emission tomography (18FDG-PET)/CT imaging in diagnosing a malignant adrenal mass in a high risk population of patients referred for adrenal biopsy.

Methods: We retrospectively reviewed 379 percutaneous adrenal core biopsies performed in our institution between 1994 and 2014. Patients’ clinical data and imaging studies (CT and 18FDG-PET/CT) were reviewed. Reference standard was based on histology in all patients. FDG uptake was measured in the adrenal mass (SUV max) and liver (SUV liver). SUV max to SUV liver ratios (ALR) were calculated.

Results: Patients were referred for adrenal biopsy mainly due to suspected or confirmed extra-adrenal malignancy (301/379, 79%) and included 237/379, 62.5% men, median age 68 (range 18-91) with 237/379, 62.5% malignant adrenal lesions (median size 3.5 cm, range 0.7-17 cm), 136/379, 36% benign adrenal adenomas (2.3 cm, range 0.6-11) and 6/379, 1.5% infiltrative infectious processes. Unenhanced CT was performed in 352 patients (223 malignant, 129 benign lesions). All malignant adrenal lesions demonstrated Hounsfield Unit (HU) measurement of >15 (sensitivity 100%, specificity 33% , positive predictive value (PPV) 72% and negative predictive value (NPV) 100%). 18FDG-PET/CT was performed in 92 patients (44 metastases, 3 lymphomas, 2 adrenocortical carcinomas and 43 adrenal adenomas). SUV max was higher in malignant lesions when compared to benign lesions (median 10.1 (range 1.9-29.4) vs 3.7 (range 1.4-24.5), p<0.001). Similarly, ALR in malignant lesions was higher than in benign lesions (median 3 (range 0.5-13.4) vs. 1.15 (range 0.6-6.6), p<0.001). ALR cutoff of 1.8 performed best in diagnosing adrenal malignancy (sensitivity 83.3%, specificity 83.7%, PPV 85.1% and NPV 81.8%).

Conclusion: In this largest retrospective study with an optimal reference standard, all malignant adrenal lesions demonstrated unenhanced CT HU >15. Although malignant
lesions had higher ALR compared to benign lesions, there was still significant overlap in this high risk population.

Abstract #145

POST-STEROID WITHDRAWAL PANNICULITIS IN A PATIENT AFTER TREATMENT OF CUSHING’S SYNDROME

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Case Presentation: A 30 year old female Army pilot was referred to Endocrinology for evaluation of the etiology of stress fractures of her feet and left femur in recent years. DXA scan showed a Z-score of -1.1 at hip and -1.0 at the spine, which meant normal bone density for her age. However, patient had history of hypertension and hyperlipidemia without any traditional risk factors. On physical exam, she was noted to have truncal fat distribution, moon facies, easy bruising, supraclavicular fullness, and dorsal cervical fat padding. Thus, evaluation for Cushing’s Syndrome was initiated as a possible underlying cause of her stress fractures.

Late-night salivary cortisol was consistently elevated at 0.581, 0.621 and 0.628 ug/dL (reference range <0.010 - 0.090) and 24 hour urine free cortisol was 210 mcg/24hr (reference range 0-50). Cortisol was 16.8mcg/dL with an undetectable ACTH after 1 mg dexamethasone suppression test, indicating an adrenal source. A pituitary MRI was normal and CT Abdomen showed a left 3.0 x 2.3 x 2.9 cm adrenal adenoma. A left adrenalectomy was performed and the patient was discharged on a maintenance dose of hydrocortisone.

A few weeks later, the patient presented with a 1-week history of painful subcutaneous nodules on arms and legs bilaterally with overlying erythema. Dermatology performed a punch biopsy of her right posterior calf. Histopathologic examination of the nodule showed mixed lobular and septal granulomatous panniculitis with fat necrosis. Special stains were negative for micro-organisms and fungal serologies and autoimmune markers were negative. Sarcoidal granulomas and foreign material were not seen. Coupled with the clinical history, she was diagnosed with post-steroid withdrawal panniculitis. Dermatology recommended treatment for this with high-dose steroids, however, this would have prolonged recovery from her adrenal insufficiency as her ACTH was still suppressed. She was continued on maintenance dose hydrocortisone and her panniculitis resolved six weeks later.

Conclusion: This case illustrates a unique cause of post-steroid panniculitis, an already rather rare condition which presents as a complication of systemic corticosteroid therapy. Post-steroid panniculitis was first described in 1956, with most cases in the pediatric population receiving high-dose systemic steroids for a variety of conditions. It usually develops within days or weeks following rapid tapering or cessation of high amounts of systemic corticosteroids. Most cases are self-limited. While there have been cases described in adults after withdrawal of steroid treatment, there has been no prior published cases of post-steroid panniculitis after Cushing’s treatment.

Abstract #146

ACUTE HEMORRHAGIC ADRENAL INSUFFICIENCY FOLLOWING CLOSTRIDIUM DIFFICILE COLITIS

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Objective: The symptoms and signs of adrenal hemorrhage are nonspecific thus making it difficult to be recognized clinically. Acute adrenal insufficiency (AI) due to adrenal hemorrhage has been reported with sepsis or infection caused by several pathogens. To the best of our knowledge this is the first case of bilateral adrenal hemorrhage associated with Clostridium difficile colitis.

Case Presentation: Fifty-four year old woman was re-hospitalized (10 days after discharge) when she presented with flank pain, nausea, vomiting, 10 pound weight loss and functional decline. The patient had been recently hospitalized for right-sided flank pain with suspected pyelonephritis in the setting of chronic self-catheterization because of neurogenic bladder. She was empirically treated with antibiotics but her initial urine and blood cultures came back negative and therefore antibiotics were discontinued. Her inpatient course at that time was complicated by Clostridium difficile colitis treated with oral Vancomycin. The patient was not on chronic anti-coagulation, nor on chronic or recent steroids. She was not known to have any chronic infections, chronic respiratory symptoms, and had no known history of cancer.

Computed Tomography (CT) of the abdomen without contrast was performed and demonstrated bilateral adrenal masses, not reported on a previous CT scan performed during her previous recent admission. Thereafter, a dedicated CT scan of the adrenal glands was performed during her previous recent admission. Thereafter, a dedicated CT scan of the adrenal glands was performed and was consistent with bilateral adrenal hemorrhage. Due to these findings, a Cosyntropin stimulation test was performed. Morning cortisol was 1.3 microgram/dL and only increased to 1.6 microgram/dL after 0.25 mg of intravenous Cosyntropin. Baseline ACTH was elevated at 237 pg/mL consistent with primary AI. Platelet
count and prothrombin time were normal and testing for antiphospholipid syndrome was negative. After the Cosyntropin stimulation test, the patient was started on glucocorticoid replacement and her symptoms significantly improved within 24 hours. She was then discharged on a chronic regimen of glucocorticoid replacement.

**Discussion:** This case demonstrates that Clostridium difficile colitis could predispose to or cause bilateral adrenal hemorrhage. The patient could have developed adrenal crisis or been at risk of death if CT scan would not have incidentally detected the adrenal hemorrhage and guided the treating physicians to assess the adrenal function.

**Conclusion:** Since AI symptoms could be nonspecific, managing physicians should be vigilant and consider this possibility in a patient presenting with such symptoms including gastrointestinal symptoms after being treated for Clostridium difficile colitis.

**Abstract #147**

**A CASE OF ADRENAL CORTICAL CARCINOMA MASQUERADING AS A GIST TUMOR**

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Advocate Christ Medical Center

**Objective:** Adrenal cortical carcinoma (ACC) is an extremely rare malignant tumor of the adrenal glands. The overall five-year survival for patients is less than 40% and many cases are diagnosed at advanced stages; hence, early detection is crucial for better outcomes. We present a case of ACC that was found unexpectedly on pathology of a large intraabdominal mass with presenting features suggestive of gastrointestinal stromal tumor (GIST).

**Case Presentation:** A 50 year old female with no past medical history presented with one month history of left upper quadrant discomfort and weight loss. Vital signs were within normal limits. On physical examination the patient had a large palpable mass in the left upper quadrant with no tenderness. Laboratory workup showed normal chemistry and microcytic anemia with hemoglobin of 7.4 mg/dL (normal 12-15). CT of the abdomen revealed a 21 cm left upper quadrant mass extending from the gastric fundal region of the stomach to the iliac crest. Initial imaging suggested GIST. To this end, upper and lower endoscopies were performed, which showed no tumors in the lumen of the gastrointestinal tract. Exploratory laparotomy demonstrated a 24 centimeter mass weighing 2480 grams which was excised. The mass had invaded into the left adrenal vein. Pathology of the mass revealed ACC with malignant features such as necrosis and invasion the adrenal vein. As an adrenal tumor was not suspected, no preoperative hormonal workup was performed. Postoperatively, urine cortisol level, plasma metanephrines and aldosterone to renin ratio were normal, which indicated a non-functioning mass. Therapy with mitotane was initiated along with radiotherapy considering the local invasion of the left adrenal vein. Subsequent evaluation after one year of therapy revealed lung and liver metastases on PET scan.

**Discussion:** ACC is a rare malignant tumor of the adrenal gland accounting for only 2% of adrenal tumors. Incidence is estimated at five per million annually with a female preponderance. Five year survival rate is less than 40% and it drops to 7% in patients with distant metastases on presentation. Tumors are usually found incidentally on imaging but can also present with compressive symptoms or as functionally active adrenal tumors. Surgery is the treatment of choice along with mitotane as adjuvant chemotherapy. Radiation is mainly used in invasive or metastatic lesions, especially if tumor has spread to the bones.

**Conclusion:** We present an unusual case of ACC presenting as a mass found in the left upper quadrant with initial features suggestive of GIST. This case highlights the fact that ACC can have a varied clinical presentation, which can hinder early diagnosis and treatment.

**Abstract #148**

**EXENATIDE SUPPRESSES TGFβ1: A NOVEL POTENTIAL ROLE FOR GLP-1 AGONISTS IN NEPHROPATHY**

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**Objective:** We have previously demonstrated that exenatide exerts potent anti-oxidant and anti-inflammatory effects in diabetic patients. TGFβ1 cytokine is fibrogenic, induces epithelial-mesenchymal transformation and is an important mediator in the pathogenesis of diabetic glomerulopathy. We now hypothesized that exenatide treatment suppresses TGFβ1 and its signal mediators in type 2 diabetes and thus might play a nephro-protective role.

**Methods:** We analyzed samples from 24 obese patients with type 2 diabetes taking insulin who were randomized (1:1) to receive either exenatide 10μg twice daily or placebo twice daily for 12 weeks. Fasting blood samples were obtained at baseline and 3, 6 and 12 weeks later. Mononuclear cells (MNC) were isolated and cellular fractions prepared.

**Results:** HbA1c fell significantly (from 8.6±0.4 to 7.4±0.5mU/ml, p<0.05) and insulin increased (p<0.05)
in the exenatide taking group while it did not change significantly in the placebo group. There was no significant change in body weight in either group. Exenatide suppressed plasma TGFβ1 concentrations by 20±7% (from 12.9±0.6 to 10.4±1.0ng/ml, P<0.05) while there was no significant change in TGFβ1 levels following placebo treatment. Exenatide also suppressed the expression of SMAD3 and SMAD4 by 28±8% and 30±7%, respectively, while it increased the expression of BAMBI (a pseudo-receptor of TGFβ1) by 98±24% over the baseline in MNC. The increase in BAMBI was evident by 3 weeks following the start of exenatide. There was no change in TAK-1 and TGFβ1 receptor expression in MNC or in CTGF and fibronectin concentrations in plasma in either group.

**Discussion:** Exenatide treatment in type 2 diabetes suppresses plasma TGFβ concentration and its downstream signaling mediators, SMAD3 and SMAD4 while increasing the expression of BAMBI, a TGFβ inhibitor.

**Conclusion:** Since TGF-β plays a critical role in diabetic kidney disease, these actions of exenatide may contribute to a potential nephroprotective effect in diabetes.
Abstract #200

CERTIFIED DIABETES EDUCATOR-AMBASSADOR (CDE-A) INVOLVEMENT IMPROVES DIABETIC CONTROL AND CARDIOVASCULAR RISK FACTORS AT PRIMARY CARE LEVEL

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Objective: We have previously shown that the involvement of a CDE, empowered by guidance from a diabetologist, termed CDE-Ambassador (CDE-A), in the management of the diabetes at the primary care level, results in marked benefits.

Results: Retrospective analysis of data obtained from 100 such patients showed improvements in glycemic control (HbA1c from 8.4% to 6.8%; p<0.0001), body weight (from 102 to 99Kg; p<0.0001), systolic blood pressure (from 134 to 128 mm; p=0.002), diastolic blood pressure (from 80 to 77 mm; p=0.003) and serum triglycerides (from 189 to 162 mg/dl; p=0.003) and LDLc concentrations (from 108 to 96 mg/dl; p=0.0004) following 2 to 3 consultations over a period of 6 months. [Micro-albuminuria did not alter significantly.]

There was no significant change in any of these indices in 45 control patients who did not consult with the CDE-A. We have now investigated the durability of this effect by getting follow up data at 12 months without further intervention after 6 months. The beneficial effect on HbA1c diminished from a reduction of 1.6% from the baseline at 6 months to 1.1% over the following 6 months without further visits to the CDE-A. However, the benefits in BMI, blood pressure, triglycerides and LDLc were largely maintained, without significant attenuation. These indices did not change in the control group.

Conclusion: We conclude that the involvement of the empowered CDE-A can contribute to improvements in diabetic control and indices of cardiovascular risk. While the maintenance of HbA1c probably requires repeated visits to CDE-A, the other indices related cardiovascular risk are effectively controlled for at least one year. A network of CDE-A, empowered by diabetologists at the primary care level could help prevent diabetic microvascular and macrovascular complications.

Abstract #201

THE DEVELOPMENT OF AUTOIMMUNE DIABETES AND THYROIDITIS BY THE USE OF PD-1 IMMUNOTHERAPY

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Objective: PD-1(Programmed cell death-1) is a key immune checkpoint inhibitor and if blocked can lead to impairment of immune tolerance and precipitation of autoimmunity.

A new class of drugs the anti PD-1 antibodies have recently been introduced for the treatment of certain cancers including melanoma, lung CA and renal cell CA. Autoimmune toxicity had been reported as a rare consequence of this immunotherapy.

Methods: A patient treated for metastatic squamous cell cancer of the lung with Nivolumab, at our tertiary care center was analyzed for the development of autoimmune DM as well as autoimmune thyroiditis with the use of Nivolumab-PD-1 inhibitor.

Case Presentation: Pt is a 63 yr old African American male, without any PMH of DM, who was otherwise healthy until Dec, 2013 when he developed cough.Work up revealed stage 3 squamous cell carcinoma of the lung.

Pt unfortunately failed multiple treatment modalities and his lung CA became widely metastatic. Given disease progression with chemotherapy, he was offered immunotherapy in light of survival benefit and more importantly potential durable response based on the recent data.

After two dose of Nivolumab patient presented to the ER with, palpitations and fatigue, and found to be in DKA.

Further investigation showed positive results for both anti GAD and TPO antibody. Patient did develop primary hypothyroidism at about three months.

Patient was continued on the Nivolumab and he received third dose on 9/28/15. Further immunotherapy is put on hold due to frequent admissions for DKA, syncope and RUE DVT.

Discussion: The critical role of PD-1 pathway in regulation of autoimmune DM had been well described in animal model. In phase 3 clinical trials of Nivolumab where it showed significant improvement in the survival in melanoma patients, one out of 206 patient developed DM.

Clinician should be aware of this rare but serious consequence.

Conclusion: PD -1 immunotherapy is an emerging treatment for Melanoma, lung and renal caner. Endocrine autoimmune disorders such, as autoimmune diabetes, thyroiditis and hypophysitis are a rare complication of this treatment. Prior
Abstract #202

RECURRENT DIABETIC KETOACIDOSIS: A CLINICAL CONUNDRUM

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UTHSC

Case Presentation: A 26-year-old Caucasian male with known history of diabetes mellitus (DM) type 1 presented to the hospital with recurrent diabetic ketoacidosis (DKA), 5 episodes in the last 25 days with hospitalizations in various hospitals in the city. During each of his hospitalizations he was taking insulin and did not have any stressor which could potentially precipitate DKA. DKA was moderately severe. Each time he was given diabetic education prior to his discharge from the hospital. His home regime included Levemir 25 units in AM and 18 units in PM and aspart insulin 7 units with each meal.

He was started on intravenous insulin, fluids and electrolyte replacement per standard DKA protocol. DKA resolved within 24 hours. Further work up was done to delineate the etiology of DKA. There was concern for possible fictitious insulin and Pharmacy was consulted to verify the authenticity of insulin. Insulin has a distinct smell and patients product smelled like insulin. Light refraction was done which showed he was using insulin at home. Results of light refraction are as follows.

Control Patients Insulin: Levemir 1.3382 1.3382; Novolog 1.3359 1.3359; Tap Water 1.3327 N/A

When DKA resolved patient was asked to draw and inject insulin under supervision. This nailed the problem as patient’s mother who used to draw insulin for him was doing it the wrong way. There was little or no insulin in the insulin syringe as the vial was kept on the table when insulin was being drawn.

Discussion: This case report illustrates two points. Firstly it reinforces the importance diligent diabetic education and perusal of cause of DKA before discharge from the hospital. This patient was admitted to the hospital 5 times before the cause of DKA was found. A team approach which included the pharmacist was the key to nail the problem. Secondly if the authenticity of insulin needs to be quickly verified at bedside then checking the refractory index and comparing to a control could be a good bedside tool. Also peculiar smell of insulin should be helpful and all healthcare professionals should be familiar with the same.

Conclusion: Diabetic education should be more practical and less verbal and should try to simulate home scenario. This would minimize errors and improve compliance.

Abstract #203

ALSTROM’S DIABETES – RARE DISEASE WITH COMMON ENDOCRINE CHALLENGES

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Objective: To emphasize on the increasing awareness of Alstrom syndrome and the challenges posed with the treatment strategies of diabetes and hypertriglyceridemia associated with this rare disease.

Case Presentation: A 33 year old male presented to the hospital for evaluation of weakness and vomiting. His medical history was significant for chronic abdominal pain and Alstrom syndrome complicated by multiple endocrinopathies including hypothyroidism, obesity, insulin resistant diabetes, dyslipidemia and binge eating disorder. Medications included metformin 1000 mg bid, pioglitazone 30 mg daily, levothyroxine 100 mcg and simvastatin 40 mg daily. Labs were remarkable for TSH-2.64 (0.35 - 4.94) mU/L, blood glucose- 378 (70-110) mg/dl, anion gap-18 (7-12) mmol/L, HCO3-16 (23-32) mmol/L, B- hydroxybutyric acid - 2.30 (0.4-0.5) mmol/L, venous PH - 7.30 (7.32 -7.42), triglycerides- 738 (0-150) mg/dL and lipase- 848 (65-230) U/L. HBA1c was 9.5 (4.0 - 5.6) % and GAD- 65 was unremarkable. CT- abdomen showed mild ductal dilatation of the main pancreatic duct, non pathological enlargement of numerous retroperitoneal lymph nodes and hepatic steatosis. The patient was treated for diabetic ketoacidosis with IV fluids and insulin. High dose statin was initiated to treat hypertriglycerideremia.

Discussion: Alstrom syndrome is an autosomal recessive disorder manifested by congenital blindness, deafness and multiple endocrinopathies. Diabetes associated with Alstrom is primarily due to severe insulin resistance. Nonetheless chronic insulin resistance and frequent episodes of pancreatitis secondary to ciliopathy and hypertriglyceridemia can lead to substantial insulin deficiency leading to severe ketoacidosis as demonstrated in our patient. We suggest that these patients should be considered for high dose statin therapy and be frequently evaluated for insulin replacement.

Conclusion: Alstrom’s Diabetes is multifactorial and can rarely present initially with diabetic ketoacidosis. We suggest vigilance in treating these patients with high
dose statins and frequent monitoring of their lipid indices. Nevertheless keen-sightedness for the transformation of insulin resistant diabetes to insulin dependent diabetes should be pursued.

Abstract #204

RAPID IMPROVEMENT OF DIABETES CONTROL AFTER A SINGLE DOSE OF LANTREOTIDE IN A PATIENT OF ACROMEGALY.

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Texas Tech University

Objective: Type 2 DM is present in a third of patients with acromegaly. Somatostatin analogues (SSA), commonly used to treat acromegaly, have the potential of worsening glycemia due to inhibition of insulin secretion. Conversely, they may improve glycemia due to a reduction in growth hormone concentrations. We report a case of remarkable reduction (by 50%) of insulin requirements in a man with acromegaly after a single dose of lanreotide.

Case Presentation: 67 year old man presented with type 2 diabetes (for last 12 years), severe obstructive sleep apnea and hypertension. He was most bothered by his worsening sinus congestion and difficulty to breath. He was taking metformin, sitagliptin, glargine and lispro for his diabetes. HbA1c was 7.4%. His BMI was 40 kg/m2. He had soft, doughy hands. Multiple skin tags were observed around his neck. Prognathism, frontal bossing and an enlarged nose dominated his facial features. Oral cavity showed enlarged tongue with dental impressions and spacing between teeth. Visual fields were normal on confrontational testing. On questioning he reported an increase in his shoe size. Serum IGF-1 level was 882 ng/ml (41-279) and Z score 5.4. Anterior pituitary hormones were normal. MRI of the Pituitary showed a 2cm pituitary mass encroaching upon the optic chiasm. Since the adenoma was abutting the medial aspect of each carotid artery in the cavernous sinus, we decided to treat the patient medically. He was started on Lanreotide 90 mg monthly. However, within a week of the first dose, he started getting hypoglycemic, necessitating a decrease in growth hormone concentrations which would lead to decreased hepatic gluconeogenesis, lipolysis and insulin resistance.

Conclusion: SSA therapy in patients with diabetes and acromegaly with markedly elevated IGF-1 concentrations can lead to a rapid reduction in their anti-hyperglycemic therapy.

Abstract #205

A RARE CAUSE OF DIABETES MELLITUS: MITOCHONDRIAL DIABETES

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Objective: A rare and commonly under-recognized form of diabetes mellitus (DM) is maternally inherited diabetes and deafness (MIDD) caused by mutations in mitochondrial DNA (mtDNA). The most commonly associated gene mutation is an A to G transversion in 3243 of the mitochondrial DNA-encoded tRNA gene (Leu, UUR). It is prevalent in 1.5% of the diabetic population worldwide. It is characterized by both a defect in insulin secretion leading to eventual insulin dependence and sensorineural hearing.

Case Presentation: A 25 year old female with a previous medical history of mitochondrial DNA defect presented after an elevated glucose on routine labs and a subsequent high HgA1C of 11.1%. There was no previous family history of diabetes mellitus. She had no classical diabetes or myopathy symptoms. Her mother, with the same defect, was recently diagnosed with mitochondrial myopathy. Vital signs were normal. Physical exam did not reveal any pertinent positives. She was started on a basal bolus insulin regimen with excellent glycemic control. A C-peptide level was 2.3 ng/mL (0.80 - 3.10 ng/mL) and GAD antibody level was <1.0 (0.0-0.15 U/mL). Her Mitochondrial DNA deficiency was seen in A3243G, the defect most commonly associated with MIDD. She did not have overt hearing loss with planned formal audiometry testing. She thus far remains on basal bolus insulin with excellent diabetes control.

Discussion: SSA have the potential of worsening diabetes control due to their inhibitory effects on the β cell, but meta-analyses have not been shown any significant effects of SSA on HbA1c or fasting glucose concentrations in patients with diabetes. However the patients studied in these trials usually underwent adenoma resection and thus had lower IGF-1 (and presumably lower growth hormone) concentrations prior to starting SSA. The probable cause of improvement in glycemia in our patient is a large reduction in growth hormone concentrations which would lead to decreased hepatic gluconeogenesis, lipolysis and insulin resistance.
loss, negative GAD antibody, elevated lactate level with a strong maternal family history of diabetes should raise the suspicion of mitochondrial diabetes though the mitochondrial DNA mutation is necessary for diagnosis. Myopathy and lactic acidosis are more commonly seen in Japanese individuals with this disease. This case is a rare presentation given that her mutation was known prior to onset of DM without a significant family history of DM and no hearing loss thus far.

Abstract #206

SLEEPRELATED EATING DISORDER: THE ENEMY OF DIABETES

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Objectives: Controlling diabetes can be very frustrating for patients. What can be even more frustrating is if there are other medical issues that are preventing good blood sugar control when it seems they are doing everything that they should be doing. Sleep related eating disorder is not often suspected in people who are having issues with diabetes, but can prevent good control and can often be treated.

Case Presentation: The patient is a 48 year old male who had type 2 diabetes since 2004. His blood sugars readings during the day have been in the low to mid 100’s but his fasting blood sugar readings were in the 200’s. His was on Aspart 10-15 units with meals, and Glargine was increased to 80 units but that caused postprandial hypoglycemias and did not improve his fasting blood sugars. When discussed with the patient, he said that he had issues with sleep eating and not remembering it for 25 years. He was sent to the sleep clinic and was found to have obstructive sleep apnea with an index of 118. He was started on CPAP and since this treatment, his sleep eating has almost completely resolved.

On Glargine 70 units and Aspart 10-15 units with meals, his fasting blood sugar readings were in the low to mid 100’s. He also says that he feels much better and has a lot more energy during the day.

Discussion: Sleep-related eating disorder is defined as parasomnia with recurrent episodes of eating that occur after an arousal with partial or complete amnesia. Predisposition to this condition has a genetic susceptibility and has a familial pattern. It is more common in females and onset usually occurs in adulthood. Conditions that increase slow wave sleep increase susceptibility including sleep deprivation, alcohol, medications, situational stress and fever. People with sleep related eating disorder are more likely to have eating disorders during the day. It is also commonly associated with other primary sleep disorders such as sleepwalking, restless legs syndrome, obstructive sleep apnea syndrome, or use of sedative-hypnotic medications. First-line treatment is the treatment of the underlying sleep disorder but if it is idiopathic it can be treated by selective serotonin reuptake inhibitors, Clonazepam, or Topiramate. Low awareness of the condition makes it very difficult to determine the prevalence.

Conclusion: Patients who are having issues with high fasting blood sugar readings despite increasing basal insulin to the point of having postprandial hypoglycemias should be assessed for sleep related eating disorder. This can be treated and help with diabetes control.

Abstract #207

UNRAVELING THE MYSTERY OF POSTOPERATIVE WEAKNESS: A CASE OF EUGLYCEMIC DKA AFTER BARIATRIC SURGERY

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Objectives: Euglycemic diabetic ketoacidosis (DKA) is diagnosed with near normal glucose, PH< 7.3, serum bicarbonate <15 and ketosis. It is a relatively uncommon entity but it can be precipitated by starvation with concurrent stress. We report a case of euglycemic diabetic ketoacidosis precipitated by starvation in a patient with insulin dependent diabetes mellitus who recently underwent bariatric surgery.

Case Presentation: A 63 year old Caucasian female with a BMI of 50 presented with generalized weakness three days after a laparoscopic sleeve gastrectomy. She denied constitutional symptoms. The patient had commenced a standard bariatric clear liquid diet on the second postoperative day which consisted of a calorie intake of about 600-700 calories/day, protein intake of 60-70 gms, and fluid intake about 60 ounces/day. On presentation, her vital signs and the physical examination were normal.

Initial labs revealed a Hb of 15.5 mg/dl, BUN 41 mg/dl, creatinine 1.5mg/dl, glucose 200 mg/dl, lactic acid 1 mg/dl and urinalysis revealed more than 500 mg/dl glucose with ketones of 20 mg/dl. Blood gas: pH 7.26, pCO2 of 29, HCO3 of 13, PO2 of 91% on room air. She had an anion gap metabolic acidosis. The patient was initially managed with IVF and nutritional supplements believing that her symptoms were secondary to starvation ketoacidosis. However, she did not improve clinically and repeat biochemistry tests a day later showed worsening anion gap metabolic acidosis. Acetone and B hydroxybutyrate were ordered and both were elevated. She was started on an insulin drip as a diagnosis of DKA was made. There was gradual closure of the anion gap and her symptoms improved. She was discharged after 2 days on a diet with
a higher caloric intake and had no untoward event. 

**Discussion:** Differentiating DKA from starvation ketoacidosis can be challenging in patients with diabetes exposed to limited calorie intake. Starvation and DKA have a similar mechanism of action where glycogen depletion, lipolysis and free fatty acid production can result in metabolic acidosis.

**Conclusion:** The main difference is normal or even low glucose levels in starvation which is contrary to the hyperglycemia of DKA. This was not the case with our patient. There can be a significant overlap in the clinical and biochemical presentation of the metabolic acidosis caused by starvation ketoacidosis and that of DKA in the face of euglycemia. This can create an arduous task in making the diagnosis and more so, initiating the correct management. It is important to understand the pathophysiology of both entities in diabetic patients in order to tailor the management and achieve clinical improvement.
collected from medical charts and interviews with patients. Comparison between diabetic group (DM), hypertensive group (HTN) and combined diabetic and hypertensive group (DM/HTN) was made.

**Results:** Total patient interviewed was seventy (N= 70), thirty-seven (53%) are female. Mean age 57 (range 21-94) years. Of those 29 patients (41.5%) in DM group; twenty one (30 %) in HTN group, and twenty (28.5%) patients had both. Only 3 (4%) completed some undergraduate degree, two (3%) completed secondary school, thirteen (18.6%) completed primary school. Average monthly income was 10, 7000 UGX. Mean fasting glucose value for the diabetes patients was 149.4mg/dl ±68.4. EQ-5D profile suggests higher rates of pain (75 %) in DM group, some to moderate problems with mobility, usual activity, and pain in HTN group (80%, 76%, and 95% respectively) and DM/HTN group (85%, 65%, and 85% respectively). Worse scores were in age group > 60 years old. Mean (Standard deviation) EQ-VAS score (0-100) was 51 (±21.5) in females and 58.4 (±18.7) in males. Mean VAS score (SD) was 56 (± 20) in DM group, 49.8 (± 22) in HTN group, and 61.7 (±20) in DM/HTN group (P-value 0.06)

**Discussion:** Studies showed variable effects of diabetes and its management on QOL measures compared to hypertension or other chronic diseases in African population. We report no statistically significant difference in the EQ-VAS scores among the DM, HTN and DM/HTN groups though a lower VAS in hypertensive patients was noted. Problems in multiple domains of health status measures reported more in HTN and DM/HTN groups, especially in elderly population.

**Conclusion:** This study suggests relative poor QOL in patients with diabetes and hypertension due to problems with pain, mobility and daily activity especially in elderly. Potential impact on social aspects and well-being and ways to minimize this deserve additional studies.

**Abstract #210**

**SGLT-2 INHIBITOR-INDUCED DKA: UNMASKING OF LATENT AUTOIMMUNE DIABETES IN ADULTS. CAN WE DO BETTER?**

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**Objective:** SGLT2 inhibitors are a new class of antihyperglycemic medications that have been associated with favorable outcomes including weight loss and decreased cardiovascular risk. However, their use in certain patients may be linked with a higher risk of diabetic ketoacidosis (DKA). Our case brings attention to the non-obese population with a diagnosis of type 2 diabetes (T2DM) and asks whether screening for autoimmunity should be recommended in these patients prior to implementing SGLT2 inhibitor therapy.

**Case Presentation:** A 40 year-old man with hypertension, non-ischemic cardiomyopathy and T2DM, was admitted to the hospital with a 2-day history of nausea, vomiting and generalized weakness. He was diagnosed with T2DM a year prior and treated initially with sulfonylurea and metformin. 2 months prior to admission, due to deteriorating glucose control, he was started on 10 units of glargine and advised to engage in a healthy lifestyle. Follow-up clinic visit, 2 weeks prior to hospitalization, showed improved glucose control; insulin was discontinued and canagliflozin 100 mg/day initiated. Family history was negative for diabetes, social history positive for weekend alcohol use. Exam revealed a lethargic patient with dry oral mucosa, BP 101/64, P 150/min, RR 34/min, T 97.6 F, BMI of 24.1 Kg/m2. He had no acanthosis nigricans or skin tags. Laboratory tests showed: serum glucose 417 mg/dL, CO2< 5 mmol/L, anion gap 28; arterial pH 6.9, urine ketones 80 mg/dL, lactic acid 2.7 mmol/L, 3 Beta-hydroxy-butyrate 8.2 mmol/L. Canagliflozin was discontinued; patient received treatment with intravenous insulin, fluid and electrolyte replacement. He was successfully transitioned to subcutaneous insulin while maintained on a high carbohydrate diet. Patient was discharged on insulin after 9 days in the hospital with a diagnosis of latent autoimmune diabetes in adults (LADA). Glutamic acid decarboxylase antibodies came back elevated at 170.1 IU/mL.

**Discussion:** Recent AACE recommendations point to the risk of DKA associated with SGLT2 inhibitor use when insulin therapy is reduced/discontinued in patients with known LADA, type 1 diabetes, or long-standing T2DM. It is estimated that 4-14 % of patients thought to have T2DM may have LADA. Our patient had a diagnosis of T2DM; improved glucose control with lifestyle changes prompted discontinuation of low dose insulin. His underlying LADA became evident only after initiating canagliflozin and developing DKA.

**Conclusion:** When considering SGLT-2 therapy, increased awareness of underlying insulin deficiency and autoimmunity may reduce the risk of DKA in patients who present with atypical features of T2DM and have undiagnosed LADA.
Abstract #211

A RANDOMIZED CONTROL TRIAL ON REDUCTION OF HEMOGLOBIN A1C USING CELL PHONES, COMMUNITY HEALTH WORKERS OR COMBINATION OF BOTH IN A DISTRICT OF COLUMBIA AFRICAN AMERICAN POPULATION

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Objective: To compare the effectiveness of A1c reduction after 3 months using cell phone text reminders, CHWs or the combination of both on a predominately African American District of Columbia Medicaid population.

Methods: Subjects between the ages of 18-70 years with an A1C of > 8% were recruited to participate in the study. Those who agreed were randomly assigned into one of 3 groups. Group 1 was assisted by the Voxiva Care4Life mobile health disease management program (C4L) downloaded on the patient’s cell phone. Group 2 was assisted by CHWs, and Group 3 was assisted by both the C4L and a CHW. Baseline and 3 month A1Cs were obtained. Paired t tests and ANOVA statistical analyses were used to assess changes in A1c within and between the groups. The study was approved by the Howard University Institutional Review Board.

Results: A total of 64 patients (44 females, 20 males) with an average age of 56.33 ± 9.52 participated in the study. Sixty three patients had baseline and 3 month A1Cs. Group 1 (20 patients), Group 2 (19 patients), and Group 3 (24 patients) showed significant reductions in average A1cs (initial A1c 10.12 ± 2.15 and 3 month A1c 8.94 ± 1.77) p=0.003. However, there was no significant difference in A1c reduction between groups p=0.292.

Discussion: DM is the 7th leading cause of death in the United States affecting 25.8 million Americans DM costs the United States $174 billion annually. Systematic literature reviews that evaluated cell phone text reminders on diabetes management have shown the benefits of these reminders in lowering hemoglobin A1C. Many studies have found that community health workers (CHWs) intervention also resulted in better control of type 2 DM (DM2). Minorities are disproportionately affected by the complications associated with DM2 and effective strategies are needed for improved management in this population.

Conclusion: Reduction in A1c were found in all three groups after 3 months. The data suggests that either cell phone, CHW or combination of both interventions can significantly reduce A1c. Further studies are warranted to assess the long term effects and cost effectiveness of these interventions. Meanwhile we recommend either cell phone text reminders and/or CHW interventions that engage a patient for better self-management to improve diabetes control.

Abstract #212

CLINICAL MANIFESTATIONS AND MANAGEMENT OF NON-HIV RELATED LIPODYSTROPHY: A SYSTEMATIC REVIEW

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Objective: Lipodystrophy (LD) syndromes are rare congenital or acquired disorders with generalized or partial absence of adipose tissue, acanthosis nigricans, hepatomegaly and often accompanied by diabetes mellitus (DM) and hypertriglyceridemia. This systematic review synthesized existing data on clinical features and management of non-HIV related LD.

Methods: Comprehensive search of databases (MEDLINE, EMBASE, Cochrane, Scopus) was conducted from database’s inception to August 2015, for congenital generalized LD (CGL), acquired generalized LD (AGL), familial partial LD (FPL), acquired partial LD (APL) and other syndromes that present with LD. Due to rarity of LD, most data were extracted from case reports and case series. Abstracts from initial search were evaluated by two authors and full texts from included abstracts were reviewed by one author.

Results: From initial 1303 citations, 333 were included. Study design in 169 studies was case-report (single patient), 143 were cohorts (number of cases ≥ 2) and 21 studies reported data from NIH registry. We present data on a total of 993 patients with LD syndromes. Mean age of onset of CGL was 1.5 y and 62% patients had history of parental consanguinity. Core features of CGL included generalized loss of adiposity, prominent musculature, DM (50%) with mean age of onset of DM at 13.3 y, acanthosis nigricans (73%), hepatomegaly (86%), hypertriglyceridemia and low leptin level. In AGL, onset was noted during childhood with female predominance (68%) and preceded by infectious (80%) and autoimmune diseases (60%). In FPL, sites of fat loss were trunk and extremities while facial and neck fat was spared; mean age of onset of DM was 24.5 y and hypertriglyceridemia and
pancreatitis were common. Onset of APL was noted during childhood (mean age 8.2 y), with cephalocaudal pattern of fat loss, commonly involving face, upper abdomen, thorax and upper limbs. Lower limbs and lower abdomen was usually spared. Lower prevalence of acanthosis nigricans (14%) and only moderately elevated fasting glucose, insulin and triglycerides distinguished it from other three types of LD. Combination therapy with leptin and insulin showed greater improvement in metabolic outcomes of acquired and congenital generalized lipodystrophy, as compared to leptin alone.

**Discussion:** LD syndromes have overlapping features with DM, metabolic syndrome and dyslipidemia. It is important for endocrinologists to distinguish subtle features of LD from these common disorders.

**Conclusion:** This is the largest reported data on LD. We have established core and supportive clinical features of LD and summarized data on available interventions and their outcomes.

**Abstract #213**

**DAPAGLIFLOZIN AS ADDITIONAL TREATMENT TO LIRAGLUTIDE AND INSULIN IN PATIENTS WITH TYPE 1 DIABETES. A RANDOMIZED CLINICAL TRIAL**

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**Objective:** We have recently demonstrated that the addition of liraglutide to insulin significantly improves the glycemic control in patients with type 1 diabetes (T1D). We have now conducted the first prospectively randomized study investigating whether the addition of dapagliflozin, a SGLT-2 inhibitor to insulin and liraglutide would further improve glycemic control.

**Methods:** Thirty T1D patients on insulin and liraglutide therapy for at least last 6 months were randomized (2:1 ratio, drug: placebo) to receive either dapagliflozin 10 mg or placebo daily for 12 weeks. Dapagliflozin was initiated at 5 mg daily for one week and increased to 10 mg daily thereafter. Twenty six patients completed the study (Placebo=9; Dapagliflozin = 17).

**Results:** All patients had T1D for at least one year, on insulin therapy and had no detectable c-peptide in plasma and were on 1.8 mg of liraglutide for 7±1 months (mean body weight: 82.69±3.43 kg; mean HbA1c: 7.68±0.15%, mean weekly glucose levels: 163±6 mg/dl, total insulin dose: 52.3±4.8 units, mean age: 54±2 years, mean age at T1D diagnosis: 29±2 years, mean BP: 122±2/76±1 mmHg, 8 males, 17 females, 23 Caucasian, 1 African American and 1 Asian) with no difference in these parameters between the two groups. HbA1c fell by 0.6±0.08% in the dapagliflozin group (p<0.01 vs placebo) with no changes in placebo group. The average weekly glucose concentration fell in the dapagliflozin group by 15±6 mg/dl (p<0.05 vs baseline, p=0.07 vs placebo) with no changes in placebo group. There was no additional hypoglycemia (<70 mg/dl; p=0.52 vs placebo). The basal insulin dose fell by 0.72±0.96 from 33.70±4.53 units while it increased by 1.9±0.5 units (p<0.01 vs baseline) in placebo group (p<0.05 vs placebo). However, total insulin dose remained unchanged in both groups. The body weight fell by 1.9±0.54 kg (p<0.05 vs placebo) in the dapagliflozin group while it remained unchanged in placebo group. The total cholesterol and LDL cholesterol increased by 6 and 8% from 167±8 and 90±7 mg/dl (p<0.01 vs placebo for both) in dapagliflozin group while it decreased by 11 and 17% in the placebo group (p<0.05 for both vs baseline) from 176±11 and 89±8 mg/dl respectively. Two of the drop-out patients in Dapagliflozin group developed DKA (one patient with euglycemic DKA with total insulin dose reduced from 33 to 26 units and the other with hyperglycemic DKA with total insulin dose unchanged at 26 units) within 24 hours of increasing the dose to 10 mg daily.

**Discussion:** Care has to be exercised in terms of the reduction in the insulin dose and increasing dapagliflozin dose to prevent the occurrence of DKA.

**Conclusion:** Addition of dapagliflozin to insulin and liraglutide in patients with T1D results in significant improvement in glycemia.

**Abstract #214**

**INPATIENT SELF MONITORING AND ADMINISTRATION STUDY (ISMAS) OF HOSPITALIZED PATIENTS WITH DIABETES MELLITUS**

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**Objective:** Inpatient management of diabetes mellitus (DM) consumes significant staff resources. In contrast to outpatient strategies, patients are typically excluded from glycemic management when hospitalized. We hypothesized that a subgroup of DM inpatients are able to self-manage their blood sugars. The aim of this pilot study was to assess whether select DM patients could self-administer insulin and self-monitor blood glucose (BG) in
the hospital and achieve care standards equal to standard nursing care.

Methods: Thirty-six patients recruited from medical and surgical wards of the Atlanta VA Medical Center were randomized to control (n=18) or self-care (n=18). Self-care patients self-administered all insulin doses and logged fingerstick BGs and insulin doses/times at bedside. Control patients received usual nursing care. Inclusion criteria were age <80 years old, pre-admission care with at least twice daily insulin and glucose monitoring, A1c <12%, and mini-mental status exam score ≥25. Exclusion criteria included recent cardiac ischemia, encephalopathy, or dialysis. All patients were seen by the endocrinology consult service who made recommendations on insulin and monitoring regimens. Primary outcomes were the number of BG measurements and insulin doses administered vs. ordered; percentage of correct insulin dosages, numbers of BG ≥200 or <70, and average BG. Data were analyzed according to intention to treat, using unpaired T test and Fisher’s test.

Results: Control patients (n=18) had greater compliance with BG checks than self-care, 95.1% vs. 90.4%, respectively (p=0.0324). Compliance with insulin administration was better in the self-care group (80.8% control vs. 89.6% self-care, p=0.0035). Correct insulin dose was more common in the control group, 97.6% of doses vs. 91.9%, p=0.0018. However, hypoglycemia (BG <70) was less common in the self-care group (5.0% control vs. 2.3% self-care, p=0.0448). Neither the frequency of hyperglycemia (BG ≥200) (28.4% control vs. 23.7% self-care, p=0.119) nor the average BG differed significantly between groups (167.2 mg/dL control vs. 167.0 mg/dL self-care, p=0.9854).

Conclusion: This pilot study demonstrates that select patients achieve diabetes care at least as good as standard nursing care. Self-care patients had inferior compliance with BG monitoring and lower rates of insulin given at correct dosages but exhibited better compliance with insulin administration and less hypoglycemia compared to those under usual nursing care. There was no significant difference in average BG or rates of hyperglycemia. While these data are promising, a study involving a larger number of patients is needed to further examine the utility of self-care in the hospital.

Abstract #215

LIRAGLUTIDE AS AN ADJUNCT TO INSULIN IN THE TREATMENT OF TYPE 1 DIABETES MELLITUS IN AN ACADEMIC SETTING

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Objective: Insulin is an essential treatment for patients with type 1 diabetes mellitus (T1D). With the obesity epidemic, obesity and insulin resistance are no longer uncommon features in these patients. This has led to increasing interest in the role of glucagon-like receptor agonists as adjunctive therapy in this patient population. The aim of this study was to assess the indications for use, efficacy and adverse effects (AEs) of liraglutide, as an adjunct to insulin in patients with T1D.

Methods: A cross-sectional retrospective study identified patients with T1D who were prescribed liraglutide from January 2014 to January 2015. Hemoglobin A1C (A1C) and body mass index (BMI) at baseline (at liraglutide initiation), next follow-up visit and at the most recent visit were compared. To create a control group for comparison, A1C and BMI were recorded approximately 3-6 months prior to initiation of liraglutide (pre-GLP-1) and compared to baseline. BMI data were log transformed to achieve a normal distribution. A1C (%) and BMI (kg/m2) results are reported as means±SD, analyzed using paired t-test.

Results: Thirty-one patients were identified, 42% were male, mean age 44.6±8.5 years. Baseline A1C was 7.9±0.8, BMI was 32.6±7.4 (log transformed 3.4±0.2). A1C was unchanged from pre-GLP-1 to baseline (mean time was 4.9±17.8 months), change was 0.08±2.1 (p=0.8), however there was a significant decrease at 3.7±3.2 months (at follow-up visit) post initiation of liraglutide: -0.53±0.8 (p=0.001). This effect persisted when comparing baseline A1C to the most recent visit, 33.9±17.8 months post liraglutide initiation, with an A1C change of -1.07±2.1 (p=0.009). There was no difference in the log transformed BMI in the pre-GLP-1 period compared to baseline 0.02±0.08 (p=0.1), but decreased from initiation to follow-up, -0.4±0.03 (p<0.001) and also from initiation to the most recent visit, -0.03±0.08 (p=0.04).

The indications for initiation of liraglutide were: preservation of pancreatic beta cell function, 9.7%; weight loss, 22.6%; poor control, 25.8%; insulin resistance, 29% and unclear, 12.9%.

Gastrointestinal AEs and hypoglycemia were common, but no severe hypoglycemia was recorded.

Conclusion: Liraglutide significantly reduced A1C and BMI in patients with T1D when used as an adjunct to insulin. The AEs were similar to those already established
Abstract #216

MODULATION OF METABOLIC PARAMETERS AND ANTIOXIDANT ENZYMES IN DIABETIC AGING FEMALE RAT BRAIN: BENEFICIAL ROLE OF METFORMIN

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Objective: The objective of this study was to investigate beneficial effects of metformin on membrane bound enzymes (monoamine oxidase, Na+ K+ ATPse,) and antioxidant enzymes (superoxide dismutase, glutathione S-transferases), lipid peroxidation, neurolipofuscin, DNA degradation in diabetic aging brain of female rats.

Methods: Young (3 months) adult (12 months) and aged (24 months) rats will be diabetic by using alloxan monohydrate. Metformin was administered at a dose of two hundred mg per kg per day for 30 days to both control and diabetic aging rats. Learning was tested in a Morris water maze. A detailed study was carried on membrane linked enzymes, membrane fluidity, neurolipofuscin, antioxidant enzymes and DNA degradation to identify the antidiabetic and antiaging role of metformin using biochemical, molecular and histiochemical study.

Results: Present study shows that there was a similar pattern of increased lipid peroxidation, neurolipofuscin, DNA degradation and monoamine oxidase activity and a decrease in membrane fluidity, Na+ K+ATPse, antioxidant enzymes activities in brain of both aging and diabetes.

Discussion: Metformin was found to be an effective treatment in stabilizing and normalizing the membrane functions; therefore this therapy can be considered an alternative to be explored further as a means of diabetic and aged related disorders control. Metformin treatment also helped to reverse the age related changes studied, to normal levels, elucidating an anti-aging, antidiabetic and neuroprotective action.

Conclusion: The results of this study will be useful for pharmacological modification of the aging process and applying new strategies for control of age related disorders including metabolic syndrome.

Abstract #217

GLYCEMIC VARIABILITY DURING PREGNANCY CAN BE DETECTED BY AMBULATORY GLUCOSE PROFILE USING FREESTYLE LIBRE PRO

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Objective: Patients with diabetes and pregnancy are asked to perform self monitoring of blood glucose (SMBG) 4 to 6 times a day. The 6 point SMBG often disliked by patients is also inadequate in detecting glycemic variability. Addressing these clinical barriers to maintain normoglycemia is essential. The objective of this study was to evaluate the maternal glycemic profile using Ambulatory Glucose Profile (AGP) in pregnant patients with diabetes.

Methods: This was a prospective study of 20 pregnant patients with diabetes attending the outpatient of a specialized diabetes hospital in Bangalore, India between April and November 2015. The study was approved by the institution’s ethics committee. All patients who consented to use AGP were included [6-gestational diabetes (GDM), 14-type 2 diabetes with pregnancy]. AGP was measured using Free Style Libre Pro by Abbot. In 4 patients with GDM who refused insulin, AGP was used to evaluate the glycemic profile with glyburide and metformin. In others, AGP was used to recognize glycemic variability. Patients performed SMBG and adjusted insulin as per standard of care. AGP values were downloaded and treatment changes were made based on the glycemic trends at the end of week 1(W1) and week 2(W2). The sensor was removed after 14 days. Patients were asked to continue SMBG and monitor more frequently the times of glycemic peaks or dips noted by AGP. Patients were followed up till delivery. Data was analysed with Microsoft Excel.

Results: The mean age was 32.1±3.4 years. The gestation period varied from 8 to 28 weeks. The frequency of SMBG was 15.3±7.5 finger pricks over 2 weeks. The number of readings obtained by AGP was 96 per day and 1,344 over 2 weeks. There was reduction in the total time spent in hyperglycemia per day by 9.35% [W1 21±15.6 % vs. W2 11.7±11.4]. The Hba1c before and after the use of AGP showed a reduction from 6.5±0.6% to 5.7±0.6%. Both observations were statistically significant. There was no change in the total time spent in hypoglycemia. GDMs on oral hypoglycemic agents did not go on to require insulin. There were no adverse pregnancy outcomes. No discomfort was reported with the use of Libre Pro.

Discussion: This study demonstrates that the use of AGP to make ‘change of treatment decisions’ in pregnant patients with diabetes reduces hyperglycemic excursions.
by 50% and improves Hba1c. In spite of infrequent SMBG, all patients showed near normal glycemic control with no increase in hypoglycemia. **Conclusion:** AGP with Libre Pro is safe and useful to monitor glycemic trends in pregnant patients. Its use can open up new areas of research to utilize this device as a therapeutic intervention.

**Abstract #218**

**PREVALENCE OF RISK FACTORS FOR DIABETIC FOOT DISEASE IN ZARIA, NORTHERN NIGERIA**

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**Objective:** Diabetic foot complications are a major cause of disability, reduced life and death; and constitute a huge economic burden on the health care system. Diabetic foot disease is preventable with appropriate management of its recognized risk factors. The purpose of this study is to determine the prevalence of risk factors for diabetic foot disease in Zaria, Nigeria.

**Methods:** This was a cross-sectional comparative study carried out at the Ahmadu Bello University Teaching Hospital, Zaria from 4th November 2014 - 4th May 2015. Subjects with diabetic foot disease were compared with those without foot disease. History, physical examination, and laboratory investigations were performed and recorded in an investigator-administered questionnaire. Data was analyzed with SPSS version 17. Statistical significance was tested with student t-test for numerical variables and χ2 for categorical variables.

**Results:** A total of 150 subjects participated in the study, 75 (diabetic foot disease group) and 75 (diabetics without foot disease). The mean ages of the subjects were 54.6 and 53.0 years for subjects with foot disease and subjects without foot disease respectively, p=0.588. The proportion of participants that were males was 36.0% in diabetic foot patients and 28.0% in those without diabetic foot, p = 0.46. The prevalence of peripheral neuropathy (64% vs. 38.7%, p = 0.027), foot deformity (74.6% vs. 50.7%, p = 0.026), hypertension (64% vs. 45.3%, p=0.035) and nephropathy (66.7% vs. 53.3%, p=0.000) were significantly higher in subjects with foot disease compared to those without foot disease. The prevalence of peripheral vascular disease (PVD) was not statistically different in both groups (21.4% vs. 17.3%, p = 0.377), however, more patients in the diabetic foot disease group have Ankle Brachial Index (ABI) ≥ 1.3 (35.7% vs. 9.3%, p = 0.005). The prevalence of diabetic retinopathy in both groups was 55.5% vs. 58.6%, p = 0.816

**Discussion:** Peripheral neuropathy, diabetic nephropathy, hypertension and foot deformity are the important risk factors for diabetic foot disease in our hospital. Though, the prevalence of peripheral vascular disease appears not statistically different between the two groups, however, a significant proportion of patients with foot disease have ABI ≥ 1.3 which signifies poorly compressible vessels. This may have been the reason for the blunting of the prevalence of PVD.

**Conclusion:** Provision of health education on these risk factors and instituting measures to mitigate them in our patients can help reduce the prevalence of foot disease in Zaria, Nigeria.

**Abstract #219**

**EFFICACY OF 5MG AND 10MG ROSUVASTATIN IN TYPE 2 DIABETES MELLITUS WITH HYPERCHOLESTEROLEAMIA.**

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**Objective:** Coronary Heart Disease (CHD) is the most important complication and the leading cause of death in patients with type 2 diabetes mellitus (T2DM). Hypercholesterolemia is an important modifiable risk factor for CHD. Statins are the first line drugs for the treatment of hypercholesterolemia in DM. Comparative studies between different statins are available but different doses of the same statin have not been compared in our population. The objective of this study is to compare mean reduction in serum LDL-C level after using 5mg and 10mg of rosuvastatin among T2DM patients with hypercholesterolemia. This study will help finding lowest effective dose of rosuvastatin to achieve internationally set low density lipoprotein cholesterol (LDL-C) goals.

**Methods:** A total of 82 patients with T2DM having fasting LDL-C levels equal or more than 100mg/dl were randomly allocated into two groups with 41 patients in each group. Baseline fasting serum LDL-C levels were obtained in all patients. Group A received 5mg while group B received 10mg of rosuvastatin daily at night. After 6 weeks, fasting LDL-C levels were obtained and analysed to compare the mean±SD reduction of LDL-C levels in both groups.

**Results:** Results: Baseline mean± SD LDL-C levels in group A and group B were 134.12±30.02 and 143.49±32.01 respectively (p 0.176). Follow up mean±SD LDL-C levels
were 81.59±28.47 and 83.24±36.06 respectively (p 0.818). Mean±SD reduction in LDL-C levels from baseline levels in group A and group B were 52.51±19.49 and 60.20±24.09 (p 0.116).

Conclusion: Rosuvastatin 5mg is as effective as 10mg in reducing the LDL-C levels in type 2 diabetic patients with hypercholesterolemia.

Abstract #220
IS REGULAR SELF MONITORING OF BLOOD GLUCOSE IN INSULIN-TREATED TYPE 2 DIABETIC PATIENTS JUSTIFIED IN RESOURCE-POOR SETTINGS?

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Objective: To evaluate the impact of regular self monitoring of blood glucose (SMBG) on metabolic control in patients with type 2 diabetes mellitus (DM) treated with insulin.

Methods: 96 type 2 DM subjects who had HbA1c above 7%, initiated on biphasic insulin aspart and procured blood glucose meters were consecutively recruited and randomly assigned to either of two groups – intensive and conventional SMBG. Subjects in the intensive group were asked to check their blood glucose at least once daily while the frequency of SMBG in the conventional group was left at their discretion. Both groups were educated on proper use of glucose meters and on self-adjustment of insulin based on test results. Both groups were asked to keep records of hypoglycemia, defined as either symptoms suggestive of hypoglycemia that resolved after ingestion of carbohydrate and/or documented blood glucose less than 70mg/dl. Participants were followed up fortnightly for 12 weeks and their HbA1c repeated at the end of the study.

Results: A total of 71 subjects completed the study. In the intensive arm (n = 25), 11 (44%) were males while 14 (56%) were females. In the conventional group (n= 46), 13 (28.3%) were males while 33 (71.7%) were females. These differences were not significant (P = 0.181). The mean age of the subjects in the intensive and conventional groups were respectively 49.4 ± 8.3 years and 48.8 ± 4.5 years; P = 0.778). There was no significant difference in the baseline HbA1c between the two groups (intensive: 8.2 ± 1.7%; conventional: 8.4 ± 1.8%; P = 0.679). Both groups witnessed a decline in HbA1c at the end of the 12 weeks. However, the decline in the intensive group was significantly more compared to the conventional group (1.5 ± 0.2% vs. 0.6 ± 0.1% respectively; P < 0.001). The monthly cost of SMBG in the intensive arm was $262.2 ± 2.8 compared to $80. ± 3.9 in the conventional group; P < 0.001). Although frequent hypoglycemia (≥ 1 episode/week) occurred more in the conventional (6; 24%) than intensive group (18; 39%), this did not reach statistical significance (P = 0.165).

Discussion: International guidelines recommend frequent daily SMBG in all type 1 and insulin-treated type 2 DM patients. Unlike type 1 DM, the usefulness of SMBG in subjects with type 2 DM has remained controversial. Managing DM in resource-poor settings such as sub-Saharan Africa is highly challenging. Regular SMBG is costly and substantially adds to this financial burden. This study has clearly demonstrated that regular SMBG is beneficial in insulin-treated type 2 DM patients and should be recommended.

Conclusion: Although costly, regular SMBG impacts positively on metabolic control in insulin-treated patients with type 2 diabetes.

Abstract #221
PROPOSAL FOR A NEW ORAL DISPOSITION INDEX

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Objective: The euglycemic clamp is the gold standard for measuring insulin action, but has disadvantages that it becomes impractical. There surrogates as Oral Glucose Insulin Sensitivity (OGIS) based on a mathematical model derived from kinetic studies in humans. Outperforms other options (Matsuda, HOMA, Quicki). In seeks to evaluate integrated manner the compensation capacity of the beta cell to different states of sensitivity to insulin, the disposition index, which serves as a predictor developed of incident diabetes. Can be calculated using surrogates both secretion and action insulin.

This study proposes a new disposition index to assess simultaneously both insulin secretion and action, utilizing OGIS as a marker of insulin action in place of 1/insulin in the original ODI formula.

Methods: This was a retrospective cross-sectional observational comparative study. Subjects who had undergone a 3 or 5 hour OGTT during the preceding 5 years in our Institute, were identified. The results of glucose and insulin in these curves, were recorded. The medical records pertaining to each subject was reviewed to obtain anthropometric data, age, lipid profile, and medication history. We considered only one OGTT curve for each patient.

Results: We analyzed 1619 oral glucose tolerance tests (OGTT) in 1177 women and 442 men. Normal glucose tolerance (NGT) was recorded in 1039 subjects (64%), impaired fasting glucose (IFG) in 175 subjects (11%),
Abstract #222

HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH DIABETIC FOOT DISEASE IN A NIGERIAN TEACHING HOSPITAL

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Objective: Diabetic foot disease cause severe morbidity and prolonged hospitalizations, which may lead to both economic and psychosocial burden. This study aimed at evaluating the impact of foot disease on the quality of life of patients with diabetes mellitus in Zaria, Nigeria.

Methods: This was a cross-sectional comparative study carried out at the Ahmadu Bello University Teaching Hospital, Zaria. Short-Form 36 version 2 (SF-36 v2) questionnaire was used to assess the quality of life of 150 diabetic patients (75 with foot disease and 75 diabetic patients without foot disease). The SF-36 score varies from 0 (worst possible health status) to 100 (best possible health status). Foot disease was defined as the presence of at least stage 1 DM foot (Wagner’s classification).

Discussion: It is necessary to validate this index in prospective studies; the discriminative performance of the new index at individuals at high risk of T2DM can be evaluated, comparing the results obtained with those from clamp studies.

Conclusion: In this study a new disposition index (EII x OGIS) was evaluated and compared with IDO. Regarding glucose tolerance status, the new index was better able to discriminate between groups than the original ODI.

Abstract #223

REAL LIFE EXPERIENCE WITH THE COMBINATION OF EXENATIDE LAR AND DAPAGLIFLOZIN IN OBSE Type 2 Diabetic Patients in Mexico City.

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Grupo Médico Rubi

Objective: Obesity complicated with Type 2 Diabetes in Mexico City has attained epidemic proportions. Therefore, an ideal treatment should provide both good glycemic control and weight loss. More experience is needed with treatments that show promise.

The primary objectives were to demonstrate the glycemic control, weight and body composition changes attained
with the use of this treatment combination. Secondary objectives were any changes in lipids and blood pressure. We present here only the primary objectives.

**Methods:** We conducted an open, longitudinal study of exenatide LAR and dapagliflozin on glycemic control and weight loss in obese type 2 diabetic patients treated for 6 months. We included 20 female and 18 male patients (between 28-60 years) who have failed to other oral treatments and did not show any relevant chronic complications or intercurrent illness. All patients followed a 1500 Kcal diet (55/30/15 nutrients ratio), 50 minutes exercise a day and were initiated with 10 mg dapagliflozin and 2 mg exenatide LAR weekly for the study period. All biochemical analysis were made in a commercial lab using Beckam automated enzymatic methods. HbA1c was measured using HPLC and insulin with RIA. Body composition analysis was made with impedance test using a MBCA115 analyzer. Comparisons were made with parametric tests between visits for HbA1c, glucose, lipids, insulin (for HOMA modeling), BMI, weight and body fat percentage.

**Results:** At start, mean weight was 101.4+-16.8 males 83.8+-6.8 females, BMI was 34+-3.7 males and 34.8+-3.21 females; HbA1c were 8.98+-0.3, 8.8+-0.5; glucose 204+-10, 208+-20 mg% males and females respectively. At 6 months a significant (p<0.01 first vs last visit) mean weight loss of 11.9/12.9 Kg; fat% decrease 9/8; HbA1c reduction 1.97/1.88, and glucose levels of 97/96 mg% (55%, 75% attained control goals of HbA1c <=7%) and HOMAR reduction 6.4/7.38 for males/females respectively. Nausea was present in around a third of patients, was severe in two patients (no discontinuation) and we recorded 8 episodes of vulvovaginitis that needed treatment.

**Discussion:** We used two different treatments with complimentary mechanisms. SGLT2 inhibitors may decrease gluco toxicity while dispose energy (glucose) in urine and GLP-1 mimetics can centrally decrease the appetite that usually accompanies SGLT2 continuous use and equilibrate insulin secretion and glucagon decreasing hepatic glucose output. This combination can obtain a greater weight reduction and better glycemic control.

**Conclusion:** A combination of 2 weight lowering antidiabetic treatments could be synergistic and a significant weight loss with adequate control obtained, upsetting any relevant side effects.

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**Abstract #224**

**LDL-C PLAY SIGNIFICANT ROLE IN THE PROGRESSION OF DIABETIC RETINOPATHY (NPDR TO PDR)**

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**Objective:** To Find Out the correlation of Lipid parameters with progression of Diabetic retinopathy

**Methods:** 200 subjects were enrolled after opthalmoscopic examination, into study group of Diabetic Retinopathy (DR, n=100) and control group of No-retinopathy (NR, n=100) respectively, on the basis of presence or absence of retinopathy. Study Group was further divided into non-proliferative diabetic retinopathy (NPDR, n=50) and proliferative diabetic retinopathy (PDR, n=50). Whereas Control Group was divided into diabetics no-retinopathy (DNR, n=50) and non-diabetics no-retinopathy (NDNR, n=50) respectively, based on presence or absence of diabetes. Fasting blood samples were collected of all subjects for the estimation of Fasting blood sugar (FBS), Aldose reductase enzyme (ALDR-2) and Fasting lipid profile (FLP).

**Results:** On comparing outcomes of NPDR & PDR, duration of diabetes (p<0.0001), LDL-C (p<0.0234) was significantly associated in the progression of NPDR to PDR, but no significant difference was observed for ALDR-2 activity (p=0.0728), Hyperglycemia (p=0.32). So, we can conclude that ALDR-2 activity and hyperglycemia does not contribute much in progression of DR, although (on comparing DNR with NPDR) increase aldose reductase activity is significantly (p<.0001) responsible in the establishment of DR initially as NPDR, in genetically predisposed diabetic individuals to ALDR gene.

**Discussion:** Establishment of DR will certainly occur sooner or later, because it is very difficult to maintain sustained euglycemia for years. Persistent hyperglycemia leads to activation of aldose reductase enzyme, which causes establishment of diabetic retinopathy initially as NPDR, and will further progress to PDR, if dyslipidemia not controlled. It is necessary to manage PDR, because PDR ensues as adult blindness in diabetic population of developed countries. We can halt progression of NPDR to PDR easily by managing dyslipidemia. The Progression of NPDR to DPR is influenced by LDLC and if we manage Dyslipidemia since begging that may alter the progression NPDR to PDR.

**Conclusion:** We can conclude that the development of NPDR in a Diabetic individual is influenced by variety of factors including the duration of Diabetes as well as activation of aldose reductase enzyme activity but the progression of NPDR to PDR is influenced by LDLC.
Abstract #225

THE VALUE OF ASSESSING THE IMMUNOLOGICAL PROFILE OF PATIENTS WITH YOUNG ONSET DIABETES IN INDIA

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Objective: Patients with type 1 diabetes (T1DM), type 2 diabetes (T2DM) and Latent Autoimmune Diabetes in Adult (LADA) have mixed characteristics. Detection of islet cell autoimmunity when the clinical diagnosis is uncertain has prognostic and treatment implications. The objective was to evaluate the clinical and immunological profile of patients less than 40 years presenting with symptoms of hyperglycemia and ketonuria at the time of diagnosis.

Methods: This was a retrospective analysis of 100 patients with previously undiagnosed diabetes, less than 40 years presenting with symptoms of hyperglycemia and ketonuria at a specialized diabetes hospital in Bangalore, India between 2013 and 2015. Diabetes was diagnosed based on ADA guidelines. Secondary diabetes and suspected MODY were excluded. Cardiovascular risk factors were evaluated in all patients. Auto antibodies against glutamic acid decarboxylase (GAD65), the 40K fragment of tyrosine phosphatase (IA2) and insulin auto antibodies (IAA) were measured by ELISA at the Diabetomics Laboratories at Portland, Oregan. C-peptide was measured by Roche Elecsys 2 weeks after recovery from the acute illness. The final diagnosis and treatment was reviewed once the antibody profile and c peptide reports were available. Microsoft excel was used for descriptive analysis.

Results: Diagnosis of T1DM, LADA and T2DM was made in 24.5%, 24.5% and 51%. Characteristics of T1DM patients: age-26±9 years, BMI-18±3 kg/m², Hba1c-13±2%, hypertension-7%, dyslipidemia-61%. Antibodies detected in T1DM were IAA (7.7%), GAD 65 (69%) and IA2 (31%). Characteristics of LADA patients: age-23±9 years, BMI-20±3 kg/m², Hba1c-12±2%, hypertension-7%, dyslipidemia-60%. GAD 65 and IA2 were present in 100% and 23% of patients with LADA. Characteristics of T2DM patients: age-22±5 years, BMI-25±4 kg/m², Hba1c-12±3%, hypertension-8%, dyslipidemia-71%.

Discussion: Heterogeneous presentation makes the diagnosis of T1DM, T2DM and LADA difficult. In this study, clinical presentation, age at diagnosis and Hba1c were similar in patients with T1DM, LADA and T2DM. Percentage of hypertension and dyslipidemia was similar across all groups. Patients with T2DM were obese. Those with T1DM and LADA had a low to normal BMI. Evaluation of the immunological profile helped in classification and subsequent treatment.

Conclusion: Overlap of phenotypical characteristics in patients with young onset diabetes makes the diagnosis challenging. This study confirms that an immunological diagnosis based on the autoantibody profile is central to the classification and management of young onset diabetes.

Abstract #226

EVALUATION OF “BASSAR”: A NEW TOOL OF THERAPEUTIC EDUCATION

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Objective: Therapeutic patient education represents a cornerstone of the diabetes management. Different modes of interventions has been proposed in the past. In this scope, we propose “BASSAR” as a new tool of therapeutic education. It represents through a video simulation, a vision model of the different diabetic eye complications such as cataract, macular edema, intravitreous hemorrhage, glaucoma.

AIM: Evaluate the impact of “BASSAR” on self-management and glycemic control among adult diabetic 2 patients.

Methods: This randomized controlled trial was conducted in the diabetic education unit. Patients were recruited on a voluntary basis. Eligibility criteria were physician confirmed type 2 diabetes and between 20 and 80 years. A total of 86 patients met the criteria and were randomly assigned to either the “BASSAR” group or the control group. The “BASSAR” group viewed the video simulation during diabetic education sessions. The sessions were interactive and patient centered. In the control condition patients were placed on the waiting list during 3 months. Background characteristics and outcome measures (glycemic control, self-management behaviors) were assessed at baseline and after 3 months.

Results: On average, participants were aged 54, 5 years and had had diabetes for 8.7 years. The results reveal a significant group by time interaction for the HbA1c. Follow up Scheffe comparisons showed that HbA1c significantly decreased in the BASSAR group whereas it remains stable in the control group. Identical changes were observed in diabetes self-management behaviors.

Conclusion: Results reveal that the education tool used in this study generate positive clinical outcomes. Additional research is needed on a largest sample size.
DETERMINANTS OF DIABETIC RETINOPATHY IN MOROCCAN TYPE 2 DIABETIC PATIENTS: WHICH PECULIARITIES IN OUR POPULATION?

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Objective: Diabetic retinopathy represents a major cause of the blindness worldwide. A variety of risk factors has been identified in several population, but to date, comprehensive data concerning our particular risk factors are lacking. The aim of the study was to determine the risk factors of diabetic retinopathy in Moroccan type 2 diabetic patients and to determine the threshold of HbA1c predicting retinopathy and to define the specific determinants in our population.

Methods: All patients 18 years or older diagnosed as type 2 diabetes and who were able to complete the laboratory data and retinal examination were invited to participate in the study. The diabetic retinopathy was classified by the ETDRS severity scale. Data were collected about duration of diabetes, smoking status, medications, evidence of macrovascular disease, blood pressure, nephropathy or neuropathy and actual therapeutics. Laboratory parameters included: HbA1c, lipid panel and microalbuminuria. Statistical analysis was performed using SPSS 16.0. The association between DR and each of the risk factors was assessed by bivariate analysis. A multivariate logistic regression analysis was performed to check the effect of independent variables on DR. the predictors on the binary logistic regression model were disease duration, HbA1c, systolic blood pressure, nephropathy, neuropathy and evidence of macrovascular disease.

Results: A total of 231 patients were included. The bivariate analysis has identified as risk factor for diabetic retinopathy: microvascular and macrovascular diabetic complications, presence of hypertension, duration of disease, glycemic control and insulin use. The multivariate regression analysis retrieved as independent risk factors: glycated hemoglobin >7% (OR: 2, 71 95% CI 1, 06-7, 43), microalbuminuria (OR : 2,6 95% CI 1,2-5,4), diabetes duration(per ten years) (OR : 2,6 95% CI 1,2-5,4) and blood pressure (per 10mmgh) (OR : 1,27 95% CI 1-1,70).

Conclusion: Our study found similar factors to those described for other populations. We emphasize on the important role of early medical intervention and adequate therapeutic education especially concerning the glycemic and blood pressure control.

CORRELATES OF ALBUMINURIA AMONG PATIENTS WITH TYPE 2 DIABETES MELLITUS IN A TEACHING HOSPITAL.

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Objective: Africa, especially the Sub-Saharan region is projected to experience the largest increment in the burden of type 2 diabetes over the next two decades. Albuminuria has been identified as a marker of high cardiovascular risk among people with type 2 diabetes (T2DM). Most previous studies from this region had focused on microalbuminuria, ignoring patients with macroalbuminuria. This study aimed to describe the burden of albuminuria among our patients and the associated clinical parameters.

Methods: In a cross-sectional design, one hundred and thirty patients with T2DM aged ≥ 30 yrs were consecutively recruited from our clinic over 3 months. Spot urine was examined for albumin and creatinine using immunoturbidimetry and enzymatic method respectively, and the albumin creatinine ratio was calculated. The blood pressure, fasting lipids, serum creatinine and HbA1c were also done.

Results: The age of the subjects ranged from 34 to 80 years, with a mean ± SD of 60 ± 9.6 years. Majority (68%) were females. The median duration of diabetes was eight years. Albuminuria was found in 34.6% of the subjects (microalbuminuria - 26.9%, macroalbuminuria -7.7%). Albuminuria was associated with older age (>65 years), history of hypertension, higher measured systolic BP and low HDL cholesterol. There was no association with duration of diabetes, body mass index, waist circumference, waist hip ratio, serum creatinine or HbA1c. On multivariate analysis, history of hypertension (adjusted odds ratio = 2.3, p = 0.035), and higher systolic blood pressure (adjusted odds ratio = 5.7, p =0.025) were the independent predictors of albuminuria.

Discussion: The prevalence of albuminuria is high in our clinic, but is much lower compared to a study carried out in our clinic 9 years ago where a prevalence of 83% was reported. This may be due to improved recognition and management of cardiovascular risk factors. Presence of hypertension and poor blood pressure control appear to be more important than degree of glycaemia or duration of diabetes in determining albuminuria. They may also be stronger predictors of cardiovascular outcomes. It is consistent with reports that blood pressure reduction and statin-induced lipid lowering...
Diabetes Mellitus/Prediabetes

ABSTRACTS – Diabetes Mellitus/Prediabetes

Abstract #229
DAR STRUCTURED EDUCATION IN MOROCCO: FASTING BEHAVIOURS AMONG T2D PATIENTS
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Objective: Fasting in Ramadan is of vital significance amongst Muslim. The Islamic regulation exempt those who are ill, however some insist on fasting despite they were advised not to fast by their HCP. The key strategies to prepare the patients and to reduce the risk of complication in diabetic patients is to provide appropriate health education to the patients prior to Ramadan and to adjust the anti-diabetic medicines during Ramadan.

The aim of our intervention is to use a specific designed Arabic language program for measured approach on diabetes and Ramadan fasting (MADAR).

Methods: The MADAR education Tool was adapted to include the local and regional traditional Moroccan dishes. A list of meals suggestions was also added to help T2d patients in their dietetic choices during Ramadan. Each MADAR session was delivered to a maximum of 8 patients to enhance the exchange between participants. Each session lasted for almost 2 hours. 2 groups had also 1 hour interview after the MADAR education program to explore their specific needs about fasting. The MADAR questionnaire was used to assess the educational impact before and after education.

Results: 82 T2 diabetic patients did attend the MADAR education sessions. the median age was 51.21 SD 8.52), female represented 65.9% of the attendees. Among the 82 patients, 82% fasted the previous year and 51 % reported hypoglycemia during the fasting. 72.3% pf patients that has hypoglycemia symptoms do not break the fasting with 83% of hypoglycemia occur around 5-6PM. The overall confidence in fasting safely was increased after the education session.

Conclusion: Our Experience has shown that the patients are motivated to take part in the MADAR education sessions. The have expressed a specific need concerning the meal composition choices especially considering the variety of dishes cooked usually during the holly month. The DAR experience in Morocco shows the critical importance of a dietetic advice tailored to Moroccan context and to the diabetic patient restrictions. The conception of a specific booklet will help Moroccan diabetic patients in their everyday choices.

Abstract #230
OPTIMAL BLOOD GLUCOSE MONITORING INTERVAL IN ICU PATIENTS ON INSULIN INFUSION
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Objective: Insulin infusion with frequent finger stick blood glucose (BG) monitoring is the preferred way of hyperglycemia management in the intensive care unit (ICU). American diabetes association and the society of critical care medicine recommends monitoring blood glucose every 1-2 hours in patients receiving insulin infusion to prevent dysglycemia (hyper or hypoglycemia); however, this is based on weak evidence.

Methods: Retrospective chart review was performed on 56 consecutive patients who required insulin drip in the ICU at Saint Vincent Hospital for persistent hyperglycemia (two consecutive BG reading of ≥ 180 mg/dL despite subcutaneous insulin therapy). Baseline characteristics were obtained and mortality probability model (MPM) II score at ICU admission was calculated to estimate the severity of illness. Finger stick BG (FSBG) readings were reviewed for compliance with hourly BG. Data was divided into three groups depending on the time interval of BG monitoring: Group A (<90 min), Group B (91-179 min) and Group C (≥180 min), and relationship of dysglycemic events (BG <70 and ≥180 mg/dL) with time interval of BG monitoring was analyzed using two way ANOVA factoring for every patient. Post hoc analysis was used to assess differences between groups.

Results: Mean age was 69 years; 48% were males, 77% patients had preexisting type 2 diabetes and mean MPM II score was 41. Of 1411 time intervals for BG monitoring in 56 patient on insulin drip, 467 (33%) were in group A, 806 (57%) in group B and 138 (10%) in group C; hourly BG monitoring compliance was 12.6% (178/1411). Hypoglycemic episodes while on insulin drip was 10 (0.7%) of 1411 BG readings. The frequency of dysglycemic episodes were similar in all three groups (p=0.55) and post hoc analysis between the groups was not statistically significant; however, there was a non-statistical trend of higher dysglycemic events in Group C vs. Group A (p= 0.08). Further analysis, showed rapid decline in BG levels in the first 16 hours of starting insulin
infusion followed by stabilization.  

**Discussion:** Strict compliance with hourly BG monitoring was only 12.6%. Overall occurrence of hypoglycemia was low (0.7%) and there was no significant difference in dysglycemia with less frequent monitoring. Rapid decline in BG levels in the first 16 hours suggests that it would be prudent to do hourly monitoring in the first 16 hours to avoid any hypoglycemia and then a longer time interval may be reasonable. Retrospective nature and small sample size limits generalization.  

**Conclusion:** Risk of dysglycemic episodes in patients requiring insulin drip for sustained hyperglycemia in ICU was not significantly different with less frequent BG monitoring.

**Abstract #231**

**INSULIN PUMP CLOCK GLITCHES: A WORD OF CAUTION TO CLINICIANS**

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**Objective:** To increase awareness amongst clinicians about glitches in time-date settings of insulin pumps, that could potentially cause dosing errors in insulin delivery. We previously reported cases of glitches in Day Light Saving Time (DST) and AM-PM settings related to patients’ errors. In this case report, we report a double time setting glitch (DST and AM-PM glitch) related to a clinician’s error.

**Case Presentation:** A 75 year old woman was brought to a tertiary teaching hospital after she had a severe hypoglycemic episode. She had diabetes due to pancreatectomy (Whipple’s procedure) managed with insulin pump. The patient was kept overnight for observation, and since neither the admitting team nor the nursing staff could handle her pump management, the oncall endocrinology team was consulted. The patient was seen just before midnight (on November, 13th), and the on-call clinician noted that the patient had forgotten to make the DST time change (that occurred on November 1st). After reducing basal and bolus doses as appropriate and changing from multiple settings to just one, the clinician corrected the pump’s time by 1 hour. When the patient was seen the following day, another clinician noted that the time on the pump’s screen was off by 12 hours (Pump’s time: 12:45 AM; actual time: 12:45 PM). The correct AM-PM setting was restored, and the endocrine team called the pump manufacturer, which investigated the time settings utilizing a remote “Connect” software: The glitch occurred when the first clinician (who corrected the DST time) failed to change the AM-PM setting, within 1 hour of the 12:00 mark (i.e. at 11:40 PM), when the pump switches AM-PM setting. This glitch caused no dose error, since the settings were not multiple.  

**Discussion:** Since pump clocks do not automatically adjust (neither are they wirelessly connected to GPS), patients have to manually set up the time. Correct setting of the pump’s internal clock is prudent to ensure delivering the correct insulin doses in the intended (actual) time of the day. If a patient uses only one basal and bolus setting, no harm is expected, because the same basal rate will be delivered at all times, and so are the boluses. But if multiple settings are used, incorrect dosing may occur, as recently reviewed in publications by our group. While patients and clinicians should be vigilant regarding pump’s time settings, recently introduced software apps can help pump users secure correct settings at all times, by alarming them to “check pump’s time”.  

**Conclusion:** This is another example of glitches of insulin pump internal clock. When adjusting the pump’s clock within 1 hour of the 12:00 time mark, it is prudent to pay attention to the AM-PM setting.

**Abstract #232**

**STARDM: A MODEL OF CARE IN SPECIALTY DIABETES CARE**

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**Objective:** Specialty diabetes care is commonly offered to patients who have not achieved clinical goals in the primary care setting, but it is unknown which care models are most effective for reaching goals in specialty diabetes settings. We describe the design, implementation and plan for evaluation of the Setting Targets Achieving Results in Diabetes Mellitus (STARDM) Program, a care model designed to improve diabetes outcomes for medically complex patients within an urban diabetes specialty care setting.

**Methods:** STARDM is an intensive disease management program that applies specialty tools to help high risk patients to achieve personalized diabetes goals within 6 months. Patients are referred by their endocrinologist based on criteria including frequent hypoglycemia or uncontrolled hyperglycemia despite adequate treatment trials. A 60 minute intake visit with the STARDM Nurse practitioner/coordinate includes a technical review, skills evaluation, goal setting and baseline measurement of disease-specific attitude (PAID survey) and quality of life (SF-36). Specific interventions are chosen from the STARDM Toolkit using shared decision making. These
include diabetes education, subspecialty referral, intensive telephonic interim care or virtual visits, frequent glucose data review and professional CGM. A personalized plan is carried out by a multidisciplinary team that includes the primary care provider. A final transition visit is conducted after 3 or 6 months to collect outcome data. After a 6 month pilot, referred patients will be randomized to receive the complete STARDM intervention vs. interdisciplinary goal-setting only.

**Results:** The primary outcome will be the percent of patients achieving the goal in the time frame. Secondary outcomes will include differences between groups in HbA1c, acute care services utilization, and the PAID and SF-36 scores. Cost-effectiveness will be measured. Variables including comorbid depression and disease complications will be tested as potential confounders.

**Discussion:** Population diabetes care models are typically developed, funded and tested in the primary care setting to improve standard clinical outcomes. However, while timing of referral to diabetes specialty care is often discussed, the relative effectiveness of different diabetes specialty care models has not been evaluated.

**Conclusion:** The STARDM program is a short-term intensive disease management program designed to augment routine specialty diabetes care in a cost-effective manner, employing existing tools and personnel to assist patients in achieving personalized goals. A planned evaluation including randomization will determine if such a care model can be cost-effective in diabetes specialty settings.

**Abstract #233**

**TYPE 2 DIABETES: IMPACT OF QUALITY IMPROVEMENT CME ON PHYSICIAN PERFORMANCE**

Amy Larkin, PharmD⁠¹, Colleen Healy, MA⁠¹, Jess Dropkin, None⁠¹, Barry Patel, PharmD², Denise Herriott, MPH², Anne Le, PharmD²

1. Medscape Education, 2. Indegene Total Therapeutic Management

**Objective:** Research has noted clinical practice gaps in the management of diabetes. We sought to determine if participating in an intervention comprising quality improvement (QI) and continuing medical education (CME) could improve performance of primary care physicians (PCPs).

**Methods:** To address clinical gaps related to type 2 diabetes (T2D), a multi-partner initiative was developed and implemented, including a baseline assessment, an educational intervention consisting of 3 CME activities and one-on-one peer coaching, and a final assessment at 6 months after CME completion. Thirty primary care providers (PCPs), each of whom cared for a high proportion of adult patients with T2D and A1c ≥7% in the past year, were included in the study. Data from 300 patient charts were abstracted, using a HIPAA-compliant, IRB-approved protocol. The baseline assessment period spanned July 2013 through June 2014. Following the final assessment, the initiative’s effect was determined as defined by the changes in PCPs’ performance relative to national quality standards and changes in patients’ metrics. The intervention site and target audience included PCPs in an accountable care organization based in the northeastern US.

**Results:** Glycemic Control:

7% (93% to 100%) increase in the proportion of patients with T2D for whom A1c testing was documented by their physicians in the past 6 months (P < 0.001)

Individualized Treatment Plan:

15% (72% to 87%) increase in the proportion of patients receiving medication counseling from their physicians (P < 0.001)

15% (72% to 87%) increase in the patients receiving lifestyle counseling from their physicians (P < 0.001)

17% (6% to 23%) increase in the patients setting weight loss goals with their physicians (P < 0.001)

17% (27% to 44%) increase in the patients setting exercise goals with their physicians (P < 0.001)

**Discussion:** The overall goal of this QI initiative was to improve the ability of physicians to provide optimal T2D treatment, focusing on appropriate measurement of A1c and individualizing treatment plans. The effectiveness of the health system-focused initiative design has implications for the scalability of the model to other healthcare provider systems. This partnership demonstrates a unique and valuable innovation in elevating clinician performance, and thus improving patient health outcomes among individuals with diabetes.

**Conclusion:** This study demonstrates the success of CME activities as educational interventions to improve physician performance related to quality- and guideline-based type 2 diabetes management. It is expected that these performance improvements will translate to improved patient outcomes in clinical practice.
REGULAR INSULIN ADMINISTERED WITH THE V-GO® DISPOSABLE INSULIN DELIVERY DEVICE IN A CLINICAL DIABETES SETTING: A RETROSPECTIVE ANALYSIS OF EFFICACY AND COST

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1. Northeast Florida Endocrine and Diabetes Associates, 2. Valeritas

Objective: The cost of diabetes therapy including insulin continues to rise for patients and insurers. Finding a more affordable treatment strategy for achieving glycemic control is a serious challenge for many patients. Rapid acting insulin analogues offer more convenient delivery options, such as with prefilled pens and devices, but are substantially more expensive than regular human insulin. Often, patients must compromise between inconvenient insulin delivery and affordability. The objectives of this retrospective analysis were to assess the efficacy and cost savings when Regular Human Insulin (RHI) U-100 was utilized in the V-Go® Disposable Insulin Delivery Device.

Methods: A retrospective analysis was conducted by querying an electronic medical records database for patients administering RHI by V-Go at a large endocrine practice.

Results: Eleven patients met the prespecified analysis criteria and were evaluated. At baseline, 7 patients were on basal-bolus insulin injections, 1 patient was on basal insulin only, 2 patients were on pre-mix insulin injections, and 1 patient was naive to insulin therapy prior to RHI+V-Go initiation. Patients had a mean baseline A1C of 8.6% (range 6.0% - 10.7%) and mean insulin total daily dose (TDD) of 82 U/day observed at baseline. After an average treatment duration of 6 months A1C was significantly reduced by -0.7% (p=0.029) and mean TDD decreased to 61 U/day reflecting a 26% dose reduction. Body weight remained stable. The monthly direct pharmacy cost (including insulin and delivery mode) was $309 per patient based on wholesale acquisition cost and retail pricing for RHI compared to baseline cost of $558.

Discussion: Using RHI in V-Go resulted in improved glycemic control with a reduction in TDD while also decreasing the associated cost of insulin therapy for the patient. Combining more affordable insulin with an alternative delivery system that allowed for simplified insulin delivery, with only one daily injection, may be a viable option when insulin therapy is required.

Conclusion: Administering RHI therapy via V-Go is safe and efficacious. Additional studies should be conducted to validate these findings and further evaluate the efficacy and safety of RHI with V-Go.

T2D MANAGEMENT: CAN CASE-BASED CME IMPROVE PHYSICIAN PERFORMANCE?

Amy Larkin, PharmD, Colleen Healy, MA, Anne Le, PharmD

Medscape Education

Objective: To make appropriate individualized treatment recommendations for patients with type 2 diabetes (T2D), it is important for physicians to understand the role of newer oral antihyperglycemic agents. We sought to determine if case-based, interactive, online continuing medical education (CME) could improve performance of primary care physicians (PCPs) and diabetologists/endocrinologists related to clinical use of newer antihyperglycemic agents and individualization of treatment plans for T2D in various clinical case scenarios.

Methods: An interactive, text- and case-based, online CME activity was developed. The educational effects of exposure to the program were assessed using a linked preassessment/postassessment study design. McNemar’s chi-squared test was used to assess differences pre to post. P values <.05 are statistically significant. Cohen’s d was used to calculate effect size (<0.4 is a small effect, 0.4-0.8 moderate, and >0.8 large). The activity launched on August 26, 2015 and data were collected through September 29, 2015.

Results: Improved performance was seen among PCPs (n = 490; P <.05) and diabetologists/endocrinologists (n = 174; P <.05) in the following areas (all P < .05):
- Increase of 29% by PCPs and 38% by diabetologists/endocrinologists in educating patients about the progressive nature, and need for additional medications, of T2D
- Increase of 54% by PCPs and 53% by diabetologists/endocrinologists in designing an individualized treatment plan
- Increase of 9% by PCPs and 10% by diabetologists/endocrinologists in designing an individualized treatment plan using newer oral agents for a given patient with T2D

Area identified as needing additional education:
- 27% of PCPs and 14% of diabetologists/endocrinologists remain unclear on the need to engage patients in their T2D care plan.

Discussion: For all physicians who participated in the CME activity, the statistically significant changes observed indicate success of the interventions as well as an increase in evidence-based practice choices. Interactive cases are an effective way to improve physician performance in the area of T2D management. While improvements were seen in all areas, additional education is needed to highlight the need to engage patients in formulating their
T2D care plans. Perhaps this gap remains as a result of time constraints with physicians having short patient visits and feeling they do not have time to involve patients in decision making.

**Conclusion**: This study demonstrates the success of an interactive, case-based, online CME activity on improving performance of PCPs and diabetologists/endocrinologists regarding clinical use of newer antihyperglycemic agents and individualizing care in T2D.

**Abstract #236**

**SUDDEN RAPID PROGRESSION TO INSULIN DEPENDENCE POST TREATMENT WITH ANTI-PD1 MONOCLONAL ANTIBODIES IN PRE-EXISTING TYPE 2 DIABETES**

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**Case Presentation**: GAD65 antibodies (GAD), a marker of immune β cell damage in type 1 diabetes (T1D) occur also in a subset of adults with type 2 diabetes (T2D), unofficially classified as type 1.5 diabetes (T1.5). Adults with T2D with and without GAD (-GAD) are of a varied phenotype, making it difficult to distinguish clinically from each other. T1.5 is more common in lean adults and require insulin more rapidly than –GAD. The inhibitory molecule Programmed death-1 (PD1), and its ligand, PD-L1 (PD1-PDL1) pathway is a therapy target against cancer. The anti-PD1 monoclonal antibodies (PD1As) pembrolizumab and nivolumab, enhance antitumor activity by breaking down tolerance and increasing tumor destruction, but also enabling reactions to self-antigens. We present 2 cases of T2D, with rapid progression to insulin dependence and +GAD, after PD1As: a 78 yr old man with chemotherapy-resistant lung cancer and T2D for 30 yrs, controlled on oral medications (OM), developed polydipsia, polyuria and nocturia, post treatment with nivolumab. Basal bolus glargine/lispro regimen was initiated, requiring frequent increments in insulin doses to achieve glucose control. A 55 yr old man with chemotherapy-refractory metastatic melanoma and 5 yr history of T2D, required basal bolus glargine/aspart post treatment with ipilimumab, from OM. Hypophysitis prompted discontinuation of Ipilimumab, and pembrolizumab was initiated. Intensive escalation of insulin doses post nivolumab were needed for glucose control, c-peptide was undetectable. Both patients were non-obese and had +GAD.

**Discussion**: PD1/PDL1 interactions are critical for the regulation of T-cells involved in the development of T1D. PD1 manipulation results in the development of autoimmunity in animal models, including T1D. Low PD1 expression has been described in human T1D and new-onset T1D has been linked to the use of PD1As. We present 2 cases of sudden rapidly progressive pre-existing diabetes, and hypothesize that in individuals at risk, fulminant autoimmune destruction may be enhanced upon treatment with PD1As.

**Conclusion**: The development of novel PD1/PDL1 targeting agents has heralded a new era in immuno-oncology and has unmasked subclinical, “latent” autoimmunity in the β cell in individuals at risk. Obtaining GAD before treatment initiation in T2D should be considered to identify those at higher risk (lean, personal and/or first degree history of autoimmunity) and alert providers on the need for close glycemic control, and to institute prompt insulin initiation. Further research is needed to assess whether GAD positivity is induced de novo by PD1As or whether these agents enhance a latent autoimmunity already present (i.e. type 1.5 diabetes), or both.

**Abstract #237**

**EVALUATING THE IMPACT ON DIABETES CONTROL WITH V-GO® FOR PATIENTS WITHIN A HIGH RISK POPULATION– A RETROSPECTIVE COHORT ANALYSIS FROM A LARGE ENDOCRINE AND SPECIALIZED DIABETES SYSTEM**

David Sutton, MD¹, Charissa Higdon, PA-C¹, Mark Carmon, PharmD, CDE², Scott Abbott, MS²

1. Northeast Florida Endocrine and Diabetes Associates, 2. Valeritas

**Objective**: Diabetes is a chronic disease that is closely monitored as part of quality improvement initiatives by healthcare providers and organizations. Patients with diabetes that have A1C measures >9% are defined as being poorly controlled and are at the highest risk for related complications and mortality. Many institutions are focusing on this high-risk patient population to improve quality of care and health outcomes. A retrospective analysis assessed the outcomes of patients with poorly controlled diabetes being switched to V-Go® Disposable Insulin Delivery Device (V-Go) to simplify insulin administration and to improve glycemic control.

**Methods**: An electronic medical records database from a large endocrine and specialized diabetes system was used to query patients. Patients with an A1C >9% at baseline were identified. The change from baseline in A1C, weight and insulin dose was evaluated.

**Results**: Thirty eight patients were identified as having a baseline A1C>9%. After a mean duration of 153 days...
on V-Go a 2.2% reduction (p<0.0001) in A1C from a mean baseline of 10.8% was achieved. Twenty seven of 38 patients achieved an A1C reduction of >1%. For those patients administering insulin at baseline a 22% reduction in total daily insulin dose (TDD) was observed. There was a mean +3.8kg change in weight. Despite the significant improvement in A1C levels the overall incidence of reported hypoglycemia was similar to baseline.

Discussion: Clinicians and healthcare institutions focusing on high-risk diabetes patients to improve quality of care and health outcomes may be able to make considerable progress when switching to a novel insulin delivery device.

Conclusion: High risk patients with poorly controlled diabetes switched to V-Go experienced improved glycemic control and achieved significant reductions in A1C levels with less total daily insulin.

Abstract #238

IMPROVING IMPACT OF GUIDELINES ON T2D: EFFECT OF ONLINE CME AND NEED FOR FURTHER EDUCATION

Amy Larkin, PharmD, Kelly Hanley, Jess Dropkin, Anne Le, PharmD

Medscape Education

Objective: Guideline recommendations for type 2 diabetes (T2D) management are rapidly evolving to reflect new clinical safety and efficacy data. In order to optimize incorporation of new information into clinical practice, we sought to determine if participation in online continuing medical education (CME) could improve the knowledge and clinical decision-making of primary care physicians (PCPs) and diabetologists/endocrinologists related to guideline-based treatment of T2D.

Methods: The effect of two educational interventions was analyzed to determine efficacy of online education presented in the form of a video roundtable and an interactive case-based text activity. The effects of education were assessed using knowledge- and case-based matched pre-assessment/post-assessments. P values are shown as a measure of significance; P values <.05 are statistically significant. The activity launched online March, 2015 and data were collected through May or June, 2015, depending on the activity.

Results: In total, 866 PCPs and 220 diabetologists/endocrinologists participated in at least 1 of the CME activities and were included in the analysis. Significant overall improvements were seen after participation in the video roundtable (PCPs: n = 314, P <.001; diabetologists/endocrinologists: n = 29, P = .705) and in the case-based text activity (PCPs: n = 552, P <.05; diabetologists/endocrinologists: n = 191, P <.05). Specifically related to (all P < .05):

- 47% more PCPs and 46% more diabetologists/endocrinologists correctly identified individualized glycemic targets
- 22% more PCPs and diabetologists/endocrinologists selected appropriate next steps for an individualized treatment plan
- 27% more PCPs and diabetologists/endocrinologists made appropriate clinical decisions regarding adjusting treatment in a patient with weight gain

Additional education needed:

- 52% of PCPs and 24% of diabetologists/endocrinologists remain unclear on when to select a higher than average A1c target
- 66% of PCPs and 52% of diabetologists/endocrinologists remain unclear on therapy selection in the presence of renal insufficiency
- 31% of PCPs and 21% of diabetologists/endocrinologists remain unclear on treatment intensification in the presence of weight gain

Discussion: For all physicians who participated in one or both of the CME activities, the statistically significant changes observed indicates success of the interventions as demonstrated by an increase in evidence-based practice choices.

Conclusion: This study demonstrates the success of CME on improving knowledge and clinical decision-making of PCPs and diabetologists/endocrinologists regarding guideline-based treatment intensification of T2D.

Abstract #239

IMPACT OF MEDICAL EDUCATION ON KNOWLEDGE OF GUIDELINE UPDATES

Amy Larkin, PharmD, Colleen Healy, MA, Anne Le, PharmD

Medscape Education

Objective: Individualization of type 2 diabetes (T2D) care is essential to achieving glycemic control, yet physicians are not developing guideline-based treatment plans for patients with T2D based on disease- and patient-specific factors that influence optimal antihyperglycemic therapy. We sought to determine if case-based online continuing medical education (CME) could improve the knowledge, competence, and clinical decision-making of primary care physicians (PCPs) and diabetologists/endocrinologists.

Methods: A video-based, case-inclusive online CME activity was developed that included 3 expert faculty discussing application of guidelines in common T2D
cases. The educational effects were assessed using a linked pre-/post-education study design. The McNemar’s chi-squared test was used to assess differences pre to post. Cohen’s d was used to calculate the effect size. P values were calculated and those <0.05 were considered statistically significant. The activity launched online June 5, 2015 and data were collected through July 20, 2015. Results: Improved clinical-decision making was seen among PCPs (n = 363; P < .05; large effect d = 0.904) and diabetologists/endocrinologists (n = 32; P <.05; medium effect d = 0.469) in the following areas: Increase of 27% by PCPs (P < .05) and 3% by diabetologists/endocrinologists (P = .768) in identifying target A1c per AACE/ACE guideline recommendations Increase of 29% by PCPs and 25% by diabetologists/ endocrinologists in selecting guideline-based add-on therapy to metformin (both P < .05) Increase of 13% by PCPs (P < .05) and 6% by diabetologists/endocrinologists (P = .545) in identifying priorities when selecting antihyperglycemic therapy (AACE/ACE guidelines) Increase of 21% by PCPs (P < .05) and 12% by diabetologists/endocrinologists (P = .226) in selecting criteria for intensification plans Additional education needed: 36% of PCPs and 44% of diabetologists/endocrinologists remain unclear on guideline-based treatment intensification Discussion: For PCPs who participated in the CME activity, the large effect observed indicates an increase in evidence-based practice choices, demonstrating the impact of the intervention. The medium effect among diabetologists/endocrinologists and lack of statistical significance for some questions was a result of a higher baseline compared to PCPs. Conclusion: This study demonstrates the success of a targeted educational intervention on improving knowledge, competence, and clinical decision-making of PCPs and diabetologists/endocrinologists regarding guideline-based treatment of T2D.

Abstract #240

COMPARISON OF TWO METHODS FOR INTENSIFIED INSULIN DELIVERY IN PATIENTS WITH TYPE 2 DIABETES INADEQUATELY CONTROLLED ON BASAL INSULIN

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Objective: With disease progression, beta cell function continues to decline resulting in a threshold in glycemic benefit when administering basal insulin despite further titration. The purpose of this analysis was to compare the clinical effectiveness of two methods to deliver intensified insulin therapy (IIT) in patients with type 2 diabetes inadequately controlled on basal insulin + concomitant antihyperglycemic agents in a real world clinical setting.

Methods: Data for this retrospective study were obtained using electronic medical records from a large multi-center diabetes system. Records were queried to identify patients transitioned to V-Go® Disposable Insulin Delivery device (V-Go) or multiple daily injections (MDI) using an insulin pen/syringe to add prandial insulin when A1C >7% on basal insulin therapy. The primary endpoint was to evaluate the between group difference in A1C change over time using follow-up A1C results.

Results: One hundred sixteen patients were evaluated (56 V-Go, 60 MDI). Baseline characteristics were similar between V-Go and MDI (A1C 9.5 vs 9.4%; weight 94.6 vs 97.6 kg; basal insulin dosing 51 vs 46 units/day and diabetes duration 13 vs 12 yrs), respectively. By 27 weeks, A1C least squares mean change (95% CI) from baseline was -1.98% (-2.36 to -1.60) with V-Go and -1.34% (-1.68 to -1.00) with MDI; for a treatment difference of -0.64% (-1.17 to -0.10; p=0.020). Patients using V-Go administered less mean + SD total daily insulin compared to patients using MDI, 56 + 17 vs 78 + 40 units/day (p<0.001).

Discussion: IIT provides both fasting and postprandial glucose coverage and is a suggested option when glycemic targets are not achieved. The use of MDI is the most common method of insulin delivery for IIT; however the majority of patients prescribed MDI report missing insulin injections which negatively impacts therapy success. V-Go facilitates the progression to IIT with minimal additional effort and does not require an added preparation process by the patient to administer prandial doses. Patients using V-Go were able to maintain a similar total daily dose compared to baseline, yet had a significantly greater reduction in A1C compared to MDI. Considering both IIT methods offer additional glucose coverage through insulin redistribution, we attribute this finding to improved adherence to prandial dosing and/or improved insulin action with V-Go.

Conclusion: Progressing to IIT resulted in significant glycemic improvement. Insulin delivery with V-Go was associated with a greater reduction in A1C and required less insulin compared to patients administering IIT with MDI. This study provides real-world evidence that V-Go is an effective and efficient method to administer IIT.
Abstract #241

HIGH PREVALENCE OF DIABETES, PRE-DIABETES AND INSULIN RESISTANCE IN SOUTH ASIANS: IMPLICATIONS FOR PUBLIC HEALTH PREVENTION BASED ON A NOVEL COMMUNITY REGISTRY

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1. South Asian Heart Foundation, 2. Atherotech

Objective: South Asian immigrants (SA) in the United States have a high prevalence of cardiovascular diseases (CVD), diabetes mellitus (DM), high triglyceride (TG), and low levels of high-density lipoprotein cholesterol (HDL-C). While DM is a CVD risk equivalent, pre-diabetes (P-DM) may also impart a 20% increase in the risk for macro-vascular diseases and DM, thereby leading to increased risk for micro-vascular diseases. Insulin resistance (IR) is also predictive of CVD. Further, an elevated TG/HDL-C ratio is a correlate of IR and is predictive of DM and CVD. However, the prevalence of P-DM and IR in SA in the United States is largely unknown.

Methods: We reviewed the clinical history and Vertical Auto Profile (VAP) + lipid panel utilizing ultracentrifugation to directly measure lipid sub-fractions, for 348 participants in a unique SA Registry in the United States. We measured the TG/HDL-C ratio in this cohort. Prevalent DM and Pre-DM were defined as HbA1c > 6.5 and 5.7-6.4, respectively.

Results: Since SA are known to have high TG levels, we stratified the results based on clinically relevant TG levels<150 (n=202), 150-199 (n=62), 200-499 (n=79), and >500 (n=5) mg/dL: the median levels of total cholesterol were: 189, 213, 205, and 189 mg/dL; low density lipoprotein cholesterol were: 114, 133, 125, and 107 mg/dL; TG/HDL-C ratio was: 1.7, 3.4, 5.8, and 18.6; non-HDL-C were: 133, 158, 161, and 162 mg/dL; TG-rich lipoprotein remnants were: 20, 27, 31, and 40 mg/dL; prevalence of DM was: 15%, 19%, 36%, 40%; and prevalence of P-DM + DM was: 67%, 68%, 74%, and 60%, respectively. The overall prevalence of P-DM was 48% and that of P-DM + DM was 69%. The risk ratio for patients with TG/HDL-C >3.5 was 1.9 for DM.

Discussion: In a large novel SA community registry in the United States, SA participants were noted to have a very high prevalence of DM, Pre-DM, and IR. With nearly 70% of the population at risk, there is a tremendous need for public health awareness campaigns for SA. The TG/HDL-C ratio is a simple inexpensive tool that may be useful to stratify risk in this population.

Conclusion: While the high prevalence of CVD in SA has been previously documented, this is the first study to document using a large community registry, the total prevalence of P-DM and DM of nearly 70% in SA adults in the United States. Public health prevention efforts for diet, lifestyle changes, and appropriate screening for DM and P-DM are needed, with treatment as indicated by guidelines, for preventing the progression of disease in SA. Such public health efforts will help prevent the downstream costs of both macro-vascular and micro-vascular complications that could reach epidemic proportions in SA living in the United States.

Abstract #242

DECREASED FREQUENCY OF HYPOGLYCEMIA AND IMPROVED GLYCEMIC CONTROL IN PATIENTS WITH T2DM PRE- AND POST-INITIATION OF A DISPOSABLE INSULIN DELIVERY DEVICE

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Objective: The introduction of wearable insulin infusion devices, including pumps and disposable devices, has been an advance in the management of diabetes with insulin. The goal of these devices is to help deliver insulin in a more physiologic manner while reducing the complexity and frequency of multiple daily insulin injections resulting in improved glycemic response. The purpose of this analysis was to utilize electronic medical records (EMR) at an endocrine specialty clinic and evaluate the safety and effectiveness of switching patients from multiple insulin injections to a disposable insulin delivery device.

Methods: An analysis of 10 patients with Type 2 Diabetes followed longitudinally up to 6 months to assess the occurrence of hypoglycemia, change in body weight and BMI as well as the change in glycemic control. All patients had initiated the V-Go® Disposable Insulin Delivery Device and had at least two follow-up visits post initiation.

Results: Patients had a mean age of 57.7 years (42 - 85 years), body weight of 204 lbs. and a BMI of 32.7. All patients were receiving insulin with multiple daily injections (8 patients with insulin pens and 2 patients with vial and syringe). Baseline mean A1C was 9.32% (7.0 -13.1%) and dropped to 6.98% (6.1 - 8.4%) and 6.73% (6.6 - 7.5%) at 3 and 6 months, respectively (p<0.05 at each
time point compared to baseline). These improvements were observed despite a reduction in baseline basal insulin doses of more than 50% and a reduction in total daily dose of 27% at V-Go initiation, both of which were maintained to 6 months. At baseline, 30% of patients reported hypoglycemic episodes on a weekly basis. After initiating V-Go only 10% of patients reported hypoglycemic events after 3 months and 0% reported hypoglycemic events at 6 months. Baseline hyperglycemia (>180 mg/dl) was reported at a frequency of >10 per week in 40% and at a rate of >20 times per week for an additional 40% of patients. At 3 months 50% of the patients reported no hyperglycemia and 40% reported only 1-2 episodes per week. At 6 months, 70% of patients reported no hyperglycemia. Mean body weight at 6 months was 203 lbs. and BMI was 32.9 indicating no meaningful change despite the improvement in glycemic control.

**Discussion:** Patient switched from traditional insulin injections to a wearable insulin delivery device demonstrated improved glycemic control and, perhaps more importantly, a reduction in glycemic fluctuations and occurrences of evident hyperglycemia and hypoglycemia.

**Conclusion:** These results demonstrate significant reductions in A1C over 6 months using V-Go without increasing risk of hypoglycemia. Frequency of hyperglycemia was nearly eliminated while using less total daily insulin.

**Abstract #243**

**THE CONCEPT OF THE “INSULIN PUMP CENTER”: COORDINATED AND CENTRALIZED CARE FOR INSULIN PUMP PATIENTS**

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**Objective:** While several diabetic centers exist in the United States, to date only one center is devoted to the care of diabetic patients utilizing insulin pump therapy (Continuous subcutaneous insulin infusion [CSII]). Our Insulin Pump Center (IPC) at the AM Diabetes and Endocrinology Center in Memphis, Tennessee centralizes all care for patients utilizing CSII and seeks to improve glycemic control as well as patients’ overall quality of care. Here we present the experience and data from the IPC’s first year as a standalone center.

**Methods:** Patients on CSII therapy were switched over to the IPC starting August 2014. The IPC is manned by staff trained in all aspects of insulin pump therapy, such as MA, RN, CDE and RD. The IPC centralizes all pump-related services (in addition to quarterly follow up visits by providers) in one location, such as walk in appointments for patients to download pump information and adjustments in therapy if needed, in between scheduled appointments, walk-in appointments to consult staff for any pump related issues, visits with a Certified Diabetes Educator (CDE) and providing troubleshooting and/or education on insulin pumps with Certified Pump Trainers (CPT).

**Results:** 601 insulin pump patients were followed between August 2014 - December 2015, with an average visit frequency of 3 months. 87.2% of patients utilized a Medtronic pump, 3.1% utilize T-slim (tandem) pumps, 5.2% use Omnipod pumps and 4.5% use Animas pumps. 29.2% of patients are on sensor augmented pump therapy with Medtronic 530G system [SAP], while 2.4% are on a sensor and pump combination. (of the patients with sensors, 92.8% utilize SAP while 8.2% use a sensor and pump). Average A1C levels for patients using a pump at the IPC is 7.943%, with a p value < 0.05, compared to A1c at time of start of care at the IPC, while average A1C levels for patients on either SAP or a sensor and pump combination is 7.69%, with a p value > 0.05 when compared to A1c before initiation of sensor use. Additionally, the A1C levels of patients on SAP have decreased 0.6% (from 7.9% to 7.3%), while the average A1C levels of patients without a sensor pump decreased about 0.2% (8.2% to 8.01%).

**Discussion:** Our experience shows that care for patients on CSII therapy in an IPC setting lead to better patient outcomes. Limitations of this data include absence of comparison to MDI treated patients (control group).

**Conclusion:** Our IPC is the first to treat patients on CSII therapy in a specialized environment and both outcomes and patient compliance have improved with this approach. More studies are needed to review the efficacy of this approach, as we feel it is a viable standard of care not just in Memphis, but also potentially across the country.

**Abstract #244**

**BODY-MASS INDEX, WAIST-SIZE, WAIST-HIP RATIO AND CARDIOVASCULAR RISK FACTORS IN NORTH INDIAN PUNJABI DIABETIC POPULATION**

Rohit Kapoor

Carewell Heart & Superspeciality Hospital

**Objective:** To determine the association of obesity, measured by body-mass index (BMI), waist-size or waist-hip ratio (WHR), with multiple risk factors in Punjabi population.
Methods: 2015 (1157 M, 858 F) T2D subjects, aged between 31-79 yrs were enrolled for the study. Waist Hip Ratio (WHR), Waist Circumference (WC), Body Mass Index (BMI), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Lipid Profile (Total Cholesterol, Triglycerides, HDL, LDL), Pulse Wave Velocity (baPWV), Ankle brachial index (ABI) and HbA1c of the subjects were analyzed. Pearson’s correlation coefficients (r) of BMI, waist and WHR with various risk factors were determined.

Results: There is a positive correlation of BMI, waist-size and WHR with SBP (r= 0.18 to 0.07), DBP (0.13 to 0.08), duration of diabetes (r=0.10 to 0.07), HbA1C (r=0.126 to 0.08), Total cholesterol (0.23 to 0.09), and LDL cholesterol (0.12 to 0.07) and negative correlation with HDL cholesterol (r=-0.11 to -0.08) in both men and women (p<0.05). Triglycerides were found to be significantly correlated with BMI and WHR only (p<0.05). No significant correlation was found with PWV & ABI.

Conclusion: There is a positive relationship of markers of obesity (body-mass index, waist size and waist hip ratio) with major cardiovascular risk factors and regular anthropometric measurements are needed in diabetic population to prevent future CV risk.

Abstract #246

OVERALL AND ABDOMINAL ADIPOSETIES AND HYPERTRIGLYCERIDEMIA AMONG NORTH INDIAN PUNJABI DIABETIC POPULATION

Rohit Kapoor
Carewell Heart & Superspeciality Hospital

Objective: To determine the association of obesity, measured by body-mass index (BMI), waist-size or waist-hip ratio (WHR), with hypertriglyceridemia in North Indian Punjabi diabetic population.

Methods: 2015 (1157 M, 858 F) T2D subjects, aged between 31-79 yrs were enrolled for the study. Waist Hip Ratio (WHR), Waist Circumference (WC), Body Mass Index (BMI) and Triglycerides of the subjects were analyzed.

Results: The mean age of the subjects was 52.9 yrs (5.09). The mean BMI of subjects was 26.5(4.4), WHR 1.1(0.02) and WC 39.7(4.1) inches. There is a positive correlation of waist circumference (r=0.01) with triglycerides. There was a significant positive correlation of BMI (r=0.08 M =0.18 F) and WHR (r=0.07 M =0.07 F) with triglycerides (p<0.05).

Conclusion: Both BMI and WHR were strongly independently associated with hypertriglyceridemia among the population. Both measurements should be considered for use in assessing health risk at clinical settings and epidemiologic research among diabetic population.
Abstract #247

SERUM FERRITIN: RELATIONSHIP WITH INDICES OF OBESITY AMONG TYPE 2 DIABETICS IN KANO, NORTHWESTERN NIGERIA.

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Objective: Markers of body iron stores have been shown to be significantly higher in persons with diabetes compared with controls, even after correction for various other risk factors for diabetes including markers of obesity and inflammation. We determined the relationship between serum ferritin and indices of obesity among type 2 diabetics attending the diabetes clinic of Aminu Kano Teaching Hospital (AKTH), Kano, Northwestern Nigeria.

Methods: We recruited 100 patients with type 2 diabetes attending AKTH. A pretested questionnaire was used to obtain data on socio-demography, duration of diabetes, treatment history and history of hypertension. Patients with liver disease, sickle cell anaemia or other haemoglobinopathies; any acute illness, malignancy and patients on iron or folate containing medications were excluded from the study. We measured anthropometric indices including height, weight, BMI, WC, WHR, waist-to-height ratio (WhtR) and blood pressure using standard methods. Laboratory investigations included serum ferritin, fasting plasma glucose and 2-hour postprandial glucose. Data were analyzed using STATA version 11. A p value <0.05 was considered significant.

Results: Of the 100 patients, 40(40%) were males and 60(60%) were females. The mean (SD) values of BMI, WC, WHR and WhtR were 26.3(5.9) kg/m², 94.5(14.9) cm, 0.98(0.13) and 0.6(0.1) respectively. The mean (SD) duration of DM was 8.6(7.6) years with a range of 1-34 years. The overall prevalence of obesity was 19.8%. The mean (SD) serum ferritin of the study subjects was 79.8(88.1) ng/ml with a range of 20-420 ng/ml. There was negative correlation between BMI and log ferritin (r= -0.02, p=0.01), while WHR correlated positively but not significantly with log ferritin (r=0.21, p=0.48). No correlation was found between log ferritin and duration of diabetes, gender, WC, WhtR, SBP, DBP, FBS and 2HPPG.

Discussion: In this study, we found the prevalence of obesity to be higher among females than males. Studies from other parts of Nigeria have reported similar findings. Of the indices of obesity assessed in this study, only WHR showed positive correlation with log ferritin. No correlation was found between log ferritin and duration of diabetes, gender, WC, WhtR, SBP, DBP, FBS and 2HPPG in our study. The limitations of our study include its cross-sectional design and the relatively small sample size employed which makes generalization of the findings difficult. Patients with subclinical conditions may have been missed.

Conclusion: Of the indices of obesity only WHR correlated positively with serum ferritin in our study.

Abstract #248

SEX AND AGE SPECIFIC ASSOCIATION AND PREVALENCE OF HYPERTENSION IN OVERWEIGHT AND OBESE NORTH INDIAN DIABETIC POPULATION

Rohit Kapoor

Carewell Heart & Superspeciality Hospital

Objective: To determine the prevalence of Hypertension in Overweight and Obese Type 2 diabetic patients and its correlation with age and gender.

Methods: 2644 Type 2 DM subjects, aged between 20 – 80 yrs. were enrolled for this study which is a cross-sectional and co-relational study.

Results: – From total sample of 2644 subjects with T2DM, 52.83% were overweight and 35.39% obese. There was an increase prevalence of overweight in male patients, whereas women had increase prevalence of obesity. According to BMI, it was noted that, there is an increase prevalence of overweight and obesity grade –II in subjects between the age group of 51- 60 yrs., while obesity grade I & III in subjects from 41-50 yrs. age group. SBP was elevated in 70 % in overweight and obese subjects. SBP is slightly high in male but there is no significant difference between genders (P = 0.84). Regarding to elevated DBP, it affects 35.4% subjects, presenting a greater proportion in males with 42.2% compared to 36.3% females. DBP has highly significant association with respect to male gender (P = 0.009). DBP affects in greater proportion the subjects ranging from 51 - 60 yr.

Conclusion: 52.8% of subjects with overweight and obese suffered from hypertension. High SBP has a greater impact in male patients regardless of age. DBP is statistically significant higher in males, specifically when they are in between 51- 60 yrs.
Abstract #249

SEX SPECIFIC ASSOCIATION AND PREVALENCE OF INSULIN RESISTANCE (HOMA-IR) IN INDIAN DIABETIC POPULATION

Rohit Kapoor
Carewell Heart & Superspeciality Hospital

Objective: Determine the prevalence of IR in Indian diabetic population and its correlation with gender and other metabolic factors.

Methods: 250 subjects (131 M / 109 F), between the age of 26–78 years were recruited for the study. After a 12-hour fasting, blood sample was drawn for biochemical measurements including plasma glucose, insulin and lipids. BMI, waist and hip circumference were also measured. IR was assessed according to HOMA (Mathew et al method) and HOMA-IR > 3.98 was used as IR.

Results: The mean±SD age of the sample population was 51.0±11.7yrs (51.3±11.6yrs males & 50.8±11.9yrs females). The BMI (24.8 kg/m² males, 22.7 kg/m² females), mean FPI (14.9 ±19.0 males & 12.5±9.2 females) and overall HOMA-IR (4.9±7.3 males & 4.2±3.8 females) was found to be higher in males than females. The prevalence of IR using HOMA-IR estimated was found to be 33.75 % (34.35% males and 33.02 % females). No significant correlation was found between HOMA-IR and Age, BMI, BP, Lipid profile in both the genders. But in males the correlation of HOMA-IR with FPG (p = 0.001), WC (p=0.013) and HC (0.019) was significant. In females, HOMA-IR was significantly correlated with FPG (p=< 0.0001). FPI was significantly correlated with HOMA-IR in the both genders (p<0.0001).

Conclusion: The study concludes that IR is relatively common in male and has correlation with obesity and FPG. Risk factors for IR should be detected in diabetics for effective preventive measures.

Abstract #250

HYPERTENSION AND SUB CLINICAL ATHEROSCLEROSIS – THEIR CORRELATION WITH METABOLIC RISK FACTORS IN DIABETIC PATIENTS BY AGE

Rohit Kapoor
Carewell Heart & Superspeciality Hospital

Objective: To evaluate correlation of hypertension with pulse wave velocity and other metabolic risk factors in type 2 diabetic population.

Methods: 3700 Type 2 diabetes patients were enrolled in this study. Patients were divided into 3 groups according to their age. Group A - (30-45yrs.) had 759, (499 males/260 females). Group B - (46 – 55 yrs.) had 1123, (697 males / 469 females). Group C - (56 – 65 yrs.) had 627, (364 males/ 263 females). baPWV (pulse wave velocity), Blood Pressure, ABI (ankle-brachial index), HbA1c, Duration of Diabetes, WHR (waist hip ratio), BMI (Body mass Index), Lipids of all the subjects in all age groups were measured. Results: Both SBP and DBP has strong correlation with Age,(p - <0.0001) baPWV (p - <0.0001), Duration Of Diabetes (p - < 0.0001) in all age groups. Younger group of patients (group A) had significant correlation with HDL, WHR, BMI (Obesity).

Conclusion: PWV and hypertension has shown strong correlation in all age groups. Since PWV is a strong future atherosclerotic disease risk marker, regular screening of pulse wave velocity is advisable in all hypertensive diabetic population in all ages to assess atherosclerosis and prevent future cardiovascular risk

Abstract #251

PREVALENCE OF VITAMIN D DEFICIENCY IN TYPE 2 DIABETES PATIENTS IN NORTH INDIAN POPULATION AND ITS CORRELATION WITH DIABETIC COMPLICATIONS AND CO-MORBIDITIES

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Objective: 1. To evaluate Vitamin D levels in type 2 diabetes patients in urban north Indians
2. To study correlations between Vitamin D levels and diabetes complications and co-morbidities in these patients

Methods: This a retrospective study carried out at Diabetes and Obesity Centre in New Delhi, India. A total of 294 adult type 2 diabetes (T2D) patients who had data available for clinical and laboratory parameters, including serum 25-hydroxy vitamin D3 (25(OH)D3 (VitD)) levels, were taken up for the study. Serum 25(OH)D3 level(ng/ml) of more than 30ng/ml was defined as VitD sufficiency; between 21-30 as insufficiency; 10-20 as deficiency; and <10 as severe deficiency. For comparison, patients with diabetes duration less than 1 year were considered recently diagnosed diabetes.

Results: Present study included 167 male and 127 female patients with T2D (n=294). Mean age was 50.32years (+10.05yrs, age group 26-76 yrs). Mean Body Mass Index
(BMI) was 29.29 kg/m² (+6.91) and average duration of diabetes was 7.97 years (+6.9 yrs). Of these 60 patients had recently diagnosed T2D (<1 year duration). Mean serum 25(OH)D3 (Vit D) level was 14.98 (+13.96) ng/ml, with only 25/294 patients (8.5%) {9/167 (5.39%) males and 16/127 (12.6%) females} having Vit D levels more than 30 ng/ml. Mean Vit D level were similar in males (14.32 ng/ml) in males and females (15.85 ng/ml). Vit D deficiency was present in 239/294 (81.3%) patients {136/167 (81.45%) of males, 103/127 (81.10%) of females} and of these 44.22% (130/294) had severe Vit D deficiency. There was no correlation seen between Vit D levels and age (r = 0.13), BMI (r = -0.007), duration of diabetes (r = 0.017), A1c levels (r = -0.018), CAD (r = -0.03), microalbuminuria (r = -0.057), peripheral neuropathy (r = 0.13).

**Discussion:** Recent studies have reported a very high prevalence of Vit D deficiency in T2D patients in North India. However, data is limited. Our study also shows a very high prevalence Vit D deficiency in north Indian T2D patients, with more than 80% T2D patients having Vit D deficiency. We did not find any correlations between Vit D and various co-morbidities and complications in 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 any correlation with age, duration of diabetes, BMI, A1c, CAD, microalbuminuria, or peripheral neuropathy in our study population.

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**Abstract #252**

CORRELATION OF MICROALBUMINURIA WITH OBESITY AND CARDIOVASCULAR RISK MARKERS IN TYPE-II DIABETIC NORTH INDIAN PUNJABI POPULATION

Rohit Kapoor

Carewell Heart & Superspeciality Hospital

**Objective:** Microalbuminuria has been identified as a predictor of renal failure and an independent risk factor for cardiovascular disease in patients with diabetes mellitus as well as in general population. This study was aimed to determine the correlation of microalbuminuria with Obesity and Cardiovascular risk markers.

**Methods:** 2044 Type II diabetes patients were enrolled in the study. Microalbuminuria in all the subjects was estimated and the albumin to creatinine ratio (A:C) was determined. Obesity parameters (BMI, WHR), HbA1c, baPWV, Blood Pressure, ABI, LDL, HDL, TGs of all the subjects were also measured. baPWV was measured with VP-2000/1000-Colin Corporation, (hyayashi komaki Japan). Microalbuminuria was measured Clinitek status Analyzer. (Bayer Health Care).

**Results:** Overall prevalence of microalbuminuria was 58.4% (54.6%M/64.2%F). Microalbuminuria had a highly significant correlation with duration of diabetes (p<0.001), HbA1c and BMI (p<0.05), Systolic and diastolic blood pressure (p<0.01). Positive correlation was found with PWV, ABI, Cholesterol, LDL & TG.

**Discussion:** The high proportion of type 2 diabetes patients with microalbuminuria raises implications for health policy in North India. Screening programs and optimized control of modifiable risk factors are needed to reduce the risk of diabetic nephropathy.

**Conclusion:** The high proportion of type 2 diabetes patients with microalbuminuria raises implications for health policy in North India. Screening programs and optimized control of modifiable risk factors are needed to reduce the risk of diabetic nephropathy.

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**Abstract #253**

RELATIONSHIP OF HYPERGLYCAEMIA AND INFLAMMATION TO OBESITY IN TYPE 2 DIABETES

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**Objective:** The physical, functional and economic burdens of diabetes lies mainly in the enormity of its complications. Obesity is a central factor in the pathogenesis of insulin resistance and hence type 2 diabetes, and also the occurrence of diabetes complications. Hyperglycaemia has also been shown to be a major risk factor for diabetic complications, especially microvascular complications. Inflammation and other non-traditional risk factors are emerging as important contributors to the pathogenesis of diabetes complications.

This study determined the occurrence of obesity among patients with type 2 diabetes and the relationship of hyperglycaemia and some inflammatory markers (high-sensitivity C-reactive protein {hs-CRP} and white cell counts) with obesity.

**Methods:** This is a cross-sectional study involving 155 patients with type 2 diabetes attending an out-patient diabetes clinic. History and anthropometric measurements were taken. Ethical approval was granted by the hospital’s ethical committee and informed consent was given by the participants. Blood sample was collected for determination
ABSTRACTS – Diabetes Mellitus/Prediabetes

of hs-CRP levels, white cell counts (total and differential) and glycated haemoglobin (HbA1c). Generalized and central obesity were defined as body mass index (BMI) ≥30 kg/m², and waist circumference (WC) of >94 cm in men and >80 cm in women respectively. Data was analysed using SPSS 20 version. Correlation between measures of obesity, inflammation and hyperglycaemia was obtained. Statistical significance was defined as p value < 0.05.

Results: Mean age of participants was 56.50 ± 8.01 years. 36 (23.3%) and 116 (74.8%) participants had generalized and central obesity respectively. There was significant correlation between WC and total white cell count (Twbc) (r = 0.184; p = 0.024), and between BMI and Twbc (r = 0.187; p = 0.022) and hs-CRP (p = 0.212; p = 0.028). There was no correlation between WC or BMI and HbA1c.

Discussion: Our study showed significant correlation between Twbc and hsCRP, which are markers of inflammation. Fat depots not only act as energy reserve, but they secrete cytokines and other mediators of inflammation which stimulate production of hs-CRP from the hepatocytes. Cytokines also promote activation and production of white blood cells. Inflammation has been postulated as a major pathogenic pathway for vascular diabetic complications.

Conclusion: This study demonstrates a high occurrence of obesity among people with type 2 diabetes, and significant relationship between measures of obesity and inflammation but not hyperglycaemia.

Abstract #254

ANTI-CCP ANTIBODY IN INDIAN PATIENTS WITH TYPE 1 DIABETES MELLITUS

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Objective: We aimed to investigate the positivity of anti-cyclic citrullinated peptide (CCP) in type 1 diabetes patients positive for anti-glutamic acid decarboxylase and/or anti-protein tyrosine phosphatase (IA2) antibodies.

Methods: Anti-GAD antibody and anti-IA2 antibody levels were measured from newly diagnosed T1DM patients with low C-peptide levels. With either of the antibodies positive, anti-CCP antibody level was measured.

Results: Ninety-four type 1 diabetes patients with low C-peptide and either Anti-GAD antibody and anti-IA2 antibody positive were included in the study. Of these, 16 patients had an anti-CCP level above the reference range. An association between anti-IA2 positivity and anti-CCP positivity was found with an odds ratio of 11.82 (95% CI: 2.50-55.78). Also, 7 of the 16 anti-CCP positive cases did not have symptoms of rheumatoid arthritis.

Conclusion: In Indian patients with type 1 diabetes mellitus, anti-IA2 positivity correlates with anti-CCP positivity.

Abstract #255

PATTERN OF GESTATIONAL DIABETES IN NIGERIA USING THE NEW WORLD HEALTH CRITERIA

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Objective: Diabetes complicating pregnancy is associated with adverse maternal and perinatal outcomes. Lesser degrees of glucose intolerance have also been shown to be harmful. However, how one defines what constitutes glucose intolerance in pregnancy has been an issue of considerable international controversy, both in clinical practice and research in the past three decades. In order to achieve a uniform/universal diagnostic criteria for hyperglycaemia in pregnancy, the World Health Organization in 2013 published a new guideline. The study was set out to determine the pattern of Gestational Diabetes in Port Harcourt, Nigeria.

Methods: A prospective study amongst antenatal attendees with a 75 gram glucose load and obtaining fasting of (5.1-6.9 mmol/L), 1 hr (≥10.0 mmol/L) and 2 hr (8.5-11.0 mmol/L) glucose values: one value being sufficient for diagnosis; and associated anthropometric and clinical factors including primary and secondary outcomes.

Results: Results revealed that 26.5% had a family history of Diabetes while 12.9%, 7.6%, 11.4% were diabetic using FBG, 1Hr PPG and 2Hrs PPG respectively of the new WHO CRITERIA. The overall prevalence of GDM in the study population was 15.2%. The outcomes of the study showed poorer outcomes as per caesarean section rate, fetal macrosomia, neonatal hypoglycemia, need for neonatal intensive care and preeclampsia for those diagnosed with GDM. The following outcomes were statistically significant (p<0.001) for the GDM cases: fetal macrosomia (70.6%), caesarian section (67.6%), neonatal hypoglycaemia (55.9%), need for neonatal intensive care (47.1%), and preeclampsia (44.1%).

Discussion: The three key biochemical parameters viz: FBG, 1HR PPG, 2HRS PPG where all useful in diagnosing GDM in this Nigerian study, thus underscoring the new evidence –based WHO criteria.

Conclusion: Diabetes Association of Nigeria has adopted these guideline and is translating the recommendation into clinical practice.
Abstract #256

PATTERN AND PREVALENCE OF CARDIOVASCULAR DISEASE IN PATIENTS WITH TYPE 2 DIABETES AT THE UNTH ENUGU NIGERIA

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Objective: Cardiovascular disease (CVD) is said to be common in patients with diabetes, and is regarded as a major cause of mortality in them. Previous studies in our environment had reported hyperglycaemic emergencies as the major cause of DM related mortality. There have been very few studies on CVD in patients with diabetes. The aim of this study was to determine the pattern and prevalence of major cardiovascular disease in patients with type 2 diabetes mellitus.

Methods: Fifty-one patients with T2DM were recruited. Socio-demographic data, risk factors and past history of CVD were extracted from the study participants using questionnaires. Anthropometric measurements were done. The glycosylated haemoglobin (Hba1C), lipid profile and fasting plasma glucose were measured. A portable doppler device was used to measure the ankle brachial index (ABPI) and Electrocardiogram (ECG) was done in 30 participants. Data was analyzed using SPSS version 21.

Results: The female: male ratio was 1.42:1. The mean (SD) age was 62.5(9.9) years, median (IQR) duration of diabetes was 7.0 (10) years. Past history of stroke was reported in 2(3.9%), heart failure in 2(3.9%). Cardiovascular risk factors were hypertension in 32(62.7%), obesity in 16(31.4%) and dyslipidaemia in 42(82.4%). Their mean Hba1C was 8.9(2.5)%, and 26(50.9%) had Hba1c > 7.0%. Features of peripheral artery disease (PAD) were present in 34(66.7%), cardiac ischaemia on ECG in 8 out of 30(26.7%). Peripheral artery disease was not associated with hypertension (p=0.39), age (p=0.36), gender (0.48) or glycaemic control (0.28). Ischaemic heart disease (IHD) was not related to age (p=0.87), gender (p=0.22), hypertension (p=1.0). PAD and IHD were significantly related (p=0.02).

Discussion: The patients were mostly elderly, with long-standing diabetes mellitus. PAD was the most common form of CVD and was significantly associated with IHD. This has been similarly reported in other studies, which showed high prevalence of PAD. ECG evidence of IHD was fairly common, though not related to hypertension or age as expected, suggesting that DM itself is a more significant risk factor.

Conclusion: Peripheral arterial disease was the most common CVD in the subjects, while stroke was the least common.

Abstract #257

INSULIN USE ON THE TOP OF THE WORLD

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Results: Along with modernization, diabetes has reached the remote Himalayan areas of Lahaul-Spiti and Kinnaur, in the Indian state of Himachal Pradesh, located in the upper reaches of the Western Himalayas. Inhabited predominantly by the tribal population, these districts are located at an altitude of 8000-16,000 feet above sea level. The unique geographic conditions and dietary patterns, which include drinking of copious amounts of liquor, dependence upon local non-vegetarian foods, go against routine diabetes diet prescriptions. These tribal areas remain cut off from the rest of the country at least for 3-4 months in the winters. People living with diabetes usually seek specialized diabetic care from the state capital, located 250-500 km away (most treacherous road in the world). The challenges posed by diabetes on top of the world have been addressed in an innovative manner. Three patients from tribal areas living at an “altitude” of 9500, 12000 & 14500 feet at a distance of 250 & 550 Km from state capital were prescribed insulin for uncontrolled blood sugar. The unique geographic condition of these areas, and peculiar social habits and dietary patterns of the inhabitants, impose unique challenges for the use of insulin in this part of the world. Besides having the danger of hypoglycemia, however, the biggest challenge remains how to store insulin in the winter when outside temperature dips to minus 30°C mostly during midnight and inside temperature of the living room, goes up to 40°C to 70°C due to constant burning of “Bukhari” made up of iron. In winters, people of these areas wear warm clothes made up of sheep and yolk wool. One such unique cloth women wear in the winter is an abdominal binder (2-3 feet in width and 5-15 feet in length). Seeing a woman wearing the traditional attire in a hospital, an innovative idea of insulin storage that was “locally” relevant and easily acceptable came to my mind: “It was planned to store insulin in multiple layers of abdominal binder, which prevents it from freezing in winter”. On their follow-up visit, they were advised to “wrap the insulin vials and/or pens in "multiple layers" in the abdominal binder (where the temperature recorded was between 5-10°C). The
success of this practice is evident from the normal HbA1c values, and the smiles on their faces, when they visit state capital for routine medical consultation.

**Conclusion:** Normally; we think of living with diabetes at normal altitude, not for those living in the extreme conditions of the world; one like those living “in the Himalayas” and this improvised method of insulin storage may be of great value for those diabetic patients living at top of the world.

**Abstract #258**

**SUBCLINICAL ATHEROSCLEROSIS & LEFT VENTRICULAR DIASTOLIC DYSFUNCTION - THEIR CORRELATION IN INDIAN T2DM PATIENTS**

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**Objective:** To assess the correlation of LVDD with CIMT (carotid intima media thickness) and baPWV - the subclinical atherosclerotic risk markers.

**Methods:** 565 diabetes mellitus, aged between 35-75 years were evaluated for left LVDD using Doppler Echo. LVDD was determined by using conventional 2-D echo and Doppler techniques & LVDD was graded as grade I, II, III & IV as per standard norms. Parameters such as CIMT, baPWV, ABI, SBP, DBP, Lipid Profile, HbA1c, Duration of diabetes, WHR were included. LVEF was considered as a measure of systolic dysfunction.

**Results:** LVDD was observed in 84.6% of patients. Predominant pattern was abnormal relaxation (58%) with highest in age group of 35 -73 yr. Out of 565 patients studied, total 478 (84.6%) had LVDD, 347 patients (69.4%) had (Grade 1 DD), 104 patients (20.8%) had (Grade 2-), 27 patients (5.4%) had (Grade 3). 87 out (15.4%) had no evidence of diastolic dysfunction. LVDD was found to have significant correlation with SBP (p= 0.015), ABI (p= 0.034), LDL (p= 0.06), HDL (p= 0.07) and TG’s (p= 0.18). Correlation of LVDD with PWV & CIMT is found to be mild significant

**Conclusion:** LVDD had mild correlation with CIMT & PWV in this group of population. Since both CIMT & PWV are future cardiovascular risk markers, such correlation warrants screening of diabetic population for these atherosclerotic risk markers for prevention of future cardiovascular risk. However, larger study is needed to observe more correlation between these parameters.

**Abstract #259**

**HOW WELL DOES SINGLE PILL COMBINATION VILDAGLIPTIN-METFORMIN COMPARE WITH METFORMIN-GLIBENCLAMIDE IN THE TREATMENT OF TYPE 2 DIABETES MELLITUS AMONG BLACK AFRICANS?**

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**Objective:** The use of Vildagliptin-Metformin (VM) compared to Metformin-Glibenclamide (MG) in type 2 diabetes mellitus (T2DM) among black Africans has not been evaluated. We aimed to compare the efficacy, tolerability and side effects profile of VM combination with MG combination in T2DM Africans resident in Kano, North-West Nigeria.

**Methods:** In a prospective open-labeled randomized comparative out-patient study of T2DM patients at the diabetes clinic of Aminu Kano Teaching Hospital, subjects were randomised to two treatment groups - VM (Group 1) and MG (Group 2). Socio-demographic, clinical and laboratory parameters were measured at baseline (study beginning), 6 weeks and 12 weeks for both groups and compared for efficacy, tolerability and side effects. Efficacy was defined as change in measured glycated haemoglobin (HbA1c) at baseline compared to end of study (12 weeks). Tolerability (attrition due to unbearable side effects) and frequency of side effects were also assessed.

**Results:** Sixty subjects were recruited but only 54 (26-VM, 28-MG) completed the study. The mean age of all subjects was 50.39±7.94 years. The mean age, duration of DM, body mass index, and HbA1c of the subjects in both groups at baseline were comparable, p > 0.05. The improvement in BMI of subjects in group 1 (30.02±4.16 at baseline, 29.71±4.12 at study end) was better than that of group 2 (31.98±6.32 at baseline, 32.62±6.30 at study end), p=0.04. The mean FPG, 2-hrPP glucose, and HbA1c of all subjects in both groups improved at study end comparably. At end of study, the efficacy of VM (HbA1c- 7.22±1.20%) was comparable to that of MG (HbA1c- 7.25±0.96), p=0.92. The tolerability of MG (attrition 6.7%) was better than that of VM (attrition 13%). The subjects on VM experienced more gastrointestinal side effects than those on MG while the major side effects experienced by those on MG was hypoglycaemia and weight gain.

**Discussion:** The reduction in HbA1c was similar to an
Iraqi study by Hassan et al which reported a 1-2% drop in HbA1c with MG after 3-6 months. Bluher et al also observed a significant reduction in HbA1c with VM at 3 months of treatment. VM was less tolerable and had more GIT side effects than MG. Although the efficacy of VM and MG was comparable, the choice of therapy in type 2 DM should be individualised considering patient peculiarities (presence of co-morbidities, side effect profile, cost of drugs and sustainability of use).

**Conclusion:** The efficacy of VM versus MG among black Africans from Nigeria is comparable. The use of VM was less tolerated and had more GIT side effects than MG. The use of single pill combination oral antidiabetic medications is associated with improved efficacy but must be individualized.

**Abstract #260**

**EFFECTS OF ENDOTHELIN RECEPTOR ANTAGONIST ON VEGF SIGNALING IN DIABETIC PENIS: A POSSIBLE CLINICAL IMPLICATION FOR DIABETES ERECTILE DYSFUNCTION**

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**Objective:** Erectile dysfunction (ED) affects about 50% of male diabetic patients possibly due to the vascular and neuropathic complications. The imbalance between vasoconstrictors and vasodilators may play an important role in the pathogenesis of erectile dysfunction. Vascular endothelial growth factor (VEGF) has been extensively documented for its pathogenic significance in different complications of diabetes and we have already reported that VEGF signaling is greatly diminished in penis in a rat model of type II diabetes. Endothelin (ET) activity is also altered in atherosclerotic and ischaemic disease, nephropathy, retinopathy, erectile dysfunction, and neuropathy, many of the well-known complications of diabetes. The present study used a three weeks duration of streptozotocin (STZ)-induced diabetic (DM) rat model to assess the VEGF expression with NO system in penile tissue and concomitantly the effects of endothelin antagonism has been studied on these changes.

**Methods:** Male Sprague-Dawley rats were administered citrate saline vehicle or STZ (65 mg/kg IP). One week after the injection, animals were separated into those receiving endothelin-A/B (ET-A/B) dual receptor antagonist (SB209670, 1 mg/kg/day), endothelin-A (ET-A) receptor antagonist (TA-0201, 1 mg/kg/day) or saline for 2 weeks by osmotic mini pump. After 2 weeks treatment, rats were sacrificed under anesthesia and the penile tissue was removed. The present experimental design was approved by the Tsukuba University School of Medicine Animal Care and Use Committee.

**Results:** The local ET-1 level in DM penis was higher by 20% than non-DM rats. ET-1 receptor A (ETAR) in penile tissue in early diabetes was increased by 27% and was remarkably downregulated by ET antagonism. ET-1 receptor B (ETBR) expression was downregulated in early DM penis and were recovered by ET antagonists. A 30% decrease in VEGF expression in penile tissue was seen in DM rats. Penile NO and eNOS level was decreased in DM rats; greatly restored by ET-A receptor antagonist while unchanged by ET-A/B dual antagonist. iNOS was not significantly changed in penile tissues among non-DM, DM and ET-A antagonist treated groups.

**Conclusion:** Thus, we conclude that (1) VEGF and pAkt were downregulated in type 1 DM penis, and that (2) the ET-A antagonist was potentially effective in reversing the decreased NO and eNOS levels in DM penis than those by ET-A/B dual antagonist. From these findings, it can be stated that ET antagonism might be beneficial to normalize the components of ET and NO systems, in early DM penile tissues. And also effective in normalizing the decrease in VEGF in early DM penile tissues.

**Abstract #261**

**ANTIMICROBIAL RESISTANCE PATTERN AMONG DIABETIC PATIENTS WITH URINARY TRACT INFECTION AT BANGLADESH**

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**Objective:** Diabetes mellitus (DM) is a worldwide health problem with an expected prevalence of 593 million by 2035. Urinary tract infection (UTI) is the most common infection among patients with DM and is responsible for considerable morbidity. Due to the emergence of
multidrug resistant (MDR) uropathogenic strains, the choice of antimicrobial agent is sometimes difficult. This study is designed to reveal the distribution of uropathogens in Diabetic patients and corresponding resistance patterns and to correlate the microbiological results with various clinical parameters.

Methods: A nine month retrospective review of 100 urine culture reports of Diabetic patients from January 2015 to September 2015 from semurban multispeciality hospital of Feni were analyzed. Only Diabetic patients were included in this study who were clinically diagnosed as UTI patients with a corresponding urine culture showing a bacterial count of more than 105 cfu/ml. Clinical data was obtained from each patients using a well structured questionnaire. Data was analyzed using the SPSS statistics 21 software.

Results: Out of 100 patients with UTI, 39 (39%) were male and 61 (61%) were female. Organisms grown in urine culture were Escherichia coli (64) followed by Klebsiella (11), Proteus (7), Staph Aureus (4), Pseudomonas (4), Acinetobacter (3), Sreptococcus (3), Enterococcus (2) and one each of Enterobacter and Fungi. Overall resistance pattern in decreasing order of various commonly used antibiotics were Amoxicillin (84%), Quinolones (72%), Cefixime (61%), Cefuroxime (39%), Ceftriaxone (32%), Amikacin (19%), Nitrofurantoin (14%), Meropenem (11%). Antibiotic resistance was more with patients having HbA1c more than 7 %. 61 (61%) of patients did not present with fever but had pus cells in urine. 46 (46 %) of patients did not have dysuria as urinary symptoms.

Discussion: This study revealed that Escherichia coli and Klebsiella were the most prevalent pathogens followed by Proteus, Staph Aureus, Pseudomonas, Acinetobacter, Sreptococcus. The most effective antibiotic overall was meropenem followed by nitrofurantoin and amikacin. The once blockbuster antibiotics such as Amoxicillin, Quinolones, Cefixime, Cefuroxime, Ceftriaxone showed resistance with 84%, 72%, 61%, 39%, 32% resistance respectively. Less symptoms but significant laboratory findings are noted, especially in uncontrolled Diabetics.

Conclusion: The significance of the study lies in the determination of common pathogens in diabetic patients with UTI and the resistance pattern of antibiotics so that physicians and pharmacists get the proper information rationalizing the rational use of antibiotics.

Abstract #262

OPTIMIZING VITAMIN D LEVELS AND IMPROVEMENT IN GLYCAEMIC CONTROL: AN OBSERVATIONAL STUDY FROM INDIA

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Objective: There is a dearth of long term follow-up data from India on vitamin D status in diabetes patients and effect of vitamin D status on glycemic control.

Methods: We followed up 2134 diabetes patients presenting at our centers for an year (34% female; age in years M:53.1, SD: 11.8). Vitamin D status was similar amongst male & female patients, with overall 60% deficient (<20ng/ml), 27% (21-30ng/ml) and 12% normal (30-80 ng/ml). Patients were given comprehensive treatment for diabetes, dyslipidemia, hypertension, vitamin D deficiency, etc. as applicable, with telemedicine-based diabetes care. 599 patients visited the clinic again within an year.

Results: At the second visit, only 23% were vitamin D deficient and 45% had normal values. Average HbA1c was 7.7+/-.1.8 at first visit and 7.1+-/ 1.5 at second visit.

Discussion: A multilinear regression with Hba1c as outcome and age, sex, insulin use, BMI, and vitamin D status (deficient, low, normal) as predictors showed statistically significant effect of final vitamin D status on final HbA1c level (β=-0.12, se=0.06,p=0.04).

Conclusion: Vitamin D status may be optimised for better glycemic control and further well-designed studies are needed to elucidate the level of effect.

Abstract #263

VITAMIN D AND ENDOTHELIAL DYSFUNCTION IN TYPE 2 DIABETES MELLITUS

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Objective: Vitamin D deficiency may be responsible for endothelial dysfunction which in turn affects the onset and progression of vascular disease including coronary artery disease and its risk factor, directly or indirectly through
various mechanisms. This study was undertaken to find out association between vitamin D and endothelial dilatation of brachial artery, which may help to suggest possible underlying mechanisms and may be of clinical importance in planning preventive and therapeutic strategies.

Methods: 50 cases of type 2 diabetes mellitus aged 40-60 years were taken. 50 cases without type 2 diabetes mellitus matched for confounding factors were taken as controls. Venous blood samples were collected for the investigations including vitamin D levels. Then Participants were subjected to ultrasound examination for measurement of flow mediated dilatation (FMD) and endothelial independent dilatation after ingestion of glyceryl tri-nitrate (GTN). Unpaired student T test and correlation coefficient analysis were used to find out association between different variables.

Results: The mean values of FMD were 18.85 ± 5.39% and 10.29 ± 4.91% in controls and cases respectively (p<0.001). The dilatation after GTN was observed to be 26.16 ± 4.25% and 18.74 ± 5.72% in controls and cases respectively (p<0.001). The mean levels of vitamin D among controls and cases were 25.41 ± 12.18 and 14.52 ± 8.28 ng/ml respectively.

Discussion: The correlation between endothelial dependent dilatation (FMD), endothelial independent dilatation (after GTN) and vitamin D was found to be more positive in cases (r=0.870, r=0.798) than controls (r=0.079, r=0.158).

Conclusion: Vitamin D deficiency state is higher among cases of type 2 DM. Endothelial dependent dilatation (FMD) was found to be lower among the patients of type 2 DM. The study gives us an insight to identify the diabetics with vitamin D deficiency which may be at higher risk of vascular complications including coronary artery disease.

Abstract #264

THE GLYCAEMIC INDEX OF AND THE INSULIN RESPONSE TO SOME INDIAN FOOD ITEMS

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Objective: Blood glucose and insulin responses to various forms of carbohydrates is called Glycaemic Index (GI). It is the area under the plasma glucose response curve for a test food divided by area under plasma glucose curve for an equivalent amount of carbohydrate derived from standard reference food taken by same individual x 100. It helps to identify beneficial foods for diabetics. We studied the GI of, and the insulin responses to some food items consumed by Indians.

Methods: 55 newly diagnosed, drug naïve, Type 2 diabetics were studied in a tertiary care center in India. The reference food was glucose and foods tested were rice, sago, chapathi, white bread, millet bread, Bengal gram, apple, potato, milk and ground nuts. Each had 50 gms of carbohydrates.

On test day, glucose was given with 300 ml water. Apple, banana and ground nuts were taken with 1/2 teaspoon salt and 300 ml water. White bread given with 2 gms of butter. Randomly patients were divided into 11 groups, 5 in each. Each group was given 1 of 11 test food items. All had a standard OGTT using 50 gms glucose, venous blood was taken at 0, 30, 60, 90 and 120 minutes for the estimation of glucose and insulin. After 2 days, the procedure was repeated using the test foods (FTT).

Results: Study comprised of 38 males and 17 females with ages ranging 30 to 60 years (mean 46.9). The GI of each food was less than 100, this being the GI of the reference meal (i.e. glucose). There were considerable intra-food variations, least with chapathi, and highest with sago. Low mean values were observed with Bengal gram, apple and banana. The highest mean GI (95.3) was of millet bread. 3 patients didn’t produce any measurable glycaemic response to milk.

Comparison of the various mean GIs by analysis of variance (ANOVA) revealed a significant difference (P<0.01). A Scheffe’s correction was applied and the significant difference was between Bengal gram and potato (p < 0.05).

Discussion: The food items may be categorised into low, medium and high glycaemics. Bengal gram, apple, banana, ground - nuts and milk have low glycaemic indices of 13.3, 21.4, 24.9, 36.5 and 26.8 respectively. Wheat chapathi, potato and millet have high GI’s of 79.4, 77.2, 95.2 respectively. Rice, sago and white bread have intermediate indices.

We found a positive correlation between the GI and insulin response since the Kendall’s coefficient of rank correlation T (tau) was determined to be +0.61.

Conclusion: We recommend that diabetic diet includes Bengal gram, banana, apple, rice, sago and white bread which have low glycaemic indices. The glycaemic index of rice is lower than of wheat chapathi and millet bread. Therefore, the exclusion of rice and other item of similar glycaemic indices not justified.
Abstract #265

COMPLICATIONS AND COMORBIDITIES IN POVERTY ASSOCIATED CHILDHOOD DIABETES IN INDIA.

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Objective: To analyze the course, complications and comorbidities of a cohort of underprivileged children with diabetes [onset 1-18 y] in India [2011-2015].


Results: I. Type 1 Diabetes 95%; II. Type 2 Diabetes 1% (discontinued insulin on follow-up); III. Other Specific Types 4% [A. Monogenic Diabetes: Permanent Neonatal Diabetes 5 (Wolcott Rallison syndrome 1; Insulin gene mutation 1; under genetic analysis 3); Wolfram syndrome 2; D. Chronic pancreatitis 3]; IV. Gestational Diabetes Mellitus 0%.

Age onset T1DM: Mean 9.6y [0-5 y: 20%; 6-10 y: 34%; 11-15 y: 39%; 16-18 y: 7%]. Duration Diabetes: 8.6y; Rural: Urban = 48: 52. Follow up 3 y.

HbA1C trend (%): Improvement-- 39%; Stable-- 50%; Worsening-- 11%

HbA1C Value:
- At Enrollment: HbA1C <8% --11; HbA1C 8.1—10% --24; HbA1C >10% --65
- Latest: HbA1C <8% --23; HbA1C 8.1—10% --34; HbA1C >10% -- 43

Nephropathy trend (%): On ACE inhibitors/ARB = 25%

Albuminuria:
- At enrollment: Normoalbuminuria—60; Microalbuminuria—32; Macroalbuminuria—8
- Latest: Normoalbuminuria—66; Microalbuminuria—27; Macroalbuminuria--8

Retinopathy: Non-proliferative: 3%; Proliferative 1%.

Hypothyroidism: 21% [At enrollment 14%; new diagnosis 7%].

Acute myocardial infarction: One 20 y girl with T1DM from age 4 y.

Growth Groups % Prevalence [% New Hypothyroid]:
- Improved 26 % [0]; Stable 64% [6]; Decline 10% [33]. “Growth decline” was associated with younger age [prepubertal], better initial height and weight SDS and higher prevalence of newly diagnosed hypothyroidism. On follow up, this group demonstrated decrease in height and weight SDS and lesser improvement of HbA1c.

Discussion: Childhood onset diabetes in economically underprivileged in India is almost exclusively type 1 [cf: type 2 diabetes in (affluent) children 16-46 % USA; ? India - but increasing]. Philanthropy based systematic highest possible standards of medical care, resulted in improvements in glycemic control and decrease / retardation of acute and chronic complications of childhood type 1 diabetes in a resource limited setting.

Conclusion: Dedicated combination of physical [insulin, BG meters/strips, and medical care] and “spiritual” [empathy and love] support can positively change the natural history of the disease and foster better health, overall well being and longevity of economically underprivileged type 1 diabetes children in India and world over.

Abstract #266

VASCULAR CONTINUUM OF COMPLICATIONS IN TYPE 2 DIABETES MELLITUS- A DECADE OF TIME FRAME EXPERIENCE

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Objective: Tight glycemic control does limit microvascular disease while macrovascular out comes remain shrouded with controversy. We emphasize a unique continuum bridging the microvascular and the macrovascular risk which is based on our evidence based studies consistently over a decade.

Methods: We collate the results from our studies conducted at our specialized premier diabetes care centre in North India, which have been presented as evidence based perspectives over last one decade and summarize to correlate to provide the contemporary insights.

Results: Prevalence of Diabetic retinopathy (DR) at our centre is 21.2%, with HbA1c, BMI, duration of diabetes and microalbuminuria as significant risk factors in the development of DR (p=0.001). Diabetic Neuropathy (DN) prevalence is reported as 15.3% across 720 patients. We
reported the association of DN, DR and microalbuminuria in 855 patients in 2011-2012. Diabetic cardiac autonomic neuropathy (CAN) had strong co-association with DR (22% vs. 14.3%), DN (14% vs. 6.8%) & poor glycemic control in our study in 2012. A positive correlation was established between autonomic neuropathy (AN) and peripheral neuropathy (p = 0.00014) in 2010. Association between AN and peripheral vascular disease (PVD) did not reach statistical significance. A direct relationship of PVD (7.4%) with duration of T2DM was documented by us in 2004. In 2004-05 we reported a strong association between microalbuminuria with DR in 50 newly diagnosed diabetics. We also documented impaired FMD as a marker of Endothelial dysfunction in Diabetics and in IGT in 2004. Discussion: Our decade of evidence based perspectives provides contemporary insights into the clinical, pathological and mechanistic correlates which demystify the complex interactions between the microvascular and macrovascular complications. Neovascular microangiopathy is an important pathological link between the microvascular and the macrovascular complications. The pathogenic mechanisms underlying diabetic nephropathy involve generation of ROS, accumulation of AGEs, and activation of intracellular signaling molecules such as protein kinase C. We propose a model of vascular continuum for the complications in diabetes. Conclusion: Our work highlights the need for implementing programs for early detection, screening and awareness to mitigate the burden of managing the complications. We recommended CAN evaluation at the time of T2DM diagnosis and thereafter annually. Glycemic control improves microvascular disease and should be implemented early, with blood pressure monitoring and effective dyslipidemia management to prevent macrovascular disease. Large scale interventional research would further strengthen our vascular continuum hypothesis.

Abstract #267

USE OF A REAL TIME CONTINUOUS GLUCOSE MONITORING SYSTEM AS AN EDUCATIONAL TOOL FOR PATIENTS WITH GESTATIONAL DIABETES

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Objective: Women with gestational diabetes mellitus (GDM) are required to control their blood glucose shortly after GDM diagnosis to avoid adverse pregnancy outcomes. This requires disease awareness by pregnant women and self-control of their blood sugar. However, these women usually have no experience in diabetes management and are less knowledgeable on blood glucose self-control. Real-time continuous glucose monitoring systems (RT-CGMS) provides the patient with continuous information about the alterations in his/her blood glucose levels throughout the day, which is immediately revealed to the patient, and helps the patient to understand how food, exercise, and insulin affect blood glucose. This visibility may empower the patient to modify his/her lifestyle and engage in therapeutic management. The purpose of this study is to determine whether a single application of a RT-CGMS to pregnant women shortly after GDM diagnosis is useful.

Methods: Design and setting: Prospective, open label randomized controlled study conducted at Maternity and Children Hospital, Medina, Saudi Arabia. Participants: 130 pregnant women with GDM were allocated to either the routine care with self monitoring of blood glucose (SMBG) alone group (n = 62), or the use of RT-CGMS in addition to the routine care (n = 68). Intervention: A single application of 3-7 days RT-CGMS within 2 weeks of GDM diagnosis in the RT-CGMS group. Main Outcome Measurement: The primary outcome was the parameters of glucose variability included mean sensor readings, the standard deviation (SD) of blood glucose, and the area under the curve for hyper and hypoglycaemia at the end of the RT-CGMS. Secondary outcomes were maternal glycemic control and pregnancy outcomes.

Results: There was significant improvement in the parameters of glucose variability on the last day of sensor application, both mean glucose and SD of glycemia were reduced significantly; P=.016 and P=.034 respectively. Although, the area under the curve for both hyper and hypoglycaemia were improved, the results did not reach statistical significance. At the end of the pregnancy; HbA1c, mean fasting and postprandial glucose levels, and frequency of hypo- and hyperglycemia were similar in both groups; except for lower glucose levels post lunch in the RT-CGMS group. Maternal and neonatal outcome were also comparable.

Conclusion: A single application of RT -CGMS shortly after GDM diagnosis can be used as an educational and motivational tool for pregnant women with GDM. However, this was not associated with improvement in glycemic control or pregnancy outcome.
Abstract #268

EFFECTIVENESS OF DAPAGLIFLOZIN IN ASIAN INDIAN TYPE 2 DIABETES PATIENTS – REAL WORLD EXPERIENCE

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Objective: Dapagliflozin is the first SGLT-2 inhibitor introduced in India in April 2015. We retrospectively assessed the effectiveness of dapagliflozin in Asian Indian patients with type 2 diabetes. Our primary objective was to study the change in HbA1c and secondary objectives were the change in body weight, blood pressure and decrease in the ongoing therapy requirements.

Methods: We evaluated the real world efficacy and safety of dapagliflozin amongst the continuous dapagliflozin users (defined as continuous treatment at 12 weeks). It was used as an add on drug to the ongoing therapy. The data was collected retrospectively from patient records. Data is presented as mean± SD and comparison between the groups has been done using Mann-Whitney and Fisher’s exact test.

Results: The study participants (n=59) had a mean age of 54.2 ± 10.56 years, diabetes duration 13.2 ± 7.9 years (CI 11.2-15.3), body weight 77.3 ± 12.8 kg (CI 74.4-81.1), BMI 30.2 ± 4.6 kg/m2 (CI 29-31) and HbA1c of 8.6 ± 1.5% (CI 8.3-9.1). HbA1c reduced significantly as compared to the baseline (7.6 vs 8.7%, difference -1.1) (p<0.0001). The proportion of patients attaining the goal of Hba1c level < 7.0% trebled (5 patients to 15 patients) after 12 weeks. The mean reduction in the body weight, blood pressure and decrease in the ongoing therapy requirements. The mean reduction in systolic and diastolic BP and weight in the Indian setting for improved glycemic control; with adverse events consistent with previous studies. Only 1 patient reported mild urinary tract infection; none developed diabetic ketoacidosis or severe urosepsis after 3 months of use. Dapagliflozin is useful in the Indian setting for improved glycemic control; with additional reduction in systolic and diastolic BP and weight. Dapagliflozin can be effectively and safely combined with other agents, including insulin, sulphonylureas, metformin, DPP4 inhibitors; and can be used either as monotherapy, or in dual or triple agent combinations. Our study is limited for a short follow up. However, this is perhaps the first largest real time, interim evaluation of the effectiveness of dapagliflozin in Indian setting.

Abstract #269

GENETIC ANALYSIS AND CLINICO-GENETIC CORRELATION OF NEONATAL DIABETES IN A COHORT OF 12 CHILDREN FROM SOUTH INDIA

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Objective: To study and report the molecular genetics, clinico-genetic disease correlation, suitability of current treatment regimens and treatment outcomes of 12 children with neonatal diabetes from a single centre in South India.

Methods: Neonatal diabetes was defined as “A Diagnosis of Diabetes prior to 9 months of age. “Ages at recruitment ranged from 5 days to 18 years. Detailed history and investigations were obtained and included HbA1c, blood glucose, liver and renal function tests and autoimmune markers. Genetic samples were sent to the Genetics Lab of University of Exeter Medical School.

Case Presentation: Genetic mutations were identified in seven of the twelve children. 2 children had mutations in INS gene (INS missense mutation, p.R89C; a novel INS intronic mutation, c.188-40C>A), one child in ABCC8 (ABCC8 nonsense mutation, p.W232*, and an ABCC8 missense mutation, p.P254S) and two in KCNJ11 (KCNJ11 missense mutation, p.R201C, heterozygous missense mutation, p.E229K). In another infant with a mutation in KCNJ11, (novel KCNJ11 missense variant, p.R29H) a causal association of the mutation with diabetes could not be proven. Another girl had a homozygous deletion of exons 2-8 of IL2RA gene and further analysis is being carried out. Two children with INS mutations and the child without an identified mutation have been continued on insulin. ABCC8 and KCNJ11 mutation children are being transitioned onto Sulphonylurea. The father of the girl with KCNJ11 p.R29H variant also has the same mutation and was diagnosed with diabetes one year ago. This mutation has been associated with transient/adult onset diabetes. The neonate with the non-causal KCNJ11 mutation died on 11th day of life, of a massive cerebral infarct, most probably consequent to very high blood sugars at presentation. The neonate with IL2RA gene...
mutation expired due to sepsis meningitis.

**Discussion:** The mutations in cohort were heterogenous and could not be identified in five children. Transition to Sulphonylureas was also not complete in any of the children started on Sulphonylureas. These findings suggest that the mutations and treatment outcomes in Indian children could probably be quite different from those in the previously extensively studied Caucasian and Arab populations.

**Conclusion:** With proper genetic analysis, research findings can be translated into accurate treatment decisions and good clinical outcomes; especially, the outcomes of transition onto sulphonylurea can be improved. Mutations in Indian children seem quite different and multicentre nation/region wide studies are necessary for further analysis.

**Abstract #270**

**ABNORMAL GLUCOSE METABOLISM AMONG TUBERCULOSIS PATIENTS ON TREATMENT: ITS PREVALENCE AND RISK FACTORS IN NIGERIA**

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**Objective:** Tuberculosis (TB) is a chronic infectious disease, the incidence of which is decreasing worldwide however, the control of TB is threatened by the high prevalence of diabetes (DM), HIV, global poverty and unhealthy lifestyle. The DM patients, have a defective phagocytic function leading to impaired innate and adaptive cellular mediated immunity which increases the risk of TB infection by 2–3 fold. The TB infection induces transient hyperglycaemia with consequent increase in prevalence of overt DM among subjects especially in those with identified risk factors. The coexistence of these two chronic conditions will put an enormous burden on the patients especially in a poor resource setting countries. The prevalence of DM in patients with TB among different population groups was found to be 1.9% to 29%. We intended to document the prevalence of DM, impaired fasting glycaemia (IFG) and their clinical characteristics among TB patients on treatment with the aim of identifying this class of patients early so as to reduce the complications and cost of managing them.

**Methods:** This was a cross sectional study involving 140 TB patients, on at least two weeks of treatment, consecutively recruited from 2 public DOT treatment centres in Jigawa State of Nigeria. All the patients consented, proforma forms were filled, anthropometric and physical examination was performed. Their fasting venous plasma was analyzed for glucose using glucose oxidase method and their urine tested for glucose and protein. The WHO criteria for diagnosis of DM (FBG >7.1mmol/L) and IFG (FBG>5.7<7.0mmol/L) was used. Student T-test was used to compare means while chi square was used for proportions. values are considered significant at P<0.05.

**Results:** Of the 140 subjects, 26(20 males, 6 females) were found to have FBG > 7.1mmol/L and of this, 8 have pre-existing DM before the commencement of TB treatment, therefore, giving a prevalence of 12.8% (18/140), 28 subjects have IFG (FBG>5.7<7.0) or a prevalence of 20% (28/140). The age and BMI were significantly higher in the TB with DM group than in the TB without DM group. Also there was a significant glycosuria and proteinuria in TB with DM group X2 = 13.7, 4.4 p<0.05 respectively.

**Discussion:** The prevalence of DM in patients with TB is high 12.8% when compared with the average national DM prevalence of 6-8% in Nigeria. There is a need to consider screening all TB patients for DM for early detection and management so as to reduce the dual burden of these chronic conditions.

**Conclusion:** It is concluded that the coexistence of DM and IFG in TB patients in Nigeria is significantly high (12.8% and 20%) majority are males, obese and tended to have renal impairment.

**Abstract #271**

**BIPHASIC ISOPHANE INSULIN 30/70 THRICE DAILY, IS IT REASONABLE?**

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**Objective:** The aim of this study was to evaluate the efficacy and safety of thrice-daily versus the traditional twice-daily injection regimen of Biphasic Isophane Insulin 30/70 on HbA1c for type 2 diabetes mellitus by a cross-over design trial.

**Methods:** The study included 22 patients with type 2 diabetes mellitus over a 6-month period. All patients were followed up prospectively. They received education on diet therapy and insulin therapy. They continued their insulin regimen as prescribed whether twice daily or three times daily injection. The regimen was changed for each patient at the end of the first 3 months, and then they were followed up for an additional 3 months on the new regimen. The main outcome measure was HbA1c. The blood glucose levels were measured using ACCU-CHEK performa glucose meter, and the measures were downloaded at each visit. The patients were given
instructions on how to titrate their insulin at each follow up visit. Hypoglycemia incidents were also recorded.

**Results:** All 22 patients completed the study protocol. Mean (SD) of age was 55.0 (10.7) years. There was a significant decrease in HbA1c level (p<0.05) at the end of the first 3 months of trial regardless on which regimen the patient started, but there was no significant difference in the mean HbA1c reduction in patients when they were on twice-daily insulin injections versus the time they were on thrice-daily insulin injections (1.1± 1.3 vs. 0.8±1.71 respectively, p>0.05). On the other hand, when patients were on thrice daily insulin injections, they had better average blood glucose readings compared to twice daily regimen (161.4 ± 62.7 and 166.0 ± 69.5 respectively, p<0.05). There was no significant difference in hypoglycemia incidents between the two regimens.

**Discussion:** The common practice of giving biphasic isophane insulin 30/70 thrice daily to achieve better glycemic control is widely used in Jordan because insurance doesn’t cover the new analogs in a lot of cases. There is no published research on the efficiency or safety of this practice. Our results indicate that the thrice daily regimen is as effective as the twice daily regimen. The significant lowering of HbA1c at the end of the first 3 months, regard less of which regimen used, could be attributed to education on diet and insulin therapy.

**Conclusion:** Compared to the traditional twice daily insulin regimen of Biphasic Isophane Insulin 30/70, a thrice daily insulin regimen is as effective and safe. Our results validate the ongoing practice of dividing the Biphasic Isophane insulin into a 3 dose regimen as a means of intensifying glucose control.

**Abstract #272**

MEDICATION ADHERENCE IN PERSONS WITH DIABETES MELLITUS IN A TERTIARY HOSPITAL

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**Objective:** Adherence poses a challenge in persons with chronic diseases including diabetes mellitus. We evaluated adherence to antidiabetic medications, diet and exercise and identified factors associated with non-adherence in persons with diabetes in our clinic with the aim of subsequently improving adherence.

**Methods:** A cross-sectional study of 113 consecutive adults with diabetes attending the diabetes clinic of a tertiary Hospital was done over a period of 3 months. Adherence was assessed by patients self-report and use of the eight-item Morisky Medication Adherence Scale (MMAS-8).

**Results:** Mean age of respondents was 59.3± 13.4 years with a male to female ratio of 1 to 2.2. Ten (8.8%) respondents had type 1 diabetes while 103 (91.2%) had type 2 diabetes (persons with gestational diabetes were excluded). Mean duration of diabetes was 9.6±9.2 years. Self-reported adherence to medications was rated as good, medium and low by 80.9%, 13.6% and 5.5% of respondents respectively. Using the MMAS-8, adherence to medications was high, medium and low in 18.6%, 59.3% and 22.1% respectively. The commonest reason for non-adherence was paucity of funds (7%) followed by forgetfulness (6.5%). Self-reported adherence to diet and exercise was 92% and 77.9% respectively (in response to whether or not they adhered). There was no significant association between adherence and age, gender, level of education and presence of comorbidities.

**Discussion:** Adherence to treatment regimen (diet, exercise and medications) was quite good in our patients. A contributing factor could be that education on diabetes and its treatment is done not only by Doctors but also by by Health Educator Nurses and Dieticians who are all located within the out-patient clinic. Patients are sent back for follow-up appointments with these personnel whenever they are found to be non-adherent and when they default from clinic attendance.

**Conclusion:** Adherence to treatment was good in our study population. Patients’ self-reported adherence was higher than was obtained using the MMAS-8. This shows that patients overestimate their adherence and standardized questionnaires would give more accurate responses. With the information provided in this study, adherence could still be improved upon by prescribing cheaper drugs and by encouraging patients to get medical insurance.
Abstract #273

BENEFITS OF EXTENDED RELEASE METFORMIN: SYSTEMATIC REVIEW OF THE ONGOING CLINICAL TRIALS

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Objective: The evidence for the benefits of metformin extended release has consistently evolved over 15 years. The insights into the ongoing clinical trials provide meaningful information for the anticipated data across various new parameters of evaluation across varied clinical perspectives.

Methods: We searched for ongoing trials recruiting patients from World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/search/en), without any date restrictions and last search on December 12, 2015. Independent sample t test were performed for statistical analysis. We compared results with the existing published evidences on pubmed and Cochrane library by using specific MeSH, Boolean operators Metformin AND Extended, prolonged, delayed release NOT Pharmacokinetics.

Results: Total 7 trials are actively recruiting 2278 patients across US, Europe and Asia with 3 international multicentric trials. The registration date ranged Dec 2012 till Feb 2015. Study designs include randomised, controlled, double blind, parallel group, cross over design studies. Two phase 2 trials are actively evaluating the benefits of metformin ER beyond diabetes for the benefits in inflammation in HIV (n=12) and effect on prostate carcinoma (n=70). The minimum age group enrolled is 10 years for the fixed dose combination of Sitagliptin and Metformin ER in paediatric T2DM, phase 3 trial for 54 weeks, across 30 countries. Analysis of target patient sample size reveal median 240, maximum 1048, mean 325.4, SD 361.9, SEM 136.8, CI -9.31- 660, p=0.05. Cumulative duration of the ongoing trials is 198 weeks with mean duration 28.2 weeks, CI 16.3-40.2, p=0.001; longest duration for 54 weeks. Highest target sample size of 1048 patients is for a phase 4 study evaluating metformin XR Vs metformin IR across 10 countries, followed by 518 patients in CONSENT trial in China. Till date, 18 clinical trials have been published for metformin ER including evaluation beyond metabolic control

Discussion: The WHO ICTRP provides a single point of access to information about ongoing clinical trials, meeting criteria for content and quality control. The primary outcome measures for these studies not only include several conventional parameters like HbA1c, PPG, FPG but also novel emerging markers like CT angiography, Prostate Specific Antigen doubling time. As these studies end closure it is likely to reveal the paradigm results which would be clinically meaningful and insightful.

Conclusion: The quality and the level of evidence for ongoing metformin ER trials promises to further substantially strengthen the existing evidence based perspectives for metformin ER.

Abstract #274

OUTCOMES OF DIET PLUS INSULIN COMPARED TO DIET ALONE IN THE MANAGEMENT OF GESTATIONAL DIABETES MELLITUS

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Objective: Maternal hyperglycemia is the main cause of maternal as well as fetal and neonatal complications. While there is strong evidence to support that treatment of gestational diabetes mellitus (GDM) reduces these complications, however the efficacy of adding insulin to diet on maternal and neonatal outcomes has not been evaluated in our high risk population. This analysis is done to assess maternal and neonatal outcomes of gestational diabetes patients treated with diet plus insulin versus diet alone.

Methods: We re-analyzed the data from earlier study in which we evaluated the effectiveness of a multidisciplinary approach in the management of GDM. In this study we evaluated for maternal and neonatal outcomes according to the type of GDM treatment. We randomly selected five percent out of 3342 GDM patients whom were diagnosed, regularly followed and delivered at our institution from October 2011 till September 2012. A total of 169 GDM patients, 38 treated with diet plus insulin and 131 treated with diet alone, were fully reviewed. In addition 169 neonates born to same mothers were assessed for pre-specified neonatal outcomes indicators.

Results: Mothers treated with diet plus insulin had a higher baseline risk factors such as higher BMI, increasing parity and higher blood glucose levels during the OGTT testing. They documented their blood glucose levels more often, had longer hospital admissions during pregnancy and delivery (table1). Pregnant ladies in this group had increased risk of preeclampsia with lower rates
of polyhydrominous and perineal tears (table 2).
The overall incidence of neonatal complications was significantly lower in the neonates born to mothers in the insulin plus diet group when compared to the diet only group (7.9% VS 21.4% respectively, P value < 0.05). Neonates born to mothers treated with diet plus insulin had significantly less macrosomia (5.3% vs 8.4%, P < 0.05) and less neonatal hypoglycemia (2.6% vs 13%, P < 0.05).

Conclusion: Our study showed that glucose lowering by adding insulin to diet in women with GDM is superior to diet alone in our population. Stringent blood glucose monitoring with prompt insulin initiation is associated with improved maternal as well as neonatal outcomes in our high risk GDM patients.

Abstract #275

EFFECTS OF LONG-TERM TESTOSTERONE UNDECANOATE (TU) THERAPY ON ANTHROPOMETRIC PARAMETERS IN HYPOGONADAL MEN WITH TYPE 2 DIABETES (T2DM): REAL-LIFE DATA FROM A REGISTRY STUDY

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Objective: To assess long-term effectiveness and safety of TU in a urological setting in comparison to an untreated hypogonadal control group.

Methods: Cumulative registry study in 656 men with total testosterone (T) levels below 12.1 nmol/L and symptoms of hypogonadism. 230 men with T2DM were analysed. 113 received parenteral TU 1000 mg/12 weeks following an initial 6-week interval. 117 men had opted against T therapy (TTh) and served as controls (CTRL). Median follow-up in both groups was 7 years. Measurements were taken at least twice a year, and 8-year data are presented. Mean changes over time between the groups were compared by a mixed effects model for repeated measures with a random effect for intercept and fixed effects for time, group and their interaction. Changes were adjusted for age, weight, waist circumference, blood pressure, and lipids to account for baseline differences between the two groups.

Results: Mean age: 63.4±4.73 years. Waist circumference progressively decreased from 110.7±7.3 to 100.5±5.4 cm in the T group and increased from 110.2±7.2 to 110.7±6.1 cm in CTRL. The model-adjusted estimated difference between groups at 8 years was -13.2 cm (p<0.0001 for all).

Weight decreased from 112.5±13.2 to 91.8±9 kg (p<0.0001) in the T group and from 97±10.2 to 96.9±9.0 kg (p<0.05) in CTRL. Difference between groups: -22.3 kg (p<0.0001).

Weight change from baseline was -19±5.6% (p<0.0001) in the T group and +1.1±2.9% (p<0.01) in CTRL. Difference between groups: -20.6% (p<0.0001).

BMI decreased from 36.1±4.2 to 29.7±2.8 kg/m2 (p<0.0001) in the T group and from 31±3.5 to 30.9±2.9 kg/m2 (NS) in CTRL. Differences between groups: -6.9 kg/m2 (p<0.0001).

Fasting glucose decreased from 6.2±0.8 to 5.2±0.05 mmol/L (p<0.0001) in the T group and remained stable at 5.8±0.3 in CTRL. Differences between groups: -0.9 mmol/L (p<0.0001).

HbA1c decreased from 8.03±0.83 to 5.77±0.43% in the T group and increased from 7.44±0.66 to 8.01±0.78% in CTRL. Differences between groups: -2.17% (p<0.0001 for all).

The triglyceride:HDL ratio, a surrogate parameter for insulin resistance, decreased from 5.4±2.4 to 2.3±0.5 (p<0.0001) in the T group and from 7.8±4.4 to 7.0±4.3 (p<0.05) in CTRL. Differences between groups: -3.8 (p<0.0001).

No patient dropped out. There was 1 death in the T group. In CTRL, there were 14 myocardial infarctions, 16 strokes, and 9 deaths.

Conclusion: Long-term TTh with TU in an unselected cohort of hypogonadal men with T2DM resulted in improvements in anthropometric and metabolic parameters. Untreated controls gained weight and glycemic control worsened. Long-term TU was well tolerated and adherence excellent.

Abstract #276

USING THE HEALTH BELIEF MODEL FOR PATIENTS WITH TYPE II DIABETES: A PROVIDER EDUCATION TOOL FOR ADVANCED PRACTICE NURSES

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Objective: The purpose of this project is to provide an educational tool for Advanced Practice Registered Nurses (APRNs) on how to incorporate health beliefs using a Health Belief Model (HBM) Survey into diabetes-self management training for patients with Type II diabetes. Objectives of the program were: rating of the health belief survey as an effective tool for use in patients with T2DM; and APRN willingness to incorporate concepts of HBM in
caring for patients with T2DM.

**Methods:** A one-group pre- and post-test design was utilized in this project. Participants were recruited from the United Advanced Practice Registered Nurses (UAPRN) of Georgia Online community group.

**Case Presentation:** Most participants (n=46) of the pilot project were Nurse Practitioners (n=45) working in family practice (n=30). Average years of practice were 6-10 (n=17). Over half (56%) were unfamiliar with HBM construct, and not confident in tailoring diabetes education based on patients’ health beliefs (90%). After completing the online educational module on HBM concepts, most indicated that they would perform HBM based assessment on patients with type II diabetes. Not surprisingly, respondents reported the greatest barrier to implementing health belief assessments into clinical practice was time (n= 41). Most (n= 43) felt that patients would find the assessment beneficial. Strategies for incorporating HBM based assessment were identified. All (n=46) agreed upon the efficacy of the Health Belief Model survey tool in assessing patients with type II diabetes prior to implementing diabetes education.

**Discussion:** The pilot project was successful in meeting objectives as APRN indicated the efficacy of the HBM in clinical practice for patients with T2DM (n=46). Participants also indicated their willingness to incorporate assessment using HBM concepts into caring for patients with T2DM (n=46).

**Conclusion:** The success of this pilot project is demonstrated by clinicians’ willingness to commit to the incorporation of a health belief assessment for patients with Type II diabetes, the identification of possible barriers to implementation, and strategizing to find methods to eliminate barriers to implementation of the health belief assessment tool in practice. The topic of the project is of great clinical and professional interest to the primary author, who plans to continue traveling throughout the State of Georgia to visit APRN meetings and various APRN educational opportunities to promote use of the HBM in diabetes education.

**Abstract #277**

**IMMUNOGENICITY IN A PATIENT WITH DKA: DO INSULIN ANTIBODIES INFLUENCE RESPONSE TO RECOMBINANT BUT NOT ANALOG INSULIN?**

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**Case Presentation:** 63 y.o. Hispanic male with uncontrolled Type 2 Diabetes Mellitus with retinopathy, neuropathy, CAD, HTN, and CKD presented with hypotension and nausea. The patient had past hospitalizations for chest pain requiring CABG and hyperglycemia. His HbA1c was 10.5% with stated adherence to a home regimen of Humulin 70/30 60 units BID. Review of systems was positive for fatigue and chest pain. Vital signs were: BP 98/48, HR 69, RR 18 SaO2 94% on 2L O2. Physical exam was significant for a healed sternotomy scar and a pacemaker in the left anterior chest wall. Admission labs confirmed severe DKA with Na+125 mmol/L, K+ 7.2 mmol/L, Cl- 80 mmol/L, HCO3- 5 mmol/L, anion gap 40 mmol/L, BUN 67 mg/dL, creat. 3.12 mg/dL, gluc. 898 mg/dL and a venous pH of 7.08. The patient was managed with fluid in the ED and an insulin drip was initiated in the ICU. The drip rate started at 8 units/hour then titrated up to 35 units/hr over 48 hours. The patient required 6 liters of saline and 915.1 units of regular insulin to close his anion gap and bring glucose levels to target. He was transitioned to a medicine floor and started on NPH 10 units with breakfast/6 units at night, insulin lispro 3 units tid-ac and low dose correctional sliding scale. Titrations were made to NPH and lispro to achieve target glucose of <180 mg/dL. The patient experienced hypoglycemia to 48 mg/dL at 7:30 am while tolerating a consistent carb diet; thus basal insulin was switched from NPH to insulin glargine to prevent future hypoglycemic episodes. Over the next 5 days, he remained hyperglycemic despite 104 units of insulin daily. His glucose reached 580 mg/dL with no nutritional changes or other identifiable modifying factors. Insulin antibodies were ordered to assess the degree of insulin resistance, and were greater than 50 U/mL. The decision was made to transition him back to NPH and insulin lispro as he was controlled on this regimen despite the episode of hypoglycemia. Upon reinitiating NPH and lispro, glucose levels improved quickly to target.**

**Discussion:** No clinical trials have determined the relationship between insulin dose and the development of insulin antibodies. There is, however, evidence that development of antibodies depends on the purity, molecular structure, and storage conditions of the insulin administered as well as HLA type. As such, in patients who are severely insulin resistant, positive antibodies can support the argument that switching from insulin analogs to non-analogs may result in achieving target glucose levels more efficiently.

**Conclusion:** We present a rare case of severe insulin resistance in a patient presenting with DKA responding to protamine insulin formulation over insulin analogs.
Abstract #278

METFORMIN-ASSOCIATED LACTIC ACIDOSIS (MALA): A CASE SERIES

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Case Presentation: We present two case reports of MALA. The first case was a 31 year old male, who was not a known diabetic, but was admitted due to ingestion of 50 tablets of metformin 500 mg/tab (equivalent to 25 g of metformin) and injected 3000 units of Regular Insulin and 1000 units of Premixed Insulin 70/30. He presented with epigastric pain and cold clammy extremities. He admitted to being stressed from work recently. Physical examination revealed an elevated blood pressure at 149/87 mmHg and tachycardia at 119 bpm. Initial random blood sugar was 54 mg/dL (3 mmol/L, Normal at >11.11 mmol/L). He also had hypokalemia and leukocytosis with segmenter predominance. Arterial blood gas showed severe lactic acidemia. He was admitted to the ICU. On chemistries the following day, there was noted acute rise in creatinine from normal to 3.96 mg/dL (350 umol/L, Normal at 59-104 umol/L). A central line was inserted and hemodialysis was instituted. After 3 sessions of hemodialysis, full clinical recovery was observed, with return to a normal serum lactate level on the fourth hospital day. The second patient was a 33 year old male, known diabetic maintained on metformin 500 mg/tab twice a day and glibenclamide 5 mg/tab once a day. He was admitted after ingesting 28 tablets of metformin (equivalent to 14 g of metformin) and 12 tablets of glibenclamide (equivalent to 60 mg of glibenclamide) with alcohol and methamphetamine. He admitted to being depressed over the loss of his partner of 10 years. He was seen thereafter to be nauseated and complained of headache with shortness of breath. Physical examination showed elevated blood pressure at 150/100 mmHg and tachycardia at 129 bpm. Initial evaluation revealed mild lactic acidosis. Capillary blood glucose, blood urea nitrogen and creatinine were normal. Due correction was given for hypokalemia. The patient did not require hemodialysis. Progressive recovery was observed and supportive measures were continued.

Discussion: Metformin remains to be the initial recommended therapeutic step with lifestyle intervention in most of the treatment guidelines for DM type 2. However, despite its proven efficacy, one feared adverse effect of metformin is lactic acidosis. Metformin increases plasma lactate in a plasma concentration-dependent manner by inhibiting mitochondrial respiration in the liver. The reported incidence of metformin-associated lactic acidosis (MALA) is 0.05 per 1000 patient-years.

Conclusion: MALA is a rare, preventable but life-threatening adverse event that should be suspected among patients presenting with elevated blood lactate levels and high-anion gap metabolic acidosis in the background of metformin intake.

Abstract #279

EFFICACY AND SAFETY OF EMPAGLIFLOZIN BY BASELINE AGE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Objective: The objective was to assess the influence of age on the efficacy and safety of empagliflozin in patients with type 2 diabetes mellitus.

Methods: Using pooled data from 4 Phase III trials (NCT01177813, NCT01159600, NCT01210001) in which patients (n=2477; mean [SD] HbA1c 7.99 [0.85]%) received empagliflozin 10 mg, 25 mg, or placebo as monotherapy or add-on therapy for 24 weeks, we assessed efficacy and safety in subgroups by baseline age (<50 [n=686], 50 to <65 [n=1330], 65 to <75 [n=395], and ≥75 years [n=66]). Changes from baseline at week 24 in HbA1c, body weight, and blood pressure were analyzed using ANCOVA in the full analysis set; safety was assessed in the treated set (randomized patients treated with ≥1 study dose) and analyzed descriptively.

Results: Across treatment groups and subgroups, mean baseline HbA1c was 7.70–8.10%. At week 24, adjusted mean (SE) differences vs placebo in change from baseline in HbA1c (%) in patients aged <50 years were −0.75 (0.07) and −0.87 (0.07) for empagliflozin 10 mg and 25 mg, respectively, in patients aged 50 to <65 years were −0.59 (0.05) and −0.63 (0.05), respectively, and in patients aged 65 to <75 years were −0.58 (0.09) and −0.55 (0.10), respectively (all p<0.001 vs placebo). In patients aged ≥75 years, mean (SE) differences were −0.21 (0.22)% and −0.33 (0.24)% for empagliflozin 10 mg and 25 mg, respectively (both p=ns vs placebo; for interaction between treatment and age groups, p=0.022). Weight and systolic blood pressure were significantly reduced...
vs placebo for both empagliflozin doses in all age groups (p=ns for interactions). Empagliflozin was well tolerated in all age groups, with an increased risk of adverse events (AEs) consistent with genital infection and, in patients on background regimens that included a sulfonylurea, there was an increased risk of confirmed hypoglycemic AEs vs placebo. The frequency of these AEs with empagliflozin did not appear to increase with age compared with placebo.

Discussion: Reductions in HbA1c with empagliflozin compared with placebo decreased with increasing age, but reductions in weight and blood pressure were not significantly affected by age. The incidence of confirmed hypoglycemic AEs in patients on sulfonylurea background therapy, and AEs consistent with genital infection was higher with empagliflozin; however, it did not appear to increase with increasing age compared to placebo.

Conclusion: Empagliflozin was efficacious and well tolerated across all age subgroups.

Abstract #280

CLUSTERIN AND CARDIOVASCULAR AUTONOMIC FUNCTION: ANY ASSOCIATION IN TYPE 2 DIABETES

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Objective: Clusterin, a glycoprotein found in the central nervous system and plasma, is implicated in many pathological processes (e.g., inflammation, apoptosis). Clusterin plays a role in inflammation and is associated with neuregenerative diseases. In rodents, clusterin was upregulated in denervated sensory pathways. Sensorimotor and autonomic neuropathies are the two main types of neuropathies in type 2 diabetes (T2D). Persons with cardiovascular autonomic neuropathy (CAN) may suffer from orthostatic hypotension, silent myocardial ischemia, and increased risk of mortality. The etiology of CAN is multifactorial with metabolic, neurovascular, and inflammatory components. An association of clusterin and CAN has not been investigated in T2D. In this study, we examined serum clusterin levels to determine if clusterin is associated with autonomic function.

Methods: RR-variation during deep breathing (i.e., mean circular resultant (MCR) and expiration/inspiration (E/I) ratio) was used to assess cardiovascular autonomic function (i.e., parasympathetic function) in 50 persons with T2D. Clusterin and other metabolic parameters (e.g., adiposity, glycemic control, insulin resistance, calcium metabolism and 25-hydroxyvitamin D [25(OH)D]) were examined.

Results: Demographic and metabolic parameters for this cohort were: age=63±10 years; BMI=32.7±5.3 kg/m2; M/F=21/29; duration=13±8 years; HbA1c=7.3±1.2%; clusterin=215±37 µg/mL. No significant Spearman rank correlations were found for clusterin and MCR r=−0.27, p=0.06; nor for E/I ratio r=−0.21, p=0.17. We used a stepwise selection procedure regressing MCR and E/I ratio on a number of metabolic parameters, including clusterin. We had previously reported significant associations of cardiovascular autonomic function with age, 25(OH)D insufficiency (i.e., 25(OH)D levels <30 ng/mL), and the interaction of age x 25(OH)D insufficiency. Neither clusterin nor other metabolic parameters (except 25(OH)D insufficiency) were selected as independent variables in the regression models.

Discussion: CAN results in abnormalities of heart rate control and vascular dynamics. The pathogenesis of CAN is complex involving a cascade of pathways activated by hyperglycemia. Several etiologies have been suggested (e.g., inflammation, 25(OH)D insufficiency, premature apoptosis) but the pathogenesis is not clear.

Conclusion: Clusterin is associated with certain forms of nerve injury but whether serum clusterin is associated with an incomplete compensatory mechanism to limit nerve dysfunction or it is involved in the pathogenesis requires further study. We did not, however, find an association of clusterin and parasympathetic function in T2D.

Abstract #281

ADDRESSING DIABETES MANAGEMENT DURING AIR TRAVEL CROSSING MULTIPLE TIME ZONES

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Objective: Approximately 10% of travelers with diabetes report that they have experienced a diabetic complication during air travel. In-flight acute complications of diabetes may have serious consequences, leading to flight diversion and hospital admission. The literature was reviewed to determine recommendations for management of insulin and oral diabetic medications during long-distance travel.

Methods: PUBMED and MEDLINE databases were queried for all English articles using search terms air travel and diabetes mellitus. References of articles identified were reviewed to screen for additional articles. Websites of national diabetes organizations were reviewed for patient-oriented advice. Recommendations were abstracted and updated to address the following issues regarding diabetes care for travelers: General preparation advice, cabin environment and equipment, medication adjustments and insulin pump use.
Results: Nine peer-reviewed articles and two diabetic nursing guidelines were identified. Five of the 6 recommendations identified were based on expert opinion, the other was based on a prospective cohort study. For short/rapid acting insulin, no dose adjustment is recommended. During eastward travel, intermediate/long-acting insulins should be reduced in dose proportional to hours lost. During westward travel, correction scale insulin with rapid acting insulin can be used or the dose to be administered during travel can be given as divided doses to span the longer travel day. Pre-mixed insulins are discouraged due to difficulty in titrating effects. Sulfonylureas and glinides should be held during eastward travel. Insulin pumps may be used per usual basal bolus dosing; however, caution needs to exercised as cabin depressurization may lead to unintended bolus dosing. Therefore, the pump should be disconnected prior to ascent and descent. In addition, any visible bubbles that form during ascent should be removed prior to reconnecting the device upon reaching altitude. Bringing backup medication is advised. Patients should be informed of differences in concentration and varying availability of international insulin products.

Conclusion: Based on clinical experience and literature review, specific regimen adjustments for diabetes management during air travel have been developed to avoid hypoglycemia during eastward travel, and severe hyperglycemia or diabetic ketoacidosis during westward travel. Further well-designed studies are needed to validate clinical practice standards.

Abstract #282

CLINICAL DETERMINANTS OF SERUM INTERLEUKIN-6 LEVEL IN ERYTHROPOIETIN-DEFICIENT AND ERYTHROPOIETIN-SUFFICIENT PATIENTS WITH DIABETIC NEPHROPATHY AND ANEMIA

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Objective: Anemia occurs early and predicts high risk of cardiovascular events and death in patients with diabetic nephropathy (DN). In our previous studies we have shown that anemia in DN is often associated with erythropoietin (EPO) deficiency and increased serum levels of proinflammatory cytokines. The aim of this study was to assess clinical determinants of serum interleukin-6 level in EPO-deficient and EPO-sufficient patients with diabetic nephropathy and anemia.

Methods: We investigated 95 anemic patients with type 2 diabetes mellitus and chronic kidney disease (stages 1-3). GFR was calculated by Cockcroft-Gault formula. Anemia was defined according to World Health Organization criteria (2008). In addition to routine clinical tests we measured serum levels of erythropoietin (EPO), interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF alpha) using immunoassay. The patients were divided into 2 groups: 53 patients who were found to be EPO-deficient (serum EPO level <5mIU/ml) and 42 patients with normal serum EPO levels. Correlations were assessed by Spearman’s correlation coefficient (rs).

Results: Elevated serum IL-6 levels were found in 71.6% of patients (with no significant difference between the groups). Serum level of IL-6 had no significant correlations with age, serum creatinine, GFR, cholesterol, erythropoietin levels and urinary albumin excretion in each group. In patients without EPO deficiency IL-6 level correlated with body mass index (rs= -0.314, p=0.029), duration of diabetes (rs= -0.503, p=0.048), hemoglobin level (rs= -0.414, p=0.005), mean cell hemoglobin content, MCH (rs= -0.732, p=0.012) and TNF alpha level (rs= 0.284, p=0.038). In EPO-deficient patients IL-6 level it correlated with duration of diabetes (rs= 0.405, p=0.038) but not with other above mentioned parameters.

Conclusion: The results of the study suggest that EPO-deficient and EPO-sufficient anemic patients with DN are characterized by different clinical correlates of serum IL-6 level. Further larger studies are needed to elucidate clinical implications of these findings.

Abstract #283

DAPAGLIFLOZIN INDUCES KETOSIS IN PATIENTS WITH TYPE 1 DIABETES

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Objective: Liraglutide and SGLT2 inhibitors have a beneficial role in the management of type 1 diabetes (T1D). We have now investigated triple therapy using a sequential combination of insulin, liraglutide and dapagliflozin in such patients. Since treatment with SGLT-2 inhibitors in T1D is associated with increased risk of diabetic ketoacidosis (DKA), we have also now investigated the effect of dapagliflozin on mediators of ketosis in patients on triple therapy.

Methods: Thirty T1D patients on insulin and liraglutide therapy for at least last 6 months were randomized (in 2:1 ratio, drug: placebo) to receive either dapagliflozin 10mg or placebo daily for 12 weeks. Dapagliflozin was
initiated at 5mg daily for one week and increased to 10mg daily thereafter. Twenty-six patients completed the study (Placebo=9; Dapagliflozin=17).

**Results:** The addition of dapagliflozin resulted in a decrease in HbA1c of 0.6±0.1% (p<0.01 vs placebo). Along with improved glycemic control there was a significant increase in glucagon concentrations by 35±13% (from 91±12 to 114±19pg/ml, p<0.05), hormone sensitive lipase (HSL) by 29±11% (from 4.95±0.66 to 16.32±0.75ng/ml, p<0.05), FFA (from 0.34±0.04 to 0.59±0.11mM; p<0.05), glycerol (from 11.2±2.4 to 13.6±3.5mg/L, NS), acetoacetate (from 0.32±0.09 to 0.53±0.11mM, p<0.05) and β-hydroxybutyrate (from 0.11±0.02 to 0.39±0.09mM, p<0.05) while there was no change in the placebo group. Urinary ketones (acetoacetate and β-hydroxybutyrate) levels also increased significantly from 0.68±0.19 to 1.28±0.34µM/mg creatinine (p<0.05). There was no change in plasma bicarbonate concentrations. There was no change in mean total insulin dose in either group. Serum β-hydroxybutyrate levels were related to FFA concentrations (r=0.374, p<0.05) and inversely to total insulin dose at 12 weeks (r=−0.297, p<0.05) but not to HSL or glucagon levels. Two patients in the dapagliflozin group suffered from DKA within a day after increasing the dose of dapagliflozin to 10mg and were withdrawn from the study. Both patients had an arterial pH of <7.10. One of these patients had euglycemic DKA with blood glucose concentrations <160mg/dl (total daily insulin dose fell from 33 to 26 units) while the other had markedly hyperglycemia.

**Discussion:** All patients treated with dapagliflozin experienced increased lipolysis stimulated by glucagon and HSL with an increase in plasma FFA concentrations; Ketogenesis increased with a greater bio-availability of FFA; ketosis not amounting to DKA.

**Conclusion:** Since treatment of patients with type 1 diabetes with dapagliflozin induced ketogenesis and DKA in 2 patients, caution needs to be exercised while decreasing insulin doses and increasing dapagliflozin doses in such patients.

**Abstract #284**

**IMPROVED GLYCEMIC CONTROL FOLLOWING CABERGOLINE USE FOR HYPERPROLACTINEMIA IN A PATIENT PRESENTING WITH HYPEROSMOLAR HYPERGLYCEMIC STATE**

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**Objective:** To present a case of uncontrolled diabetes mellitus (DM) with drastically decreasing insulin requirements while treated with cabergoline for macroprolactinoma.

**Case Presentation:** A 77 year old male with prior history of dyslipidemia, hypertension and pituitary adenoma, presented with lethargy and polyuria. Upon admission he was found to be hypotensive (60/40 mmHg), with a serum glucose of 1,028 mg/dl. He weighed 107.4 kg (BMI 38.2 kg/m2). He was found to be in a hyperosmolar hyperglycemic state and was treated initially with intravenous fluids and an insulin infusion, requiring up to 17.5 units/hour of insulin. He was subsequently transitioned to glargine 56 units at bedtime and lispro 18 units before meals three times daily. HbA1c was 12.3% consistent with newly diagnosed DM2. Prolactin level was 476.2 ng/mL and MRI sella showed a 1.8 cm pituitary adenoma, consistent with macroprolactinoma. The patient carried this diagnosis in the past but discontinued cabergoline previously due to cost of the medication. He was restarted on cabergoline 0.5 mg twice weekly. Over the course of his 3 week hospitalization which was complicated by pulmonary embolus, insulin requirements significantly decreased. Blood glucose ranged from 77-164mg/dl. Prolactin decreased to 4.2 ng/mL. Discharge medications included glargine 10 units daily, metformin 1000mg daily and bromocriptine 2.5mg daily for decreased cost. At one month post-hospitalization, diabetes was well controlled and insulin was discontinued. While maintained on metformin his follow-up HbA1c was 6.5%.

**Discussion:** While typically used for the treatment of hyperprolactinemia, dopamine agonists (i.e. bromocriptine and cabergoline) have been shown to affect various metabolic parameters. Bromocriptine (Cycloset) is approved as an adjunct medication for diabetes but cabergoline is not used in this capacity. There have been few small studies of cabergoline’s effects on metabolic parameters during treatment of hyperprolactinemia including weight loss, glucose tolerance, insulin sensitivity, HbA1c, and lipids. One study showed reductions in fasting and post prandial glucose levels as well as HbA1c in patients receiving cabergoline with DM2 and on oral agents only. Cabergoline is longer acting and better tolerated than bromocriptine. This case is the
first reported in the literature demonstrating improvement of insulin-treated DM with cabergoline.

**Conclusion:** There has been minimal research on cabergoline for treatment of DM2. As a longer acting agent with fewer adverse effects than bromocriptine, this drug has the potential to be a suitable option for patients. Further research is needed.

**Abstract #285**

**OPTIMIZING INSULIN THERAPY IN OLDER ADULTS IN THE LONG-TERM CARE SETTING: AN EFFICACY AND SAFETY COMPARATOR ANALYSIS**

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**Objective:** According to HHS, people who reach the age of 65 have a 40% chance of entering a nursing home. More than 25% Nursing Home (NH) residents aged 65 years and older have diabetes. Evidence supports that patients with poor glycemic control are more likely to experience complications and higher healthcare costs. Poorly controlled diabetes mellitus (DM) and fluctuations in blood glucose (BG) present a significant challenge for patients and their healthcare team in long-term care (LTC) setting. The purpose of this analysis was to assess whether introducing V-Go in patients requiring basal bolus insulin therapy can improve glycemic control and reduce glycemic fluctuations compared to a matched cohort in the LTC setting.

**Methods:** A retrospective chart review evaluated two groups of 4 patients each that were matched on mean 30-day BG values to compare the effect of utilizing V-Go vs. standard of care (SOC). Daily blood glucose (BG) readings were obtained by nursing staff at up to 4 time points each day for 8 weeks. Efficacy variables included proportion of time in range (100mg/dl -200mg/dl), change in mean daily BG and change in glucose excursions.

**Results:** A total of 1937 BG values were collected during 8 weeks of therapy (969 V-Go and 968 SOC). The mean (SD) baseline BG of the comparator groups was 213.6 (90.7) for the standard of care (SOC) group and 208.1 (91.8) for the V-Go treatment group (p=0.934). A statistically significant improvement in BG Time in Range (100-200mg/dl) was observed for the V-Go group compared to the SOC group (59.09% vs. 34.02%, respectively; p<0.001) with decreased BG fluctuations in the V-Go group as measured by standard deviation (61.2 vs. 92.1; p<0.001). The mean daily BG decreased in favor of V-Go as compared to SOC (159.38 vs. 223.86, respectively; p<0.001). Significant improvements in BG measures were observed at all 4 daily BG testing time points for the V-Go group as well. The number of glucose excursions >200mg/dl was significantly lower with the V-Go group (23.24% vs. 56.77%; p<0.001). The calculated HbA1C, based on the criteria utilizing known BG averages, decreased to 7.2% from 9.4% in favor of the V-Go group (p<0.001). Hypoglycemic events as measured by blood glucose measurements were similar between both groups.

**Discussion:** Insulin therapy utilizing the V-Go disposable insulin delivery device, when compared to SOC insulin therapies in the LTC patients with diabetes, demonstrated favorable changes in overall glycemic control, increased time in range and decreased glucose fluctuations.

**Conclusion:** Given these findings larger controlled studies are needed to fully evaluate the use of V-Go in this patient population.

**Abstract #286**

**LINAGLIPTIN (LINA) AS ADD-ON TO EMPAGLIFLOZIN (EMPA) AND METFORMIN (MET) IN PATIENTS WITH TYPE 2 DIABETES MELLITUS (T2DM): TWO 24-WEEK RANDOMIZED, DOUBLE-BLIND, DOUBLE-DUMMY, PARALLEL-GROUP TRIALS – STUDY DESIGN**

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**Objective:** Triple therapy options in T2DM patients with poor glycemic control (HbA1c >7.0%) may include a combination of a sodium-glucose cotransporter 2 (SGLT2) inhibitor (e.g. EMPA) with a dipeptidyl peptidase-4 (DPP-4) inhibitor (e.g. LINA) added to MET background therapy. The present studies (NCT01778049) were designed to investigate the efficacy and safety of LINA 5 mg/day (d) versus placebo (PBO) as add-on therapy in T2DM patients inadequately controlled on EMPA (10 mg/day (d) or 25 mg/d) plus MET.

**Methods:** These randomized, placebo-controlled, double-blind (DB), double-dummy, parallel-group, multinational, Phase 3 trials of adults with T2DM treated with stable doses of MET used the following “filter” design. A total of 1324 patients were screened. Eligible patients (n=709) with HbA1c ≥8.0% and ≤10.5% were randomized 1:1 to a 16-week open-label (OL) treatment period with EMPA 10 mg/d (Study 1) or EMPA 25 mg/d (Study 2), in addition to background MET. Patients then entered a 1-week PBO
add-on phase, receiving EMPA 10 mg/d (Study 1) or 25 mg/d (Study 2) plus PBO, during which further eligibility evaluations were performed. Patients (n=227) were “filtered out” for reasons including adequate glycemic control (HbA1c $<7.0\%$) on OL EMPA (10 mg or 25 mg) plus MET, failure to meet other DB eligibility criteria, discontinuation during the OL phase, and target sample size already having been met. The remaining eligible patients with HbA1c $\geq 7.0\%$ and $\leq 10.5\%$ (n=482) entered a 24-week DB, double-dummy treatment period, and were randomized to receive daily treatment with a single-pill combination (SPC) of LINA 5 mg/EMPA 10 mg (n=126) or PBO+ EMPA 10 mg (n=130) in Study 1, and an SPC of LINA 5 mg/EMPA 25 mg (n=114) or PBO + EMPA 25 mg (n=112) in Study 2. The primary endpoint in both studies was the HbA1c change from baseline after 24 weeks of DB treatment. The key secondary endpoint was the change from baseline in fasting plasma glucose after 24 weeks of DB treatment. Safety was assessed by monitoring the incidence and intensity of adverse events (AEs), serious AEs, and AEs of special interest (e.g. decreased renal function, hepatic injury, skin reactions, hypersensitivity and pancreatitis).

Results: The last patient visit for collection of data was in March 2015 and external presentation of the final results is expected imminently.

Discussion: Study NCT01778049 will inform on the efficacy and safety of LINA added on to background EMPA + MET when EMPA therapy is replaced by LINA/EMPA SPCs.

Conclusion: Combining a DPP-4 inhibitor with an SGLT2 inhibitor may provide the potential to further decrease HbA1c in T2DM patients with inadequate glucose control on EMPA and MET.

Abstract #287

ASSESSMENT OF DIABETES KNOWLEDGE USING MICHIGAN BRIEF DIABETES KNOWLEDGE TEST AMONG PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Objective: Type 2 Diabetes Mellitus (T2D) represents a growing health threat globally. The International Diabetes Federation (IDF) in 2014 estimated that 387 million of adult people have diabetes and this number is expected to exceed. In Saudi Arabia the prevalence over that decades shows a higher progression. Diabetes knowledge has been shown to improve self-management skills and glycemic control. The primary goal is to assess the Diabetes knowledge and its impact on diabetes control and complications.

Methods: We conducted a cross-sectional study at the King Abdulaziz Specialist Hospital, Taif, Saudi Arabia, Division of Endocrinology. T2D age $>$18 years who had a routine visit to the Endocrine clinic Jun 2014 - Oct 2015 were asked to participate. Baseline characteristics and measurement were obtained at the time of visit. Laboratory data was collected from patients’ medical Records. We excluded patients with T1D. We used Michigan Brief Diabetes Knowledge Test to assess patient’s knowledge. Those answered $>$65% of the questions considered having good knowledge about diabetes.

Results: Total of 264 patients participated, 131 (49.6%) were male and 132 (50.0%) were female, 44.7% has diabetes $>$10 yrs. and 29.8% has it for 5-10 yrs., mean A1c 8.56%, mean BMI 30.5%, 64% did high school or less and 38% did college degree or higher, 41.7% considered to have low income, 37.9% were on oral medications only, 41.3% were on insulin and the mean correctly answered knowledge questions was 48.26%. 28% of the participants think that A1c reflect Blood Glucose control over the past week, 44.3% don’t know what is A1c. 29.5% think that diet soda can be used to treat low blood glucose. 57 patients (21.6%) considered having good knowledge about diabetes. Compare to those with poor-knowledge, diabetics with good knowledge has mean age of 49 yrs. vs. 54.3 yrs. (p <.05), 59.7% vs. 28.5% has college degree or higher (p <.05).

76.4% of the diabetics with good knowledge report sedentary lifestyle compare to 85.5% in the poor-knowledge (p .10). Diabetics with good knowledge have mean A1c 7.6 vs 8.8 (p<.05), mean TC 167.2 vs 176.3 (p.16), mean LDL 108.6 vs 143.10 (p.37), mean HDL 44 vs. 41 (p.20), and mean TG 167.4 vs. 183.6 (p.11).

All diabetics with good knowledge aware that poorly controlled diabetes cause retinopathy compare to 74.4% (p<.05) And nephropathy 87.7% vs 75.7% (p .13) in patients with poor knowledge respectively.

Conclusion: The majority (78.4%) of the screened T2D patients considered having poor knowledge about diabetes. Poor knowledge associated with higher A1c, non-significant increase in most of the measured cardiovascular markers, and those are less aware about diabetes related complications.
Abstract #288

SCREENING, DIAGNOSIS, AND INITIATION OF LONG-TERM THERAPY FOR DIABETES MELLITUS IN A HOSPITAL 24 HOUR OBSERVATION UNIT

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Objective: Observation Units allow Emergency Department (ED) patients to be monitored for up to 24-36 hours, resulting in decreased ED overcrowding, increased patient satisfaction, and avoidance of inpatient hospital admissions. These units have become increasingly popular, with nearly 5 million admissions in the USA annually. They also provide a unique venue to screen for, and initiate long-term treatment for Diabetes Mellitus (DM).

Methods: In this demonstration project, patients with no history of DM presenting to an urban ED Observation Unit between February 7 and October 31 of 2015 were screened for DM with a hemoglobin A1c(HbA1c) test. New diagnoses of DM and Pre-DM were based on the ADA HbA1c diagnostic criteria. Newly diagnosed patients were given DM education and encouraged to follow-up with their primary care providers. If patients had an HbA1c ≥6.5% and were <80 years old, they were given a 28-day prescription for metformin unless contraindicated. Patients with an HbA1c ≥ 9.0% received an endocrine consult to assist with their treatment plan. Follow-up home phone calls were conducted at 1 month to patients newly diagnosed with DM who received a DM medication.

Results: Of the 2,855 patients presenting to the Observation Unit, 2193/2855 (76.8%) had no history of DM, and 2022/2193 (92.2%) of these received an HbA1c test. A total of 996/2022 (49.3%) had an HbA1c ≤5.6%, 886/2022 (43.8%) had an HbA1c between 5.7%-6.4%, 115/2022 (5.7%) had an HbA1c between 6.5%-8.9%, and 25/2022 (1.2%) had an HbA1c ≥9.0%. Of the 140 patients with an HbA1c ≥ 6.5%, 70/140 (50.0%) were prescribed only metformin and 48/70 (68.6%) were reached for a 1-month follow-up. Of these, 36/48 (75.0%) had follow-up with their primary care physician and 26/48 (54.2%) were still taking a DM medication. Of the 25 patients with an HbA1c≥9.0%, 19/25 (76.0%) were prescribed insulin or multiple DM medications, 10/19 (52.6%) were contacted for a 1-month follow-up, 7/10 (70.0%) had followed-up with their primary care physician, and 9/10 (90.0%) were still taking the medications.

Discussion: Undiagnosed DM is common among adults admitted to ED Observation Units. Since Observation Units are typically staffed with PAs or physicians around the clock, there is ample opportunity for initiation of DM education, outpatient medication, and referral for follow-up. Conclusion: The relatively high frequency of undiagnosed DM suggests that ED Observation Units are appropriate settings for large-scale identification, education, and initiation of outpatient treatment. More work is needed to increase adherence to outpatient treatment plans, particularly among patients prescribed only metformin.

Abstract #289

ASSESSING UNMET NEEDS FOR TYPE 2 DIABETES PATIENTS TREATED WITH BASAL INSULIN IN THE UNITED STATES

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Objective: Assess patient demographics and clinical characteristics for adult type 2 diabetes (T2DM) patients in the United States (US) treated with basal insulin who 1) did not intensify therapy, 2) intensified with a GLP-1 receptor agonist (RA), 3) intensified with oral anti-diabetic medication (OAD) or 4) intensified with bolus insulin.

Methods: All adult (age≥18 years) GLP-1 and bolus insulin naïve patients with T2DM and continued (>180 days) basal insulin use in the General Electric Centricity electronic medical records database were retrieved. Intensification was defined, consistently with American Diabetes Association’s treatment guidelines, as the first prescription of GLP-1 RA, OAD or bolus insulin >180 days after basal insulin initiation 1/1/2011-12/31/2013. Mean age, HbA1c and BMI were assessed at time of intensification. For patients not intensifying an “average intensification date” was constructed, based on intensification dates in the three groups with actual intensification dates.

Results: A total of 37,594 adult T2DM patients were included. The majority (55.9%) had no treatment added to their basal insulin, 3.9% added GLP-1 RA, 15.3% added OAD and 24.8% added bolus insulin. Across groups, mean age/HbA1c/BMI were 63.9 years/7.8%/33.1kg/m2 for basal insulin, 57.9 years/8.7%/37.9kg/m2 for GLP-1 RA add-on, 61.6 years/8.9%/34.4kg/m2 for OAD add-on and 61.7 years/9.1%/34.4kg/m2 for bolus add-on. Gender distribution was similar across groups. Of patients on basal insulin without intensification, 67% had uncontrolled HbA1c values (≥7%). Significant shares of patients adding GLP-1 (36%), OAD (40%) or bolus (48%) were severely uncontrolled (HbA1c≥9%) at time of intensification.
Discussion: Multiple strategies are used in the US to intensify basal insulin. Patient characteristics varied across treatment groups (e.g. older patients were less often intensified and less often received GLP-1 RA; patients adding bolus insulin had highest HbA1c level (all p<0.001)). A substantial number of patients not intensifying basal insulin showed elevated levels of HbA1c and BMI. Similarly, many patients had very high HbA1c levels (≥9%) when intensification occurred indicating potential lack of timely insulin intensification. Elevated BMI levels across groups indicated a possible unmet need for diabetes therapies that exhibit weight neutrality or weight loss. Study limitations include: 1) basal insulin doses could not be assessed so potential titration was not accounted for, 2) it was not known how long patients had been uncontrolled for at time of index.

Conclusion: This study points to a need for more effective disease management for basal insulin users.

Abstract #290

EFFICACY AND SAFETY OF ONCE-WEEKLY SEMAGLUTIDE VS ONCE-DAILY INSULIN GLARGINE IN INSULIN-NAÏVE SUBJECTS WITH TYPE 2 DIABETES (SUSTAIN 4)

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Objective: This trial evaluated the efficacy, safety and tolerability of subcutaneous semaglutide vs insulin glargine (IGlar) in insulin-naïve subjects with T2D.

Methods: In this phase 3a, open-label study, 1089 adults with T2D (HbA1c 7–10%) were randomized to semaglutide 0.5 mg (n=362) or 1.0 mg (n=362) once weekly or IGlар (n=365; starting dose 10 IU/day) once daily for 30 weeks, added to stable metformin +/- sulfonylurea (SU). In both semaglutide groups, 51% of subjects were on metformin + SU vs 52% with IGlар. Investigators were instructed to titrate to a pre-breakfast SMPG target of 4.0–5.5 mmol/L. In both semaglutide groups, 51% of subjects were on metformin + SU vs 52% with IGlар. Investigators were instructed to titrate to a pre-breakfast SMPG target of 4.0–5.5 mmol/L. In both semaglutide groups, 51% of subjects were on metformin + SU vs 52% with IGlар. Investigators were instructed to titrate to a pre-breakfast SMPG target of 4.0–5.5 mmol/L. In both semaglutide groups, 51% of subjects were on metformin + SU vs 52% with IGlар. Investigators were instructed to titrate to a pre-breakfast SMPG target of 4.0–5.5 mmol/L. In both semaglutide groups, 51% of subjects were on metformin + SU vs 52% with IGlар. Investigators were instructed to titrate to a pre-breakfast SMPG target of 4.0–5.5 mmol/L. The primary endpoint was change in HbA1c from baseline to Week 30.

Results: Mean HbA1c (baseline 8.2%) was reduced with semaglutide 0.5 and 1.0 mg by 1.2% and 1.6% vs 0.8% with IGlар (estimated treatment difference vs IGlар [ETD] −0.38% and −0.81%; p<0.0001 for both). Mean IGlар dose at Week 30 was 29.2 IU/day. HbA1c <7% was achieved by 57.5% and 73.3% of 0.5 and 1.0 mg semaglutide-treated subjects vs 38.1% with IGlар. HbA1c ≤6.5% was achieved by 37.3%, 54.2% and 17.5% of subjects, respectively. Mean FPG (baseline 9.7 mmol/L) was reduced with semaglutide 0.5 and 1.0 mg by 2.1 and 2.7 mmol/L vs 2.1 mmol/L with IGlар (ETD 0.07 mmol/L [p=0.7] and −0.61 mmol/L [p=0.0002]). Mean 8-point SMPG (baseline 10.9 mmol/L) was reduced by 2.4, 2.9 and 2.4 mmol/L, respectively (ETD −0.07 mmol/L [p=0.6] and −0.58 mmol/L [p<0.0001]). Mean body weight (BW; baseline 93.4 kg) decreased with semaglutide 0.5 and 1.0 mg by 3.5 and 5.2 kg vs a 1.2 kg increase with IGlар (ETD −4.62 kg and −6.34 kg; p<0.0001 for both). Overall treatment satisfaction (DTSQ; baseline 26.9) improved by 4.9, 5.4 and 4.0 points, respectively (ETD 0.07 [p=0.025] and 1.38 [p=0.0005]). The proportion of subjects reporting adverse events (AE) was 69.9%, 73.3% and 65.3% with semaglutide 0.5, 1.0 mg and IGlар, respectively; 6.1%, 4.7% and 5.0% reported serious AEs. Fatal AEs were reported in 4 semaglutide subjects (1 pancreatic cancer, 3 cardiovascular) and 2 IGlар subjects (both cardiovascular). Discontinuation due to AEs occurred in 5.5%, 7.5% and 1.1% of patients, respectively. The majority of discontinuations with semaglutide were due to gastrointestinal (GI) AEs; mild, transient GI AEs were the most common AEs with semaglutide. The proportion of subjects reporting GI AEs was: 21.3%, 22.2% and 3.6% for nausea; 16.3%, 19.2% and 4.4% for diarrhea; and 6.6%, 10.3% and 3.1% for vomiting. Severe BG-confirmed hypoglycemia was reported by 4.4%, 5.6% and 10.6% of subjects, respectively.

Conclusion: Semaglutide (0.5 and 1.0 mg once weekly) provided superior glycemic control and BW reduction vs IGlар in patients with T2D treated with metformin +/- SU.
Abstract #291

EFFICACY AND SAFETY OF LIRAGLUTIDE ADDED TO INSULIN TREATMENT IN TYPE 1 DIABETES, THE ADJUNCT ONE TREAT-TO-TARGET RANDOMIZED TRIAL

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Objective: To investigate if adjunct treatment with liraglutide (lira), a glucagon-like peptide-1 analog, improves glycemic control and reduces insulin requirements and body weight in type 1 diabetes (T1D).

Methods: A 52-week double-blinded multinational treat-to-target (TTT) trial in adults with T1D in suboptimal glycemic control (HbA1c 7-10%). Subjects (n=1398) were randomized in a 3:1 ratio to receive once-daily subcutaneous injections of lira (1.8 mg, 1.2 mg or 0.6 mg) or placebo as adjunct to insulin. Endpoints, primary: change in HbA1c, fasting body weight, total insulin dose and secondary: symptomatic hypoglycemic episodes.

Results: At baseline, the mean age, T1D duration, HbA1c and body weight were 44 years, 21 years, 8.2% and 86.2 kg, respectively. There were 52% women, 28% on CSII treatment, 7% had severe hypoglycemia in the last year, 6% had hypoglycemic unawareness and 17% had a fasting C-peptide ≥ 0.03 nmol/L. HbA1c was reduced 0.34-0.54% across groups at week 52. Despite the TTT design, reductions in HbA1c in lira1.8 mg and 1.2 mg compared with placebo (estimated treatment differences (ETD) 95% confidence interval (95% CI) = 1.8 mg: -0.20 % (-0.32; -0.07), 1.2 mg: -0.15 % (-0.27; -0.03), 0.6 mg: -0.09% (-0.21; 0.03)). Reductions in body weight were significantly larger for all lira groups compared with placebo (ETD (95%CI) = 1.8 mg: -4.9 kg (-5.7; -4.2), 1.2 mg: -3.6 kg (-4.3; -2.8), 0.6 mg: -2.2 kg (-2.9; -1.5)). Reductions in total insulin dose were significantly larger for lira 1.8 mg and 1.2 mg compared with placebo (estimated treatment ratios (95% CIs) = 1.8 mg: 0.92 (0.88;0.96), 1.2 mg: 0.95 (0.91;0.99), 0.6 mg: 1.00 (0.96;1.04)). Significantly more symptomatic hypoglycemic episodes (def. severe or by a plasma glucose < 56 mg/dL and hypoglycemic symptoms) were seen for 1.8 mg and 1.2 mg than for placebo (estimated rate ratio (95%CI) = 1.8 mg: 1.31 (1.07;1.59), 1.2 mg: 1.27 (1.03;1.55), 0.6 mg: 1.17 (0.97;1.43)). There were no significant differences for severe hypoglycemic episodes (1.8 mg (45), 1.2 mg (31), 0.6 mg (40), placebo (57)). Significantly more hyperglycemic episodes with ketosis >1.5 mmol/L were seen for 1.8 mg (77) than for placebo (37), but not for 1.2 mg (44) or 0.6 mg (54). There were 8 diabetic ketoacidosis episodes (1.8 mg (3), 1.2 mg (1), 0.6 mg (4), placebo (0)). The most frequently reported adverse events with lira were nausea and vomiting.

Conclusion: Liraglutide 1.8 mg and 1.2 mg, as adjunct to insulin, lead to greater reductions in HbA1c, body weight and total insulin dose compared with placebo, but the higher rates of symptomatic hypoglycemia seem to limit the clinical utility for a broad T1D population as studied in this trial.

Abstract #292

DESIGN OF A 24-WEEK TRIAL OF EMPAGLIFLOZIN ONCE DAILY IN HYPERTENSIVE BLACK/AFRICAN AMERICAN PATIENTS WITH TYPE 2 DIABETES MELLITUS (T2DM)

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Objective: African Americans are disproportionately affected by T2DM, diabetes-related complications, and hypertension, but they are often underrepresented in clinical trials. In a primarily white population with T2DM and hypertension, the SGLT2 inhibitor empagliflozin was associated with significant reductions in HbA1c and blood pressure (BP)—both in office and ambulatory BP monitoring. The present study has been designed to similarly assess empagliflozin in a self-identified black/African American population.

Methods: This is an ongoing multicenter, randomized, double-blind, placebo-controlled, parallel group phase IIib study (NCT02182830) assessing the safety and efficacy of empagliflozin (10 or 25 mg/day) versus placebo in black/African American patients with uncontrolled T2DM and hypertension (mean seated systolic BP [SBP] 140-180 mmHg; diastolic BP [DBP] 90-110 mmHg). Enrolling 154 patients (77 per treatment group) was calculated to provide ≥80% power to detect meaningful differences in HbA1c, BP, and body weight. For glucose-lowering therapy, patients will be drug-naïve (no antidiabetic therapy for 12 weeks; pioglitazone for 16 weeks) or pre-treated with either metformin, a sulfonylurea (SU), a DPP-4 inhibitor, metformin plus SU, or metformin plus DPP-4 inhibitor (stable dose for ≥12 weeks before randomization). For antihypertensive therapy, patients will be on at least 1 but not more than 3 antihypertensive drugs for ≥4 weeks. After a 2-week placebo run-in, eligible patients will be
randomized (1:1) to empagliflozin or placebo. From a starting dose of 10 mg, a dose escalation to 25 mg will be introduced at Week 4. The primary endpoint is the change from baseline in HbA1c at Week 24. Key secondary endpoints are change from baseline in: trough seated SBP at Week 12, mean 24-hr ambulatory SBP at Week 12, mean trough ambulatory SBP at Week 12, and body weight at Week 24. Other secondary endpoints include change from baseline in: mean 24-hr ambulatory DBP at Week 12 and 24, mean 24-hr ambulatory SBP at Week 24, trough seated SBP and DBP at Week 24, and trough seated DBP at Week 12. Safety and tolerability will be assessed by incidence of adverse events, including hypoglycemia and orthostatic changes in BP.

**Results:** The study is currently recruiting patients at 111 centers across the United States, and is expected to complete in 2017.

**Discussion:** This is the first trial of an SGLT2 inhibitor specifically conducted in black/African American patients.

**Conclusion:** Results of this study will add to our understanding of the efficacy and safety of empagliflozin in self-identified black/African Americans with T2DM and hypertension.

Abstract #293

**POST-OPERATIVE INSULIN REQUIREMENTS IN BARIATRIC SURGERY**

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**Objective:** 1) Determine perioperative glycemic control in patients with type 2 diabetes (DM) on insulin who have undergone bariatric surgery. 2) Compare pre and post-operative insulin regimens and dosage in these patients.

**Methods:** Retrospective chart review of patients with type 2 DM on insulin who underwent Roux-en-Y bariatric surgery at Cleveland Clinic 2010-2014. Time points used were prior to admission (Baseline), day of surgery (DOS), and post-operative days 1-2 (POD 1, POD2). Comparisons between the time points were done using paired t-test. Subgroup analysis was performed on patients with good control (BG 100-140mg/dL for >50% of the time on POD2), and was compared with the subjects not in control with t-test.

**Results:** N=114, 55% females, 75% Caucasian, mean age 52.8±9.8 years (SD), BMI 46.2±8.0 kg/m2, A1c 8.3±1.7%. HTN was present in 79%, lipid disorders in 82%. Sixty-six% were on insulin plus non-insulin medications, the rest on insulin only. Mean blood glucose (BGs) (mg/dL): Baseline N/A, DOS 185±43, POD1 171±41 (p <0.0001 vs DOS), POD2 160±36 (p <0.0001 vs DOS). Mean daily insulin dose (units): Baseline 85.8±62.9, DOS 11.5±13.2, POD1 16.8±21.2, POD2 11.5±15.3, with p <0.0001 for all time points vs Baseline. Mean insulin dose per body weight (unit/kg): Baseline 0.65±0.45, DOS 0.04±0.05, POD1 0.13±0.15, and POD2 0.09±0.11, with p <0.0001 for all time points vs Baseline. On POD2 95% were on insulin only, the rest on insulin plus non-insulin medications. In subgroup with good control, A1c 7.9%±1.6, mean daily insulin doses (units) were: Baseline 75.6±55.7, DOS 7.7±7.6, POD1 8.7±11.6, and POD2 4.0±6.2, all with p <0.0001 vs Baseline. Mean doses of insulin per body weight (unit/kg): Baseline 0.58±0.42, DOS 0.03±0.03, POD1 0.07±0.11, and POD2 0.03±0.06, all with p value <0.0001 vs Baseline. Subgroup with good control vs subjects not in control comparisons were: A1c p=0.0354, BG POD2 p<0.0001, total insulin POD2 p<0.0001, insulin per body weight POD2 p<0.0001.

**Discussion:** Most patients were managed on insulin alone post-operatively, consistent with recommendations for inpatient DM. Glycemic control on POD1 and POD2 was fair, falling in the upper end of the ADA guidelines of 100-180 mg/dL in hospitalized patients. An 86% reduction in the total daily dose of Insulin was seen by POD2. In the subgroup with good glycemic control, there was an even larger reduction, 95%, in total daily insulin use despite lower BGs.

**Conclusion:** Mean BGs were 160-170 mg/dl on 0.09-0.13 units/kg (86% reduction) on POD1 and 2, when patients are on clear liquids q1hr. This will assist in developing algorithms for insulin titration after bariatric surgery.

Abstract #294

**POTENTIAL RELEVANCE OF CHANGES IN HEMATOCRIT TO CHANGES IN LIPID PARAMETERS WITH EMPAGLIFLOZIN IN PATIENTS WITH TYPE 2 DIABETES MELLITUS (T2DM)**

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**Objective:** Empagliflozin (EMPA), either as monotherapy or as add-on therapy, has consistently reduced HbA1c in patients with T2DM. Changes in lipid parameters have been observed following EMPA treatment. To test our hypothesis that these lipid changes could be partly due
to hemoconcentration as a result of increased urinary volume and subsequent volume contraction, we used pooled data from four 24-week, Phase III, randomized trials (NCT01177813, NCT01159600, NCT01210001) to analyze the contributions of % changes in hematocrit (HCT, a marker of plasma volume changes) to % changes in LDL-C, HDL-C, triglycerides (TG) and apolipoprotein B (Apo B).

**Methods:** Patients with T2DM received 24 weeks’ placebo (PBO), EMPA 10 mg, or EMPA 25 mg as monotherapy or add-on therapy (N=2477; mean [SD] age 55.6 [10.2] yrs, HbA1c 7.99 [0.85]%, BMI 28.7 [5.5] kg/m2). ANCOVA models were used to assess % changes in LDL-C, HDL-C, TG, and Apo B, and changes in these variables after adjustment for % changes in HCT.

**Results:** Increases in LDL-C, HDL-C and Apo B, and decreases in TG from baseline were seen with EMPA 10 mg (PBO-subtracted adjusted mean % change [95% CI] from BL 3.30% [0.32, 6.29], 5.58% [4.09, 7.07], 1.33% [−0.78, 3.43] and −7.12% [−11.51, −2.73]) and EMPA 25 mg (4.38% [1.40, 7.36], 5.25% [3.76, 6.74]; p<0.05), 1.91% [−0.20, 4.02], and −3.75% [−8.15, 0.64]). At week 24, the PBO-corrected adjusted mean (SE) % changes from BL in HCT were 5.2 (0.3)% with EMPA 10 mg and 5.5 (0.3)% with EMPA 25 mg (both p<0.001). Changes in % HCT with EMPA 10 and 25 were significantly associated with changes in % LDL-C, HDL-C, TG, and Apo B (p<0.05). After adjusting for the change in % HCT, the remaining % change in each lipid fraction was only significant for HDL-C and TG (EMPA 10 mg, 25 mg: LDL-C 1.33% [−1.84, 4.50], 2.29% [−0.89, 5.47]; HDL-C 4.09% [2.51, 5.68], 3.66% [2.07, 5.26]; TG −12.08% [−16.75, −7.41], −9.02% [−13.72, −4.32]; Apo B, −1.40% [−3.64, 0.84], −0.97% [−3.23, 1.29].

**Discussion:** The % changes in HCT were associated with % changes in LDL-C, HDL-C, TG and Apo B. As the observed increase in HCT may reflect hemoconcentration, the lipid parameter changes seen may be partly due to hemoconcentration. Percentage changes in HDL-C and TG that were independent of % changes in HCT were more pronounced than for the other lipid parameters.

**Conclusion:** Percentage changes in LDL-C, HDL-C, TG and Apo B following treatment with EMPA in patients in T2DM may partly reflect hemoconcentration. Improvements in metabolic control may drive HCT-independent % changes in HDL-C and TG.

**Abstract #295**

**ROLE OF ANGIOTENSIN-CONVERTING ENZYME GENE INSERTION/DELETION POLYMORPHISM IN DIABETIC PATIENTS WITH CHRONIC KIDNEY DISEASE**

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**Objective:** Genetic susceptibility plays an important role in the risk of developing chronic complications in patients. This study investigated the effects of ACE I/D polymorphism on chronic kidney disease (CKD) risk in patients with diabetes.

**Methods:** The allele frequency and the genotype distribution of the ACE (I/D) polymorphism were studied in 208 patients with diabetes type 1 and type 2 aged 21-79 years (50.55±14.96). Polymorphisms of ACE (I/D) were examined by polymerase chain reaction and restriction fragment length polymorphism. Glomerular filtration rate (eGFR) was defined and calculated using the CKD-EPI. Chi-square and analysis of variance (ANOVA) were used for association studies and to assess the differences in the values among the groups.

**Results:** Patients carrying the ACE DD genotype had a higher odds ratio (OR) = 2.00 [1.09;4.31] of CKD. In measured genotype analyses, the ACE I/D polymorphism was not associated with urinary homocysteine level, urinary NGAL level and albumin excretion rate. However, the association with albumin excretion rate was of borderline statistical significance (ANOVA P = 0.055), with eGFR was significant (ANOVA P = 0.01). Homozygosity for the D allele was associated with decreased eGFR (87.54±3.36 ml/min/1.73 m2) compared with homozygosity for the I allele (89.11±3.12 ml/min/1.73 m2) and with heterozygotes (97.92±2.12 ml/min/1.73 m2) (post hoc pairwise comparisons DD versus DI, P=0.012; DD versus IL, P=0.756; DI versus II, P = 0.047).

**Conclusion:** The risk of having CKD was increased in homozygous (DD) diabetic patients with I/D polymorphism of the ACE gene. However, more investigations are required to further this association.
Abstract #296

EFFICACY OF CANAGLIFLOZIN (CANA) IN COMBINATION WITH METFORMIN (MET) IN PATIENTS WITH TYPE 2 DIABETES MELLITUS (T2DM): RESULTS FROM 3 STUDIES

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Objective: In the AACE clinical practice guidelines, SGLT2 inhibitors, such as CANA, are the first oral medication recommended for patients inadequately controlled on MET. This analysis assessed the efficacy of CANA in patients with T2DM in combination with MET in 3 studies.

Methods: Changes in A1C, body weight (BW), and systolic blood pressure (SBP) were assessed in 3 randomized, double-blind, Phase 3 studies of CANA in combination with MET. CANA 100 and 300mg were assessed vs placebo (PBO) at Week 26 and sitagliptin 100 mg (SITA) at Week 52 in Study 1 (N=1,284; A1C, 7.9%; BW, 87kg; SBP, 128mmHg), and vs glimepiride (GLIM) at Weeks 52 and 104 in Study 2 (N=1,450; A1C, 7.8%; BW, 87kg; SBP, 130mmHg). In Study 3, drug-naïve T2DM patients (N=1,186; A1C, 8.8%; BW, 91kg; SBP, 129mmHg) received initial combination therapy with MET+CANA 100mg (CANA100/MET) or MET+CANA 300mg (CANA300/MET) vs MET alone for 26 weeks.

Results: In Study 1, CANA 100 and 300mg significantly lowered A1C vs PBO at Week 26 (–0.79%, –0.94%, –0.17%; P<0.001); CANA 100mg demonstrated noninferiority and CANA 300mg demonstrated superiority vs SITA at Week 52 (–0.73%, –0.88%, –0.73%). In Study 2, CANA 100 and 300mg significantly lowered A1C vs GLIM at Week 52 (–0.82%, –0.93%, –0.81%); reductions were –0.65%, –0.74%, and –0.55% at Week 104. In Study 3, CANA100/MET and CANA300/MET significantly lowered A1C vs MET at Week 26 (–1.77%, –1.78%, –1.30%; P<0.001). Significant BW reductions were seen in Study 1 with CANA 100 and 300mg vs PBO at Week 26 (–3.7%, –4.2%, –1.2%; P<0.001) and vs SITA at Week 52 (–3.8%, –4.2%, –1.3%; P<0.001). In Study 2, CANA 100 and 300mg significantly lowered BW vs GLIM at Week 52 (–4.2%, –4.7%, 1.0%; P<0.001); BW changes were sustained at Week 104 (–4.1%, –4.2%, 0.9%). In Study 3, significantly greater weight loss was seen with CANA100/MET and CANA300/MET vs MET at Week 26 (–3.5%, –4.2%, –2.1%; P=0.001). CANA 100 and 300mg were associated with reductions in SBP vs PBO at Week 26 (–3.8, –5.1, 1.5mmHg; P<0.001) and SITA at Week 52 (–3.5, –4.7, –0.7mmHg; P<0.001) in Study 1, and vs GLIM at Week 52 (–3.3, –4.6, 0.2mmHg) and Week 104 (–2.0, –3.1, 1.7mmHg) in Study 2. In Study 3, SBP reductions were –2.2, –1.7, and –0.3mmHg with CANA100/MET, CANA300/MET, and MET at Week 26. CANA was generally well tolerated in each study, with increased incidence of adverse events related to SGLT2 inhibition (eg, genital mycotic infections) and low rates of hypoglycemia.

Conclusion: In 3 studies, CANA in combination with MET improved A1C, BW, and SBP, suggesting that a fixed-dose combination of CANA+MET may be beneficial in patients with T2DM.

Abstract #297

IS ABNORMAL BNP PREVALENT IN RANDOMLY SELECTED ASYMPTOMATIC NON CARDIAC T2DM PATIENTS?

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Objective: BNP is a natriuretic peptide secreted by the heart in response to a pressure or volume overload. It has been shown to be a reliable marker of myocardial dysfunction in both diabetic and non diabetic patients. Furthermore it has been shown to be a prognostic indicator in diabetic patients predicting increased risk for cardiac morbidity and mortality. We report the prevalence of abnormal BNP or NT-proBNP in a sample of randomly selected, asymptomatic, non cardiac, T2DM patients.

Methods: The prevalence of abnormal BNP or NT-proBNP was determined in 21 patients, 12 males mean age 63.3 yrs (38-85 yrs) and 9 females mean age 64.2 yrs (45-88 yrs) being followed in an office based diabetic practice. Patients had neither history nor clinical evidence of cardiac disease. All had T2DM. Therapy, duration of disease, obesity, HbA1c, atherosclerotic risk factors, cardiac test results, and renal function were not considered in patient selection. BNP or NT-proBNP was measured at the patient’s next blood sampling using the methodology of the laboratory where the patient routinely had their blood work done. All laboratories met provincially and federally mandated standards.

Results: Twenty out of 21 patients tested had normal BNP or NT-proBNP was determined in 21 patients, 12 males mean age 63.3 yrs (38-85 yrs) and 9 females mean age 64.2 yrs (45-88 yrs) being followed in an office based diabetic practice. Patients had neither history nor clinical evidence of cardiac disease. All had T2DM. Therapy, duration of disease, obesity, HbA1c, atherosclerotic risk factors, cardiac test results, and renal function were not considered in patient selection. BNP or NT-proBNP was measured at the patient’s next blood sampling using the methodology of the laboratory where the patient routinely had their blood work done. All laboratories met provincially and federally mandated standards.

Discussion: Essentially all patients in this study had normal BNP or NT-proBNP. One patient, a 72 yr old female, had a BNP value 1 unit above the upper limit of normal for her age.
ABSTRACTS – Diabetes Mellitus/Prediabetes

Results: ANCOVA regression modeling analyzed with descriptive statistics, logistic, binomial, and (blood glucose ≤70 mg/dL/ third-party assistance) were <7.5%, weight change, and combined hypoglycemia >65 y), hemoglobin A1c (A1C), % patients reaching A1C studies. In four age groups (<55 y, 55–≤60 y, 60–≤65 y, >65 y), randomized to Gla-300 or Gla-100 QD for 6 months hypoglycemia were generated for patients with T2D mean duration of T2D 11.2 y; mean BMI 33.8 kg/m2). At 12 months’ follow-up, A1C reduction was comparable for Gla-300 and Gla-100 across age ranges (A1C change for Gla-300 vs Gla-100 for age categories: –0.77 vs –0.81%; –0.99 vs –0.74%, –0.86 vs –0.84%; –0.96 vs –0.95%), as was the proportion of patients reaching A1C <7.5% (Gla-300 vs Gla-100: 45.0 vs 54.3%; 55.2 vs 43.6%; 50.9 vs 52.2%; 56.4 vs 54.7%; age*treatment interaction P=0.04 ). Hypoglycemia incidence and rates were significantly lower for Gla-300 patients at all ages (% patients, Gla-300 vs Gla-100: 58.7 vs 64.9%; 62.5 vs 71.6%; 64.1 vs 72.0%; 60.7 vs 71.5%, treatment P=0.0005, region P=0.005 [higher for non-US patients], age*treatment*region interaction P=0.0028. No. events/patient-year for Gla-300 vs Gla-100: 9.2 vs 13.3; 12.5 vs 17.1; 12.8 vs 14.0; 12.3 vs 14.7; treatment P=0.0047, age*treatment*region interaction P=0.0009). There was a significant effect of age on weight change (kg for Gla-300 vs Gla-100: 1.31 vs 1.83; 0.25 vs 1.05; 0.29 vs 0.77; 0.64 vs 0.70, age P=0.0002, treatment P=0.04 ). There was no significant dose/kg change from 6 months to 12 months in either treatment arm.

Discussion: Among T2D patients, efficacy in reducing A1C in younger and older age groups was similar for Gla-300 and Gla-100, while hypoglycemia was lower with Gla-300. These data are consistent with results seen at 6 months.

Conclusion: The aging diabetes population may benefit from treatment with Gla-300, which shows a lower rate of hypoglycemia while maintaining similar efficacy compared with Gla-100.

Abstract #298

MAINTAINING GLYCEMIC CONTROL ON GLA-300 WHILE DECREASING HYPOGLYCEMIA IN AN AGING TYPE 2 DIABETES (T2D) POPULATION: 12-MONTH RESULTS (EDITION 2, EDITION 3)

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Objective: Glycemic control is suboptimal in many patients with T2D on insulin and higher rates of hypoglycemia lead to hospitalization in older patients. We compared efficacy and hypoglycemia risk for insulin glargine 100 U/ml (Gla-100) and new insulin glargine 300 U/ml (Gla-300), a formulation with a more constant pharmacokinetic profile and prolonged duration of action, in an aging population.

Methods: Pooled data on glycemic control and hypoglycemia were generated for patients with T2D randomized to Gla-300 or Gla-100 QD for 6 months from the EDITION 2 (basal insulin + oral antidiabetes drugs [OADs]) and EDITION 3 (insulin-naive on OADs) studies. In four age groups (<55 y, 55–≤60 y, 60–≤65 y, >65 y), hemoglobin A1c (A1C), % patients reaching A1C <7.5%, weight change, and combined hypoglycemia (blood glucose ≤70 mg/dL/ third-party assistance) were analyzed with descriptive statistics, logistic, binomial, and ANCOVA regression modeling.

Results: A total of 1,670 patients (<55 y, n=553; 55–≤60 y, n=343; 60–≤65 y, n=364; >65 y, n=410) were included (mean age 58.0 y; age range 24.0 – 87.0 y; mean A1C 8.4%; mean duration of T2D 11.2 y; mean BMI 33.8 kg/m2). At

12 months’ follow-up, A1C reduction was comparable for Gla-300 and Gla-100 across age ranges (A1C change for Gla-300 vs Gla-100 for age categories: –0.77 vs –0.81%; –0.99 vs –0.74%, –0.86 vs –0.84%; –0.96 vs –0.95%), as was the proportion of patients reaching A1C <7.5% (Gla-300 vs Gla-100: 45.0 vs 54.3%; 55.2 vs 43.6%; 50.9 vs 52.2%; 56.4 vs 54.7%; age*treatment interaction P=0.04 ). Hypoglycemia incidence and rates were significantly lower for Gla-300 patients at all ages (% patients, Gla-300 vs Gla-100: 58.7 vs 64.9%; 62.5 vs 71.6%; 64.1 vs 72.0%; 60.7 vs 71.5%, treatment P=0.0005, region P=0.005 [higher for non-US patients], age*treatment*region interaction P=0.0028. No. events/patient-year for Gla-300 vs Gla-100: 9.2 vs 13.3; 12.5 vs 17.1; 12.8 vs 14.0; 12.3 vs 14.7; treatment P=0.0047, age*treatment*region interaction P=0.0009). There was a significant effect of age on weight change (kg for Gla-300 vs Gla-100: 1.31 vs 1.83; 0.25 vs 1.05; 0.29 vs 0.77; 0.64 vs 0.70, age P=0.0002, treatment P=0.04 ). There was no significant dose/kg change from 6 months to 12 months in either treatment arm.

Discussion: Among T2D patients, efficacy in reducing A1C in younger and older age groups was similar for Gla-300 and Gla-100, while hypoglycemia was lower with Gla-300. These data are consistent with results seen at 6 months.

Conclusion: The aging diabetes population may benefit from treatment with Gla-300, which shows a lower rate of hypoglycemia while maintaining similar efficacy compared with Gla-100.

Abstract #299

EFFICACY AND SAFETY OF LIRAGLUTIDE ADDED TO CAPPED INSULIN TREATMENT IN TYPE 1 DIABETES, THE ADJUNCT TWO RANDOMIZED TRIAL

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Objective: To investigate if treatment with liraglutide (lira), a glucagon-like peptide-1 analog, added to individually capped insulin treatment improves glycemic control and reduces weight and insulin dose in a broad population of adults with type 1 diabetes (T1D).
Methods: The 26-week, double-blind, multinational trial enrolled adults with T1D on basal-bolus or CSII therapy with HbA1c 7–10%. Subjects with a history of severe hypoglycemia, hypoglycemia unawareness, DKA or renal impairment (with estimated GFR >30 mL/min/1.73 m2) were not excluded. Subjects were randomized 3:1 to receive once-daily subcutaneous injections of lira (1.8 mg, 1.2 mg, 0.6 mg) or placebo. Each subject titrated insulin with total daily dose capped at their own average dose from the week prior to randomization.

Results: At baseline, n = 835, mean age = 43 years, T1D duration = 21 years, HbA1c = 8.1%, BMI = 29 kg/m2 (60%, >27 kg/m2) and body weight = 83.9 kg; 54% of subjects were women, 26% used CSII, 7% had severe hypoglycemia in the last year, 6% had severe hypoglycemia-unaware and 15% had baseline fasting C-peptide >0.03 nmol/L. Lira treatment at all doses reduced HbA1c, body weight and insulin dose, both absolutely and relative to placebo, after 26 weeks. For lira 1.8 mg, 1.2 mg and 0.6 mg, respectively: HbA1c estimated treatment differences (ETDs) [95% confidence intervals] to placebo were -0.35% [-0.50;-0.20], -0.23% [-0.38;-0.08] and -0.24% [-0.39;0.10]; body weight ETDs were -4.8 kg [-5.5;-4.1], -3.7 kg [-4.4;-3.0] and -2.2 kg [-2.9;-1.5]; insulin dose estimated treatment ratios to placebo were 0.90 [0.86;0.93], 0.93 [0.90;0.96], and 0.95 [0.92;0.99]. The rate of symptomatic hypoglycemic episodes (severe by ADA classification or <56 mg/dL with symptoms) was increased relative to placebo with lira 1.2 mg (estimated rate ratio, ERR=1.31 [1.03;1.68]). Rates of severe hypoglycemic episodes were similar across groups. The percentage of subjects achieving HbA1c reduction >1.0% with no severe hypoglycemia was greater at all lira doses (all p≤0.0078) compared to placebo (1.8 mg, 15.3%; 1.2 mg, 11.3%; 0.6 mg, 11.1%; placebo, 3.7%). The most frequent adverse events with lira were dose-dependent nausea and vomiting. The rate of hyperglycemic episodes accompanied by ketosis (>1.5 mmol/L) was increased with lira 1.8 mg (ERR=3.96 [1.49;10.55]; lira n=42; placebo n=10).

Conclusion: Liraglutide (1.8 mg, 1.2 mg and 0.6 mg) added to caged insulin treatment led to greater reductions in HbA1c, body weight and insulin dose compared to placebo, but a higher rate of symptomatic hypoglycemia (liraglutide 1.2 mg) may limit the clinical utility of liraglutide for a broad T1D population as studied in this trial.

Abstract #300

CASE OF EXTREME INSULIN RESISTANCE SECONDARY TO INSULIN ANTIBODY: SUCCESSFUL TREATMENT WITH COMBINATION IMMUNOSUPPRESSIVE THERAPY USED FOR TYPE B INSULIN RESISTANCE

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Objective: Immunological insulin resistance can occur in ≤ 0.1% of insulin treated patients manifesting as postprandial hyperglycemia and fasting hypoglycemia. Previous cases were treated with plasmapheresis or various immunosuppressants. We present a case of extreme insulin resistance secondary to insulin antibody successfully treated using rituximab, cyclophosphamide and dexamethasone.

Case Presentation: A 60-year-old African American man with type 2 DM was admitted with diabetic ketoacidosis. Two years prior to presentation, he was well controlled on 24 units/day of insulin. He then experienced deterioration of glycemic control requiring 174 units/day of insulin and HgA1c of 10.8% at admission. On exam, he did not have acanthosis nigricans, lipodystrophy or Cushingoid features. He required 1020 units of IV insulin to close the anion gap and we could not safely transition him from IV insulin to a steady dose of U500 due to fluctuating daily insulin requirements, ranging from 900 to 1500 units/day without significant fasting hypoglycemia. Further evaluation for type B insulin resistance revealed adiponectin level of 467 IU/mL (0-5 IU/mL). Given adiponectin level > 7 ug/dL, positive ANA with titer of 1:320 (< 1:40) and elevated rheumatoid factor level to 467 IU/mL (0-5 IU/mL). Given adiponectin level > 7 ug/mL, reported to have a 97% positive predictive value for insulin receptoropathy, and non-elevated triglyceride level with evidence of rheumatologic illness and extreme insulin resistance, suspicion for type B insulin resistance was very high. Therefore, we initiated treatment with protocol developed at the NIH using rituximab, cyclophosphamide and dexamethasone. He received two cycles of treatment and his insulin requirement diminished drastically. He was discharged on total daily dose of 57 units of insulin. Interestingly, to confirm our diagnosis, a serum sample had been sent to an experienced research laboratory to test for insulin receptor antibody prior to initiating the above treatment protocol. The result of insulin receptor antibody test returned 4 weeks after discharge. Surprisingly, he did not have insulin receptor antibody but rather had extremely high titer of anti-insulin antibody.

Discussion: Extreme insulin resistance secondary to insulin antibody can masquerade as type B insulin...
resistance. Both entities cause extreme insulin resistance and should be distinguished but a treatment regimen using rituximab, cyclophosphamide and dexamethasone appears to be effective for both conditions.

**Conclusion:** Immunological insulin resistance from insulin antibody can present with extreme insulin resistance without fasting hypoglycemia and can be effectively treated using combination immunosuppressive therapy.

**Abstract #301**

**CONTEMPLATING AN ADDITIONAL ORAL AGENT FOR YOUR PATIENT WITH TYPE 2 DIABETES? CONSIDER POSSIBLE INTERACTION BETWEEN QUALITY OF YOUR CONVERSATION WITH PATIENT’S ATTEMPTS AT BARGAINING AND SELF-REPORTED OUTCOMES - LESSONS FROM THE INTRODIA™ STUDY**

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**Objective:** IntroDia™ is investigating physician-patient communication during early treatment of type 2 diabetes (T2D); at diagnosis and at the time, often months or years post-diagnosis, when an additional medication is added (“add-on”). Here we examine the issue of patient bargaining (to delay additional medication) and its association with self-reported outcomes.

**Methods:** As part of IntroDia™, 4235 T2D patients from 26 countries (median age, 46 years; male gender, 52%) were surveyed about their experience with their physician during oral medication add-on conversations (which had occurred, on average, 7.42 months ago). Patients were asked whether, during these conversations, they tried to convince their physician to postpone the additional medication. Patient-perceived communication quality (PPCQ) (using elements from Consumer Assessment of Healthcare Providers and Systems [CAHPS®], Trust in Physician Scale [TIP], and Interpersonal Process of Care [IPC] questionnaires) was measured, as well as current psychosocial status (Diabetes Distress Scale [DDS®] and WHO-5® Well-being index), and self-care behaviors (Summary of Diabetes Self-Care Activities [SDSCA]).

Results: At add-on, 80% of patients did not bargain (DNB), while 20% did bargain (DB). Of note, within the DB group, approximately 60% of patients managed to delay initiating additional medication, while 40% did not. There were no clinically relevant differences between DNBs and DBs on key demographic variables. The mean PPCQ score (scale 1=poor to 4=high [SD]) was significantly higher (p < 0.001) for DNBs versus DBs (3.25 [0.71] vs. 3.01 [0.68]). DNBs were significantly less distressed by diabetes than DBs (Emotional DDS score: 2.63 [1.25] vs. 3.45 [1.28]; p < 0.001). In addition, well-being and self-care scores were significantly higher for DNBs versus DBs, respectively (WHO-5: 62.5% [24.5] vs. 54.3% [24.0]; SDSCA general diet: 4.81 [1.94] vs. 4.14 [1.92]; SDSCA medication: 5.92 [1.72] vs. 4.82 [1.93]; in all cases, p < 0.001).

**Discussion:** These data show that at least 20% of patients are reluctant to start an additional medication and actively bargain with their physicians to avoid doing so. Those who bargain report poorer PPCQ, greater diabetes distress, and poorer well-being and self-care than those who do not bargain.

**Conclusion:** Patient bargaining in T2D is associated with poorer PPCQ and poorer self-reported outcomes.

**Abstract #302**

**ACHIEVEMENT OF GLYCEMIC GOALS WITHOUT HYPOGLYCEMIA WITH CANAGLIFLOZIN VERSUS GLIMEPIRIDE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS**

Michael Davies, PhD,1 Katherine Merton, PhD, MBA,2 Ujjwala Vijapurkar, PhD,2 James Simples, None1, Amy Carroll, None1, Dainius Balis, PharmD,3 Frank Vercruysse, MD,3


**Objective:** Guidelines for the management of type 2 diabetes mellitus (T2DM) recommend lowering A1C levels to <6.5% or <7.0% for most patients as long as they can be achieved safely, while avoiding hypoglycemia. In a 52-week, Phase 3 study of patients with T2DM on background metformin (MET), canagliflozin (CANA), a sodium glucose co-transporter 2 inhibitor, improved glycemic control and reduced body weight with fewer episodes of hypoglycemia versus glimepiride (GLIM). This post hoc analysis evaluated the proportion of patients achieving A1C <7.0% and <6.5% without hypoglycemia with CANA versus GLIM.

**Methods:** Patients with T2DM (N = 1,450; mean age, 56.2
ABSTRACTS – Diabetes Mellitus/Prediabetes

Abstract #303

EFFICACY OF TITRATED CANAGLIFLOZIN IN PATIENTS WITH TYPE 2 DIABETES MEL-LITUS INADEQUATELY CONTROLLED ON METFORMIN AND SITAGLIPTIN

Michael Pfeifer, MD1, Jochen Seufert, FRCPE2, Naresh Aggarwal, MD, CCFP, FCFP3, Anjun Cao4, Albert Fung4, Maria Alba, MD4, Helena Rodbard, MD, FACP, MACE5


Objective: The efficacy and safety of canagliflozin (CANA), a sodium glucose co-transporter type 2 inhibitor, were evaluated in patients with type 2 diabetes mellitus (T2DM) inadequately controlled on metformin (MET) and sitagliptin (SITA).

Methods: In this randomized, double-blind, placebo (PBO)-controlled study, patients with T2DM (N=218; mean age, 57.4 y; mean A1C, 8.5%; mean BMI, 32.0 kg/m2; mean estimated glomerular filtration rate [eGFR], 90.5 mL/min/1.73 m2) on MET ≥1,500 mg/day (mean dose, 1,984 mg/day) and SITA 100 mg received CANA 100 mg or PBO for 6 weeks; patients were then uptitrated from CANA 100 mg to CANA 300 mg or matching PBO if they met the following criteria: baseline eGFR ≥70 mL/min/1.73 m2, fasting self-monitored blood glucose ≥100 mg/dL, and no volume depletion–related adverse events (AEs) within 2 weeks prior to uptitration. Those not meeting these criteria remained on CANA 100 mg or matching PBO, and were reassessed every 2 weeks through Week 18 to determine eligibility for uptitration. The overall incidence of adverse events (AEs) was similar with CANA 100 and 300 mg versus GLIM (64.4%, 68.5%, respectively). Incidences of male and female genital mycotic infections and osmotic diuresis–related AEs were higher with CANA 100 and 300 mg versus GLIM, consistent with other Phase 3 studies of CANA.

Conclusion: More patients with T2DM achieved A1C <7.0% and <6.5% without hypoglycemia with CANA versus GLIM over 52 weeks as add-on to MET.

Results: At Week 52, CANA 100 mg was non-inferior, and CANA 300 mg was superior to GLIM in A1C-lowering (LS mean changes of –0.82%, –0.93%, and –0.81%, respectively). The proportion of patients who achieved A1C <7.0% at Week 52 was similar across treatment groups (53.6%, 60.1%, and 55.8% with CANA 100 and 300 mg and GLIM, respectively); 25.5%, 30.6%, and 30.7% achieved A1C <6.5%, respectively. The incidence of documented hypoglycemia was significantly lower with CANA 100 and 300 mg versus GLIM (5.6%, 4.9%, and 34.2%, respectively; P <0.001). A greater proportion of patients achieved A1C <7.0% without documented hypoglycemia with CANA 100 and 300 mg versus GLIM (49.8%, 56.5%, and 32.8%, respectively; with relative ORs [95% CI] vs GLIM of 2.1 [1.6, 2.8] and 2.9 [2.2, 3.8], respectively). Similarly, a greater proportion of patients treated with CANA 100 and 300 mg versus GLIM also achieved A1C <6.5% without documented hypoglycemia (23.0%, 28.5%, and 18.4%, respectively; with relative ORs [95% CI] vs GLIM of 1.3 [0.9, 1.8] and 1.8 [1.3, 2.5], respectively). The overall incidence of adverse events (AEs) was similar with CANA 100 and 300 mg versus GLIM (64.4%, 68.5%, and 68.5%, respectively). Incidences of male and female genital mycotic infections and osmotic diuresis–related AEs were higher with CANA 100 and 300 mg versus GLIM, consistent with other Phase 3 studies of CANA.

Abstract #303

EFFICACY OF TITRATED CANAGLIFLOZIN IN PATIENTS WITH TYPE 2 DIABETES MELLITUS INADEQUATELY CONTROLLED ON METFORMIN AND SITAGLIPTIN

Michael Pfeifer, MD1, Jochen Seufert, FRCPE2, Naresh Aggarwal, MD, CCFP, FCFP3, Anjun Cao4, Albert Fung4, Maria Alba, MD4, Helena Rodbard, MD, FACP, MACE5


Objective: The efficacy and safety of canagliflozin (CANA), a sodium glucose co-transporter type 2 inhibitor, were evaluated in patients with type 2 diabetes mellitus (T2DM) inadequately controlled on metformin (MET) and sitagliptin (SITA).

Methods: In this randomized, double-blind, placebo (PBO)-controlled study, patients with T2DM (N=218; mean age, 57.4 y; mean A1C, 8.5%; mean BMI, 32.0 kg/m2; mean estimated glomerular filtration rate [eGFR], 90.5 mL/min/1.73 m2) on MET ≥1,500 mg/day (mean dose, 1,984 mg/day) and SITA 100 mg received CANA 100 mg or PBO for 6 weeks; patients were then uptitrated from CANA 100 mg to CANA 300 mg or matching PBO if they met the following criteria: baseline eGFR ≥70 mL/min/1.73 m2, fasting self-monitored blood glucose ≥100 mg/dL, and no volume depletion–related adverse events (AEs) within 2 weeks prior to uptitration. Those not meeting these criteria remained on CANA 100 mg or matching PBO, and were reassessed every 2 weeks through Week 18 to determine eligibility for uptitration. The overall incidence of adverse events (AEs) was similar with CANA 100 and 300 mg versus GLIM (64.4%, 68.5%, and 68.5%, respectively). Incidences of male and female genital mycotic infections and osmotic diuresis–related AEs were higher with CANA 100 and 300 mg versus GLIM, consistent with other Phase 3 studies of CANA.

Conclusion: More patients with T2DM achieved A1C <7.0% and <6.5% without hypoglycemia with CANA versus GLIM over 52 weeks as add-on to MET.

Results: At Week 52, CANA 100 mg was non-inferior, and CANA 300 mg was superior to GLIM in A1C-lowering (LS mean changes of –0.82%, –0.93%, and –0.81%, respectively). The proportion of patients who achieved A1C <7.0% at Week 52 was similar across treatment groups (53.6%, 60.1%, and 55.8% with CANA 100 and 300 mg and GLIM, respectively); 25.5%, 30.6%, and 30.7% achieved A1C <6.5%, respectively. The incidence of documented hypoglycemia was significantly lower with CANA 100 and 300 mg versus GLIM (5.6%, 4.9%, and 34.2%, respectively; P <0.001). A greater proportion of patients achieved A1C <7.0% without documented hypoglycemia with CANA 100 and 300 mg versus GLIM (49.8%, 56.5%, and 32.8%, respectively; with relative ORs [95% CI] vs GLIM of 2.1 [1.6, 2.8] and 2.9 [2.2, 3.8], respectively). Similarly, a greater proportion of patients treated with CANA 100 and 300 mg versus GLIM also achieved A1C <6.5% without documented hypoglycemia (23.0%, 28.5%, and 18.4%, respectively; with relative ORs [95% CI] vs GLIM of 1.3 [0.9, 1.8] and 1.8 [1.3, 2.5], respectively). The overall incidence of adverse events (AEs) was similar with CANA 100 and 300 mg versus GLIM (64.4%, 68.5%, and 68.5%, respectively). Incidences of male and female genital mycotic infections and osmotic diuresis–related AEs were higher with CANA 100 and 300 mg versus GLIM, consistent with other Phase 3 studies of CANA.
The overall incidence of AEs (39.8% [n=43] vs 44.4% [n=48]), AE-related discontinuations (0.9% [n=1] vs 2.8% [n=3]), volume depletion-related AEs (0.9% [n=1] vs 1.9% [n=2]), and fracture AEs (0% vs 0.9% [n=1]) was similar with CANA and PBO. The incidence of male genital mycotic infections (GMIs) was 1.5% (n=1) and 0%, female GMIs was 12.2% (n=5) and 2.0% (n=1), and osmotic diuresis-related AEs was 5.6% (n=6) and 3.7% (n=4) with CANA and PBO, respectively. The incidence of documented hypoglycemia (≤70 mg/dL) was 3.7% (n=4) with CANA and 1.9% (n=2) with PBO; there were no reports of severe hypoglycemia.

**Conclusion:** Titrated CANA significantly improved A1C, FPG, body weight, and SBP, and was generally well tolerated over 26 weeks in patients with T2DM as add-on to MET and SITA in a triple therapy regimen.

**Abstract #304**

**DIABETIC CHOREA PRESENTING AS SUDDEN ONSET INVOLUNTARY AND NON-SUPPRESSIVE GENERALIZED MOVEMENTS: CASE REPORT**

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**Case Presentation:** 72 year old female with medical history of diabetes mellitus type 2, hypertension and morbid obesity admitted to the hospital with generalized movements that started one week before. The movements were sudden in onset, progressive and generalized. They involved the four extremities and head, were involuntary, not suppressible, and interfered with ambulation, sleep and daily activities. She denied any new medications or drugs. Her physical exam showed vital signs within normal limits and she was completely oriented. Cardiovascular and abdominal exam was unremarkable. Laboratory results reported normal CBC, normal liver enzymes, mildly increase creatinine of 2.1 mg/dl that normalized 12 hours later to 1.1, normal electrolytes with high glucose = 450 mg/dl and high A1C = 12%. X-ray of the chest and CT of the brain were normal. MRI showed small bilateral diffuse hyperintensities in T1 in the basal ganglia. She was started on basal/bolus insulin with average glucose below 140 mg/dl and 4 days later she was discharged with almost 80% resolution in the choreiform movements.

**Discussion:** Chorea is described as an irregular involuntary movement disorder that can be unilateral or bilateral and can be secondary to different diagnoses including cerebrovascular insufficiency, neurodegenerative, neoplastic, immunologic, infectious or metabolic diseases. Chorea associated with non-ketotic hyperglycemia has been described since 1960. In the last years few meta-analysis described three main characteristic that are included in this syndrome: chorea, non-ketotic hyperglycemia and a high signal basal ganglia lesion on T1 brain MRI. It is reported as more frequent in elderly females with a mean A1C of 14.4%. Presented as hemichorea in 88% of the cases or bilateral chorea in 11.4%. Usually involves the upper and lower extremities and only a small group has facial involvement. MRI show that basal ganglia involvement is usually the putamen and in some cases the caudate nucleus or globus pallidus. The lesion is contralateral in hemichorea or bilateral in generalized presentation. The exact mechanism involved in this syndrome is not completely understood. There are multiple hypotheses, including an incomplete transient dysfunction of the striatum with hypoperfusion and hypometabolism partially proven in SPECT studies. The clinical course usually involves a good prognosis with full recovery after normalization of blood glucose, and only a few patients require additional therapy with antipsychotics or medications with GABA agonist properties.

**Conclusion:** Diabetic chorea is an infrequent complication of a very common disease and an early diagnosis will usually improve the symptoms with a good prognosis.

**Abstract #305**

**DENTITION AND DIABETES: A CASE STUDY**

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**Case Presentation:** Periodontal disease is a dangerous epidemic. Although the number of patients with the disease have recently been on the decline, NHANES reports 64.7 million adults older than 30 have had periodontitis. Worldwide, 15 to 20% of the total adult population between the ages of 34 and 44 have severe periodontal disease. We present a case of a woman with severe periodontal disease and prediabetes. The patient is a 51 year old white female with past medical history of COPD, migraine headaches, chronic pancreatitis, remote drug abuse and prediabetes who presented to the Riverside Methodist Hospital in diabetic ketoacidosis. Patient admitted to symptoms of hyperglycemia and twenty pound weight loss during the prior month. On arrival, hemoglobin A1c was 12.9. She was diagnosed with diabetes mellitus type two and started on an insulin drip. Cardiac and infectious evaluations were unremarkable. Physical exam revealed poor dentition. During hospitalization, diabetes education was arranged. The patient was discharged on 20 units basal insulin and 8 units prandial insulin. Referral was made for oral
surgery to evaluate the patient’s dentition outpatient. She had frequent follow ups with her primary care physician after hospitalization, where blood glucose remained in the 200s prior to bed, and fasting levels in the 80s. During this time, the patient reported eating smaller meals. Three months later, oral surgery was performed and extracted all upper teeth. Surgery noted a deep abscess with significant pus, concerning for chronic infectious disease invading the jaw. During the week after the procedure, the patient experienced hypoglycemia and blood glucose in the 40s overnight. Repeat hemoglobin A1c improved to 5.9. Total daily insulin was reduced, and patient plans to follow up with her primary care physician after her bottom teeth are surgically removed in December.

Conclusion: This case is an example of chronic inflammation in association with diabetes mellitus. It is complicated by the presence of diabetic ketoacidosis and chronic pancreatitis. Many studies have attempted to find correlation between periodontal disease and diabetes mellitus, but at this time remain inconclusive. The patient’s drastically reduced hemoglobin A1c was identified one week after her dental procedure. The effect of treatment to her dentition, so closely to drawing the lab, should not have had a significant impact on hemoglobin A1c. It is assessed that her rapid drop in hemoglobin A1c came from good adherence to her new insulin regimen and resolution of her associating glucotoxicity. Overall, further analysis of the correlation between periodontal disease and diabetes should be attempted.

Abstract #306

CANAGLIFLOZIN PROVIDES GREATER IMPROVEMENT IN RISK FACTORS ASSOCIATED WITH METABOLIC SYNDROME VERSUS GLIMEPIRIDE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND METABOLIC SYNDROME ON BACKGROUND METFORMIN

Katherine Merton, PhD, MBA1, Michael Davies, PhD1, Ujjwala Vijapurkar, PhD2, Dainius Balis, PharmD3, Mehul Desai, MD2


Objective: Metabolic syndrome (MetS) refers to a collection of risk factors associated with the development of cardiovascular disease and type 2 diabetes mellitus (T2DM). Canagliflozin (CANA), an SGLT2 inhibitor, increases urinary glucose excretion, leading to decreased plasma glucose levels and a net caloric loss. In patients with T2DM on background metformin (MET), CANA improved glycemic control and reduced body weight (BW) and blood pressure (BP) versus glimepiride (GLIM) over 52 weeks; this post hoc analysis assessed the effects of CANA versus GLIM on the components of MetS in patients with T2DM and MetS.

Methods: In this randomized, double-blind study, patients with T2DM (N=1450; mean age, 56.2y; A1C, 7.8%; BMI, 31.0kg/m2) received CANA 100 or 300mg or GLIM as add-on to MET over 52 weeks. In addition to T2DM, MetS was diagnosed if patients met ≥2 of the following criteria: triglycerides (TG) ≥150mg/dL; high-density lipoprotein cholesterol (HDL-C) <40mg/dL (men), <50mg/dL (women); waist circumference (WC) ≥102cm (non-Asian men), ≥88cm (non-Asian women), >90cm (Asian men), >80cm (Asian women); diagnosis of hypertension or BP-related criteria (systolic BP [SBP] ≥130mmHg or diastolic BP [DBP] ≥85mmHg). Changes from baseline in A1C, fasting plasma glucose (FPG), BP, WC, BW, BMI, and lipids were evaluated at Week 52.

Results: At baseline, 80.6% of patients with T2DM (n=1169) met the criteria for MetS; proportions were similar across treatment groups. Among patients with data available to assess all MetS criteria (n=1160), 39.7%, 33.7%, and 17.2% of patients met 3, 4, or 5 MetS criteria, respectively. Of those with MetS at baseline, 1132 patients had data available to assess MetS criteria at Week 52; the proportion of patients with MetS was lower in the CANA 100 and 300mg groups (86.7% and 85.8%) compared with GLIM (92.7%). CANA reduced A1C more (300mg) and similarly (100mg) compared with GLIM (LS mean changes of –0.9%, –0.8%, and –0.8%, respectively). Relative to GLIM, CANA 100 and 300mg provided reductions in FPG (–7.1 and –9.5mg/dL), SBP (–3.4 and –4.8mmHg), DBP (–1.7 and –2.4mmHg), WC (–3.0 and –3.3cm), BW (–4.5 and –4.8kg), and BMI (–1.6 and –1.8kg/m2). CANA showed increases in low-density lipoprotein cholesterol (LDL-C, 300mg only) and HDL-C (both doses) versus GLIM (differences of 2.7 and 8.6mg/dL, and 3.0 and 3.9mg/dL with CANA 100 and 300mg, respectively). Relative to GLIM, reductions in TG were greater with CANA 100mg and similar with CANA 300mg (differences of –19.5 and –10.3mg/dL). CANA was generally well tolerated.

Conclusion: CANA improved all components of MetS compared with GLIM over 52 weeks in patients with T2DM and MetS on background MET.
Abstract #307

GEOGRAPHICAL VARIABILITY AND DEMOGRAPHIC/CLINICAL CHARACTERISTICS BY GENDER AMONGST ELDERLY PATIENTS WITH DIABETES AND DYSLIPIDEMIA IN PROVINCE OF ONTARIO, CANADA

Pendar Farahani, MD, MSc, FRCP, DABIM, FACP, Ana Johnson, PhD, Marlo Whitehead, MSc PSTAT, Susan Rohland, None

Objective: Geographical differences and regional variation in the prevalence and management of diabetes and dyslipidemia have been described in several previous studies around the globe. The objective of this study was to explore demographic and clinical characteristics of elderly patients with diabetes and dyslipidemia who had exposure to statins for more than 12 months in accordance to geographical disparities and gender in Ontario, Canada.

Methods: A cohort of patients with diabetes aged 65 and older was constructed using the Ontario Diabetes Database for a ten-year period between 2003 and 2013. The medication data for statin utilization was obtained from the Ontario Drug Benefit program for the same time period. Sub-cohorts of patients according to the Local Health Integration Networks (LHINs) were compared by gender and age. LHINs 13 and 14 (North Ontario) was compared with LHINs 1 to 12 (South Ontario). Charlson Comorbidity Index (CCI) was utilized for clinical characteristics.

Results: The sample size was N=231,824 patients (49% female). The majority of patients (91.6%; 212,127) lived in LHINs 1-12 (South Ontario), while the remainder lived in LHINs 13-14 (North Ontario). Over a third (36.5%) of patients in LHINs 13-14 lived in rural areas versus 13.5% in LHINs 1-12 [p-value less than 0.001]. There was no clinically significant difference for average age at diagnosis for diabetes between patients who lived in LHINs 13-14 (69.44 ± 9.29 years old) and patients who lived in LHINs 1-12 (70.73 ± 9.34 years old). Average Charlson Comorbidity Index (5 years look back) was 1.42 ± 1.84 for total cohort (1.36 ± 1.79 for female and 1.47 ± 1.89 for male; p-value less than 0.001). Average Charlson Comorbidity Index was 1.59 ± 1.86 for patients who lived in LHINs 13-14 (North Ontario) and 1.40 ± 1.84 patients who lived in LHINs 1-12 (South Ontario) [p-value less than 0.001].

Discussion: This study illustrated that the pattern of comorbidities amongst elderly patients with diabetes and dyslipidemia on statins were dissimilar according to gender and geographical regions. Male patients and patients who lived in North Ontario on average were sicker and had more comorbidities than patients who lived in South Ontario.

Conclusion: This calls for further studies on the impact of geography and gender on health disparities, and potential implications on health care services and policies.

Abstract #308

DIABETIC KETOACIDOSIS WITHOUT PROFOUND HYPERGLYCEMIA SECONDARY TO THE USE OF A SODIUM/GLUCOSE COTRANSPORTER 2 INHIBITOR

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GRMEP/ Michigan State University

Objective: Objective: Diabetes (DM) is becoming an increasingly prevalent part of American society partly related to the American lifestyle. As such there has been a boon in recent years in the development of new classes of medications to treat DM. One of the newest classes of medications are SGLT2s which facilitate glycosuria as a means to obtain glucose control in patients with DM type 2 (DM2). We present the case of a patient with a label of DM2 when in reality he had DM type 1 (DM1) who presented with Diabetic Ketoacidosis (DKA) while being on an SGLT2.

Case Presentation: Case Presentation: A 54 year old gentleman who carried a diagnosis of DM2 since age 18 presented to the hospital with increasing nausea, vomiting, abdominal pain and hyperglycemia over the course of one day. He had been treated as an outpatient for his DM on a total of 110 units daily via his pump and metformin for insulin resistance. His hemoglobin A1C was 7.7 and because there were no contraindications he was placed on an SGLT2. Several months later he presented as above with a blood glucose of 264 mg/dL and an anion gap acidosis with elevated beta hydroxybutyrate consistent with DKA. Workup for precipitating factors were negative and patient was compliant with his medications. Patient was placed on an insulin drip and his DKA resolved. Subsequent testing showed an undetectable C-peptide and positive GAD autoantibodies consistent with a diagnosis of DM1.

Discussion: Discussion: SGLT2s represent a novel mechanism for treatment of DM inhibiting a sodium-glucose cotransporter which is responsible for reabsorption of roughly 90 percent of renally filtered glucose as their mechanism of action. DKA is one of the true endocrine emergencies with a mortality rate of almost 20 percent. Patients have an anion gap from ketogenesis and typical have profound hyperglycemia with a blood
Abstract #309

THE RELATIONSHIP BETWEEN VITAMIN D DEFICIENCY AND DIABETIC RETINOPATHY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Objective: Diabetic retinopathy (DR) is one of the leading cases of blindness throughout the world. The role of vitamin D in the pathogenesis of diabetic retinopathy remains an area of debate. The purpose of this study was to comprehensively determine the strength of association between vitamin D deficiency (VDD) and DR. The secondary objective of this study was to determine if there exists any significant difference in serum vitamin D levels between patients with DR and control group patients.

Methods: Two authors independently searched published studies indexed in the MEDLINE and EMBASE from their date of inception to July 2015. We conducted a systematic review and meta-analysis of observational studies that assessed the association between diabetic retinopathy and vitamin D deficiency. Vitamin D deficiency is defined as a serum level less than 20 ng/mL. Optimal vitamin D level was defined as a serum level greater than 30 ng/mL. Pooled odds ratios (OR) and mean difference (MD) with 95% confidence intervals (CIs) were calculated using a random-effect, Mantel-Haenszel analysis.

Results: The initial search yielded 122 articles. Data were extracted from 13 studies involving 9,350 participants with diabetes mellitus who had undergone assessment for both DR and VDD. There is a statistically significant association between diabetic retinopathy and vitamin D deficiency with a pooled OR of 1.44 (95% CI: 1.15 to 1.81, P=0.001). There was also a statistically significant lower serum 25-hydroxyvitamin D level in patient subgroups with diabetic retinopathy vs control groups with a mean difference (MD) of -2.25 ng/mL (95% CI: -3.64 to -0.87, P=0.001)

Conclusion: Our meta-analysis and systemic review demonstrates a significant association between VDD and DR and demonstrates a statistically significant difference in mean serum vitamin D levels between DR and non-DR patients. Vitamin D supplementation as a protective mechanism against the development and progression of DR, particularly in elderly female patients, warrants further investigation.

Abstract #310

ACUTE PERICARDITIS AS A RARE CONSEQUENCE OF SEVERE DIABETIC KETOACIDOSIS

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Case Presentation: A 33-year-old Hispanic man with insulin-dependent diabetes of 15 years’ duration was admitted to the hospital with a 2-day history of nausea, vomiting, and worsening shortness of breath. He endorsed loss of appetite and was unable to hold food down. He vomited a number of times after attempts to drink soup. There were no changes in urinary frequency. He decided to stop taking insulin yesterday because of poor oral intake. He stated that he had been compliant to his insulin until yesterday. His normal insulin regimen includes lispro 15 units before meals and glargine 20 units at bedtime. On examination he was alert and oriented to person, place, and time. He was found to have had Kussmaul’s respirations. The temperature was 35.3°C, pulse 135/minute, and blood pressure 118/58 mmHg. Auscultation of the heart and lungs was normal. The abdomen was soft and bowel sounds were present. Initial labs showed a blood glucose of 900 mg/dL, plasma bicarbonate 3 mmol/L, blood urea 33 mg/dL, plasma sodium 133 mmol/L, potassium 5.7 mmol/L, with a calculated serum osmolality of 299 mosmol/kg. There was no evidence of any precipitating infection on history. Blood cultures, throat swab for viral infections, and urine culture were all sterile. He was diagnosed with severe DKA and was treated with intravenous fluids and insulin infusion. After 48 hours of hospitalization, he began to complain of substernal chest pain. This pain was very sharp in character, worse on deep inspiration. Electrocardiogram was done and shown definite ST elevation in leads I-III, AVL,AVF and V2-V6. Troponin T was elevated to 29 ng/mL from 0.01 on admission. The Echocardiogram showed normal left ventricular size and contractility with LVEF 63%. He was diagnosed with acute pericarditis.
and given aspirin. He showed improvement clinically. He denied pleuritic chest pain 1 day after aspirin was started. He was discharged home 5 days after admission

**Conclusion:** DKA is a medical emergency in DM type 1 patients which may result in severe complications if not treated effectively. Acute Pericarditis was described as one of the very rare complications of DKA which is uncommon in mild to moderate DKA but has been reported in severe cases of DKA. The following report is a case of acute pericarditis that developed while treating a patient with severe diabetic ketoacidosis.

This case illustrates a rare complication of diabetic ketoacidosis. Although most cases of acute pericarditis are not life-threatening and considered a benign condition, it is important for clinicians to recognize this complication, so that they can provide appropriate treatment for their patients.

**Abstract #311**

**TYPE IV HYPERSENSITIVITY TO INSULIN COMPLICATED BY FACTOR V LEIDEN THROMBOPHILIA: A CASE STUDY**

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**Objective:** Allergies to insulin are commonly type I hypersensitivity reactions. Type IV hypersensitivity reactions are rarely documented and are often due to insulin additives rather than insulin itself. Here, we discuss a patient with type 2 diabetes and a rare type IV hypersensitivity to human insulin complicated by her factor V Leiden thrombophilia.

**Case Presentation:** A 40-year old female with a history of type 2 diabetes and factor V Leiden thrombophilia presented with painful erythematous reactions at her injection sites developing several hours after insulin administration. Initially assumed to be from a zinc allergy, she was transitioned to continuous subcutaneous insulin glulisine, however her lesions began to develop areas of necrosis. Serology revealed IgE antibodies against human insulin and protamine. Initial biopsy showed perivascular and interstitial dermal infiltrate of lymphocytes and eosinophils with fibroblastic proliferation. The patient was referred to Allergy and Immunology and biopsy of her lesions confirmed a type IV hypersensitivity reaction. Diphenhydramine injections at the site of her insulin injections and trials of oral prednisone and methotrexate provided no relief. The patient was transitioned to intravenous insulin delivered by a central venous catheter. She did well until her case was further complicated by recurrent catheter thromboses secondary to factor V Leiden thrombophilia. Due to increasingly difficult vascular access, the patient finally underwent subcutaneous insulin desensitization therapy. Following desensitization, she was transitioned to subcutaneous insulin with no adverse effects.

**Discussion:** There is an estimated 0.1-0.3% incidence of hypersensitivity reactions to human insulin and its analogues, with an IgE-mediated type I allergy reaction as the most frequently documented condition. T-cell mediated type IV hypersensitivity reactions are also documented but less common, dominated by reactions to preparation additives like zinc, latex, and protamine. Few cases have documented a type IV hypersensitivity to human insulin itself. These cases reported strategies such as transitioning to oral medications, replacing insulin with non-additive preparations, continuous infusion of subcutaneous insulin, and finally, by insulin desensitization therapy.

**Conclusion:** This case is unique because this patient with type IV hypersensitivity to human insulin also had complications from factor V Leiden thrombophilia. Vascular access remained challenging, necessitating insulin desensitization therapy. As a result, this patient achieved glycemic control with an improved quality of life, highlighting the value of early desensitization in the management of an insulin allergy.

**Abstract #312**

**INTERNAL MEDICINE RESIDENTS’ KNOWLEDGE, PERCEPTIONS, AND BARRIERS REGARDING TREATMENT OF HYPERGLYCEMIA IN NON-CRITICALLY ILL INPATIENTS WITH DIABETES**

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**Objective:** Hyperglycemia in non-critically ill inpatients is associated with higher complications and mortality, and is frequently undertreated. Previous studies showed that residents underestimate the importance of managing hyperglycemia in non-critically ill inpatients and that they have limited knowledge about both blood glucose (BG) targets and subcutaneous insulin therapy. In the previous study performed at our institution, we found that non-critically ill inpatients under residents’ care were frequently on sub-optimal insulin regimens, resulting in BG above the recommended targets. Therefore, our objective was to assess the internal medicine residents’ knowledge, perceptions, and barriers regarding treatment of hyperglycemia in non-critically ill inpatients with diabetes.

**Methods:** Residents were asked to complete an online questionnaire adjusted from the previously published one. Significance of difference among postgraduate years
Results: Out of 115 residents, 62 (54%; age 29±3 years, 61% male) completed the questionnaire. All levels of training were represented (20 PGY1 (32%), 22 PGY2 (35%), 20 PGY3 or higher (32%), 41 (66%) and 36 (58%) residents chose correct targets for fasting and random BG, respectively. Only 22 (35%) chose correct optimal insulin regimen. Most residents felt “very comfortable” with managing hyperglycemia (43 or 69%), hypoglycemia (42 or 68%), and subcutaneous insulin therapy (38 or 61%). Risk of hypoglycemia was the most frequently identified barrier to optimal hyperglycemia management (30 or 48%), followed by unpredictable changes in patient diet and mealtimes (28 or 45%), and unpredictable timing of procedures (26 or 42%). While there was no difference in proportions of correct answers on BG targets and optimal insulin regimen between different PGY, there was a significantly lower proportion of PGY1 residents, compared with PGY2 and PGY3 or higher, who were “very comfortable” with managing hyperglycemia (25% vs. 86% vs. 95%, p<0.0001), hypoglycemia (40% vs. 86% vs. 75%, p<0.05), and subcutaneous insulin therapy (15% vs. 82% vs. 85%, p<0.0001).

Discussion: While most residents knew the recommended BG targets, only a minority knew the optimal insulin regimen. Risk of hypoglycemia was the most frequently identified barrier to optimal hyperglycemia management. Senior residents had more confidence, but not more knowledge, regarding management of hyperglycemia.

Conclusion: Structured effort is needed to better educate residents on subcutaneous insulin therapy, prevention of hypoglycemia, and the importance of optimal hyperglycemia management in non-critically ill inpatients with diabetes.

Abstract #313

EUGLYCEMIC DIABETIC KETOACIDOSIS: THE CLINICAL CONCERN OF SGLT2 INHIBITOR

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Objective: The objective of this study is to increase awareness of Euglycemic DKA (EuDKA) caused by SGLT2 inhibition, a new drug approved to treat type 2 diabetes mellitus (T2DM), and used off-label use in type 1 diabetes mellitus (T1DM).

Methods: A 39 year old obese woman with presumed T2DM for many years presented with three days of nausea/vomiting and abdominal pain.

Case Presentation: The patient had been non-adherent to prescribed multiple dose of insulin (MDI). One week prior to presentation, she had been started on canagliflozin and liraglutide to increase medication adherence. Denied alcohol, starvation, or recent illness. Examination: Temperature 97.7 F, blood pressure 120/80 mmHg, heart rate 133 BPM, respiratory rate 24/min. Patient appeared ill, had dry mucus membranes, and a diffusely tender abdomen. Labs: bicarbonate 6 meq, anion gap 25, lactic acid 1.4 mmol/L, blood glucose 167 mg/dl, HbA1c 11.1%. Urine dipstick was positive for ketones. Arterial blood gas: pH 7.08; PCO222 mmHg; HCO3–6.5 mEq/L. Given her unimpressive blood glucose level, the diagnosis of DKA was unrecognized initially. The patient did not improve with intravenous fluid hydration or antiemetics Upon admission to MICU, dextrose water 5% /half normal saline, and an insulin drip were initiated. Her DKA resolved after 36 hours and she was discharged on MDI.

Discussion: EuDKA is a rare syndrome defined as DKA without marked hyperglycemia. When SGLT-2 inhibitors are used in T1DM, the insulin dose is often lowered by the clinician or the patient to prevent hypoglycemia. DKA then develops due to decreased carbohydrate availability and a reduction in circulating insulin levels. In T2DM, SGLT-2 inhibitors increase urinary glucose excretion and decrease blood glucose, stimulating glucagon and depressing insulin release. This hormonal shift enhances lipid oxidation at the expense of carbohydrate oxidation and stimulates lipolysis. Augmented free fatty acid delivery to liver promotes ketogenesis.

One case series study of EuDKA from canagliflozin found that six out of twelve patients had T1D or late autoimmune diabetes in an adult. Our patient tested positive for Glutamic Acid Decarboxylase (GAD 65) autoantibodies. There have been >70 cases reported to FDA since the release of this drug class. Most patients and clinicians fail to recognize the symptoms of DKA, given near normal blood glucose. Insulin reduction, low caloric/fluid intake, current illness, starvation, and alcohol use were other factors leading to the development DKA.

Conclusion: Given the increasing incidence and the insidious nature in which the diagnosis can be missed, vigilance is necessary to decrease morbidity and potentially mortality.
ABSTRACTS – Diabetes Mellitus/Prediabetes

Abstract #314

MATURITY ONSET DIABETES OF THE YOUNG: A CASE REPORT

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Objective: Maturity-onset diabetes of the young, also known as MODY, is the most common form of monogenic diabetes. The term MODY encompasses a group of clinically variable forms of diabetes, which are often non-insulin dependent. It accounts for approximately 2-5% of all patients with diabetes. Some clinical features that are used to identify patients with diabetes include young age of onset, typically less than 25 years of age, absence of autoantibodies, and family history of diabetes.

Case Presentation: Patient is a 4 years and 10/12 month old thin, Native American male who presented initially with an incidental finding of abnormally elevated blood glucose levels. His mother, who has Type 2 diabetes, had brought in glucometer readings from home which revealed a mean blood sugar of 163mg percent with two readings above 200mg percent. Subsequent laboratory testing revealed HbA1c of 6.2%. His islet cell antibody, glutamic acid decarboxylase, and insulin autoantibody were all negative. He was diagnosed with early Type 1 diabetes and was placed on an insulin regimen. At 14 years of age despite increasing weight and entering puberty his insulin requirements had not changed. He had not experienced any episodes of diabetic ketoacidosis (DKA) or hypoglycemic unawareness. A repeat islet cell antibody, glutamic acid decarboxylase, and insulin autoantibody tests were once again negative however a C-peptide level came back at 1.71, within normal range. He was then transitioned onto Glipizide 5mg before breakfast and dinner. He is well controlled (HbA1c 6.7%) without any episodes of DKA or hypoglycemia.

Discussion: So far a total of 11 mutations in genes have now been implicated in causing MODY, however, mutations in only three – GCK, HNF1A, HNF4A – account for a majority of cases, approximately 70% or above. Identifying which mutation a patient has is strongly suggested as certain MODY subtypes can be managed with oral medications, namely sulfonylureas, versus other subtypes can be managed with proper diet control.

Conclusion: Given this patient’s clinical history, treatment changes and subsequent results of good glycemic control, he was diagnosed with maturity-onset diabetes of the young. Thus, proper identification of this disease process is vital for appropriate treatment, cost effectiveness and management.

Abstract #315

SUPER ELEVATED LACTIC ACIDOSIS IN THE SETTING OF METFORMIN USE

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Objective: The major toxicity of metformin is lactic acidosis (LA) and is associated with high mortality rates (as high as 50% of cases - Journal Of Medicine Case Reports 2007). Metformin associated lactic acidosis can occur with renal insufficiency, hepatic impairment, and hemodynamic instability. LA can also occur in acute metformin overdose. Mortality correlates with increased LA levels and low pH. Mental status may also be impaired secondary to low plasma glucose and/or acidosis.

Case Presentation: We had a 72 year old woman with a history of Type 2 DM on oral anti hyperglycemics medications with no history of renal disease. On presentation she was found to be minimally responsive with stable vitals other than tachycardia. WBC 24.4K/ CMM, Band 12%, K 5.5mmol/L, Bicarbonate 6mmol/L, Glucose 36mg/dL, Calcium 6.6mg/dL, LA 20mmol/L, Cr 6.3mg/dL, AG 42, UA and cardiac enzymes were negative. ABG 6.80/21/117. Physical exam revealed mild epigastric tenderness. CT head and abdomen were unremarkable. EKG showed sinus tachycardia, rate 101, later converting to atrial fibrillation. She was given 1 ampule of D50, 2L NS Bolus, 2 ampules of NaHCO3, and HCO3 drip. Mental status improved at which time she confirmed that she was taking metformin. She was admitted to the ICU with severe acidosis, placed on hemodialysis (HD) and given empiric antibiotics. Repeat labs, LA 18mmol/L and Cr 2.61mg/dL, with an AG of 36. The next day her AG was 26 and LA 8.1mmol/L, HD was then stopped. Eventually her LA normalized to 1.4. All cultures remained negative. The rest of her clinical course was uneventful and she was discharged in good health.

Conclusion: Work up for LA in this patient included sources of infection (sepsis), Type A LA, Type B LA and medication induced LA. Type A LA is typically secondary to shock. Type B LA occurs in impaired cellular metabolism, tissue ischemia, metformin use, alcoholism and HIV patients. It was suspected that this patient’s LA was due to metformin use with new underlying renal insufficiency. Metformin induced LA typically presents with AMS, lethargy and metabolic acidosis along with other electrolyte derangements. Mortality with this condition is closely related to underlying comorbid conditions and death is caused by multi-organ failure.
Early identification and treatment is necessary to reduce mortality. Treatment is supportive with the use of dialysis (i.e. HD or CRRT) and a bicarbonate drip (especially if the pH is <7.10). Use of sodium bicarbonate is controversial but is suggested if the pH is <7.10. HD is also suggested if the pH is <7.10.

Abstract #316

LATENT AUTO-IMMUNE DIABETES IN ADULTS (LADA): IS IT MORE PREVALENT THAN WE THINK? A CASE SERIES

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Objective: Latent autoimmune diabetes in adults (LADA) is a form of autoimmune diabetes defined by adult onset, presence of auto-antibodies and insulin independence at diagnosis; with estimated prevalence between 10 to 25%. In clinical practice, they are often misdiagnosed as DMT1 and DMT2. We present a case series of 7 patients who presented as Type 1 or Type 2 DM, found to have LADA on further work up.

Case Presentation: Case 1: A 75 year old Caucasian female with no history of DM was hospitalized with DKA. HbA1c 11.7%, GAD ab >30 u/ml (ref <1.5), C peptide 0.5 ng/ml (0.8-3.8); Insulin ab and Islet cell ab were negative.

Case 2: A 64 year old African American female with type I DM since age 40, on insulin pump since 20 years. HbA1c 8.5%, C-peptide 2.44 ng/ml, Insulin Ab 1.6 u/ml (ref <0.4), GAD and Islet cell Ab negative.

Case 3: A 43 year old Caucasian female, diagnosed as type 2 DM since 10 years, on insulin pump since 7 years. She had 3 admissions for DKA in 1 year. HbA1c 9.1%, GAD Ab 1.9 unit/mL (<1.5), C peptide <0.1 ng/ml and Insulin Ab 22 unit/mL (ref<0.4).

Case 4: A 59 year old African American female, diagnosed as type 2 DM since 5 years, on insulin glargine, insulin aspart, metformin and sitagliptin. HbA1c 13.2%, C peptide level 1.42ng/ml (0.8-3.8) and insulin ab 8.3 (ref<0.4).

Case 5: A 32 year old African American female, with type II DM since 3 years treated with insulin pump during pregnancy. After delivery, she was started on canagliflozin and metformin. Patient presented with DKA 2 months later. Insulin pump was restarted. HbA1c 9.1%, GAD ab 104.1u/ml (ref<1.5), C peptide 1.6ng/ml and Insulin Ab 68unit/ml (ref<0.4).

Case 6: A 65 year old white male, diagnosed as type II DM at age 50 years, on insulin pump for many years. HbA1c 8.4%, GAD ab 14.1u/ml (ref<1.5), Insulin ab 8.2u/ml (ref <0.4), C peptide <0.1 ng/ml and Islet cell ab negative.

Case 7: A 60 year old female patient diagnosed with DMT2 since 10 years, presented with DKA; started on treatment with insulin. HbA1c 7.9%, GAD Ab 39.1 unit/ml (0.0- 5.0), C peptide <0.004 ng/ml and Insulin Ab 106 unit/ml (ref <0.4).

Conclusion: LADA cases are quite prevalent but are often misdiagnosed as DMT1 or DMT2. There still exists confusion in the medical community about distinction between LADA and other forms of diabetes. Management of LADA is challenging as there are no randomized control studies on treatment of LADA. 

Abstract #317

MUCORMYCOSIS IN DIABETIC KETOACIDOSIS: AN INFECTIOUS AND LETHAL COMPLICATION OF METABOLIC DISEASE

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Objective: Infection is a known precipitating factor for the development of diabetic ketoacidosis (DKA). Conversely, in mucormycosis, the metabolic conditions in DKA predispose to the onset of infection. We present a case of rhino-orbital mucormycosis, a highly lethal infection known to affect patients with uncontrolled diabetes, particularly in the setting of DKA.

Case Presentation: A 53 year-old woman with hepatitis C and poorly controlled diabetes with complications, presented to the hospital with a 3 day history of shortness of breath, lethargy and altered mental status. Initial vital signs were: BP 73/53 mmHg, HR 65/min, RR 19/min, and T 32.1 C. She was cachectic, lethargic and disoriented. Laboratory tests showed a blood glucose of 880 mg/dL, anion gap of 38, pH of 6.95, bicarbonate of 9.0 meq/L, HbA1c of 12.1%, ketonuria (40 mg/dl), and serum β-hydroxybutyrate of >9 mmol/L. The patient was diagnosed with DKA and hyperglycemic hyperosmolar state and received intravenous fluids and insulin infusion. On hospital day 3, she developed left periorbital swelling and erythema. A maxillofacial computed tomography
showed pre-septal cellulitis; a nasal endoscopy showed no evidence of mucormycosis. 5 days after admission, the patient suffered cranial nerve IV palsy. Nasal endoscopy was repeated revealing black mucosa; tissue biopsy was positive for mucor. The patient was started on amphotericin and underwent nasal cavity and sinus debridement with left orbital decompression. Her clinical condition deteriorated. An MRI identified orbital involvement and the patient underwent orbital exenteration. Due to her terminal condition, the patient was discharged home to hospice and subsequently expired.

**Discussion:** This patient presented with a long history of uncontrolled diabetes, recurrent ketoacidosis, and malnutrition, conditions known to increase mucor infection risk. The acidic and hyperglycemic environment of DKA, together with iron abundancy, favor the expression of endothelial cell glucose-regulated protein 78 (GRP78), promoting angioinvasion, the hallmark of mucormycosis. The rapid progression and high lethality of mucor, as seen in our patient, underscore the importance of improved metabolic control in the prevention of this acute complication of diabetes.

**Conclusion:** Physicians need to be familiar with the high susceptibility of patients with uncontrolled diabetes and DKA to mucor infection. Further understanding of the molecular mechanisms underlying mucor susceptibility may offer new approaches to improve patient survival.

**Abstract #318**

**GLYCOGENIC HEPATOPATHY: A RARE COMPLICATION OF UNCONTROLLED TYPE 1 DIABETES**

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**Objective:** To describe a case of hepatomegaly and elevated transaminases in a patient with glycogenic hepatopathy (GH), a rare complication of uncontrolled type 1 diabetes.

**Case Presentation:** An 18 year-old male with uncontrolled type 1 diabetes (HbA1c 18.1%) and history of recurrent diabetic ketoacidosis (DKA) presented with abdominal distention and hyperglycemia. Physical exam revealed massive hepatomegaly. Laboratory evaluation showed DKA and elevated transaminases (AST 1,162 U/L, ALT 598 U/L). DKA was managed in the ICU with insulin infusion and subsequently transitioned to a basal-bolus insulin regimen. Despite resolution of DKA, transaminases continued to increase with no signs of liver failure (peak AST 3,725 U/L, ALT 1,049 U/L). Abdominal ultrasonography (US) revealed an enlarged liver (25 cm) with moderate echogenicity, consistent with steatosis. Extensive evaluation for causes of hepatitis including toxins, autoimmune, genetic, and infectious diseases was unrevealing. Liver biopsy showed swollen hepatocytes with glycogen accumulation. After 4 days of hospitalization and improved glycemic control, transaminases started to decrease and patient was discharged with close outpatient follow-up.

**Discussion:** Based on the clinical presentation and liver biopsy, we concluded that GH was the final diagnosis. GH is the hallmark pathological finding of Mauriac syndrome, first described in 1930 in children with uncontrolled type 1 diabetes, delayed growth, cushingoid features, hepatomegaly, and/or hypercholesterolemia. As seen in our case, adolescents and young adults with uncontrolled diabetes may present with hepatomegaly and elevated transaminases without the other classic features of Mauriac syndrome. In uncontrolled diabetes, excess glucose enters hepatocytes by insulin-independent passive diffusion. Concomitant presence of insulin activates glycogen synthase, a key enzyme in glycogen synthesis which converts glucose to glycogen in hepatocytes. Thus, repeated episodes of hyperglycemia and insulin therapy lead to excessive hepatic glycogen accumulation.

**Conclusion:** After excluding common causes of hepatomegaly and elevated liver transaminases, clinicians should consider GH in patients with uncontrolled diabetes. Liver US cannot differentiate this condition from non-alcoholic fatty liver disease (NAFLD), the most common cause of hepatopathy in patients with diabetes. Further evaluation with MRI, CT scan, or liver biopsy with PAS staining may be helpful. Unlike NAFLD, GH does not usually progress to liver cirrhosis and improvement of glycemic control has been shown to improve the hepatomegaly and elevated transaminases in these patients.
Abstract #319

INTERNAL MEDICINE RESIDENTS’ PRACTICE REGARDING TREATMENT OF HYPERGLYCEMIA IN NON-CRITICALLY ILL INPATIENTS WITH DIABETES

Sandra Aleksic, MD, Elaine Zhai, DO, Tanzila Razzaki, MD, Zhen Wang, MD, Adam Kibola, MD, Neil Kothari, MD, Mirela Feurdean, MD

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Objective: Hyperglycemia in non-critically ill inpatients is associated with an increased risk of complications and mortality. Still, diabetes is frequently overlooked in inpatients and hyperglycemia is undertreated. Current guidelines recommend targeting fasting blood glucose (BG) levels of <140mg/dL and random BG of <180mg/dL. Insulin is the recommended pharmacotherapy, and prolonged use of sliding-scale insulin (SSI) without basal insulin is not recommended. Our objective was to assess the practice of Internal Medicine residents in our institution with regard to the treatment of hyperglycemia in non-critically ill inpatients with diabetes during the initial 72h of admission.

Methods: We reviewed the charts of all patients admitted to the teaching teams from August 1st to October 31st 2014. We included patients with prior diagnosis of diabetes, admitted to general medicine or telemetry beds, and hospitalized for ≥72h. Patients admitted for diabetic ketoacidosis, hyperosmolar hyperglycemic state, or hypoglycemia, were excluded. McNemar’s test for correlated proportions was used to test the difference in the proportion of patients getting basal insulin on day 1 vs. day 3 of admission.

Results: Among 445 patients admitted to teaching teams, 53 patients (57% men, median age 57 years) met the inclusion criteria; 34 were admitted to general medicine beds and 19 to telemetry beds. 36 (68%) of patients had documented ≥4 BG/day. The most common initial treatment was SSI (31 or 58%), followed by SSI with basal insulin, and 4 (8%) were on no insulin. There was no significant difference in the proportion of patients getting basal insulin on day 1 compared with day 3 of admission (30% vs. 40%, p>0.05).

Discussion: The most common initial treatment was SSI, with most patients remaining on SSI only through 72h of their admission. Hypoglycemic episodes were very infrequent, while patients’ random BG levels were frequently above the recommended targets, suggesting the need for more intense treatment of hyperglycemia.

Conclusion: Non-critically ill inpatients with diabetes under residents’ care were frequently on sub-optimal insulin regimens resulting in higher than recommended BG levels. Residents’ understanding of treatment of hyperglycemia in non-critically ill inpatients needs to be assessed in order to identify potential areas of improvement.

Abstract #320

USING CONTINUOUS GLUCOSE MONITORING WITH INSULIN PUMPS TO TREAT DIABETES: CLINICAL EXPERIENCE IN AN ACADEMIC TRAINING PROGRAM

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Objective: Personal continuous glucose monitoring (pCGM) with interstitial fluid glucose sensing can provide data which can be available in real-time therapy. We report our experience in an academic Diabetes Unit with minimally invasive pCGM used with continuous subcutaneous insulin infusion (CSII, or insulin pump) vs. CSII alone to improve glycemic control in patients with diabetes.

Methods: We reviewed all patients treated with insulin pumps at the Diabetes Unit of the University of South Carolina fellowship training program over a one-year period. Group A (CSII alone) used meters alone to self-monitor blood glucose, and while Group B additionally used pCGM integrated with CSII to modify pump settings, including adjustment of basal and/or short-acting bolus insulin doses, and change insulin-to-carbohydrate ratio and supplemental factor. The data was analyzed with respect to age, gender, glucose control as assessed by glycosylated hemoglobin (HbA1c), and severe hypoglycemia.

Results: (Table 1) There were 39 patients in group A and 47 in group B. They were comparable in mean age and gender breakdown (45.4 vs 44.4 years, and 64.1% vs 63.8% females, respectively). The average glycosylated hemoglobin (HbA1c) changed from 8.9% to 8.4% and from 8.1% to 7.2% from baseline to the end of one year in the two groups respectively. The number of severe hypoglycemic episodes per patient during the one year was 0.2 and 0.08 respectively.

Discussion: CSII patients who used pCGM were similar in demographics to those who used insulin pumps alone, but had a lower baseline A1c, exhibited a larger decrease in A1c at one year (0.9% vs 0.5%), and had fewer severe hypoglycemic events.
Conclusion: The better outcomes with pCGM-integrated pump therapy may be explained by a higher motivation for self-care, and by the pCGM being a valuable additional informational tool in assessing glucose trends when used in well-trained pump patients under professional expertise.

Abstract #321

EFFICACY AND SAFETY OF A COMPUTERIZED INTRAVENOUS INSULIN DOSING PROTOCOL IN THE CRITICAL CARE SETTING

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Objective: Hyperglycemia and insulin-induced hypoglycemia are common in critical care settings; both are associated with significant morbidity and mortality. Achieving a balance between reasonable blood glucose control and hypoglycemia is a challenge. Recommended glycemic targets for intensive care unit (ICU) patients have risen, largely due to the results of the NICE-SUGAR study which showed that patients treated to a target of 81-108mg/dL had significantly higher rates of mortality and severe hypoglycemia (glucose <40mg/dL) than patients treated to a target of<180mg/dL (27.5%vs24.4% and 6.8%vs0.5%). Computerized insulin infusion protocols are now being utilized for glycemic management. We compared the efficacy and safety of the GlucoCare insulin dosing calculator using different target glucose ranges.

Methods: Via electronic medical records, we retrospectively reviewed glycemic data, as measured by bedside glucose readings, of all critically ill patients at Westchester Medical Center treated with GlucoCare between 1/2010 and 12/2015. Different glucose targets were used: 100-139mg/dL(1/2010 – 6/2013), 120-140mg/dL(6/2013 – 11/2014), and 140mg/dL(11/2014-12/2015).

Results: 3085 patients were managed with GlucoCare,1761 in the 100-139mg/dL, 815 in the 120-140mg/dL, and 509 patients in the 140mg/dL groups. 82% of the patients had undergone cardiothoracic surgery. After eliminating the patients whose baseline glucose was <180mg/dL and those whose infusions were stopped before target glucose was reached, mean glucose after achieving target was 132mg/dL,138mg/dL,146mg/dL and percent of patients with glucose <70mg/dL was 22.1%, 10.4%, 7.7% for each group respectively. In the target 140mg/dL group if glucose readings performed >25% late were eliminated from the calculation, the percent of patients with glucose <70mg/dL was reduced to 2.8%. The percent of patients with glucose <40 mg/dL was 0.5% in the 100-139 mg/dL group, and 0% in the other groups.

Discussion: With each GlucoCare protocol mean glucose was maintained in the target range, but the oldest version had the highest rate of hypoglycemia and the current version the lowest. With the protocol target 140mg/dL mean glucose was at the lower end of the range (140-180 mg/dL) suggested by most current guidelines. With GlucoCare 120-140mg/dL and 140mg/dL there were no glucoses <40mg/dL. Delay in performance of glucose determination was associated with higher rates of hypoglycemia.

Conclusion: A computerized protocol for delivery of IV insulin in the ICU can maintain mean glucose in the target range with a low incidence of hypoglycemia. Adherence to the protocol with determinations of glucose readings on a timely basis is key to preventing hypoglycemia.

Abstract #322

RECOGNIZING LOW ENDOGENOUS INSULIN PRODUCTION AS A PRECIPITATING FACTOR OF DKA IN TYPE-2 DIABETIC PATIENTS TAKING SGLT2 INHIBITORS: A CASE REPORT

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Objective: To recognize the importance of practicing caution while prescribing Sodium Glucose Co-Transporter 2 inhibitors (SGLT2i) in patients who have poorly controlled Diabetes and diminished beta cell reserve in addition to other precipitating factors for diabetic ketoacidosis (DKA) such as recent surgery.

Methods: We reviewed the patient’s clinical course along with relevant literature.

Case Presentation: We present a case of a 66 year old man with type 2 Diabetes Mellitus, historically on metformin, glipizide, levemir, and recently started on SGLT2i. He underwent a knee surgery and 3 days later presented with nausea, vomiting, dizziness, and Kussmaul breathing. His initial labs showed severe ketonemia, high anion gap (35) metabolic acidosis with pH 7.16, serum bicarbonate of 5 mg/dl, and blood glucose of 361. The patient was treated in ICU for DKA with IV fluids, insulin infusion, and sodium bicarbonate for more than a week before the acidosis resolved and anion gap closed. The C-Peptide level showed diminished endogenous insulin production and therefore, the patient was re-classified as type 1 diabetic and started on basal bolus insulin regimen before discharge.

Discussion: SGLT2i belong to a unique class of anti-diabetes medications that work by increasing urinary glucose excretion. They have shown promising impact on glycemic control in diabetic patients in addition to several other benefits. DKA is a rare side effect associated with...
the use of SGLT2i. Several plausible mechanisms have been proposed about their metabolic effects that lead to development of DKA. We hypothesize that to gain more confidence in prescribing SGLT2i, we need to understand risk factors associated with the development of DKA. While administering SGLT2i, physicians should carefully monitor the possibility of high insulin demand in the event of diminished endogenous insulin production and in other stressful events such as a recent surgery. Future research should be geared towards identifying whether a patient taking SGLT2i is at a greater risk of developing DKA and how to prevent it with appropriate medical therapy.

**Conclusion:** SGLT2i represent a new class of anti-diabetic drugs, which is safe and effective. However, one must not forget that over 90% of type-2 diabetic patients end up requiring insulin, and at times become insulin dependent. Therefore, the longer a type-2 diabetic patient has had diabetes, the more beneficial it is to order a fasting C-peptide test to make the distinction between type-2 and type-1 diabetes.

Abstract #323

**INSULIN PRESCRIBING SKILLS AMONG INTERNAL MEDICINE RESIDENTS DURING TRANSITION-OF-CARE FROM THE HOSPITAL TO OUTPATIENT SETTING**

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**Objective:** Errors in prescribing insulin and insulin-related supplies during transition-of-care from the hospital to outpatient settings have been associated with increased readmissions, morbidity, and mortality. Accordingly, we assessed insulin prescribing skills among internal medicine (IM) residents when discharging patients with diabetes on insulin therapy.

**Methods:** An anonymous survey of multiple-choice questions was distributed among IM residents at an academic medical center in September 2015. Insulin prescribing skills were assessed by overall comfort level, whether prescriptions of insulin-related supplies (e.g., pen-needles, syringes, lancets, test strips) were given, whether insulin preparations (pen or vial) were specified in the prescription, and whether glucagon emergency kit was prescribed.

**Results:** Seventy-one residents (PGY-1: 35%, PGY-2: 30%, PGY-3: 35%) completed the survey. 48% of PGY-1 reported feeling uncomfortable prescribing insulin and insulin-related supplies. This number decreased as the training level advances (PGY-2: 19%, PGY-3: 4%). Most residents (73%) reported that they prescribed insulin pen at discharge, but 32% were unaware that pen-needles and glucose testing supplies needed to be co-prescribed. Only 1% of residents reported that they consistently prescribe glucagon emergency kit while 83% were either unaware or never prescribed it. The main barriers in prescribing insulin were “multiple testing supplies to prescribe”, followed by “items not available in electronic medical record (EMR) discharge interface”, and “no formal training in prescribing insulin”.

**Discussion:** Although a large proportion of PGY-1 reported feeling uncomfortable prescribing insulin, the comfort level increases as training level advances as 96% of PGY-3 reported feeling comfortable. We also identified that a large number of residents (32%) were unaware to co-prescribe pen-needles and glucose testing supplies when discharging patient on insulin pen which may lead to undesirable post-hospitalization outcome. Also, despite being potentially life-saving for some patients, 83% of residents were either unaware or never prescribed glucagon emergency kit. These findings, along with several barriers mentioned above may be modifiable and should be subject to future quality improvement project which include providing formal training in prescribing insulin and improving EMR discharge interface.

**Conclusion:** Avoiding insulin prescribing errors is essential to improve patient safety during transition-of-care from the hospital to outpatient settings. Focusing training and supervision towards PGY-1 while addressing modifiable barriers may reduce errors and cover current gaps in insulin prescribing skills of IM residents.

Abstract #324

**NATIONAL TRENDS IN MORTALITY, LENGTH OF STAY AND COSTS OF HOSPITALIZATION OF DIABETIC KETOACIDOSIS AND HYPEROSMOLAR HYPERGLYCEMIC CRISIS FROM 2005-2011 IN THE UNITED STATES**

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University of Tennessee Health Science Center

**Objective:** Acute hyperglycemic crisis such as diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic crisis (HHS), account for significant morbidity, mortality and healthcare costs in the United States. Methods: Using Nationwide Inpatient Sample (NIS) database, we identified all US hospitalizations from 2005-2011 of adults >18 years diagnosed with DKA and HHS...
using International Classification of Diseases version 9, clinical modification (ICD-9-CM) codes 250.1x and 250.2x respectively. Mortality rates were adjusted for age (less than or greater than 65 years) and Charlson/Deyo Comorbidity index using poisson regression methods. Trends in adjusted mortality was studied using Average Annual Percentage Change (AAPC). One way analysis of Variance (ANOVA) was used to calculate the yearly trend in length of stay and cost of hospitalization. Statistical analysis was done using STATA 13.0 (College Station, Texas). All p values were two sided and the level of significance was chosen at 0.05.

Results: A total of 33,901 hospitalizations for HHS (estimated 167,948) were identified. The mean age was 56 ±16 years & 45% were females. From 2005 to 2011, adjusted mortality rates declined from 1.92% in 2005 to 1.29% in 2011 at an AAPC of -8.98% (95% CI -14.51% to -3.12%, p value <0.001). During this period, the mean length of stay significantly declined from 5.19 days in 2005 to 4.53 days in 2011 (p value <0.001), whereas the mean cost of hospitalization increased from $ 25264 in 2005 to 30,743 in 2011 (p value <0.001).

During the same time period, a total of 219641 (estimated 1,079,976) hospitalizations for DKA were identified. The mean age was 40.7±16.1 years and 49.9% were females. From 2005-2011, the adjusted mortality rates declined from 0.69% in 2005 to 0.57% in 2011 at an AAPC of -3.08 (95% CI -5.54 to -0.67, p value 0.004). During this period, the mean length of stay significantly declined from 4.14 days in 2005 to 3.97 days in 2011 (p value <0.001), whereas the mean cost of hospitalization increased from $ 21,964 in 2005 to $ 29975 in 2011 (p value <0.001).

Discussion: Our study suggests declining trends in mortality and length of stay among patients admitted with acute diabetic complications in US hospitals from 2005-2011. A previous study from Wang et al in 2006 had suggested declining death rates among US adults with hyperglycemic crisis between 1985-2002. Our study suggests that this declining trend has continued more recently, more so among patients with HHS as compared to DKA.

Conclusion: Between 2005-2011, mortality and length of stay among patients with DKA and HHS improved along with a small but acceptable increment in the costs of hospitalization.
patients with acute renal failure, there are very few case reports utilizing SLED in the treatment of MALA.9

**Conclusion:** The above cases highlight an evolving role of SLED in the management of MALA in critically ill patients.

**Abstract #326**

**CO-MORBIDITY BURDEN DRIVE OUTCOMES AMONG PATIENTS WITH DIABETIC KETOACIDOSIS IN THE UNITED STATES**

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**Objective:** Diabetic Ketoacidosis (DKA) remains one of the most serious acute complications of diabetic decompensation and is associated with a high in-hospital mortality. Charlson-Deyo (C/D) co-morbidity index is an easily computed tool for assessing the co-morbidity burden of a patient. We assessed, if the C/D index can reliably predict mortality among patients with DKA in a cohort of patients selected from a large national database.

**Methods:** The Nationwide Inpatient Sample (NIS) database is the largest all-payer inpatient care database in the United States containing data on more than seven million hospitalizations. We identified all adults >18 years diagnosed with DKA between 2009-2011 from the database using International Classification of Diseases version 9, clinical modification (ICD-9-CM) code 250.1x as one of the top three diagnosis. Co-morbidity burden assessment was done by using C/D Index. Two level hierarchical logistic regression model with patient level factors nested within hospital level factors, were used to identify the predictors of mortality in the study population. Statistical analysis was done using STATA 13.0 (College Station, Texas). All p values were two sided and the level of significance was chosen at 0.05.

**Results:** A total of 103818 hospitalizations for DKA were identified. The mean age was 41 ±16.3 years and 49.8% (n=51717) were females. The total overall in-hospital mortality rate was 0.99% (n=1026). The median length of stay was 3 days (range 0-143 days), and the average cost of hospitalization was 27883 ± 4141 USD. Majority of patient (70%) had a Charlson/Deyo (C/D) index of 0, whereas 16% had an C/D index of 2 or higher. The in-hospital mortality was 0.44% among patients with C/D of 0, 1.65% among patients with C/D of 1 and 2.76% among patients with C/D of 2 or higher. In a multivariate regression, C/D score of 2 or more predicted a significantly higher in-hospital mortality (OR 2.80; 95% CI 2.38-3.30; p value <0.001) after adjusting for both patient level factors (age, gender, race, insurance status) and hospital level variables (location, bedsize and teaching status).

**Discussion:** C/D comorbidity Index is a method of assessing comorbidity burden of a patient and has been shown to predict outcomes among patients with a variety of medical and surgical conditions. Using a large inpatient database, we have shown that C/D can be used to reliably predict outcomes among patients with DKA.

**Conclusion:** Our study suggests that C/D co-morbidity index is a strong independent predictor of in-hospital mortality among patients with DKA. Being an easily computed score, it could potentially used as a tool for predicting prognosis and patient counseling for this disease.

**Abstract #327**

**FACTORS DETERMINING THE SUCCESS AND FAILURE OF TYPE 1 DIABETES CARE IN KERALA**

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**Objective:** Type 1 diabetes being a challenging metabolic disorder, with majority of patients failing to achieve glycemic goals, we assessed multiple determinants which could predict success and failure of type 1 diabetes care in Kerala over a period of 6-12 months.

**Methods:** The multidisciplinary diabetes team specialised in diabetes care at our center were assigned the task of identifying patient characteristics unique to type 1, characteristics of parents of children with diabetes, socio economic factors, influence of level of education, impact of job and lifestyle of parents, support at school/college, role of sibling and their impact on overall diabetes control.

**Results:** 1. Our diabetes team could identify the following predictors of success enumerated in descending order:
   a. Educational status of the mother or father
   b. Motivation and willingness to periodically attend diabetes education
   c. Disease known to family, friends and teachers
   d. Affection and care from an elder sibling
   e. Affordability to procure newer devices
   f. Accepting the disease

2. Predictors of failure in descending order include the following:
   a. Getting attracted to magical remedies and alternate therapies
   b. Anxiety, depression and mood swings
   c. Parents unwilling to understand the severity and intricacies of type 1 diabetes
   d. Those parents repeatedly requesting for oral medications and lesser number of injections
**Abstract #328**

**HIGH INCIDENCE OF ABNORMAL GLUCOSE METABOLISM IN ACUTE CORONARY SYNDROME PATIENTS AT MODERATE ALTITUDE: A SUB-HIMALAYAN STUDY.**

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**Objective:** The aim was to study the prevalence of abnormal glucose metabolism in acute coronary syndrome patients and to compare the different methods of diagnosing diabetes in ACS patients.

**Methods:** We did a prospective study. 250 consecutive non-diabetic patients (200 men and 50 women) with ACS admitted to a tertiary care institute of Himachal Pradesh in 1 year were enrolled. Admission plasma glucose (APG), next morning fasting plasma glucose (FPG), A1C and a standardized 75- g oral glucose tolerance test (OGTT) 72 hour after admission were done. Glucose metabolism was categorized as normal glucose metabolism, impaired glucose metabolism (Impaired fasting glucose or impaired glucose tolerance), and diabetes. Diabetes was arbitrarily classified further as undiagnosed (HBA1c ≥ 6.5%) or possibly stress diabetes (HBA1c < 6.5percentage). A repeat OGTT after 3 month in objects with impaired glucose tolerance. 75-g OGTT has highest sensitivity and specificity to diagnose diabetes where as A1C most specific to rule out stress hyperglycaemia.

**Discussion:** The high prevalence of diabetes (24%) and impaired glucose tolerance (38%) in our study demonstrates that majority of Indian patients with ACS have abnormal glucose metabolism irrespective age, socioeconomic status and place of living and substantiate the rising prevalence of diabetes and IGT among adult Indian population. Unrecognized diabetes and stress hyperglycaemia at admission to coronary care unit in ACS patients increase the risk of cardiovascular events and intervention improves the outcome.

**Conclusion:** Our results showed high prevalence of dysglycaemia in ACS patients in this small sub-Himalayan state of Indian where working in the fields and walking is the routine daily practice. These abnormal glucose abnormalities can be detected early in the post admission period, where as OGTT remains the gold standard test in detecting diabetes in ACS. Routine APG, FPG, A1C and OGTT 72 hours after the admission should be standard of care in coronary care unit before discharge for early detection and appropriate action to avoid future complications.

**Abstract #329**

**IS SWITCHING FROM LIRAGLUrrIDE TO ExENATIDE USEFUL?**

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**Objective:** Lisproglutide (L), a GLP1 analogue, and exenatide (E), a GLP1 mimetic, can both result in improved glycemic control without hypoglycemia and in weight loss. It has been reported that switching from E to L may be beneficial. The effect of switching from L to E has not been reported. We report the results of switching from L to E in a “real world” clinical setting.

**Methods:** Nine consecutive obese T2DM males, mean age 53 yrs (33-70 yrs) on L 1.8 mg daily for a mean 26.9 months (8 -36 months) who were no longer losing weight or who were gaining weight despite continuing L were offered to switch to E in an attempt to restart weight loss. Compared to when L had been initiated, 5 patients had stabilized at a mean weight loss of 10.8 lbs (-2 to -29 lbs), 1 retained his original weight and 3 had gained a mean 26.7 lbs (2-41 lbs). All patients accepted the switch. Treatment otherwise remained unchanged. E was titrated to 10ug BID. Weight was recorded at a mean 7.8 months (3-17 months) after E introduction. HbA1c, patient tolerance of E, and patient satisfaction with E were also recorded.
ABSTRACTS – Diabetes Mellitus/Prediabetes

Results: Five patients (55.6%) lost a mean 5.6 lbs (1-13 lbs). Two patients (22.2%) gained a mean 8.5 lbs (3 and 14 lbs respectively). Two patients' (22.2%) weight did not change. The patient who had lost the most weight while on L gained the most weight on E and the two patients who had gained the most weight while on L lost the most weight on E. HbA1c increased by a mean of 0.008 (0.003-0.017) in 8 patients (88.9%) and decreased by 0.003 in one patient (11.1%). All patients tolerated E and were equally satisfied with E as with L.

Discussion: L and E differ in their amino acid structure and homologies to native GLP1. They differ in their dosing frequency and dosing schedule and in their pharmacodynamics. Studies have shown L to have a slight advantage in glucose lowering while both drugs result in roughly similar weight loss. L is generally better tolerated. Response is not consistent across all patients to neither drug.

Conclusion: Some patients whose weight loss has plateaued or who are gaining weight while on L lose weight when switched to E. Most patients’ glycemic control however deteriorates when switched from L to E. Patients with the most dramatic weight shifts while on L may show the most dramatic opposite shifts when switched to E. Patients who tolerate L also tolerate E and are equally satisfied with E as with L.

Abstract #330

SEX SPECIFIC ASSOCIATION AND PREVALENCE OF METABOLIC SYNDROME IN TYPE 2 DIABETIC SUBJECTS OF NORTH-INDIAN POPULATION.

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Objective: We have examined the prevalence and association of metabolic syndrome clustering among male (aged 58-85 years) and female (aged 55-77 years) Punjabi population.

Methods: This cross-sectional study was carried out on total of 301 (186 males and 115 females) type 2 diabetic mellitus subjects. The risk factors to assess the metabolic syndrome were included body mass index (BMI), waist circumference (WC), high density lipoprotein (HDL), triglycerides (TG), fasting blood glucose (FBS), systolic blood pressure (SBP), diastolic blood pressure (DBP) and to determine the cut-off points of these risk factors for Asian Indians used National Cholesterol Education Program (NCEP) - ATP III and International Diabetes Federation (IDF) criteria. The cut-off points were determined for WC>90 cm in males and >80 cm in females, BMI>23 kg/m2 and impaired fasting glucose (IGF)>100 mg/dl.

Results: It was observed that overall type 2 diabetic males (49%) were at risk of developing metabolic syndrome as compared to females (31%). The risk factors of metabolic syndrome such as BMI (34.6% for males and 70.4% for females), SBP (58.8% for males, 53% for females), DBP (38.4% for male, 30.4% for females) and triglycerides (85.48% for males, 85.2% for females) consistently higher in males as compared to females in which waist circumference (75.1% for males, 89.6% for females), HDL (65.9% for males and 89.6% for females) and FBS (64.9% for males and 72.9% for females) were higher. However, the overall mean differences between males and females of all studied risk factors were not found to be statistically significant (p<0.05).

Conclusion: The risk of metabolic syndrome is observed more in type 2 diabetic male Punjabi population due to sedentary lifestyle as compared to female

Abstract #331

COST OF FOOT ULCER TREATMENT AMONG PATIENTS WITH DIABETES IN KANO, NORTH-WESTERN NIGERIA

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Objective: We aimed to estimate the cost of illness among patients with Diabetes foot ulcer in secondary and tertiary health facilities in Kano.

Methods: The study was a cross-sectional evaluation involving ninety patients with diabetes having various degrees of foot ulcerations. A structured questionnaire was used to estimate the direct medical, non medical and Indirect costs of illness. Ulcer was examined clinically. Glycated haemoglobin was done to determine the glycaemic control of subjects.

Results: The mean±SD age of the subjects was 59.3±15.1 years with M:F ratio of 4:1. Among the male participants, 68.1% were the breadwinners of their families. About 60% of the participants earn less than $100 monthly. The total cost of illness of diabetic foot ulcer for the 90 participants per annum was $164484.38 (Average= $1827.61). The direct cost of illness was $125987.81 (Average=$1399.86). The direct non-medical cost was $40900.94 (average = $454.49). The total indirect cost was $38497.38 (average = $427.74). Drugs accounted for the largest share of the total cost (21.9%). Out of pocket
payment accounted for 90% of payment. The duration and location of foot ulcer, duration and frequency of hospital admission, average monthly income and presence of co-morbidities were significantly associated with increase cost of illness p<0.05. Low average monthly income (OR 4.9, 95% CI 1.1-22.6, p=0.04)and plantar location of foot ulcer (OR 2.8, 95% CI 2.8-6.8, p=0.03) were found to be determinants of increased cost of diabetic foot ulcer illness using binary logistic regression.

Discussion: The total cost of treating diabetic foot ulcer from the study is similar to what was found in studies from Canada and China. However, it was lower than what was obtained from a similar study done in Lagos South western Nigeria and another one done by Holzer et al in the United States. These variations could be attributed to differences in centers where care was obtained, expertise and equipment used. Drug purchase accounted for the largest share of cost of illness from the study while other studies found cost of hospitalization to contribute the largest percentage. The study found that insurance coverage among the participants was poor and mode of payment was mostly out of pocket.

Conclusion: The cost of diabetic foot ulcer in Kano is prohibitive and the patients mostly affected are poor, unemployed and the breadwinners of their families. Improved healthcare funding for diabetes care and subsidy on DM medications is advised to stem the tide of the disease.

Abstract #332

CLINICAL DECISION SUPPORT SOFTWARE VER-SES PRIMARY CARE TREATMENT RECOMMENDATIONS FOR PATIENTS WITH TYPE 2 DIABETES

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Objective: In the setting of increasing numbers of patients with type 2 diabetes and a shortage of specialists, decision support tools may become important for population health management. This study examines treatment decisions of PCPs for patients with type 2 diabetes compared to a software driven clinical decision support system.

Methods: Path, a decision support tool for Type 2 Diabetes, was developed based on efficacy, cost, ease of adherence, comorbidities, side effects, and pleiotropic benefit. Efficacy was estimated using published clinical data in terms of placebo controlled and head-to-head studies. Additional information regarding agents was added with regard to FDA package inserts as well as post marketing studies. Cost of intervention was described in terms of estimated copay drawn from insurance plan and average retail price.

PCPs from a multi-specialty group were ranked based on the average HbA1c values in Type 2 Diabetes patients under poor control (HbA1c >7). Chart review of patients seen during a 30 day period was performed for PCPs ranking at the top, median, and bottom. Information was placed into a decision engine. Results were compared to PCP intervention in terms of estimated cost of therapy, projected HbA1c and a custom multivariable efficacy score.

Results: Pre-intervention scenarios demonstrated a mean projected cost of $110 monthly, mean HbA1c of 8.3, and efficacy score measured as 50.6 of 100. After PCP intervention, mean projected cost was $127 monthly. Mean projected HbA1c was 7.8. Efficacy score was measured at at 80.0 of 100. Comparisons showed p values < 0.01.

Subanalysis was performed top, median, and bottom PCPs ranked by mean HbA1c > 7. Mean post-intervention cost totals were $103, $107, and $170 for top, median, and bottom PCPs respectively, compared to Path total cost of $37, $43, and $72. Projected A1c values were 7.2, 8.0, and 8.0 for top, median, and bottom PCPs respectively, compared to Path projected HbA1c values of 6.7, 6.8, and 6.8. Composite efficacy scores were 62.2, 57.6, and 49.9 for top, median, and bottom PCPs respectively, compared to Path projected A1c values of 84.5, 79.6, and 75.7. Comparisons showed p values < 0.01.

Conclusion: A software powered decision support tool has the capacity to create a diabetes medication regimen superior to physician driven interventions. This effect was observed in terms of hemoglobin A1c, cost, as well as other factors such as cost, impact on weight, and side effects. The largest impact of this intervention was observed in median and bottom physician performers.
Abstract #333

TRAINED NURSE OPERATED TELEMEDICINE BASED RETINAL EXAMINATION – A NOVEL COST EFFECTIVE MODEL FOR THE DEVELOPING WORLD

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Objective: To study the cost effectiveness of a novel telemedicine based digital retinal imaging process compared to conventional ophthalmologic fundus examination for screening and early diagnosis of diabetic retinopathy (DR).

Methods: We evaluated 206 diabetic patients at a diabetes centre by teleophthalmology using the Forbes fundal camera, operated by a trained nurse and images transferred by icloud to a retina centre for interpretation. The cost of telemedicine based digital retinal imaging examination included cost for devices, training, annual costs, reporting fee by retina specialist and were compared with conventional cost of referral to a retina specialist for fundus examination. Patients with moderate to severe DR were referred for further evaluation to Retina clinics.

Results: Patients included 90 females and 116 males with average age of 52.7±9.2 yrs, duration of diabetes 1-19 yrs (Mean=9.4±6) of which 52% had a duration<5yrs, 26% were 6–10yrs & 22% had duration>10yrs. Duration of diabetes was a strong predictor of severity of retinopathy (p=0.001) 18.2% (n=38) had retinopathy, 8.7% had mild NPDR, 4.8% moderate NPDR, 3.8% severe NPDR and 0.9% had PDR. The primary direct cost of the telemedicine based reporting was only $5.00 per patient. Total cost of the telemedicine based digital retinal imaging by medical assistant and interpretation by ophthalmologist, capital cost, equipment maintenance and reporting fee was <$10. Conventional fundus examination by an ophthalmologist costs $20. Referral to retina specialist was required for 19 (9.5%) patients with clinically significant disease on telemedicine evaluation, which additionally costed $15 per patient.

Discussion: Telemedicine based DR screening by trained nurse costs much less ($10vs$25) than conventional retinal examination by an ophthalmologist. Telemedicine-based digital retinal imaging is cheaper strategy with greater convenience and access for the remote population. This cost effective technology driven model would reduce the screening costs and also facilitate early detection of DR with timely intervention to help prevent blindness in the developing world.

Conclusion: Large scale adoption of telemedicine should be encouraged as a means of early detection of diabetic retinopathy providing easier access at a low cost for all patients with diabetes in the developing countries where access to an ophthalmologist is more expensive and also limited in remote areas. This also reduces the mass referral of all diabetic patients to specialized eye clinics for basic retina screening drastically bringing down not only the cost but also the burden on specialist retina clinics by filtering only clinically significant referrals to them for further management.

Abstract #334

CLINICAL CHARACTERISTICS AND COMPLICATIONS OF LATENT AUTOIMMUNE DIABETES IN ADULTS (LADA), TYPE 1 AND TYPE 2 DIABETES IN THE UNITED STATES

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Objective: We investigated and compared the clinical and biochemical phenotypes of patients with latent autoimmune diabetes in adults (LADA), type 1 diabetes and type 2 diabetes. The relationship between GADA (glutamic acid decarboxylase antibody) titers and complications in LADA patients was investigated.

Methods: This is a prospective case control study conducted in the Southeastern United States. Clinical characteristics of patients with LADA (n=154), type 1 diabetes (n=305) and type 2 diabetes (n=639) were compared. GADA ≥20 units/ml was defined as “high GADA titers” and those GADA ≤20 units/ml were defined as “low GADA titers.”

Results: Compared with type 1 and type 2 diabetes, patients with LADA seem to be intermediate with lower fasting c-peptide secretion compared with type 2 diabetes (p<0.001) but higher compared with type 1 diabetes (p<0.001). Patients with LADA had a larger BMI than type 1 diabetes (p<0.001) but lower BMI compared to type 2 diabetes (p<0.001). LADA patients had higher prevalence than type 1 diabetes of dyslipidemia (p<0.001) and hypertension (HTN) (p<0.001) but lower prevalence than type 2 diabetes (p=0.007 and p=0.0001 respectively). Complications such as coronary artery disease, neuropathy and autonomic dysfunction were also intermediate. Patients with low GADA titers had higher prevalence of HTN (p=0.042) and dyslipidemia (p=0.023). Patients with...
high GADA titers had lower BMI (p=0.001) and lower fasting c-peptide levels (p=0.011).

Discussion: According to the “accelerator hypothesis”, type 1 diabetes, type 2 diabetes and LADA are not separate entities, but variations in the tempo of β-cell failure involving different contributions of insulin resistance and genetic susceptibility to it. Our data seems to support this hypothesis. Our current study has several strengths. First, to our knowledge, this is the first study in the United States to characterize and compare the clinical characteristics of patients with LADA and divide the prevalence of complications in LADA based on GADA titers. Second, we included all consecutive patients evaluated by a single investigator. This avoided selection bias.

Conclusion: LADA patients were intermediate between type 1 diabetes and type 2 diabetes with respect to clinical characteristics and chronic complications. High titers of GADA have the clinical features of type 1 diabetes while low titers are associated with the clinical and metabolic phenotype of type 2 diabetes patients.

Abstract #335

ADVANCED ALGORITHMIC CONTROL OF A COMMERCIAL SENSOR-AUGMENTED INSULIN PUMP: PROGRESS TOWARD CLOSING THE LOOP

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Medtronic, Inc.

Objective: Several features for automated control of insulin delivery are now available, including suspend on low (pump suspension in response to a low sensor glucose [SG] value), suspend before low (suspension prior to a predicted low value), and auto-resume (restarting the pump in the presence of normal and upwardly-trending SG values). We compared SG values from subjects using various combinations of these features.

Methods: Anonymized data that had been voluntarily uploaded to the CareLink database were studied. To assess the incremental benefit of suspend before low, we used data from 851 patients who switched from using Veo pumps with available suspend on low to using 640G pumps with available suspend on low and suspend before low. To assess the auto-resume feature of the 640G pump, we used data from 167,536 suspend before low events (9584 patients) that were terminated either automatically or manually. Hypoglycemia and hyperglycemia were defined as SG values ≤70 and ≥300 mg/dL, respectively. We compared glycemic excursions with respect to their durations (min/day), areas under the curve (AUC, in mg/dL × day), and frequencies (intervals with ≥2 consecutive hypo- or hyperglycemic SG values, per day) using paired t-tests.

Results: Of the 851 patients who switched from Veo to 640G, 86% used the suspend on low feature before switching, at an average of 82±30% of the time. After switching, 92% used the suspend before low feature, at an average of 88±24% of the time. Favorable reductions were noted for intervals of 640G use compared to intervals of Veo use with respect to hypoglycemia duration (37% less), hyperglycemia duration (8% less), hypoglycemia AUC (27% less), hyperglycemia AUC (17% less), hypoglycemic excursions per day (23% fewer), and hyperglycemic excursions per day (11% fewer). In a separate analysis of the 167,536 Suspend Before Low events, 60.4% were automatically resumed and 39.6% were manually resumed. Compared to automatically-resumed events, manually-resumed events had shorter durations. The time spent with low SG values in the 6 hours after automatically-resumed suspension events was significantly lower than after manually-resumed events.

Conclusion: Switching from the Veo pump system and its suspend on low feature to the 640G system and its suspend on low, suspend before low, and auto-resume features was associated with favorable changes in SG values, suggesting reductions in both hypo- and hyperglycemia. Advanced features for automatic suspension and resumption of insulin pumps represent a further advance toward closed-loop insulin delivery.
HYPOGLYCEMIA

Abstract #400

HYPERKALEMIA TREATMENT-INDUCED HYPOGLYCEMIA IN THE HOSPITAL

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Objective: To characterize hypoglycemia resulting from the treatment of hyperkalemia in the hospital in patients with and without diabetes mellitus and to develop a hospital wide hyperkalemia treatment care set. Methods: Patients with hyperkalemia are frequently treated with insulin and glucose which can result in hypoglycemia. Since many of these patients (with and without diabetes) have renal insufficiency, insulin action may be prolonged and hypoglycemia can occur 6 hours after insulin administration. The optimal duration for glucose checks following administration of insulin in the management of hyperkalemia is not known. A case of severe hypoglycemia of this type was presented at a Safety Conference at our community teaching hospital and highlighted the need for closer glucose monitoring after the use of insulin for the treatment of hyperkalemia.

Results: A subgroup of our Glycemic Care Team including a medical resident, hospitalist, endocrinologist and medical informaticist developed and implemented a hyperkalemia management care set which included a pretreatment glucose and post treatment glucoses at 15 minutes post and then hourly for 6 hours. Hypoglycemia, if present, was treated with our Hypoglycemia Protocol. The electronic orders would “crossover” from the emergency room to the hospital units, so that if a patient was admitted and started treatment in the emergency room, the glucose checks would continue on the hospital unit. The non-glucose aspects of the hyperkalemia management care set were modeled after that proposed by the Renal Association. We developed an electronic alert which is triggered when intravenous insulin is prescribed to encourage use of the care set. We are tracking care set utilization and reviewing the glucose data.

Discussion: The electronic care set encouraged standardized surveillance for hypoglycemia following insulin administration; practices varied widely prior to care set implementation and often glucoses were checked intermittently or not at all post treatment and patients with diabetes had more glucoses than those without. Preliminary data indicate that hypoglycemia can be detected several hours after treatment of hyperkalemia.

Conclusion: The use of an electronic care set to manage hyperkalemia can mitigate the risk hyperkalemia treatment induced hypoglycemia by including post treatment glucose checks and use of the Hypoglycemia Protocol. Our data will be reviewed and recommendations will be made regarding the optimal duration of glucose checks after treatment of hyperkalemia, including diabetic patients. Hyperkalemia treatment induced hypoglycemia in the hospital is high risk and can be managed and tracked more effectively with use of an electronic care set.

Abstract #401

PSEUDO-HYPOGLYCEMIA IN CRITICALLY ILL PATIENTS: DO NOT BE FOOLED!

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 Advocate Illinois Masonic Medical Center

Objective: We describe a very interesting case of pseudo-hypoglycemia resulting in an inappropriate management.

Case Presentation: A 55 year old male with past medical history significant for HIV, heart failure and polysubstance abuse presented with seizure and was admitted to the medical intensive care unit (MICU) for acute respiratory failure. Imaging tests were unremarkable and laboratory studies were significant for finger stick glucose (FSG) <10 mg/dL, blood glucose (BG) 74 mg/dL, lactic acid 8.1 mmol/L, procalcitonin 0.39 ng/mL, INR 3.1, creatinine 1.74 mg/dL, BUN 30 mg/dL, AST 4897 U/L, ALT 997 U/L, Ammonia 34 mmol/L and urine toxicology screen positive for cannabinoids and opiates. He was started on pressors, empiric antibiotics and Dextrose 10%. During his MICU stay he had multiple episodes of hypoglycemia reported on FSG testing, ranging from <10 to 44 mg/dL. Subsequently, he received numerous Dextroxe 50% intravenous ampules since symptomatic evaluation was not possible while he remained intubated. Initially, his hypoglycemia was thought to be secondary to impaired hepatic gluconeogenesis in the setting of acute liver failure. Further hypoglycemia work up revealed an appropriately elevated cortisol level, HbA1c 5.7%, negative sulfonylurea panel, normal TSH, C-peptide, and insulin levels. Finally, it was noted that despite the very low reads on FSG, antecubital venous BG was within normal limits or elevated. Furthermore, the patient’s glucose was checked in his ear lobe with the same device, finding normal blood glucose levels. Concomitant arterial blood gas sampling confirmed pseudo-hypoglycemia.

Discussion: Pseudo-hypoglycemia is the discrepancy between capillary glucose values and plasma glucose concentrations. Most of the reported cases are related to Raynaud’s phenomenon, acrocyanosis or peripheral vascular disease. In our case, pseudo-hypoglycemia was mostly secondary to peripheral underperfusion in the setting of shock. In 1991 Atkins et al reported that in critically-ill patients FSG readings were 67.5% lower than BG values, with 32% of them being incorrectly diagnosed with
hypo-glycemia likely due to terminal vasoconstriction in shock. Therefore, pseudo-hypo-glycemia should always be considered in such asymptomatic patients before initiating hypoglycemia workup and treatment.

**Conclusion:** High index of suspicion for Pseudo-hypo-glycemia should always be maintained in asymptomatic patients with discordant FSG and BG, since repetitive inappropriate treatment can lead to hyperglycemia-induced adverse events.

**Abstract #402**

**REACTIVE HYPOGLYCEMIA IN A NON-DIABETIC ADULT WITH POSITIVE GAD-65 ANTIBODIES**

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Augusta University

**Objective:** We present a nondiabetic patient with reactive hypoglycemia and positive GAD-65 antibodies successfully treated with prandial acarbose.

**Case Presentation:** A 26 year old female was seen for evaluation of hypoglycemic symptoms for 3 years. In the last year, these events occurred on a daily basis and she had withdrawn socially. Self-monitoring of blood glucose (BG) revealed her lowest BG value of 55 mg/dL. Her HgbA1c was 4.6%. We performed a glucose tolerance test (OGTT) and her 2-hour BG was 11 mg/dL. At 1-hour her BG was 62 mg/dL and insulin level was elevated at 32.8 mcIU/mL (2.6-24.9) with a high-normal C-peptide of 4.2 ng/mL (1.1-4.4). We admitted her for a 72-hour fast and during the fast she did not experience any hypoglycemic symptoms. Her lowest BG was 50 mg/dL. Insulin autoantibodies, IgF-1, and IgF-2 were normal, and oral hypoglycemic screen was negative. Her insulin, C-peptide, and proinsulin levels were low and her β-hydroxybutyrate level increased during the fast. She was started on acarbose 25 mg orally with meals after the 72-hour fast. On follow up, she reported improved symptoms and quality of life. We ordered a continuous glucose monitor (CGM) for her to use at home. Data from her CGM revealed fasting BG values above 60 mg/dL and postprandial BG up to 130 mg/dL. We obtained glutamic acid decarboxylase (GAD)-65 antibodies which were elevated at 14 nmol/L (<0.02).

**Discussion:** We present a nondiabetic patient with reactive hypoglycemia and positive GAD-65 antibodies, likely indicating a “pre-diabetic” phase of autoimmune activity that may progress to latent autoimmune diabetes in an adult (LADA). Our evaluation showed marked hypoglycemia at two hours during an OGTT and a negative 72-hour fast. We successfully managed her with the use of CGM and prandial acarbose, an approach that allowed this patient to return to her usual activities and quality of life. Due to the positive GAD-65 antibodies, we believe she may progress to LADA.

**Conclusion:** The evaluation and management of hypoglycemia in patients without diabetes is often challenging. The 72-hour fast may not yield a diagnosis and results of the OGGT are often difficult to interpret. Some patients with reactive hypoglycemia may develop diabetes and measuring islet autoantibodies may indicate a “pre-diabetic” phase where close monitoring of BG may confirm progression to overt diabetes. In these patients, BG monitoring with a CGM and prandial acarbose should be considered. Obtaining an OGGT and a 72-hour fast to rule out endogenous and exogenous sources of excessive insulin in a non-diabetic adult with reactive hypoglycemia may be necessary. The significance of positive GAD-65 antibodies in these patients has not been studied.

**Abstract #403**

**SEVERE HYPOGLYCEMIA IN A PATIENT WITH GASTRIC ADENOCARCINOMA: AN IGF-II SECRETING TUMOR?**

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Medical University of South Carolina

**Objective:**
1. Review non-islet cell tumor hypoglycemia (NICTH).
2. Recognize IGF-II secreting tumors as a cause of hypoglycemia.

**Case Presentation:** An 80 year old African American female with a history of stage IIIB gastric adenocarcinoma and prediabetes (A1c 5.6) was admitted from clinic with intractable nausea and vomiting. Computerized axial tomography (CT) scan revealed gastric outlet obstruction and she was taken for endoscopy to place a pyloric stent. The procedure was complicated by gastric perforation and she was not able to take anything by mouth. She began to have progressive dizziness and diaphoresis. A finger stick blood glucose (FSBG) level was <20 (lowest reading by the glucometer) and she was started on IV dextrose. She was transitioned to total parenteral nutrition (TPN) containing 200 g of dextrose daily. Despite this she continued to have FSBG levels less than 55 and symptoms of hypoglycemia. Her symptoms resolved when her blood glucose increased, but required 275 g of IV dextrose daily to maintain low normal serum glucose. Due to the patient’s symptoms she refused reducing the dose of IV dextrose to obtain hypoglycemia labs. Therefore her serum glucose was 78 – 97 when labs were obtained. Beta hydroxybutyrate was <0.2, C-peptide 3.9, cortisol...
16, growth hormone 2, chromogranin A 59 (normal 0-95), IGF-1 78 (normal 54-205), insulin 6 and human insulin antibodies were negative. A send out IGF-2 was 508 (normal: 288-736). The patient went to a skilled nursing facility while receiving TPN and was supposed to follow up as an outpatient. Unfortunately she developed sepsis from her TPN line and she elected for hospice care.

**Conclusion:** Cancers can cause hypoglycemia. Islet cell tumors that secrete insulin are a major cause of hypoglycemia. There are multiple mechanisms for NICTH. Production of incompletely processed IGF-II (big IGF-II) is the most common mechanism of NICTH. This is most commonly seen in mesenchymal tumors but can also occur with fibromas, carcinoids, myelomas, lymphomas, hepatocellular, colon or gastric tumors. Big IGF-II causes hypoglycemia by increasing skeletal muscle glucose utilization along with decreased gluconeogenesis and glucose release in the liver. Another mechanism is metastatic disease causing destruction of the liver or adrenal glands. Finally, production of insulin or insulin receptor antibodies are rare causes of hypoglycemia. Some cases are probably multifactorial. Our case was most likely from tumor secretion of big IGF-II. Although the measured IGF-II is in the normal range, it is the best explanation for this patient’s severe hypoglycemia.

**Abstract #404**

**IS THIS INSULIN AUTOIMMUNE SYNDROME**

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UTHSC

**Case Presentation:** A 76-year-old Afro American non diabetic female was admitted to the hospital with recurrent hypoglycemia and change in mental status. She was diagnosed with septic shock and was intubated and started on goal directed septic shock protocol. She was also started on Glucerna at 30-50ml/hour. Endocrinology was consulted after 3 days when she kept having periods of intermittent hypoglycemia. She was switched to 20% dextrose (D20) at 35ml/hour which was gradually titrated to 100ml/hour. She continued to have intermittent episodes of hypoglycemia. She was empirically started on octreotide 100mcg subcutaneously every 8 hours for possible insulinoma although scans remained negative for any pancreatic mass. But her periods of intermittent hypoglycemia continued. Her sulphonylureas screen was negative. Significant labs included cortisol level of 109.7 mcg/dl, 206 mcg/dl and 127mcg/dl without hydrocortisone supplementation. Her insulin level was measured thrice during the course in the hospital and the numbers were 70.9,46 and 51(Normal range 4.2-27 milliunit/L). Her C peptide level was 8.7.7 and 7.8 ng/ml (Normal range 0.8-3.8ng/ml). CT abdomen did not show any pancreatic mass. Further work up was not done and patient was palliatively extubated because of poor functional status prior to the current illness. After extubation patient was started on oral feeds and after a brief period of hypoglycemia she became euglycemic

**Discussion:** No insulin antibodies were done but her clinical presentation was consistent with insulin autoimmune syndrome (IAS). Typically the condition is described as hypoglycemia 3-4 hours after a meal. Since our patient was on continuous feeds the hypoglycemic episodes were more erratic and did not follow a predictable pattern. Most commonly the condition is described to be associated with methimazole which our patient was taking. Sulphonylureas screen was negative and the patient continued to have intermittent hypoglycemia even after a week of high calorie supplementation. Also failure to respond to octreotide helped in excluding insulinoma

**Conclusion:** IAS could be clinically missed among the multiple clinical conundrums which often accompany the patient in the critical care settings. Careful perusal for underlying risk factors could help in nailing the diagnosis.

**Abstract #405**

**INSULINOMA: SPONTANEOUS REMISSION WITH CALCIUM STIMULATION SCINTIGRAPHY AND RECURRENCE AFTER 10 YEARS**

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**Objective:** To determine the significance of Calcium stimulation test in the diagnosis of Insulinoma, its potential complications and the disease course of Insulinoma.

**Case Presentation:** We describe a case of 52-year-old dentist with PMH of Multiple Endocrine Neoplasia, which is complicated by hyperparathyroidism s/p parathyroidectomy. After 5 years, he had sudden onset palpitations and seizures and was taken to a local Emergency room. Vitals: T: 98.6 F, HR: 100 bpm, RR: 16/min, BP: 126/76 mm Hg, Blood glucose: 38 mg/dl. Screening for sulfonylurea was negative. There was a concern for Insulinoma and was referred the NIH for the further management. In the NIH, we performed 72-hour fasting (we stopped it in 16 hours given the positive results confirming insulinoma). Lab values: Serum Insulin levels: 29 µU/ml, C-Peptide: 7.5 ng/ml, elevated proinsulin levels with sulfonylurea negative screen. A repeat test has showed almost similar lab values. CT
and MRI were positive for 2.2 x 2.1 cms inhomogenous hypoechoic lesion in the body of the pancreas. Calcium stimulation scintigraphy (CSS) was done to confirm the location of the tumor. It was complicated by Acute pancreatitis (Lipase 800 U/L) and the patient was made NPO. To our surprise, his blood sugars never dropped to < 70 mg/dl. We have repeated 72-hour fasting test, which showed Serum Insulin levels: 7 µU/ml, C-Peptide: 1.6 ng/ml and BS of 67 mg/dl. A repeat test revealed similar results. The patient was discharged home with follow-up with us in 3 months. The patient lost follow-up for 10 years for which he was symptom-free and the symptoms recurrent while he was fasting for Ramzan. Repeat 72-hour fast has confirmed Insulinoma biochemically, which was later confirmed anatomically with CT and MRI (2.3 x 2.0 cms mass in body of pancreas). CSS has confirmed the functional location of the tumor. He had enucleation done and post-surgical 72-hour fast has showed normal insulin and blood sugar levels. The patient was free of symptoms for 2 years since surgery.

**Discussion:** The selective intra-arterial CSS has greatly facilitated the precise regionalization of insulinomas smaller than 2 cm. At the NIH we perform CSS even after CT/MRI localizes the tumor to confirm both anatomical and functional localization before proceeding to surgery. Our patient had a complication of acute pancreatitis with calcium-stimulated scintigraphy and spontaneous remission of Insulinoma. He had functional recurrence of tumor after 10 years, which was later surgically removed.

**Conclusion:** Spontaneous remission of Insulinoma can occur as a consequence of CSS and these patients should be followed up at least annually by an Endocrinologist as there can be recurrence as seen in our patient.

**Abstract #406**

**THE ROLE OF CONTINUOUS GLUCOSE MONITORING (CGM) IN THE DETECTION OF HYPOGLYCEMIA IN OLDER ADULTS (>65 YEARS OLD)**

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**Objective:** Hypoglycemia remains the main limiting factor in the management of diabetes in older individuals. The outcome associated with severe hypoglycemia may result in serious events such as seizures, cardiac arrhythmias, joint dislocations and bone fractures. The incidence of hypoglycemia in older adults (>65 years) is difficult to estimate and recognize due to the paucity of clinical studies, lack of standardization in hypoglycemia diagnosis, and nonspecific symptomatology. The aim of this study was to determine the prevalence of hypoglycemic episodes in elderly patients (>65 years) treated with insulin.

**Methods:** We conducted a retrospective study to investigate the use of continuous glucose monitoring (CGM) as a tool to recognize and prevent hypoglycemia in older diabetic patients. Data was collected from patients with a diagnosis of either type I or type II diabetes mellitus that attended the Endocrinology Clinic of the University of Florida – Jacksonville Campus and had a diagnostic CGM. Records of 67 patients (>65 years old) who underwent CGM were reviewed. Only 51 patients met study criteria which included at least 72 hours of CGM use, records of self-monitored capillary blood glucose level, self-reported history of hypoglycemia and glycosylated hemoglobin (HbA1c) within 30 days of CGM.

**Case Presentation:** The study population included 19 males (37%) and 32 females (63%) with ages ranging from 65 to 89 years with a mean age of 70. All subjects except for one were type II DM. Participants had an average A1C of 7.8% +/-1.4. Of the 51 patients, 10 were treated with at least one oral agent plus basal insulin and 41 with basal/bolus insulin regimens. Only 16 out of 51 patients self-reported hypoglycemic episodes during CGM office visit. However, CGM records revealed 32 patient with hypoglycemic episodes defined as blood sugar <70 mg/dL and a total of 85 events. Further analysis showed 42 hypoglycemic episodes defined as blood sugar <70 mg/dl but > 50 mg/dl in 11 patients. Twenty-one patients had a total of 43 hypoglycemic episodes with blood sugar readings ≤50mg/dL on CGM. The CGM monitoring was generally well tolerated by all participants.

**Conclusion:** Currently most physicians rely on self-monitored capillary blood glucose, self-reported hypoglycemic events and target HbA1c as a tool to detect and manage hypoglycemia in elderly adults. Unfortunately all three have limitations in regards to the ability to provide information about glucose variability. Based on our observations, we believe CGM is a helpful and additive tool to detect hypoglycemia in older adults that can be easily missed by customary methods. Prospective randomized trials with long-term follow up are needed to validate these results.
A RARE CAUSE OF ORGANIC HYPOGLYCEMIA

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University of Alabama at Birmingham

Objective: Insulin producing pancreatic adenoma is a serious cause of hypoglycemia in non-diabetic patients.

Methods: We present a 47 year old Caucasian female with an unusual proinsulin only secreting pancreatic endocrine adenoma as a case study.

Case Presentation: A 47 year old Caucasian female presented to our clinic with history of hypoglycemia, associated with symptoms of altered mentation and peripheral numbness for a year. Her physical examination was unremarkable. Further laboratory work-up done revealed a blood glucose 51 mg/dL, plasma insulin 2.9 micro IU/ml (normal range 3-25 micro IU/ml), plasma c-peptide 1.90 ng/ml (normal range 0.81-3.85 ng/ml), proinsulin 207 picomol/L (normal range <18.8 picomol/L, sulfonylurea screen was negative, insulin antibodies were negative, Insulin like growth factor- 2 was within normal limits, normal renal function panel and normal hepatic function panel. She was admitted for 72 hour fast and similar results were obtained at 12 hours into the fast with a blood glucose of 41 mg/dl. Blood glucose 60 minutes after glucagon injection went up to 62 mg/dl. There was an appropriate response to standard cortisol stimulation test and thyroid function test were normal. A CT scan of abdomen and chest did not show any abnormality of the pancreas. She then underwent an endoscopic ultrasound and biopsy which revealed an 8x7 mm hypoechoic well circumscribed lesion in the body of the pancreas inferior to the main pancreatic duct. Pathology was consistent with a neuroendocrine neoplasm with chromogranin and synaptophysin positivity. She underwent a distal pancreatectomy with resection of a 1.2 cm grade-1 pancreatic neuroendocrine tumor and subsequent fall in proinsulin levels fell to less than 5 picomols/L two weeks post-surgery.

Discussion: The clinical history of the patient was highly suggestive for an organic cause of hypoglycemia. Patient however had an appropriately low insulin levels in relation to low blood glucose but proinsulin level was significantly high. Proinsulin-only secreting tumors are extremely rare while pancreatic endocrine tumors usually produce and secrete both insulin and proinsulin.

Conclusion: The most common cause of organic hypoglycemia in the adult is insulin producing pancreatic adenoma. However proinsulin levels should be checked and proinsulinoma suspected in cases where there is high clinical suspicion despite low insulin levels.

FACTITIOUS HYPOGLYCEMIA

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Case Presentation: We present a 32 year old Caucasian female with history of type 2 diabetes (DM) found to have serum glucose of 54 mg/dL with complaints of blurry vision and hunger during outpatient foreign body removal. DM was diagnosed 2 years prior to presentation and was treated with metformin 250 mg BID and Humalog insulin on a “sliding scale”. She reported being NPO since the night before and stopping metformin 1 day before surgery. Her home blood glucose ranged from 135 to 155 and she denied recent insulin use. She reported having multiple episodes of symptomatic hypoglycemia in the past. She is divorced and admitted to tobacco, marijuana and alcohol use. Initial laboratory results included morning cortisol 14 ug/dl (3.7-19.4), blood glucose 55 mg/dL and A1c 5.8% (<= 6.5). Insulin and C peptide were pending. Patient was admitted to the ICU with hourly blood glucose checks and 10% dextrose infusion. Hypoglycemia eventually resolved. The rest of her labs were later available and revealed insulin 66.7 uU/ml (5-25), C-peptide 0.47 ng/ml (0.78-5.19) with blood glucose of 57 mg/dL (70-110) consistent with factitious hypoglycemia. When the patient was informed of this result, she admitted to taking 8 units of Humalog the night before admission for a blood glucose of 650 mg/dL.

Discussion: Hypoglycemia is a clinical syndrome defined by the presence of the Whipple triad: a low blood glucose concentration, characteristic symptoms and/or signs, and symptom resolution when blood glucose is normalized. Factitious hypoglycemia occurs secondary to the surreptitious use of insulin or insulin secretagogues (sulfonylureas, meglitinides).

A detailed history including the conditions that are associated with symptoms, current medications and a social history are important components of the evaluation. Laboratory evaluation should be obtained during a hypoglycemic episode (glucose <55 mg/dL) including; glucose, Insulin, C-peptide, Beta-hydroxybutyrate and Proinsulin. Sulfonylurea and meglitinide screen should be considered if clinical picture is suggestive of their use. A mixed meal diagnostic test is performed when reactive hypoglycemia is suspected. The long-term treatment of factitious hypoglycemia involves changing abnormal behavior patterns. Confrontation may be more effective when it is a collaborative intervention by the medical provider and psychiatrist.
Conclusion: Careful history taking and interpretation of laboratory results are important in the evaluation of patients presenting with hypoglycemia in order to arrive at the proper diagnosis and management approach.

Abstract #408

THE USE OF DIAZoxide IN THE TREATMENT OF HYPOGLYCEMIA SECONDARY TO RELATIVE HYPERINSULINEMIA IN PATIENTS WITH END STAGE RENAL DISEASE (ESRD)

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Objective: Hypoglycemia rarely occurs in the absence of exposure to hypoglycemic agents in some non-diabetic patients with ESRD. The main mechanism of hypoglycemia in patients with ESRD is likely reduced gluconeogenesis. In healthy individuals, renal gluconeogenesis is critical for maintaining euglycemia as it represents roughly 50% of endogenous glucose output. We present a case series of hospitalized patients with ESRD on hemodialysis (HD) in whom we have used Diazoxide to treat hypoglycemia.

Case Presentation: Case 1: A 60 year old man, with history of HIV/AIDS, ESRD on HD without prior diagnosis of diabetes was admitted with septic shock and persistent hypoglycemia. Continuous dextrose drip to maintain euglycemia was required. Elevated fasting insulin and C-peptide levels during hypoglycemia without evidence of pancreatic mass were noted. AM cortisol level was normal. After initiating diazoxide serum glucose levels normalized. Case 2: A 54 year old woman, with history of type 2 diabetes, was started on HD due to hypertensive nephropathy. After starting HD, diabetes medications were slowly tapered off due to frequent hypoglycemic episodes. Two months after discontinuation of all diabetes medications serum blood sugar was 57 mg/dl, with inappropriately normal proinsulin and C-peptide levels. After starting diazoxide hypoglycemic episodes resolved. Case 3: A 51 year old woman with history of hypertensive nephropathy, on HD and a history of HIV/AIDS was admitted with C-spine fracture. She had many episodes of hypoglycemia with blood sugars 37-50 mg/dl requiring continuous dextrose infusion. C-peptide level was found to be elevated with serum blood sugar of 56 mg/dl. After treating with diazoxide, she was weaned off dextrose, and fasting glucose remained >60 mg/dl.

Discussion: Diazoxide acts by inhibiting insulin secretion from the pancreas through its effect on potassium channels in beta cells. It is used in the treatment of hypoglycemia caused by insulinomas. While hospitalized, our patients suffered multiple episodes of hypoglycemia requiring treatment with dextrose. In addition to ESRD, these patients suffered from other comorbidities such as HIV, malnutrition, and deconditioning. Laboratory tests revealed inappropriately normal to elevated plasma insulin and C-peptide levels during episodes of hypoglycemia. We believe that hypoglycemia was triggered by a state of relative hyperinsulinemia in the setting of poor renal clearance of endogenous insulin, in addition to the poor nutritional status and reduced gluconeogenesis in these patients. Our suspicion of an insulinoma was very low.

Conclusion: Diazoxide is a beneficial treatment option in patients with ESRD and recurrent hyperinsulinemic hypoglycemia.

Abstract #410

PARANEOPLASTIC HYPOGLYCEMIA IN HEPATIC HEMANGIOPERICYTOMA

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Objective: 1. Identify hepatic hemangiopericytomas as a cause of refractory paraneoplastic hypoglycemia. 2. Describe the pathophysiology of hypoglycemia in patients with hepatic hemangiopericytomas.

Case Presentation: A 45-year old female presented with severe right-upper quadrant and epigastric pain associated with early satiety and weight loss. Ultrasonography showed a 17 cm liver mass that was eventually biopsied and consistent with hemangiopericytoma. Over the next 6 months, she was admitted to the hospital several times with symptoms of hypoglycemia and blood sugar levels frequently less than 20 mg/dL despite frequent, carbohydrate-rich meals. Laboratory findings revealed low levels of circulating insulin, C-peptide and insulin-like growth factor I (IGF-I). Glucagon and octreotide trials were unsuccessful for refractory hypoglycemia. She eventually required continuous dextrose infusions and total parenteral nutrition. Despite all interventions, and extensive medical therapy, she remained clinically and biochemically hypoglycemic and died before she could undergo orthotopic liver transplantation (OLT).

Discussion: Hemangiopericytomas are uncommon tumors that are derived from vascular pericytes. These tumors, on rare occasions, can develop in the liver and cause a paraneoplastic syndrome resulting in hypoglycemia. In the presence of a liver mass, hypoglycemia can arise from impaired gluconeogenesis due to replacement of normal liver tissue by the tumor. However, in the case
of hemangiopericytomas, hypoglycemia is caused by paraneoplastic production of insulin-like growth factors. As seen in this patient, levels of insulin and IGF-I can be low since the tumor-induced hypoglycemia can be attributed to insulin-like growth factor II (IGF-II) and a high-molecular-weight variant of IGF-II called big IGF-II. Paraneoplastic hypoglycemia in patients with hemangiopericytomas can be devastating since no medical therapy has shown to be effective in adequately controlling blood glucose levels. Surgical intervention after pre-operative embolization to shrink the tumor may be effective in patients but depends on the size of the mass and stage of the disease. OLT can also be curative but is dependent on the availability of donor organs and other qualifying parameters for transplantation.

Conclusion: Hepatic hemangiopericytomas can cause refractory paraneoplastic hypoglycemia that can be difficult to manage. Surgical resection or OLT can be curative but overall prognosis is poor.

Abstract #411

THE PREVALENCE OF FASTING-EVOKED EN-ROUTE HYPOGLYCEMIA IN DIABETES (FEEHD) IN CLINICAL PRACTICE: A PILOT SURVEY STUDY

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Objective: To increase awareness of an overlooked form of hypoglycemia, referred to as fasting-evoked en-route hypoglycemia in diabetes (FEEHD), occurring in patients who are routinely asked to fast overnight for laboratory tests without adjusting hypoglycemic medications. We recently published observational studies, a case series and a review article addressing FEEHD, but there are no other studies evaluating the prevalence of this iatrogenic, potentially harmful adverse diabetes management event.

Methods: Adult patients were surveyed at outpatient clinic visits. Inclusion criteria included diagnosis of diabetes and being on anti-diabetic medications especially those that could cause hypoglycemia, mainly insulin and sulfonylureas. Patients were asked if they recalled experiencing hypoglycemic events (plasma glucose < 70 mg/dL) while fasting for laboratory tests. Additional information regarding circumstances surrounding the event and any directed medication adjustments were obtained.

Results: Between October, 2014 and October 2015, 168 patients from 4 clinics, including a diabetic clinic, were invited to participate in the survey study, of whom 166 patients (98.8%) completed the survey. The mean age of the 166 respondents was 55 (SD 15) years, and 79 (47.6%) were females. Of the 166 respondents, 119 patients (71%) had type 2 diabetes, and all respondents were taking insulin and/or oral hypoglycemic agents or other injectable antidiabetic medications. Forty five patients (27.1%) reported having one or more lab-related hypoglycemic events (FEEHD) during the preceding 12 months. Notably, only 31.1% of the patients who experienced a FEEHD event informed their providers of the hypoglycemic event, and only 40% of FEEHD events reportedly resulted in any subsequent provider-made medication change(s) to prevent future events.

Discussion: This is the first study to evaluate the prevalence of FEEHD in a real life clinical setting, confirming a significant prevalence (27.1%), as well as the conceivable unawareness of clinicians about its occurrence in their patients. It is hoped that this study will serve as a means of increasing awareness about the occurrence of FEEHD in clinical practice, which clinicians may often appear to underestimate.

Conclusion: This study confirms the significant prevalence of FEEHD in clinical practice, suggesting that patients with diabetes are put at risk when fasting for lab tests. The study sends an alarming message that challenges the deeply rooted tradition of fasting for lipid profiles, and calls for larger studies in different populations to evaluate its actual prevalence.

Abstract #412

INSULIN AUTOIMMUNE SYNDROME

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Objective: To present a case of Insulin autoimmune syndrome (Hirata’s syndrome) secondary to alpha-lipoic acid use.

Case Presentation: 50 year old lady presented with repeated episodes of palpitations, anxiety and feeling of impending doom along with trembling of hands and sweating that responded to intake of food, especially sweets of 15 days duration. The first episode occurred in the evening but later she began to have these episodes every few hours during the day, not related to her major meals. She used to keep eating to keep herself free of symptoms. Blood glucose(BG) monitoring revealed spot BG values of 45-65 mg/dl (75-100 mg/dl). Her fasting BG 62 mg/dl (75-100 mg/dl), fasting insulin >3000 μU/mL (2-20 μU/mL), 2post mealBG 52 mg/dl (100-140 mg/dl) and insulin>4000μU/mL(up to 200 μU/mL)raising a suspicion of insulinoma. Other differential diagnosis considered...
were surreptitious exogenous insulin administration, sulphonylurea intake or insulin autoimmune syndrome (IAS). Dual phase CECT abdomen was normal and endoscopic USG abdomen did not reveal any tumour in pancreas. Patient underwent 72 hour fasting test. She developed severe hypoglycaemic symptoms within 3 hours. BG 38 mg/dl, insulin 22360 µU/mL (<3µU/mL), C-peptide 26.73 ng/ml (0.8-3.5 ng/ml) at that time. This ruled out exogenous insulin intake. Sulphonylurea and proinsulin assays were not available. Insulin antibody levels were 299.12 U/ml (0.0). Based on high levels of insulin antibodies (>100 U/ml) and high levels of insulin(>300 µU/mL) in the presence of hypoglycaemia a diagnosis of IAS(Hirata’s syndrome) was made. Patient was reevaluated and medical history reviewed which revealed that she was taking alpha lipoic acid, vitamin B12, pregabalin and diclofenac for shoulder and back pain of six weeks duration. She was put on oral prednisolone and frequent small carbohydrate meal and alpha lipoic acid was withdrawn. She was offered plasmapheresis which the patient declined. Severity and frequency of hypoglycaemia decreased markedly. Prednisolone was tapered over 10 weeks. She was asymptomatic over 6 months of follow up. A final diagnosis of IAS secondary to alpha lipoic acid was made.

Conclusion: Hirata’s syndrome is a rare cause of hypoglycemia and should be considered in evaluation of hypoglycemia. Apart from alpha lipoic acid, other drugs implicated are penicillamine, isoniazid and hydralazine.

Abstract #413

PSEUDOHYPOGLYCEMIA: UNRELIABLE CAPILLARY GLUCOSE MEASUREMENTS IN A PATIENT WITH IMPAIRED MICROCIRCULATION

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Objective: We present a case of pseudohypoglycemia to raise awareness about this phenomenon, avoiding unnecessary work-up and delays in diagnosis.

Methods: The clinical presentation, evaluation, and management of this case are presented.

Case Presentation: 54-year-old male with hypertension, diabetes mellitus type 2, end-stage renal disease on dialysis, and recently diagnosed giant cell arteritis. Patient was sent to the hospital from outpatient clinic for impaired mentation. Finger-stick glucose (FSG) measurement performed by paramedics revealed a critically low glucose level and he was given one ampule of 50% dextrose. On arrival, his vitals were stable but he was lethargic and disoriented. On exam his hands were pale, cool to touch, with weak pulses. A FSG revealed a level of 35 mg/dL, although the plasma glucose measured simultaneously revealed a level of 121 mg/dL. Other results were significant for urea nitrogen of 100 mg/dL and creatinine of 12.70 mg/dL. Subsequent FSG were between 55 and 78 mg/dL, for which he received multiple ampules of 50% dextrose and was then started on a 5% dextrose drip. Despite these interventions there was no change in his mental status and no major improvement in the FSG values. Work-up for causes of hypoglycemia was negative. Patient’s mental status improved after dialysis, making uremia the most likely etiology for his altered mentation. During his hospital stay, measurements of plasma glucose were noted to be normal or high when FSG were low. Patient was asymptomatic during these episodes. The physical finding of poor distal pulses lead to the possibility of impaired microcirculation causing false FSG values. A non-invasive flow study revealed nearly no pulsatile flow in all fingers. Patient was diagnosed with Raynaud’s phenomenon, which was attributed as the cause of the falsely low FSG measurements. Thereafter, alternate sites for glucometer checks were used, correlating well with the plasma glucose levels. His vascular symptoms improved with nifedipine, but he was advised to avoid glucometer checks from fingertips.

Discussion: Pseudohypoglycemia can arise when there are discrepancies between low capillary glucose and normal plasma glucose levels. In our patient this was likely due to Raynaud’s phenomenon causing decreased capillary flow and increased glucose consumption by peripheral tissues. Our patient was altered which could have been initially attributed to low glucose levels, but the lack of improvement with dextrose went against the diagnosis of true hypoglycemia.

Conclusion: Alternate sites for glucose measurement should be used in patients with impaired microcirculation when pseudohypoglycemia is suspected.
LIPID/CARDIOVASCULAR DISORDERS/HYPTERTENSION

Abstract #500

A CASE OF VERY SEVERE HYPERTRIGLYCERIDEMIA WITH UNUSUAL TRIAD

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Objective: Very severe hypertriglyceridemia is defined when triglyceride level is greater than 2000 mg/dL and its prevalence is about 1.8 cases per 10,000. Hypertriglyceridemia can be inherited or can be caused by obesity, metabolic syndrome, and diabetes mellitus. Although mild and moderate hypertriglyceridemia are common, severe hypertriglyceridemia in combination with uncontrolled diabetes mellitus can lead to unforeseen consequences. We present an unusual case of a triad of diabetic ketoacidosis, very severe hypertriglyceridemia, complicated by acute pancreatitis.

Case Presentation: Patient is a 28 year old man with a past medical history significant for obstructive sleep apnea and morbid obesity, who was found unresponsive at home. Emergency Medical Services intubated the patient in the field for unresponsiveness. He was admitted to a critical care unit. He had a BMI of 72 kg/m^2. Blood glucose level was 2400 mg/dL and there was anion gap metabolic acidosis with ketones. The patient was started on insulin infusion for diabetic ketoacidosis. Further workup revealed triglyceride level of 2930 mg/dL. CT abdomen showed acute pancreatitis. Insulin infusion was continued and intravenous heparin was added. The patient was started on plasmapheresis, but it was challenging due to hyperviscosity. He was in hemodynamic shock requiring multiple vasopressors and was in acute renal failure requiring dialysis. CT brain and electroencephalogram revealed findings consistent with anoxic brain injury. Despite aggressive management, the patient remained critically ill with multi-organ failure. He eventually died.

Discussion: Hypertriglyceridemia is related to numerous metabolic disorders and diabetes mellitus is one of the major causes. In insulin deficient state, increased rate of adipose tissue lipolysis leads to increased availability of free fatty acids as substrates for triglyceride synthesis. Treatment for hypertriglyceridemia includes dietary restriction and lipid lowering drug therapy. In severe cases, urgent plasmapheresis is recommended. Insulin infusion is used when there is concurrent hyperglycemia or when apheresis is not available. Heparin is also used but its role is controversial.

Conclusion: The triad of diabetic ketoacidosis, severe hypertriglyceridemia, and acute pancreatitis is rare, but it is crucial to check for such conditions as they can coexist. Also, diabetic ketoacidosis can mask symptoms of pancreatitis, and vice versa. In some cases, those conditions may lead to multi-organ failure and even death. Therefore, early recognition and appropriate management are warranted to prevent possible dire consequences of severely uncontrolled metabolic abnormalities.

Abstract #501

A RARE CASE OF FAMILIAL PARTIAL LIPODYSTROPHY II (DUNNIGAN’S SYNDROME) IN A POSSIBLE AUTOSOMAL DOMINANT PATTERN

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Objective: Lipodystrophic syndromes are a rare group of heterogeneous disorders that can be both genetic and acquired. Patients with these syndromes are noted to have multiple metabolic abnormalities in conjunction with abnormal fat distribution. Familial Partial Lipodystrophy (FPLD 2), also known as Dunnigan’s syndrome is a subclass of these syndromes which involve mutation of the LMNA gene. Here we present a 35 y/o mother of three children being managed for FDLP 2 with severe insulin resistance, dyslipidemia and gross elevations of liver transaminases. Patient also gives history of multiple members of her family (both male and female) over 3 consecutive generations having a similar phenotype.

Methods: Patient’s metabolic derangements are currently being managed with insulin and optimization of anti-dyslipidemic medications. Patient is also being managed for documented hypoleptinemia (1.7 ng/mL).

Case Presentation: Patient has marked improvement of serological biomarkers.

Discussion: FDLP 2 is mostly noted to be inherited in an X-linked dominant pattern with very rare cases being found to present as autosomal dominant. Further work up will now be carried out to ascertain the genotype of all concerned individuals in this family.

Conclusion: Lipodystrophic syndromes are a rare group of congenital or acquired disorders that present with metabolic imbalances and paucity of adipose tissue. FDLP 2, which is a subgroup of these syndromes, has a mode of inheritance which is usually X-linked dominant. In this family, the mode of inheritance appears to be autosomal dominant, which is only rarely reported in the literature.
Abstract #502

NEWLY DIAGNOSED DIABETES MELLITUS PRESENTING AS CHYLOMICRONEMIA SYNDROME AN UNCOMMON PRESENTATION OF A COMMON DISEASE

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Objective: It is not uncommon for hypertriglyceridemia induced pancreatitis, to occur in patient with underlying genetic lipid metabolism defect in the presence of established uncontrolled Diabetes. However Newly diagnosed diabetes should also be highly considered and treated in all patients presenting with chylomicronemia syndrome.

Case Presentation: Patient is 29-year-old male with history of obesity and hypertriglyceridemia, presented with severe abdominal pain and vomiting. He doesn’t consume alcohol and otherwise healthy. Examination revealed epigastric tenderness, and xanthomas on the back. Laboratory data showed serum Amylase 517U/L (26-100), lipase 602 U/DL (22-51), and normal hepatic panel. Fasting glucose was 199 (<100 mg/dl), random glucose 250 (<140 mg/dl), and HbA1c 10.8 (<5.7 %). Fasting lipid panel showed HDL 26 (40-85 mg/dl), LDL 24 (50-150 mg/dl), triglycerides 3749 (20-160 mg/dl). Further workup for diabetes was consistent with type 2 DM.

Abdominal Computed Tomography showed diffusely enlarged pancreas with severe inflammatory changes consistent with acute pancreatitis.

Patient treated in MICU with insulin infusion. Subsequently, triglyceride level and hyperglycemia improved. He was discharged on insulin, gemfibrozil, drastic dietary modification, and genetic testing as out-patient.

Discussion: It is well established that hypertriglyceridemia is exacerbated by insulin resistance and often seen as part of metabolic syndrome. Insulin resistance enhances TG release form adipocytes and decreases its clearance by inhibiting lipoprotein lipase in peripheral tissues. Patients with Poorly controlled diabetes (established or newly diagnosed) are therefore at higher risk for severe hypertriglyceridemia and chylomicronemia syndrome. Hypertriglyceridemia induces pancreatic injury through several hypothesized mechanisms such as inflammation, hyperviscosity and ischemia. Poorly controlled diabetes independently increases pancreatitis risk by 1.5-2.5 folds, however in the setting of severe HTG (1000-2000mg/dl) the risk of acute and recurrent pancreatitis increases remarkably (10-20%). Clinically, presence of eruptive xanthoma and lipemia retinalis strongly suggests chylomicronemia syndrome. Other precipitating factors like alcohol, pregnancy and hypothyroidism should be considered.

Infusions of insulin, heparin, and plasmapheresis are common treatment strategies to lower TG level. Achieving glycemic control in hyperglycemic patients promotes faster recovery.

Conclusion: Chylomicronemia as an initial representation of more common endocrine abnormalities such as DM has a great clinical relevance, especially when the serious complication of pancreatitis occurs.

Abstract #503

KNOWLEDGE AND PRACTICES TOWARDS RISK FACTORS FOR HYPERTENSION AMONG URBAN & SUBURBAN BANGLADESI HYPERTENSIVE SUBJECTS.

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Objective: To evaluate and compare knowledge & practice pattern towards risk factors for hypertension among urban and suburban Bangladeshi hypertensive subjects.

Methods: Cross-sectional observational study (April-September 2014). 352 Bangladeshi hypertensive subjects [men 25.60%, women 74.40%, aged >18 yrs] were selected randomly from OPD in MARKS Medical College & Hospital. With consent, set-written questions were asked by investigator by face-to-face interview. Statistical analysis was done with IBM SSPS ver 16.

Outcome: evaluate and compare knowledge & practice pattern towards risk factors for hypertension in urban and suburban hypertensive subjects.

Results: 222(63.06%; men=50%, women=50%) and 130(36.93%; men=31.53%, women=68.46%) lived in urban & suburban respectively. Urban versus suburban subjects had age (yrs):49.44±1.10 vs 52.59±1.10, p 0.01; hypertension duration (yrs):5.57±4.44 vs 5.97±4.51, p 0.42; BMI (kg/m2):25.83±3.99 vs 25.49±4.03, p 0.43. Monthly expenditure [0.002] & educational status [0.000] were different among urban and suburban Bangladeshi hypertensive subjects.

Knowledge & practice pattern towards risk factors (urban vs suburban):avoid alcohol intake: know=87.83% vs 80.76%(p0.07), practice=95.95% vs 94.61%(p0.56); avoid smoking :know=88.28% vs 80%(p0.03), practice=83.63% vs 86.15%(p0.41);hightersalt(Na+)consumption(>5grams/day): know=89.63% vs 84.61%(p0.14), practice=69.81% vs 58.46%(p0.03); Low intake of K+ containing foods :know=39.63% vs 36.92%(p0.61), practice=38.28%
vs 33.07%(p=0.32); Unhealthy diet: know=83.63% vs 76.92%(p=0.04);
Stress: know=80.18% vs 73.84%(p=0.16), practice=54.95% vs 54.61%(p=0.95); Sedentary life style: know=51.35% vs 37.69%(p=0.01), practice=33.33% vs 23.07%(p=0.05);
Obesity: know=82.43% vs 70%(p<0.007), practice=49.09% vs 40.76%(p=0.23); Drug induced: know=24.32% vs 16.15%(p=0.07), practice=52.70% vs 46.15%(p=0.23).

Discussion:
Knowledge & practice about risk factors for HTN were not satisfactory and did not differ significantly between urban & suburban hypertensive subjects except for avoiding smoking, higher salt intake, sedentary life style & drugs that induced HTN.

Conclusion:
Risk factors knowledge & practice pattern of urban and suburban Bangladeshi hypertensive subjects were not much different and satisfactory. There is still lack of information on the actual knowledge and practices on this condition among them.

Abstract #504
ALIROCUMAB EFFICACY AND SAFETY IN INDIVIDUALS WITH METABOLIC SYNDROME: POOLED DATA FROM PHASE 3 TRIALS
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Objective: Persons with metabolic syndrome (MetS) are at increased risk of cardiovascular (CV) disease as well as type 2 diabetes. We compared efficacy and safety of alirocumab (ALI), a PCSK9 monoclonal antibody, in patients with hypercholesterolemia and with or without MetS by pooling data from 10 Phase 3 studies (3308 patients studied for 24–104 weeks).

Methods: Efficacy data were analyzed in 4 pools according to study design. Eight studies (n=1776) used ALI 75 mg every 2 weeks (Q2W), increasing to 150 mg Q2W at Week 12 if LDL-C was above a pre-defined level at Week 8. The other 2 studies (n=1532) used ALI 150 mg Q2W from the outset. Control was placebo in 5 studies and ezetimibe in the other 5. Six studies used background maximally tolerated statin, 2 used commonly used statin doses. MetS was defined as ≥3 of: body mass index >30 for non-Asians or >25 kg/m2 for Asians; triglycerides (TG) ≥150 mg/dL or use of TG-lowering medication; high-density lipoprotein cholesterol (HDL-C) <40 in men or <50 mg/dL in women; blood pressure ≥130/85 mmHg or diagnosis of hypertension; fasting plasma glucose (FPG) 100 to <126 mg/dL. Results for patients with diabetes are not presented.

Results: Across the study pools, baseline LDL-C levels in ALI-treated patients were 128.1–130.5 mg/dL (with MetS, n=1207) and 127.6–132.3 mg/dL (non-MetS, n=907). In the 3 pools of studies with initial ALI dose of 75 mg Q2W, percent LDL-C reduction at Week 12 (prior to possible dose increase) was 45.0–49.1% (MetS) and 46.9–52.2% (non-MetS); at Week 24, LDL-C was reduced by 45.0–52.5% (MetS) and 44.9–51.7% (non-MetS). In the pool using 150 mg Q2W from the outset, LDL-C was reduced with ALI at Week 12 by 65.4% (MetS) and 58.9% (non-MetS) and at Week 24 by 63.4% (MetS) and 56.4% (non-MetS). Across the pools, by Week 24 ALI reduced apolipoprotein B by 36.4–54.7% (MetS) and 37.0–51.6% (non-MetS) and triglycerides by 8.1–17.2% (MetS) and 6.4–16.1% (non-MetS). ALI had no effect on HbA1c or FPG levels. Adverse event (AE) rates were similar in ALI-treated patients with versus without MetS (71.6–77.4% versus 68.1–75.1% respectively; range across pools according to control). The most common AEs in ALI-treated patients with and without MetS were nasopharyngitis, injection-site reaction, influenza and upper respiratory tract infection.

Discussion: Robust efficacy was observed with both ALI doses, with Week 24 LDL-C reductions of up to 52.5% (MetS) and 51.7% (non-MetS) with 75/150 mg Q2W and 63.4% (MetS) and 56.4% (non-MetS) with 150 mg Q2W.

Conclusion: Significant LDL-C reductions were observed in ALI-treated patients with and without MetS, with similar safety between groups.

Abstract #505
MYELOMA HYPERTRIGLYCERIDEMIA
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Objective: To present a case of hypertriglyceridemia in multiple myeloma in a 36 yr old woman.

Case Presentation: 36 years old woman presented with vomiting and continuous pain in mid chest and epigastrium of 10 days duration. Vomiting was associated with nausea; vomitus had bilious fluid but no blood. Pain in mid chest and epigastrium was continuous and increased during...
vomiting episode. There was no H/O fever, pain elsewhere in abdomen, urinary or bowel complaints. No H/O any drug intake (prescription or OTC), alcohol, tobacco, recreational drug abuse. She had regular menstruation, no H/O amenorrhoea of recent onset and no other positive history. Examination revealed normal vitals, mild dehydration, and tenderness in epigastrium. A working diagnosis of gastritis/pancreatitis was kept and treated with IV fluids, injectable pantoprazole and antiemetic.

Investigations: Hb: 12gm/dl (12.0-15.8gm/dl), TLC 5,100/mm3 (4,000-11,000/mm3), DLC: N-60%(40-70%), L-36%(20-50%), M-2%(4-8%), E-2%(0-6%), Platelet count: 2.4 lac/mm3 (1.6-4.1 lac/mm3). AST 30.0U/L (<50), ALT 25U/L (<50), bilirubin 1.1 mg/dl (0.3-1.3), total protein 8.8g/dl (6.6-8.8), albumin 3.4g/dl (3.4-5.5), alkaline phosphatase 268.0U/L (<50), creatinine 1.0mg/dl (0.6-1.2), fasting blood glucose 90mg/dl (75-100mg/dl), HBA1c 5.5% (4.5-6.5%). Urine examination normal. Amylase 988U/L (30-110U/L), lipase 655 U/L (23-300 U/L), cholesterol 167mg/dl (150-250), triglyceride (TG) 1580 mg/dl (50-200). Upper GI endoscopy and USG abdomen normal. She was put on low fat diet and fenofibrate 145mg/day.

Four weeks later TG levels were 1868 mg/dl and she had vomiting off and on & pain was less. CT chest revealed lytic lesions in sternal body raising suspicion of multiple myeloma. CECT abdomen was normal. Multiple myeloma was confirmed by bone marrow aspiration and presence of ‘M’band in urinary electrophoresis. Triglyceride levels fluctuated between 1500 to 2000 mg/dl in spite of continued anti-lipid therapy. TG levels normalised after receiving three cycles of chemotherapy for multiple myeloma. Patient was put in bone marrow transplant programme.

Conclusion: Highlight of this case is that hypertriglyceridemia was due to multiple myeloma, a very unusual cause. The possible mechanism is either binding of ‘M’ protein to the receptor or lipoprotein resulting in decreased clearance of lipoprotein or auto antibodies against LPL resulting in raised triglycerides.

**Abstract #506**

**PREVALENCE OF METABOLIC SYNDROME IN HOSPITALIZED PATIENTS WITH PSYCHIATRIC ILLNESS IN TAIF CITY, SAUDI ARABIA**

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Objective: Metabolic syndrome (MetS) is a cluster of the most dangerous cardiovascular risk factors, dysglycemia, abdominal obesity, high cholesterol and high blood pressure. NHANES 2003–2006 showed the ~ 34% of adults met the criteria for MetS. In a study which evaluated the prevalence of MetS in a 100 patients attending psychiatric day centers, 55% met the criteria for MetS.

Methods: We conducted a cross-sectional study at Taif Inpatient Mental Hospital, Saudi Arabia. Patient’s age > 18 years who were chronically hospitalized were asked to participate. Baseline characteristics and measurement were obtained by the participated physicians. The waist circumference (WC) was measured according to WHO STEPS protocol. MetS diagnosis was made based on the International Diabetes Federation (IDF) definition. The primary goal of this study is to evaluate the prevalence of MetS its clinical characteristics.

Results: Total of 313 patients participated, 76.2% were male and 23.8% were female, mean age 43.4 ± 10.81 yrs old, 22.9% have hypertension, 26.1% have hyperlipidemia, 8.6% have T2DM, mean BMI 26.52 ± 6.2 kg/m2, mean WC was 96.53 ± 14.04 cm, 68.3% did high school or less, 83.1% reports sedentary lifestyle, and 55.6% were active smokers. The mean hospitalization duration was 12.7 ± 7.62 yrs, 74.9% have schizophrenia, 8.2% are mentally retarded, 1.4% has bipolar, 1.4% has personality disorders, and 23.4% have other diagnosis.

Conclusion: Highlight of this case is that hypertriglyceridemia was due to multiple myeloma, a very unusual cause. The possible mechanism is either binding of ‘M’ protein to the receptor or lipoprotein resulting in decreased clearance of lipoprotein or auto antibodies against LPL resulting in raised triglycerides.
duration, BMI, physical activity and smoking; between MetS and Psychiatric diagnosis (r = -0.08, p = 0.461), MetS and antipsychotics (r = 0.131, p = 0.056), MetS and SSRI (r = 0.012, p = 0.44), and MetS and TCA (r = 0.888, p = 0.144).

**Conclusion:** 38.4% of the participated hospitalized patients met the criteria for MetS. Those with MetS tends to have significantly higher BMI, WC, and LDL and more likely to have comorbid conditions and be active smokers. Non-significant positive correlation between MetS and both psychiatric diagnosis and the treatment modalities.

**Abstract #507**

**THERAPEUTIC GAP, RACIAL GAP AND GENDER GAP FOR LDL-C GOAL ATTAINMENT IN INSURED PATIENTS WITH DIABETES**

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**Objective:** Complications and mortality associated with diabetes appear to disproportionately affect female gender and racial minorities. Several reports on racial and gender differences for LDL-C goal attainment in insured patient populations with diabetes have been published. The objective of this study was to explore racial and gender differences for LDL-C goal attainment in insured patient populations with diabetes through a systematic review.

**Methods:** A systematic literature search was performed using EMBASE and PubMed databases, with several combinations of MeSH terms. Bibliography mining was also done on relevant articles to be as inclusive as possible.

**Results:** These studies demonstrated coexistence of therapeutic gap, racial gap and gender gap. In insured populations despite insurance coverage, a large proportion of patients with diabetes did not attain LDL-C goals [39% (95% CI: 21% - 58%)] regardless of gender or race (therapeutic gap). Significant differences in LDL-C goal attainment were observed by race (racial gap) [59% for Caucasian versus 48% for blacks] as well as by gender (gender gap) [69% for men versus 58% for women]. In general men had 10.5% ± 3% (Mean ± SD) better chance to achieve LDL-C goals compared to women (p-value = 0.001). Caucasians achieved LDL-C goals in much higher rates in comparison to minorities (5% to 16%; p-value = 0.001). Atainment of LDL-C goals are the lowest in non-white women and the highest in Caucasian men (gender and race interaction; p-value = 0.001).

**Discussion:** This study illustrates that even amongst insured population with diabetes, who have equal access to medical care, there are gender and racial gaps beyond therapeutic gaps for LDL-C goal attainment.

**Conclusion:** The concepts of gender and race are useful for understanding the distribution of disease in the population and for identifying at-risk groups for prevention and treatment efforts. This calls for further study to determine causes of possible health disparities to tailor interventions to address the impact of gender and race.

**Abstract #508**

**DIABETES INDUCED ALTERATION ON CARDIAC VEGF SYSTEM IN ESTROGEN/ESTROGEN RECEPTOR MANIPULATED ANIMAL MODEL**

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**Objective:** Both types of estrogen receptors (alpha and beta) exist in cardiovascular system. Postmenopausal women have high prevalence of diabetes than the women of premenopausal. In addition, we previously demonstrated that estrogen receptors especially estrogen receptor alpha plays crucial role in maintaining coronary microcirculation and vascular endothelial growth factor (VEGF) signaling in female heart. In our series of studies, we found that loss of VEGF from early diabetes is the initial trigger for all the structural and functional changes responsible for diabetic retinopathy. In this present study, we tried to clarify how estrogen/estrogen receptor affects coronary VEGF signaling in diabetic model.

**Methods:** We induced both types of diabetes (type 1 and type 2) in estrogen receptors knockout (ERKO) female mice. In addition we also induced diabetes in female rat with or without ovariectomy. After injection with streptozotocin, we checked blood sugar level after 48 hours and then every week up to the day of scarify.

**Results:** We found that, VEGF angiogenic signaling is much more decreased in ovariectomized female rat heart in presence of diabetes compared to the absence of diabetes which has direct correlation with the functional impairment of heart. There is great imbalance between VEGF and the soluble forms of VEGF receptors in female heart in
the states of ovariectomy, diabetes or in ovariectomized diabetic condition. Estrogen replacement is partially effective in normalizing impaired/downregulated VEGF angiogenic signaling in female heart in ovariectomized rats in presence or absence of diabetes. The induction of diabetes in ERαKO female mice has more detrimental downregulation of cardiac VEGF angiogenic signaling compared to ERαKO mice without diabetes. Whereas, the streptozotocin administration in ERβKO female mice could not further worsen the VEGF angiogenic signaling in heart compared to ERβKO female mice heart without diabetes. Diabetes induction in ERαKO female mice has further worsened the cardiac function compared to ERαKO mice without diabetes. This cardiac functional impairment has not been clearly evident in streptozotocin administered ERβKO female mice compared to ERβKO female mice heart without diabetes. **Conclusion:** Presence of diabetes affects cardiac VEGF system in estrogen depleted female subject more significantly compared to non-diabetic subjects and estrogen receptors alpha has predominant role in downregulating the cardiac VEGF level in diabetic female subjects. Estrogen receptor alpha plays more dominant role in regulation of coronary microcirculation and VEGF angiogenic signaling cascade in female heart in diabetes.

Abstract #509

**STUDY OF IMPACT OF HYPERGLYCEMIA ON LEFT VENTRICULAR FUNCTION IN INDIAN POPULATION**

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**Objective:** There is an increasing recognition that diabetic patients suffer from an additional cardiac insult other than coronary artery disease termed ‘diabetic cardiomyopathy’ leading to ‘ventricular dysfunction’. Some studies also suggested that poor glycemic control adversely affects LV function. This study was carried out to find out impact of glycemic control on LV function in type II diabetes mellitus patients, which may help to suggest possible underlying mechanisms and may be of clinical importance in planning preventive and therapeutic strategies.

**Methods:** We studied 100 consecutive type 2 diabetic patients in age group of 40 to 65 years admitted in our hospital during the period of January 2014 to December 2014. 18 patients, who were subsequently found to be either hypothyroid and/or having ECG signs of IHD were excluded. Remaining 82 patients were examined clinically and 2D echocardiography was done in all of them by the same cardiologist. LV dysfunction and its severity was graded as mild, moderate and severe for systolic dysfunction and grade I, grade II, grade III, grade IV for diastolic dysfunction. All routine blood investigations, fundus examination, biothesiometry and other necessary examinations were performed. Multifactorial ANOVA test and univariate and multivariate stepwise regression analyses were used to find out association between different variables.

**Results:** The mean values of HbA1C for moderate and severe LV systolic dysfunction were 9.08% and 9.60% respectively (p<0.001). The mean values of HbA1C for grade I, grade II, grade III and grade IV were 6.72%, 7.36%, 8.70% and 9.68% respectively (p<0.001). Correlation of systolic and diastolic dysfunction with different variables shows that all the variables had highly significant differences with systolic function like BMI, duration of diabetes, serum creatinine, triglyceride, HDL, LDL, VLDL and HbA1C (p<0.001 in all).

**Discussion:** Correlation of diastolic dysfunction with different variables also shows that BMI, LDL and HbA1C had highly significant correlation with diastolic function (p<0.001), while duration of diabetes, serum creatinine, triglyceride, total cholesterol, HDL, VLDL were significantly correlated with diastolic dysfunction (p<0.05).

**Conclusion:** We concluded that poor glycemic control in type II diabetic patients is very significantly associated with LV systolic and diastolic dysfunction. We also concluded that various factors like increasing duration of diabetes and dyslipidemia are also significantly associated with LV systolic and diastolic dysfunction in type II diabetic patients.
Abstract #510

PREVALENCE OF METABOLIC SYNDROME COMPONENTS AMONG EARLY AGE ONSET ACUTE CORONARY SYNDROME PATIENTS IN BANGLADESH

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Objective: Metabolic Syndrome (MetS) is a major risk factor for coronary artery disease. MetS is defined as a cluster of metabolic risk factors that are associated with a high risk for cardiovascular disease (CVD) and diabetes. Its prevalence is rising worldwide. The prevalence of metabolic syndrome and coronary artery disease is also increasing in South Asian developing country like Bangladesh. A large number of young population with acute coronary syndrome have MetS. The cardiovascular risk arising from different combinations of the components of MS is not uniform; each component is an independent risk factor for CVD, and they all interact synergistically, further increasing risk. This highlights the epidemiological importance of the concept of MetS, which can help identify a subgroup of individuals with increased cardiovascular risk among the overall population at low absolute risk of coronary events. Aim of this study was to determine the prevalence of metabolic syndrome and the combination of components in patients with early age onset (age<50 years) acute coronary syndrome.

Methods: This is a prospective study comprised 750 consecutive patients age <50 years hospitalized for acute coronary syndrome. The patients were categorized according to NCEP ATP III definition. According to the NCEP ATP III definition, MetS is diagnosed when 3 or more of the following 5 components are present: (1) elevated waist circumference (WC ≥ 88 cm in women), (2) elevated triglyceride (TG ≥ 150 mg/dl, ≥ 1.7 mmol/L), (3) reduced HDL cholesterol (HDL < 50 mg/dl or < 1.29 mmol/L in women), (4) elevated blood pressure (BP ≥ 130/85 mmHg), and (5) elevated fasting plasma glucose (FPG ≥ 110 mg/dl or ≥ 6.1 mmol/L) or pre-existing diabetes mellitus (DM).

Case Presentation: Among 750 acute coronary syndrome patients (561 were male, 197 female), 229 (31.11%) patients met the criteria of MetS. The mean age of study participant was 43.25 ± 0.27 years. MetS was more common in female than in male (45.71% VS 26.56%, P < 0.001). One component of MetS was found in 28.13%, two components in 29.87%, three components in 30.67% of acute coronary syndrome patients. The most highly two prevalent components of MetS in this study population were low HDL (51.8%) and high triglyceride level (44%).

Conclusion: We conclude that prevalence of metabolic syndrome in patients with early age onset (Age <50 years) acute coronary syndrome is high in Bangladesh. Low HDL and high TG are the most common components of metabolic syndrome in our study. Strategies are needed for the early detection and treatment of cardiometabolic risk factors to prevent coronary artery disease progression and prognosis.

Abstract #511

HS CRP IN ACUTE CORONARY SYNDROME

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Objective: To study the relation between hs-CRP level and angiographic severity of the lesion in Acute Coronary Syndrome (ACS). and hs-CRP level and in-hospital complications and complications on 30 day follow up of patients with ACS

Methods: Prospective Cross sectional study conducted in KMC hospital tertiary care referral hospital , Manipal university. Sample size-105. Patients were included in study after informed consent all patients with iist acute coronary event.Patients were excluded if patients had infections in last 3 weeks, inflammatory conditions, acute pancreatitis, malignancy, hepatic/renal failure & patients on statins for more than one month. hs CRP was calculated in all patients. hs CRP was measured at admission in unstable angina, in acute myocardial infarction at presentation or at 1 month follow up. All patients underwent angiogram & severity of coronary artery stenosis was assessed by Gensini scoring.

Results: 108 patients were studied out of which 84 were STEMI, 17NSTEMI & 7 were unstable angina. 37 patients had high hs CRP(>3mg/L) and 71 patients had normal or low hs CRP.Left ventricular dysfunction was seen in 48 patients (62.9%) out which 22 patients were in high CRP group 7 had normal or low CRP. There was significant
correlation with hs CRP & LV dysfunction (p 0.002). Hs CRP levels were correlated with angiographic scoring of coronary artery showed that patients belonging to hs-CRP low risk group had a median angiographic Gensini score of 20, moderate risk group 33, and high risk group 38 mg/L. Using Kruskal Wallis analysis the median Gensini scores showed an increasing trend from lower to higher hs-CRP risk groups [p<0.002].

Discussion: C reactive protein is an acute phase reactant & sensitive marker of inflammation. Several studies indicate that elevated levels of hs-CRP among healthy men and women are a strong predictor of future cardiovascular events. hs-CRP not only predicts first myocardial infarction but also recurrent events. Defining the relationship between CRP and disease markers such as CAD extent as assessed by coronary angiography will enhance our understanding of whether ‘inflammation markers’ such as CRP would be complementary or redundant when combined with clinical risk prediction with other risk markers. In this study we discuss role of CRP in acute coronary syndrome.

Conclusion: There is significant correlation between the plasma level of hscrp and angiographic severity of coronary atherosclerosis as assessed by gensini score. The combined evaluation of both hscrp and LDL cholesterol may be superior as a method of risk detection to measurement of either biologic marker alone. In patients with ACS elevated hscrp is associated with higher rate of complications.

Abstract #512

IS LONG-TERM TESTOSTERONE THERAPY EFFECTIVE IN SECONDARY PREVENTION OF MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE) IN HYPOGONADAL MEN WITH A HISTORY OF CARDIOVASCULAR DISEASE (CVD)? REAL-LIFE DATA FROM A REGISTRY STUDY

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Objective: Controversies exist regarding potential cardiovascular risk associated with testosterone therapy (TTh). We investigated long-term TTh in hypogonadal men with previous cardiovascular events or diagnosis in a urological setting compared to an untreated hypogonadal control group.

Methods: Cumulative registry study in 656 men with total testosterone (T) levels below 12.1 nmol/L and symptoms of hypogonadism. 151 men with a CVD history were analysed. 68 received parenteral TU 1000 mg/12 weeks following an initial 6-week interval. 83 men had opted against T therapy (TTh) and served as controls (CTRL). Median follow-up was 6 years in CTRL and 9 years in the T group. Measurements were taken at least twice a year, and 8-year data are presented. Mean changes over time between the groups were compared by a mixed effects model for repeated measures with a random effect for intercept and fixed effects for time, group and their interaction. Changes were adjusted for age, weight, waist circumference, blood pressure, and lipids to account for baseline differences between the two groups.

Results: Mean age: 63.4±4.9 years. In the T group, 40 men had had a myocardial infarction (MI), 6 stroke, and 40 had been diagnosed with coronary artery disease (CAD). In CTRL, 23 had had a MI, 24 stroke, and 65 CAD. Waist circumference (cm) declined from 112.1±8 to 99.9±6.3 in the T group and increased from 108.1±9 to 109.4±7.1 in CTRL. The model-adjusted estimated difference between groups at 8 years was -13.2 (p<0.0001 for all). Fasting glucose (mmol/L) decreased from 6.0±0.9 to 5.2±0.1 (p<0.0001) in the T group and increased from 5.6±0.4 to 5.7±0.4 (NS) in CTRL. Difference between groups: -0.8 (p<0.0001). Lipids (mmol/L): HDL increased from 1.7±0.5 to 2.1±0.5 in the T group and from 1.3±0.5 to 1.4±0.7 in CTRL. Difference between groups: 0.51 (p<0.0001 for all). Triglycerides decreased from 3.5±0.6 to 2.2±0.1 (p<0.0001) in the T group and increased from 2.9±0.5 to 3±0.5 (NS) in CTRL. Difference between groups: -1.2 (p<0.0001).

Blood pressure (BP, mmHg): Systolic BP decreased from 167.8±11.0 to 134.6±7.5 (p<0.0001) in the T group and from 159±9.3 to 156.6±6.3 (NS) in CTRL, difference between groups: -36.9 (p<0.0001). Diastolic BP decreased from 102.3±8.2 to 76.4±4.7 (p<0.0001) in the T group and increased from 89.1±6.4 to 90.6±5 (NS) in CTRL, difference between groups: -22.4 (p<0.0001).

No patient dropped out. There were no MACE in the T group. In CTRL, there were 12 MIs, 14 strokes, and 21 deaths.

Conclusion: In hypogonadal men with CVD history receiving long-term TTh, there was not a single MACE whereas there were 47 MACE in CTRL. Long-term TTh with TU may provide effective secondary prevention of cardiovascular events.
Abstract #513

PREVALENCE AND DETERMINANTS OF METABOLIC SYNDROME AMONG HIV INFECTED PATIENTS RECEIVING HIGHLY ACTIVE ANTIRETROVIRAL THERAPY (HAART) IN KANO, NORTHWESTERN NIGERIA

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Objective: We aimed to determine and compare the prevalence and associated factors of metabolic syndrome (MS) among HAART exposed versus HAART naïve HIV infected patients at the Aminu Kano Teaching Hospital, (AKTH) Kano.

Methods: It was a cross sectional comparative study of HIV infected persons attending the HIV clinic of the AKTH. We evaluated 300 participants divided into two age and sex matched groups – HAART-exposed and HAART-naïve. Metabolic Syndrome was diagnosed using ATP-III criteria. Insulin resistance among participants with MS was estimated using HOMA-IR.

Results: The mean±SD age of study participants was 35.7±10.0 years (HAART exposed) and 34.0±9.7 years (HAART naïve). The prevalence of MS among HAART exposed participants was found to be 19.3% while it was 5.3% among HAART-naïve controls, p=0.001. With respect to gender, 8.7% of males and 10.7% females in the HAART exposed group had MS while 1.3% of males and 4.0% of females in the HAART naïve group had MS with no statistically significant difference. Advanced age, longer duration of HIV diagnosis and HAART exposure, increased BMI, weight gain after HAART exposure, exposure to PIs and increased mean CD4 cell count were found to be significantly associated with MS, (p<0.05). However, only age (OR 4.3, 95% CI 1.6-11.8, p=0.005) and BMI (OR 4.2, 95% CI 1.5-11.9, p=0.007) were found to be independently associated with the development of MS. The prevalence of insulin resistance among participants with MS that were HAART exposed was 79.3% while that among HAART naïve with MS was 25.0%, (p=0.008).

Discussion: In this study, the prevalence of MS was found to be higher among the HAART exposed participants compared to HAART naïve participants. This is similar to results obtained from similar studies across the globe. This could be due to the effect of the drugs that cause insulin resistance particularly PIs in addition to the HIV inflammation. Participants that had MS and were on HAART were much older, were diagnosed to have HIV infection much longer and had higher average BMI and waist circumference (females only) with significantly higher mean CD4 cell count when compared with their HAART naïve counterparts in the study. This is not surprising going by the fact that HAART exposure leads to improvement in health and well-being, weight gain and hence longer survival.

Conclusion: Metabolic syndrome is common among HIV patients treated with HAART mostly related to use of PIs. Advanced age and increased BMI are independent determinants of MS in HAART treated patients. Life style measures and regular monitoring of anthropometric indices of HIV patients will help to reduce the metabolic problems associated with drug treatment.

Abstract #514

HYPERTRIGLYCERIDEMIA: AN OPEN DOOR FOR CANCER TREATMENT?

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Objective: 1. To identify the correlation between cancer and lipid metabolism
2. To understand the aggressiveness of the tumor based on the lipid levels, to open a new era of treatment

Methods: 67 year old man with multiple comorbidities presented with back pain.

Case Presentation: A 67-year-old Caucasian man with past medical history of COPD, diabetes, hypertension, status post coronary artery bypass graft, stents, atrial fibrillation on coumadin, pulmonary embolism status post inferior vena cava filter and no history of familial hypertriglyceridemia presented with intermittent back pain for 1 month with significant weight loss. Physical exam showed positive straight leg test. Initial imaging studies showed multiple lesions in liver with metastasis in ribs and vertebra. Biopsy of the liver confirmed large B-cell non-hodgkin lymphoma. During his hospital stay, the patient was found to have triglycerides (TG): 1154 mg/dL, cholesterol 204 mg/dL, HDL 4 mg/dL, LDL and VLDL were unable to calculate. Decision was made to increase lantus with additional novolog and gemfibrozil. After 6 days of treatment, TG decreased to 690 mg/dL, HDL 7 mg/dL. Unfortunately, the patient passed away prior to initiation of the chemotherapy regimen after experiencing respiratory distress and hypotension.

Discussion: Altered lipid metabolism in cancer poses growing evidence for the link between deregulated FA
and cholesterol metabolism and cancer. Production of lipids is prerequisite for cell growth and proliferation. Many cancers express high levels of fatty acid synthase (FAS). A study of patients with leukemia and lymphoma exhibited lipid alterations initially with interesting findings of normal values in remission. This points out the correlation between degree of lipid abnormality and the underlying tumor burden. That finding opened the doors to new research in targeting the enzyme for more focused treatment therapy, better understanding of cancer and possible even prevention of cancer. Since lipid metabolism in cancer cells is regulated by the common oncogenic pathways, there are several drugs under development or in clinical trials (most prominently fatty acid synthase inhibitors) that are based on targeting the altered lipid metabolic pathways in cancer cells. Another interesting point is use of insulin in severe hypertriglyceridemia. Insulin is a potent triglyceride lowering agent that acts by promoting the synthesis of lipoprotein lipase, the essential enzyme for the hydrolysis of triglycerides.

Conclusion: Recognition of a definitive link and pathogenesis between altered lipid metabolism and cancer can possibly lead to earlier, focused treatment, and essentially lessen mortality. A plethora of novel therapeutic opportunities are awaiting.

Abstract #515

EFFECTS OF BARIATRIC SURGERY ON METABOLIC SYNDROME IN OBESE WOMEN WITH POLYCYSTIC OVARIAN SYNDROME

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Objective: Polycystic ovary syndrome (PCOS), characterized by hyperandrogenism, insulin resistance, and anovulation, is the most common female reproductive disorder. Women with PCOS are at increased risk for metabolic syndrome, a constellation of cardiometabolic risk factors including central adiposity, elevated BP, hypertriglyceridemia, low HDL, and glucose intolerance. Obesity exacerbates the metabolic phenotype in PCOS. Healthy lifestyle changes (diet and exercise) and the insulin sensitizer metformin ameliorate the metabolic phenotype, primarily by increasing insulin sensitivity. We asked if bariatric surgery decreases the prevalence and severity of metabolic syndrome in obese women with PCOS.

Methods: We performed a retrospective cohort study using data across Medstar facilities. Women ≥18 yo with PCOS who had undergone a bariatric surgical procedure were included (n=19). We compared metabolic syndrome components (body weight, BMI, SBP, DBP, TG, HDL, and HbA1C%) before and ≥6 months following surgery. We also compared prevalence of metabolic syndrome features and percentages meeting metabolic syndrome criteria (3/5 present) pre- and post-bariatric surgery.

Results: Mean (±S.D.) age of subjects was 18.4±3.7 years. Time between surgery and follow-up testing was 7.9±3.4 months. 53% of women were black, 41% white, and 6% Asian. Compared to pre-bariatric surgery, women had significant reductions in body weight (P<0.0001), BMI (P<0.0001), SBP (P= 0.0002), DBP (P= 0.007), TG (P= 0.04) and HbA1C (P= 0.03), and increased HDL (P= 0.04), following bariatric surgery. Mean (±S.D.) number of metabolic syndrome components per individual was 2.7±1.1 pre-surgery compared to 1.9±1.2 post-surgery (P<0.01). Percentage of women meeting metabolic syndrome criteria was 47% pre-surgery compared to 21% post-surgery, a >2-fold prevalence reduction.

Conclusion: These data suggest that bariatric surgery in obese women with PCOS decreases the rate and severity of metabolic syndrome, a known risk factor for diabetes and cardiovascular disease. Bariatric surgery should thus be considered in obese women with PCOS to reduce metabolic complications and cardiovascular morbidity.

Abstract #516

OSTEOPROTEGERIN TRUMPS OSTEOPONTIN AS A SERUM BIOMARKER OF CORONARY ARTERY CALCIFICATION IN TYPE 2 DIABETES

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Objective: Coronary artery calcification (CAC), a marker for overall coronary atherosclerotic burden, provides evidence for the risk of cardiovascular disease (CVD) in asymptomatic persons with type 2 diabetes (T2D). Furthermore, CAC is associated with CVD events. Osteoprotegerin (OPG) and osteopontin (OPN) are key factors in vascular remodeling and development of atherosclerosis. Increased OPG have been shown to be associated with increased CAC scores in T2D. In this study, we examined serum OPG and OPN levels to determine which biomarker may be more strongly associated with CAC.

Methods: Fifty T2D individuals were examined. CAC imaging was performed by multidetector computed tomography. Individuals were grouped based on abnormal CAC scores of ≥10 and ≥100, expressed in Agatston units. Logistic regression was used to assess the association between normal vs. abnormal CAC scores (dependent variable), serum bone biomarkers, and other metabolic parameters.
Results: Abnormal CAC scores were found for 64% (CAC scores ≥10) and 34% (CAC scores ≥100) of the study cohort (age=63±10 years, duration=13±8 years). OPG and OPN levels were significantly elevated (OPG 6.0±1.7 vs. 4.5±1.9 pmol/L, p<0.01; OPN 73±28 vs. 60±17 ng/mL, p<0.05) for those with CAC scores ≥100. Significant Spearman rank correlations for total CAC scores and bone biomarkers were also found (OPG r=0.38, p<0.01; OPN r=0.30, p<0.05). Logistic regression revealed that an increase in both OPG (odds ratio=5.7, 95% confidence interval[CI]=1.3-26.0, p=0.023) and OPN (odds ratio=1.1, 95% CI=1.0-1.13, p=0.045) was significantly associated with an increase in CAC scores ≥10. Similar findings were found for the model when CAC scores ≥100 were used as the dependent variable (OPG odds ratio=2.4, 95% CI=1.2-5.0, p=0.015; OPN odds ratio=1.1, 95% CI=1.01-1.13, p=0.023). Gender, age, duration, systolic blood pressure, HOMA-IR, HbA1c, leptin, adiponectin, and BMI were included as covariates in the models (Nagelkerke R2=0.74 and R2=0.62, respectively).

Discussion: With regard to the role of OPG and OPN in vascular calcification, OPG and OPN are reported to act as protective factors inhibiting CAC. Nonetheless, previous studies of persons with known CVD have shown increased serum levels of OPG and OPN. Whether elevated serum OPG and OPN are a result of an incomplete self-defensive regulatory mechanism to limit disease progression or if OPG and OPN are involved in the pathogenesis of atherosclerosis requires further study.

Conclusion: Although both OPG and OPN appear to be serum biomarkers for identifying those at increased risk of CAC, our results suggest that OPG may be a stronger biomarker than OPN.

Abstract #517

NECK CIRCUMFERENCE AS A CARDIOMETABOLIC RISK PREDICTOR AMONG SAUDI SUBJECTS

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Objective: Neck circumference (NC) is a marker of upper body subcutaneous fat and presents an extra cardiovascular risk beyond waist circumference (WC). There are no studies looked at the NC as a measure of metabolic risk from Saudi Arabia. The aims of this study are to determine the utility of NC as an indicator of overweight/obesity among Saudi subjects and to investigate its usefulness as a predictor of cardiometabolic risk.

Methods: A total of 785 adult participants aged ≥ 18 years, 370 men and 415 women, were recruited during one of public health awareness program at Medinah, Saudi Arabia. Body mass index (BMI), WC were measured and compared with neck circumference. Presence of cardiometabolic risks were assessed by a questionnaire. Blood pressure and random blood glucose were measured. Pearson’s correlation, receiver operating characteristic, Chi-square analysis and independent t-test, were analysed to evaluate the association of the NC to other anthropometric indices and to cardio-metabolic risks.

Results: Sixty percent of the participants were overweight or obese; 68% of men and 55.3% of women. Pearson’s correlation coefficients revealed a significant association between NC and: BMI (r = 0.4;p < 0.01), weight (r = 0.54, p < 0.01), waist circumference (r = 0.62, p < 0.01), age (r = 0.27, p < 0.01), random blood sugar (r = 0.099, p < 0.05), systolic blood pressure (r = 0.34, p < 0.01), and diastolic blood pressure (r = 0.102, p < 0.01). The mean NC for normal weight men were 36.74±2.8 cm and 33.5±3.4 cm for women. Receiver operating characteristic analysis showed that the area under the curve for NC and WC was 0.86 for men and 0.77 for women (P =0.000). NC ≥39.25 cm for men and ≥34.75 cm for women were the best cutoff levels for determining the subjects with central obesity; defined as WC ≥102 cm for men and ≥88 cm for women, with 89% sensitivity and 71% specificity for men, and 80% sensitivity and 65% specificity for women. These cutoff levels of NC were associated with significant increase the risk for T2DM, dyslipidemia, and hypertension with odd ratio of 2.6, 2.6, and 1.9 respectively.

Conclusion: Neck circumference can be used as a screening tool for overweight/obesity. It is positively related with BMI and waist circumference and can be used as indicator of cardiometabolic risk. A neck circumference ≥39.25 cm in men and ≥34.75 cm in women might be considered the cutoff value to identify overweight/obesity in Saudi individuals.
Abstract #518

USE OF A DIGITAL HEALTH OFFERING TO OPTIMIZE STATIN TREATMENT IN PATIENTS WITH TYPE 2 DIABETES

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Objective: Optimal use of statin medications is recommended to help prevent cardiovascular complications in patients with type 2 diabetes (DM). Proteus Discover, a digital health offering (DH) consisting of sensor-enabled medicines, a wearable sensor, patient app, and provider portal facilitates optimal use of medications. DH directly measures medication adherence and health behaviors (activity, rest) for display on a patient app and provider portal to support patient self-management and adherence, and facilitate therapy optimization. We evaluated change in LDL-C and total cholesterol (TC) in DM patients who were treated with sensor-enabled atorvastatin.

Methods: This IRB-approved, 12-week study enrolled subjects with uncontrolled DM (glycated hemoglobin ≥7%) and hypertension (systolic blood pressure ≥140 mm Hg), and treated with metformin and/or sulfonylurea and ≥2 anti-hypertensives. Subjects received DH with sensor-enabled medications for 4 or 12 weeks, or usual care (UC) based on 2:1 cluster randomization. This sub analysis evaluated changes in LDL-C and TC at week 4 in a subset of DH subjects treated with sensor-enabled atorvastatin (n=40) and a subset of UC subjects receiving conventional statin therapy (n=20).

Results: This cohort had mean age of 60 years, 53% female, 30% Hispanic, 57% low income of ≤$20,000 per year, and 17% psychiatric comorbidity. Mean baseline LDL-C and TC values for DH were 103.4 ± 9.5 mg/dL and 176.6 ± 9.1 mg/dL (mean ± standard error), respectively; values for UC were 95.3 ± 3.0 mg/dL and 172.9 ± 9.6 mg/dL, respectively. DH had a significantly greater reduction in LDL-C (-29.7 ± 8.8 mg/dL) compared to UC (-1.3 ± 2.5 mg/dL; mean difference [DH-UC] -28.4 mg/dL [95% CI: 45.8, -11.0]). DH also had a significantly greater reduction in TC (-34.8 ± 6.4 mg/dL) compared to UC (-8.2 ± 7.0 mg/dL; mean DH-UC: -26.7 mg/dL [95% CI: -47.1, -6.3]). The mean adherence to sensor-enabled atorvastatin in DH was 84%. Adherence could not be measured in UC. Thirty-one subjects have completed DH use and have responded to the satisfaction survey. Over 90% of the respondents agreed that DH was easy to learn and use, helped them with taking medicines more regularly, and improved conversations with their providers.

Discussion: Significantly greater reductions in LDL-C and TC were observed in subjects who used DH for 4 weeks (29% and 20% decreases, respectively) compared to subjects who receive UC (1% and 5% decreases, respectively).

Conclusion: A digital health offering that is focused on improving patient engagement, medication adherence and treatment optimization can help patients and providers achieve greater reductions in LDL-C and total cholesterol when compared to usual medical care.
METABOLIC BONE DISEASE

Abstract #600

THE ROLE OF BISPHOSPHONATE THERAPY IN MONOSTOTIC FIBROUS DYSPLASIA INVOLVING THE ORBIT

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Objective: Fibrous dysplasia (FD) describes the benign, abnormal development of fibrous tissue in the bony matrix. Clinical manifestations include pain, deformities, and fractures.

Case Presentation: A 68-year-old male with a past medical history of CAD, GERD, BPH, HTN was seen in an outpatient endocrinology setting for intermittent headaches, right-sided blurry vision, nausea and imbalance. He had a long history of asymmetry of the right frontal bone, but this had become more prominent in recent months. Prior to presentation, the patient was initially treated for migraines with no symptomatic improvement on prednisone, muscle relaxants, or abortive therapy. He was referred to a retinal specialist who obtained a CT scan. Imaging was significant for a fairly large expansile lesion occupying the right frontal bone, with caudal most extent involving the orbital roof, with extensive central lucent component, compatible with fibrous dysplasia. A bone scan demonstrated increased uptake at this site in addition to the thoracic and lumbar spine. Plain films of the spine were remarkable for diffuse idiopathic skeletal hyperostosis. Physical exam revealed prominence over the right orbital area and along the right temple. The thyroid was normal to palpation. Pulmonary, cardiac and abdominal exams were grossly unremarkable. No café au lait spots or findings suggestive of hypercortisolism were noted.

Laboratory studies revealed an alkaline phosphatase of 80 IU/L, calcium 9.1 mg/dL and creatinine of 0.8 mg/dL and a normal TSH and Free T4. Bone turnover markers revealed a normal serum osteocalcin level of 30ng/mL and normal N-telopeptide value of 13.6 nM BCE. Formal visual field testing was normal.

Conclusion: This case illustrates the underlying clinical symptoms often seen in FD. However, craniofacial orbital involvement with fibrous dysplasia is rare in monostotic disease (10-15% of cases). CT findings for FD typically illustrate well-defined, expansile lesions. Ground-glass opacities and endosteal scalloping may also be present on imaging. Bone pain is theorized to be secondary to bone remodeling and sensory nerve fiber derangement. In the absence of visual field defects, bisphosphonate therapy may play a role in this patient in the treatment of his bone pain reduction by inhibiting osteoclast resorption in surrounding fibrous tissue. For this patient, the use of intravenous zolendronic acid is anticipated. Denosumab has been reported to have similar activity in a small number of case reports.

Abstract #601

VITAMIN D REPLACEMENT PRACTICES IN VETERANS WITH VITAMIN D INSUFFICIENCY/DEFICIENCY: ARE WE ACHIEVING OUR GOALS?

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Objective: Vitamin D deficiency is defined as 25-hydroxyvitamin D (25(OH)D) level of <20ng/mL and vitamin D insufficiency is defined as 25(OH)D level between 20-29.9ng/mL. Current guidelines recommend replacing vitamin D with high-dose vitamin D2 therapy to the goal 25(OH)D of 30-50ng/mL. Subsequent maintenance therapy with vitamin D2 or D3 is recommended in order to prevent recurrent vitamin D insufficiency/deficiency. Our objective was to evaluate the outpatient practice of vitamin D replacement and its effects on vitamin D levels in veterans with vitamin D insufficiency/deficiency.

Methods: In this retrospective study we reviewed charts of 281 veterans (91% males, age 61.2±16.6 years) for whom electronic consults for vitamin D replacement were requested from the Endocrine Service between January 2nd and March 26th 2013. The significance of difference between groups was tested using t-test (continuous variables) and chi-square test (categorical variables).

Results: Majority of patients (95.4%) received initial high-dose replacement therapy with vitamin D2 for 6 weeks, most frequently with 50 000 units 3 times per week (63.3%), followed by 50 000 units 2 times per week (24.9%), and 50 000 units once per week (7.1%). Most patients were prescribed maintenance therapy with vitamin D3, most frequently 2000 units/day (55.9%), followed by 50 000 units 2 times per week (24.9%), and 50 000 units once per week (11.4%). 29.2% of patients were not prescribed any maintenance therapy. 82.6% of patients had repeated 25(OH)D level measured after replacement, with or without maintenance therapy, at the median of 23 weeks after the initial 25(OH)D measurement. Repeated 25(OH)D was significantly higher comparing to the initial one (25.9±9.9 vs. 14.1±5.5, p<0.0001). While there was no difference in initial 25(OH)D levels in patients who received maintenance therapy comparing to those who did not, increase in 25(OH)D levels between the measurements was higher in patients who received maintenance therapy compared to those who did not, increase in 25(OH) D levels between the measurements was higher in patients who received maintenance therapy, at the median of 23 weeks after the initial 25(OH)D measurement. Repeated 25(OH)D was significantly higher comparing to the initial one (25.9±9.9 vs. 14.1±5.5, p<0.0001). While there was no difference in initial 25(OH)D levels in patients who received maintenance therapy comparing to those who did not, increase in 25(OH) D levels between the measurements was higher in patients who received maintenance therapy (13.1±10.8 vs. 8.3±8.6, p<0.001) and they had higher proportion of patients reaching the goal 25(OH)D level of >30ng/mL (27% vs. 17%, p=0.05).

Discussion: Majority of investigated veterans with vitamin D deficiency were treated with high-dose vitamin D replacement therapy, and the majority of patients had 25(OH)D levels >30ng/mL after replacement, with or without maintenance therapy. However, a significant proportion of patients (29.2%) were not prescribed maintenance therapy, which may lead to recurrent vitamin D insufficiency/deficiency.
D insufficiency/deficiency had delayed repeated measurement of 25(OH)D levels and did not reach therapeutic goal. Almost one third of patients did not receive maintenance therapy after the initial replacement, which resulted in further reduced therapeutic response. **Conclusion:** Better compliance with the treatment guidelines and closer follow up of veterans with vitamin D insufficiency/deficiency in outpatient practice is needed to prevent adverse effects of low vitamin D levels on veterans’ skeletal and extraskeletal health.

**Abstract #602**

**CHONDROCALCINOSIS: COMMON AND IMPORTANT MANIFESTATION OF PRIMARY HYPERPARATHYROIDISM**

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**Objective:** Classic primary hyperparathyroidism (PHPT) has been associated with rheumatologic manifestations. Chondrocalcinosis in patients with primary hyperparathyroidism is caused by the combined effects of sustained hypercalcemia and age-related changes in articular cartilage.

We present a case of a 61 year old patient who was diagnosed and treated for osteoarthritis for 10 years before subsequent x-rays showed chondrocalcinosis leading to a diagnosis of parathyroid adenoma.

**Case Presentation:** A 61 year old man attended Meharry Internal Medicine clinic in 2006 because of arthritis of his knees. He had been in good health until 2006 when he gradually developed pain, stiffness and swelling in both knees. Pain was increased with weight bearing and at night. Morning stiffness lasted for about 60 minutes. Past medical history was remarkable for hypertension, nephrolithiasis, and chronic kidney disease. Bilateral knee x-rays showed mild patellofemoral joint space narrowing; demineralized osseous structures and moderate size suprapatellar effusion - changes consistent with osteoarthritis. He was initially managed with NSAID and physical therapy.

The symptoms worsened progressively to the point that he could scarcely walk. Conservative management was escalated to narcotics, but patient remained symptomatic and was referred for orthopedic evaluation.

Examination showed considerable effusion in both knees, with crepitus and instability. Repeat knee radiographs showed predominant patellofemoral joint osteoarthritis, but also noticed was early chondrocalcinosis involving both menisci and hyaline cartilage; superior patellar spur formation and hazziness of the suprapatellar area suggesting a moderate amount of fluid within the suprapatellar bursa. The calcifications were suspicious for chondrocalcinosis. Biochemical studies indicated hyperparathyroidism: serum Ca 11.2mEq/L, phosphorus 1.8mEq/L, PTH 126pg/dl, alkaline phosphatase 91U/l, creatinine 1.4mg/dl, BUN 15mg/dl, total protein 8.1g/dl, Albumin 4.1g/dl.

The patient was referred to Endocrinology where a parathyroid scan showed a parathyroid adenoma. The adenoma was surgically removed. His serum calcium and PTH returned to normal postoperatively. The patient’s symptoms improved and he continues to be followed in the clinic; his pain is managed with chronic pain medications and he walks with a cane.

**Conclusion:** PHPT has a variable clinical presentation in which musculoskeletal symptoms predominate, and one of the causes of rheumatologic manifestations is chondrocalcinosis.

The knowledge of this condition and its association with hyperparathyroidism will allow early diagnosis and therefore, minimize clinical complications.

**Abstract #603**

**CT-GUIDED RADIOFREQUENCY ABLATION IN RECURRENT TUMOR-INDUCED OSTEOMALACIA**

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**Objective:** To present a case of tumor-induced osteomalacia (TIO) refractory to surgical intervention which responded to CT-guided radiofrequency ablation (RFA).

**Case Presentation:** A 56 year-old male with history of TIO status-post two surgical curettage procedures presented with pain and swelling in the right leg with imaging confirming tumor regrowth. He was diagnosed with TIO 7 years prior after having poor healing of a trauma-induced fracture in his right foot. Laboratory studies at that time showed low phosphorus, high FGF-23 and osteoporosis on DXA. He underwent MRI which showed a mesenchymal tumor in the right proximal tibia. Within a year, he underwent two surgical curettage interventions to remove the tumor. After the procedure, the patient had some improvement in his pain and mobility. He was also maintained on appropriate phosphorus, calcium and vitamin D supplementation. However, one year after his last surgery his FGF-23 gradually increased and repeat MRI and SPECT imaging showed residual post-operative phosphaturic mesenchymal tumor. Despite medical treatment, he continued to have pain in his right leg and his FGF-23 level increased to 1510 RU/mL early this year. He underwent RFA of his residual tumor...
4 months ago for progressive disease. He had excellent results post-operatively with significant improvement in his symptoms, and a dramatic reduction in his FGF-23 to near-normal levels (297 RU/ml) 3 months later.

Discussion: Currently, the mainstay of TIO treatment is functional and anatomical imaging followed by surgical resection. This is usually curative if the tumor is completely removed with associated rapid normalization of lab values (FGF-23 and phosphorous). However, in some patients surgery can be more complicated due to anatomy and/or difficult localization of the tumor. Additionally, because wide margins are needed to ensure complete resection, destruction of healthy bone can be risky or debilitating to the patient. To date, CT-guided RFA in TIO has been documented in a few international case studies with promising results. Our patient had persistent tumor activity as indicated by high post-procedure FGF-23 levels and imaging despite surgical and medical treatment. The abrupt improvement in his symptoms and drop in FGF-23 after CT-guided RFA is promising and consistent with the results noted in other case studies. The effectiveness of RFA in TIO is likely related to more precise intraoperative localization and should be considered in those patients in whom surgical intervention is non-curative.

Conclusion: In patients with TIO who have recurrent TIO despite surgical excision and medical management, CT-guided RFA should be strongly considered as a potential treatment option.

Abstract #604

ACUTE HYPOCALCEMIA IN THE PERIOPERATIVE SETTINGS

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UTHSC

Case Presentation: Bisphosphonates are first line drugs in the treatment of osteoporosis. Their clinical utility is limited by the fact that they cannot be used in patients with chronic kidney disease (CKD) although these patients are at very high risk for osteoporosis. In this regards Denosumab is a relatively recent drug which is approved for use in patients with CKD. Denosumab, a monoclonal antibody against RANKL has been demonstrated to reduce osteoporosis and solid bone tumor related bone loss. Here in we describe a case of severe hypocalcemia associated with use of Denosumab in a patient with CKD. Patient is a 67 year old male with past medical history significant for CKD stage 4-5 who presented with a 5 day history of nausea and vomiting. He was found to have an acute coronary syndrome and acute severe hypocalcemia with total calcium of 5.8 and ionized calcium of 0.74. His vitamin D level was 12.8 although he was on calcium and vitamin D supplements as an outpatient. Angiography was significant for triple vessel disease and surgery was recommended. Surgery was deferred due to severe hypocalcemia. Work up by endocrinology showed that patient had Denosumab about 12 days back. Calcium was aggressively repleted with intravenous calcium gluconate given every six hours along with oral calcium. Intravenous calcitriol was also supplemented until calcium levels normalized and then switched to oral. Patient had an uneventful surgery and post-operative course.

Discussion: In this scenario surgery could have worsened the hypocalcemia by chelation of calcium by the citrate in transfused red blood cells and respiratory alkalosis which is often associated with induction of anesthesia. Also most anesthetic drugs have potential to cause cause QT prolongation. With underlying hypocalcemia there was very high probability of QT prolongation and torsade’s de pointes with possible cardiac arrest. So a critical event was prevented by delaying the surgery.

Conclusion: Extreme caution should be used in the use of Denosumab in patients with end stage CKD. Hypocalcemia is known to occur with more frequency and severity in patients with denosumab as compared to zolendronic acid which is a bisphosphonate. So the use of Denosumab in CKD stage 4-5 should be reconsidered.

Abstract #605

CRITERIA FOR SURGERY IN A SERIES OF APHPT PATIENTS

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Objective: Asymptomatic primary hyperparathyroidism (aPHPT) is defined as PHPT without specific symptoms or signs traditionally associated with PTH excess or hypercalcemia and is currently the most frequently diagnosed form of the disease.

Management options for aPHPT patients vary among surgery, medications and follow-up. To deal with this issue, four International Workshops have taken place in order to draw up criteria to stratify asymptomatic patients as eligible for surgery.

The latest guidelines defined as criteria for surgery: serum calcium 1 mg upper normal limit; creatinine clearance < 60 mg/cc; 24h urine for calcium > 400 mg/dl; the presence of nephrolitiasis; T score under -2.5 at lumbar spine, hip femoral neck or distal forearm; the presence of vertebral fracture and age under fifty years old.
The majority of aPHPT patients meet surgical criteria but the prevalence of each criteria has not been established yet. We thus evaluated the prevalence of each surgical criterion in a consecutive series of 172 patients with aPHPT, referred to our Division from January 1998 to December 2013.

**Methods:** Patients with nephrolitiasis and patients with vertebral fractures (detected by morphometric DEXA or standard RX and TC) were classified as symptomatic. We selected 75 out of 172 aPHPT patients showing all of the parameters proposed by current Guidelines for surgical decision.

The selected patients were not statistically different from the remaining 97 aPHPT patients as for age, sex, serum creatinine, PTH, total and ionized calcium, phosphate, 25OHD and BMD levels.

**Results:** In our series, osteoporosis at any site was the most frequently met criterion for surgery (45/75, 60%): 29 (38.7%), 27 (36%) and 14 (18.7%) patients had T score < -2.5 at lumbar spine, distal forearm and femoral neck, respectively.

Serum calcium resulted 1 mg/dl upper normal limit in 14 (18.7%) of aPHPT patients; 13 (17.3%) had renal impairment; 24-h urine for calcium resulted > 400 mg/dl in 11 (14.7%) patients while only 8 (10.7%) were younger than 50 years old.

**Conclusion:** In conclusion, our data confirm that the majority of aPHPT patients meet surgical criteria as defined by the latest international guidelines. Osteoporosis at any site is the most commonly met criterion in asymptomatic PHPT. On the other hand, only a minority of aPHPT patients meet the remaining surgical criteria.

**Abstract #606**

**HIGH COST OF HYPERCALCEMIA: A CASE OF PRIMARY HYPERPARATHYROIDISM LEADING TO ACUTE PANCREATITIS AND A SPONTANEOUS ABORTION**

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**Objective:** Hypercalcemia is associated with significant gestational complications. Here, primary hyperparathyroidism (PHPT) induced hypercalcemia led to acute pancreatitis (AP) and resulted in a spontaneous abortion.

**Case Presentation:** A 24 year old G1P0 female at 18 weeks with a history of nephrolithiasis presented with acute non-radiating LUQ pain with nausea, vomiting and a 2 day prodrome of polyuria and polydipsia. At presentation, labs included: lipase 10,261 IU/L, albumin 2.3 g/dL, calcium 13.6 mg/dL, phosphorus 1.7 mg/dL, ionized calcium 6.9 mEq/L, AST 38 IU/L, ALT 18 IU/L, bilirubin 0.79 mg/dL, blood glucose 90 mg/dL, and a glycosylated hemoglobin of 5.3%. She was hospitalized for pancreatitis and received aggressive IV fluids and electrolytes followed by furosemide for her hypercalcemia. A RUQ US revealed cholelithiasis and gallbladder sludge but no dilation of common bile duct. Her PTH was 568.3 pg/mL with a simultaneous ionized calcium of 6.9 mEq/L. A repeat PTH on day 3 was 1,984 pg/mL. An ultrasound of the neck showed no evidence of parathyroid adenoma. Her course would be complicated by new onset diabetes with diabetic ketoacidosis, associated with a glutamic acid decarboxylase-65 (GAD-65) antibody titer of 4.7 units/mL. Unfortunately, on hospital day 3, she suffered a spontaneous abortion. Her hypercalcemia work-up then concluded with a Sestamibi scan, which revealed evidence of a left superior parathyroid adenoma. After discharge, she underwent parathyroidectomy with removal of a 2.9 x 2 x 0.9 cm hypercellular left-upper parathyroid.

**Conclusion:** PHPT can be difficult to recognize in pregnant women as the physiologic changes decrease the normal serum range of calcium to 8.6 – 9.2 mg/dL. Nonetheless, the condition is associated with morbidity, including a miscarriage rate up to 3.5 times greater than uncomplicated pregnancies. Complications occur in 67% of mothers and 80% of neonates, including intrauterine growth restriction, neonatal tetany, and preterm delivery. These complications occur more often when maternal serum calcium levels exceeds 11.4 mg/dL. Another potential consequence of hypercalcemia is pancreatitis. PHPT is a relatively uncommon cause of pancreatitis in the general population accounting for less than 0.5% of all cases of AP. However, the incidence of AP amongst pregnant women with PHPT has been shown to be as high as 11%, compared to 0.5 to 1.5% of those with PHPT who are not pregnant. This case highlights the importance of recognizing and evaluating hypercalcemia in gravid patients. Hypercalcemia from PTHP is associated with significant morbidity, including pancreatitis particularly in gravid patients, and fetal mortality.
Abstract #607

YOUNG AND FRACTURABLE

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Objective: The purpose of this investigation was to determine the cause of hypophosphatemia and multiple stress fractures in a 20 year old male college student living with chronic bone pain and anxiety about suffering further fractures.

Methods: Laboratory evaluation of serum included a CMP, magnesium, phosphorus, intact PTH, 25-OH Vit D, 1,25-OH Vit D, TSH, and FGF-23. Urine studies included a spot creatinine, phosphorus, glucose, amino acids, and a fractional excretion of phosphorus (FEPi), in addition to 24 hour urine phosphorus, calcium, and creatinine. Imaging with a bone survey was completed. Genetic testing was pursued to screen for mutations involved in abnormal renal handling of phosphorus including CLCN5, PHEX, ENPP1, DMP, SLC34A3, and FGF-23 sequentially as appropriate.

Case Presentation: Results include an alkaline phosphatase of 384 units/L and a serum phosphorus as low as 1.3 mg/dl, both of which were persistent on repeat. His intact PTH was 27.1 pg/ml, 25-OH Vitamin D of 36 ng/ml, 1,25-OH Vitamin D of 21, magnesium of 2.4 mg/dl, calcium of 9.2 mg/dl. A 24hr urine collection contained 149mg of calcium, 950mg (>100mg) phosphorus, and his FEPi was 26.3% (>5%) suggesting significant phosphorus wasting. An FGF-23 level was 108. A bone scan & skeletal bone survey revealed multiple areas suggestive of prior small stress fractures. DXA is scheduled.

Discussion: Phosphorus is a key component of bone and a deficiency results in poor mineralization along with other systemic symptoms of hypophosphatemia. This young man with a propensity toward stress fractures appears to have significant urinary wasting of phosphorus in the setting of normal PTH and calcium balance. He has no family history of similar symptoms. Suspicion is raised for an isolated sodium-phosphorus co-transport defect based on inappropriately normal FGF-23 and borderline-low 1,25 OH Vit D, which can result in bone changes along the rickets-osteomalacia spectrum. This includes the possibility of an oncogenic FGF-23 secreting tumor. 1mcg calcitriol and 2Gm phosphorus replacement was started daily with increasing requirements. Progress of genetic testing thus far suggests a normal CLCN5 with evaluation of other possible mutations pending.

Conclusion: The presence of multiple fragility-type fractures, isolated low serum phosphorus with significant ongoing renal wasting, together with inappropriate FGF-23 and 1,25 OH Vit D levels suggest that this young man may have one of various rare genetic mutations involved in renal co-transport of phosphorus vs a possible oncogenic tumor with autonomous secretion of FGF-23. Ongoing genetic testing and imaging for a mesenchymal tumor remain warranted at this time.

Abstract #608

THIS GERD CAN HURT!

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Objective: Gastroesophageal Reflux Disease (GERD) is a common disorder with up to 44% of the population reporting monthly heartburn. Proton Pump Inhibitors (PPIs) are one of the most commonly prescribed treatments. Hypomagnesemia is a described, but infrequently considered, side effect from long term PPI use. We describe a case of severe electrolyte abnormalities including hypomagnesemia and hypocalcemia from long term omeprazole use.

Case Presentation: A 63 year old female presented to the Emergency Department with complaints of dizziness and intractable nausea and vomiting for 2 weeks. She mentioned being on omeprazole 40 mg daily for >2 years and 4 weeks prior to admission, the dose was doubled to 40 mg BID for worsening symptoms. Soon after, she began complaining of nausea and vomiting and was given ondansetron and compazine which did not help. In emergency department, she was found to have a magnesium of <0.2 (1.3-2.1 meq/L), potassium 2.3 (3.5-4.9 meq/L), calcium of 6.69 (8-10.5 mg/dl) with albumin 3.9 (3.6-5g/dl), ionized calcium 0.8 (1.1-1.3 mmol/L). Parathyroid hormone levels were also low at 9.5 (14-55.7 pg/ml). Omeprazole was stopped and electrolyte replacement started. Renal magnesium wasting syndrome and Gittleman’s syndrome were ruled out. Her symptoms slowly improved with electrolyte replacement and she was discharged home on ranitidine. Her electrolytes have remained normal since her discharge with continued resolution of symptoms.

Discussion: PPIs reduce intestinal magnesium absorption; however the mechanism is not entirely clear. It is also not known if all PPI users are potentially susceptible or if it is an idiosyncratic reaction. It is speculated that PPIs affect the enzymes and/or the channel functions of the active transport system either directly or by intestinal pH changes. While low levels of magnesium stimulate parathyroid hormone secretion, very low serum concentrations induce a paradoxical block leading to parathyroid hormone suppression and hypocalcemia. Of interest,
magnesium works on parathyroid-calcium homeostasis in a conflicting manner: While magnesium is physiologically needed for the secretion of parathyroid hormone (hence hypomagnesaemia leads to hypoparathyroidism and hypocalcemia), excessive magnesium levels will (also) cause hypoparathyroidism and hypocalcemia. The latter is believed to reflect the fact that magnesium in excessive levels will act like calcium (in suppressing parathyroid hormone production), and possibly by competing with calcium in the kidney, favoring magnesium reabsorption. 

Conclusion: PPIs can lead to severe electrolyte derangements. Hence clinicians should choose wisely and prescribe them only when clear indications exist.

Abstract #609
SHOULD WE REVISIT THE ROLE OF BI-PHOSPHONATES IN METASTATIC MALIGNANCY

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UTHSC

Case Presentation: A 74-year-old African American gentleman with stage IV metastatic prostate cancer was admitted to the intensive care unit with acute kidney injury, generalized weakness, hypotension, and suspected sepsis. Initial work up for sepsis was negative. He was started on intravenous (i/v) fluids, antibiotics and vasopressors. Endocrinology was consulted as his calcium was found to be less than 5mg%. Work up by endocrinology showed that 2 weeks ago he was given 5mg i/v Zolendronic acid in the oncology office. He was not on calcium or vitamin D supplements. His vitamin D level was found to be less than 13 ng/ml and his ionized calcium was 0.60 mmol/liter. He was started on i/v elemental calcium at 50 mg per hour and i/v calcitriol 0.5 mcg twice a day. As his calcium started to trend upwards his pressures normalized. Work up for sepsis remained negative and his antibiotics were stopped.

Discussion: This report reinforces three points. First it exposes the potential risks associated with lack of integration of electronic medical records in physician offices and hospitals. The etiology behind hypocalcemia could have been easily missed in this case. Bisphosphonates in patients with underlying metastatic bone disease are often given in physician offices who usually have a different electronic medical record and patient has little knowledge as to the potential complications of the drugs that are being given. Second this case also raises the question that if it is justified to give bisphosphonate to a patient with stage IV malignancy. In current era of health care reform the definition of quality is not just increased utilization but improved outcome and reduced cost. Thirdly if bisphosphonates are used the physician should make sure that the patient is getting adequate vitamin D and calcium supplements.

Conclusion: There is need to reassess guidelines on use of bisphosphonates in patients with metastatic malignancy.

Abstract #610
A POSSIBLE CASE OF HYPERPARATHYROIDISM-JAW TUMOR (HPT-JT) SYNDROME?

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Objective: Hyperparathyroidism-Jaw Tumor (HPT-JT) syndrome is a rare condition first described in 1958. It is characterized by parathyroid adenomas or carcinomas, fibro-osseous lesions of the mandible or maxilla, and renal cysts and tumors. Here we present a 63 year old woman referred to the clinic for hyperparathyroidism with a 1 year history of a large oral cavity/mandibular mass with 10 pound weight loss and elevated PTH (134.4 pg/mL) and calcium level (10.7 mg/dL).

Methods: Patient underwent successful surgical removal of the tumor with pathology showing a giant cell-containing lesion widely involving the jaw bone and extending in to the soft tissues.

Case Presentation: Post-procedure, the patient was noted to have hypocalcemia which recovered back to normocalcemia along with recovering levels of PTH.

Discussion: HPT-JT syndrome is a rare condition with approximately 200 reported cases noted in the literature. It involves mutation of the HRPT2/CDC73 gene, a tumor suppressor gene that has been mapped to Ch. 1q21-32. Further work up is being carried out to ascertain whether this patient has the HRPT2/CDC73 gene mutation associated with this condition.

Conclusion: HPT-JT syndrome is a rare disorder involving maxillary or mandibular growths along with hyperparathyroidism and renal manifestations. Surgery is curative. Post-operative management involves follow up of calcium levels and tumor surveillance, including of family members at risk, which are important components of following these patients long term.
Abstract #611

SARCIDOsis masquerading an undeRlying hypoparathyroidisM

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Medical College of Wisconsin

Objective: To recognize the challenges in the diagnosis and treatment of sarcoidosis, we present a patient with hypercalcemia related to an unusual presentation of sarcoidosis masquerading an underlying post-operative hypoparathyroidism.

Case Presentation: A 68-year-old Caucasian female was diagnosed with primary hyperparathyroidism at another facility in 2008 when she developed symptomatic hypercalcemia secondary to 4-gland hyperplasia which was cured after 3-gland parathyroidectomy. She was asymptomatic until she presented in July 2010 with fatigue and weakness and was found to have hypercalcemic crisis with a corrected calcium of 13.5 mg/dL and acute kidney injury. She was treated with intravenous pamidronate and aggressive hydration. Initial work-up showed non-parathyroid hormone (PTH) mediated hypercalcemia with low PTH, low 25-hydroxy vitamin D (25-OH Vit D) and normal 1,25-dihydroxy vitamin D (1,25-OH Vit D) and angiotensin converting enzyme level (ACE). Previous labs from outside facility showed elevated 1,25-OH Vit D level of 68 pg/dl and a mildly elevated ACE. Subsequent tests for Tuberculosis, Histoplasmosis and Blastomycosis were negative. She noted a rash in her forehead and cheeks since 2007 which was biopsied and showed granuloma annulare. Because of her history of myelodysplastic syndrome, there was a concern for hypercalcemia of malignancy. Bone marrow biopsy was consistent with myelodysplastic syndrome and also showed non-caseating granulomas. Computed tomography of the chest showed mediastinal lymphadenopathy. Left upper lobe transbronchial biopsy was consistent with sarcoidosis. The rash on her forehead was re-biopsied which showed sarcoid infiltrates. She was treated with prednisone 20 mg daily for sarcoidosis. She developed hypocalcemia (6.9 mg/dl) with perioral numbness and muscle cramps after being on prednisone for 3 weeks. An underlying iatrogenic hypoparathyroidism was then revealed once steroid treatment for her sarcoidosis was initiated. Prednisone dose was adjusted to keep her calcium levels normal to avoid symptoms of hypercalcemia and hypocalcemia.

Conclusion: Sarcoidosis is a state of functional hypoparathyroidism characterized by episodic hypercalcemia and elevated 1,25-OH Vit D levels. In our patient, the increase in calcium caused by sarcoidosis has made her underlying hypoparathyroidism quiescent for a few years. Permanent hypoparathyroidism due to her previous parathyroidectomy has been unmasked following steroid treatment of her sarcoidosis.

Abstract #612

osteonecrosis of palatal torus secondary to bisphosphonate therapy

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Objective: To contribute to the literature a case of Bisphosphonate related osteonecrosis of a Palatal Torus.

Case Presentation: We report a case of 67 yr old lady with osteoporosis on Bone Densitometry, who had been treated with alendronate and ibandronate over the course of 4-5 yrs. She had been on a drug holiday for last 7 yrs and had demonstrated stable bone densities. She had no past or recent history of malignancy, radiation, chemotherapy, smoking or dental procedures. On one of her follow up visits she complained of an overtly sensitive palate and was found to have osteonecrotic palatal tori. She was successfully treated with loco-regional antiseptic therapy and oral antibiotics. The calcified growth spontaneously fell off and she had complete resolution of her pain and necrosis.

Discussion: Osteonecrosis of jaw (ONJ) is a rare but known complication associated with Bisphosphonate therapy (BP). The incidence ranges from 0.04 to 0.1%. It mostly affects the mandible but can occur in any bony structure of the mouth. Palatal torus (PT) is type of bony exostosis, usually occurring in postmenopausal women with a genetic predisposition. It may possibly be associated with a high bone density. The maxilla is a site of excessive bone remodeling and is more prone to a mucosal breach. This increases the risk of PT being a site of osteonecrosis secondary to BP treatment. Only two cases have been reported in literature to date.

Conclusion: This case highlights the importance of considering the possibility of an increased incidence of osteonecrosis of PT in patients with BP usage. Also, it would be prudent to establish regular dental screening and preventative guidelines in patients treated with BP, importantly if they have additional high risk factors for ONJ.
Abstract #613

MILK-ALKALI SYNDROME IN A PRE-MENOPAUSAL BULIMIC FEMALE WITH OSTEOPOROSIS AND PEPTIC ULCER DISEASE

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Case Presentation: 49 year old female with history of bulimia presented with nausea, emesis, muscle aches, increase urination and ten pound weight loss in one month. Patient was taking ibuprofen everyday for a year. She started to self-medicate herself with tums, rolaids and, milk for her nausea. She would take up to two bottles of tums everyday. She had been doing this for past six months and within that time was diagnosed with osteoporosis. Upon admission calcium was 17.2, BUN 54 and Cr 4.3. Treatment included: IV fluids, pamidronate and calcitonin. Calcium improved to 9.6 upon discharge as well as renal function with BUN 20 and Cr 1.8. PTH and SPEP were within limits. Granulomatous disease was unlikely with unremarkable chest x-ray and ACE level. Vit D levels were low. At this point it was determined patient had milk-alkali syndrome given her presentation of hypercalcemia with acute renal failure and antacid ingestion.

Discussion: This case is unique due to its presentation of hypercalcemia in a premenopausal bulimic patient with osteoporosis that was self-medicating herself with calcium carbonate for peptic ulcer disease. Often times patients do not consider over the counter antacids as medications in their history therefore a good history by the physician is important when trying to diagnose the etiology of the hypercalcemia.

Conclusion: Osteoporotic females and those with peptic ulcer disease have been considered to be at increased risk for Milk-Alkali Syndrome, but it is important to note that bulimic females are also at risk due to their poor oral intake and vomiting.

Abstract #614

SKELETAL FLUOROSIS RELATED TO HABITUAL TEA CONSUMPTION: RESULTS OF LONG-TERM FOLLOW UP

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Mayo Clinic

Objective: Systemic fluorosis due to excessive tea consumption is a cause of acquired osteosclerosis. We previously reported four patients with fluoride excess due to tea. Herein, we report long-term follow up on two of these subjects.

Case Presentation: Case 1: A 67-year-old female with history of anorexia and multiple stress fractures was evaluated for a DXA BMD which revealed a T-score of +2.3 at the lumbar spine (LS) and a femoral neck (FN) T-score of -1.7. She underwent menopause in her early 40s and was not on hormone replacement therapy. Physical examination revealed a BMI of 15.2 kg/m2. Laboratory studies revealed elevated bone alkaline phosphatase 149 U/L (nl, 11-67), 25-hydroxyvitamin D 19 ng/mL, and serum calcium 9.7 mg/dL. Lumbar spine x-ray showed diffusely increased bone density. Plasma fluoride was 15.4 µmol/L (nl, 0-4). The patient confirmed consumption of an estimated 10-16 cups of black tea daily with an estimated daily fluoride intake of 13 mg/day (typically ≤ 2.5 mg/day). She reduced tea consumption. Her gastrointestinal symptoms improved. She declined osteoporosis therapies. Over 10 years of follow-up, her BMD progressively declined by 40 % at the lumbar spine (LS) and 35.1 % at the femoral neck (FN). Plasma fluoride levels plateaued at year one after reducing tea intake to 8.8 µmol/L and upon last measure at year 10 remained 8.8 µmol/L. Her eGFR improved from 25.5 ml/min at baseline to 46.9 mL/min at year 10.

Case 2: A 62-year-old female was referred for an elevated DXA BMD with a T-score of + 6.1 at the lumbar spine and + 0.9 at the femur neck. She had no prior history of fractures. She admitted to consuming generous amounts of iced tea (30-40 eight-oz. glasses of tea /day) for about 30 years with an estimated daily fluoride intake of 14 mg/day. Physical examination was unremarkable. Serum creatinine 1.7 mg/dL and plasma fluoride level of 17.3 µmol/L. A skeletal survey demonstrated axial sclerosis. The patient stopped drinking tea completely. Myalgia and gastrointestinal symptoms improved shortly after. Over 8 years of follow-up, her DXA BMD declined by 11.4 % at the LS and 2.6 % at the FN. Plasma fluoride levels plateaued at 33 months after tea discontinuation to 7.2 µmol/L and upon last measure at year 8 was 7.4 µmol/L. Her eGFR improved from 40.6 mL/min at baseline to 50.4 mL/min at year 8.

Conclusion: Chronic excessive tea consumption can result in fluoride related metabolic bone disease. Reduction or discontinuation of tea intake is associated with improvement of renal function and gastrointestinal symptoms. A prompt initial decrease in plasma fluoride levels followed by a plateau at above normal levels persists up to 10 years thereafter.
Abstract #615

HYPOCALCEMIA SECONDARY TO PARATHYROID HORMONE RESISTANCE

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Case Presentation: 34 year old man with history of tetralogy of fallot (TOF) status post repair in childhood and intellectual disability admitted to our hospital with heart failure due to failure of his TOF repair. On admission, patient was found to be hypocalcemic and Endocrinology was consulted for management. His initial calcium is 7.3 mg/dl (8.1-10.6 mg/dl) with albumin of 3.6 g/dl (3.8-5.1 g/dl), ionized calcium of 0.86 mmol/L (1.12-1.32 mmol/L), 25 hydroxyvitamin D of 9 ng/ml (>30 ng/ml), Parathyroid hormone (PTH) of 105.2 pg/ml (7-53 pg/ml), phosphorus of 7.1 mg/dl (2.5-4.5 mg/dl), creatinine of 1.12 mg/dl (0.8-1.1 mg/dl), 1.25 dihydroxy vitamin D was 6.3 pg/ml (19.9-73.9 pg/ml). Patient was asymptomatic from hypocalcemia. On examination, Chvostek and Trouseau sign were absent. No family history of calcium disorders. However, patient had previously been on calcium and vitamin D supplements which he self-discontinued six months ago. Diagnosis of PTH resistance was considered based on high phosphorus, hypocalcemia with high PTH. He was treated with calcitriol and calcium carbonate which led to normalization of his calcium, phosphorus and PTH. X-ray of his hands did not show brachydactyly. Patient has been referred for genetic testing for PTH resistance to delineate the type of PTH resistance.

Discussion: PTH resistance also known as pseudohypoparathyroidism are rare highly heterogeneous genetic disorders. Their prevalence is estimated to be 0.79 per 100,000. It was first described by Albright et al. in 1942. PTH resistance disorders type 1 has four subtypes of genetic disorders leading to end organ resistance to PTH. Type 1a is due to maternal inheritance of GNAS1 mutation leading to inactivation associated with hypocalcemia and features of Albright’s osteodystrophy which consists of round facies, shortening of 3rd and 4th metacarpals, short stature, developmental delay, subcutaneous calcifications. Type 1b PTH resistance is confined to kidneys leading to hypocalcemia, hyperphosphatemia and high PTH. Patients with Type 1b PTH resistance lack phenotypic abnormalities of Albright’s osteodystrophy. Type 1c is due to mutation affecting coupling of G protein to the PTH receptor. Adenyl cyclase is no longer coupled to the binding of PTH and its receptor. Type 2 PTH resistance does not demonstrate phenotypic features of Albright’s osteodystrophy however, mutation correlating has not been identified yet.

Conclusion: Considering that our patient lacked phenotypic features of Albright’s osteodystrophy, patient likely has PTH resistance type 1b or type 2. Genetic testing will aid in diagnosis, results of which are pending.

Abstract #616

PARATHYROID CARCINOMA ASSOCIATED WITH MULTIPLE BROWN TUMORS MIMICKING FIBROUS HISTIOCYTOMA—A UNIQUE CASE OF TWO RARE CONDITIONS.

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Objective: Both parathyroid carcinoma and brown tumors are rarely associated with primary hyperparathyroidism (pHPT). Brown tumors are a late complication of chronic untreated pHPT that is now seldom reported as a result of early diagnosis. In contrast, these tumors are less frequently reported with parathyroid carcinoma due to its less insidious onset. A few cases of this unusual presentation are published in the literature. We present a unique patient with pHPT and multiple brown tumors caused by parathyroid carcinoma.

Case Presentation: A 54-year-old female was referred to our institution with 2 months of worsening left hip pain and concern for fibrous histiocytoma on bone biopsy. 2 years prior at an outside facility, she was diagnosed with pHPT after an accidental left distal femur fracture but did not seek further treatment for HPT. On examination she was morbidly obese and bedridden with limited range of movement of the extremities. No neck or bony masses were palpable. Lab testing showed elevated calcium (12.8 mg/dL), parathyroid hormone (PTH) (1466 pg/ml), alkaline phosphate (459 IU/L) and low vitamin D at 7ng/ml. Computer tomography (CT) of the lower extremities and a bone survey had multiple lytic lesions of the axial and appendicular skeleton and a pathologic fracture of the proximal left femur. A 4D CT scan of the neck identified a 4.8 cm mass in the left inferior thyroid with mild tracheal narrowing. Review of the bone biopsy of the left femur done at an outside facility showed fibrohistiocytic proliferation of uncertain malignant potential. She received intravenous hydration and vitamin D supplementation followed by a dose of intravenous bisphosphonate. Resection of the left proximal femur confirmed brown tumor. She then underwent left radical parathyroidectomy,
left thyroid lobectomy and neck dissection. Intraoperative PTH dropped from >1900 to 270 pg/mL. Histopathology showed a 5.5 cm hypercellular gland favoring parathyroid carcinoma with soft tissue but not lymphovascular invasion or necrosis and all 12 resected lymph nodes were negative. Postoperatively patient developed hungry bone syndrome characterized by profound hypocalcemia requiring prolonged intravenous calcium and substantial doses of calcitriol and oral calcium.

**Conclusion:** Brown tumors can mimic fibrous histiocytoma and other bony metastasis. Workup of these suspect bone lesions should include a PTH level. Although parathyroid carcinoma has rapid and aggressive clinical course and is rarely associated with brown tumors, the presence of significantly elevated PTH and calcium levels should raise suspicion for the rare combination of parathyroid carcinoma with brown tumors.

**Abstract #617**

**BONE-SPECIFIC ALKALINE PHOSPHATASE FLARE IN A PATIENT WITH HEPATITIS C: CASE REPORT AND REVIEW OF LITERATURE**

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University of Maryland School of Medicine

**Objective:** Bone-specific alkaline phosphatase (BAP) synthesized by osteoblasts is a highly sensitive and specific marker of bone-forming activity of osteoblasts. ALP flare phenomenon is an acute elevation of serum ALP levels. It has been described after chemotherapy and is thought to represent an osteoblastic reaction after treatment initiation. We describe the case of a patient with Hepatitis C (HCV) infection who had a sudden and significant elevation of BAP (ALP flare) and performed a review of the literature.

**Case Presentation:** A 53-year-old man with orthotopic liver transplant in 2004 due to HCV cirrhosis, on chronic immunosuppression with cyclosporine and mycophenolate, was hospitalized for an acute elevation of serum ALP to 1077 (nl: 39-117 IU/L). Five days before admission, he had completed a 24 week course of sofosbuvir/ribavirin for the treatment of HCV. One month prior to starting HCV treatment ALP was 151 IU/L. Admission liver panel showed a serum ALP 965 IU/L, AST 37 (nl: 0-40 IU/L), ALT 13 (nl: 0-44 IU/L), TBil 1.3 (nl: 0-1.2 mg/dL), GGT 86 (nl: 15-73 U/L). ALP isoenzyme showed a peak of the BAP of 95% (nl: 12-68%). Additional work up was significant for leukopenia, Cr 2.62 (nl: 0.76-1.27 mg/dL), PTHi 254 (nl: 8-54 pg/mL), 25OH-D 26.7 (nl: 30-100 ng/mL), 1,25OH-D 46.2 (nl: 10-75 pg/mL), Urine calcium <1.0 mg/dL, C-telopeptide (CTX) 2401 (nl: 115-748 pg/mL), and LDH 877 (nl: 313-618 U/L). He had normal calcium, albumin, phosphorus, and thyrotropin levels. Skeletal survey radiographs and Tc-99 MDP bone scan did not reveal osseous lesions or Paget’s disease of bone. ALP continued to increase from 965 IU/L to 1992 IU/L after 5 days, and up to 2323 IU/L after 10 days. One month after hospital discharge ALP had declined to 221 IU/L. During his hospitalization, he got G-CSF (filgastrim) for leukopenia; a temporal relationship between this medication and further acute rise in ALP was observed.

**Discussion:** BAP flare phenomena after HCV treatment has not been described before. In this patient, concomitant BAP and CTX elevation suggests increased bone turnover. Possible explanations are: 1) Bone remodeling process starting after the completion of the HCV treatment; however, in most of the cases, bone turnover markers will normalize after treatment; 2) Ribavirin induced osteoclast activity by indirect effect on TRANCE/RANKL gene expression in osteoblasts; however, this effect has been observed in vitro, and clinical data is non-conclusive regarding the effect of ribavirin on bone.

**Conclusion:** BAP flare phenomena is an uncommon finding after chemotherapy initiation. We describe an unusual case of BAP flare after initiating therapy for HCV with sofosbuvir/ribavirin, further exacerbated by G-CSF injections.

**Abstract #618**

**IMPORTANCE OF MAGNESIUM IN THE PATHOPHYSIOLOGY AND THERAPY OF HYPOCALCEMIA**

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University of Tennessee Health Science Center

**Case Presentation:** Magnesium is necessary for parathyroid hormone (PTH) production and, hence, is important in regulation of calcium metabolism. Here, we report a case of a male presenting with significant hypomagnesaemia restraining hyperparathyroidism in response to severe hypocalcaemia.

**Discussion:** Patient is a 71-year old male with unknown past medical history but a social history significant for chronic alcohol abuse. He was brought to the Emergency Department (ED) by his daughter who found him at home in a confused state. In the ED, he was found to have a calcium level below 5.0mg/dL beyond the lower level of detectability in our institution’s assay. His 25-OH vitamin D level was also undetectable at less than 13ng/mL, albumin was 2.2 g/dL, creatinine was 1.28 mg/dL.
phosphorus was 2.2 mg/dL and 1,25 di-hydroxyvitamin D level was <8 pg/mL (normal 18-72pg/mL). Other biochemical parameters on admission were noted for PTH of 110.3 pg/mL and magnesium level of 0.6mg/dL. He was found to have a prolonged QT interval on his ECG. Following infusion of 4 grams of magnesium, the PTH level increased substantially by the next day to 436 pg/mL. Magnesium supplementation was further continued. In addition, calcium infusion was started in the ED and continued following the patient’s admission to the hospital. After five days of therapy, his calcium level was 7.4mg/dL. He was then transitioned to oral calcium carbonate at 1.25 gram BID. In treating this patient’s hypocalcaemia, we also treated his severe Vitamin D deficiency. From day 3 of hospitalization, he did receive 3 doses of calcitriol 0.25mcg and high dose ergocholecalciferol. Once magnesium and calcium levels were corrected, patient’s PTH level decreased to 229 pg/ml. At time of discharge, his magnesium level was 1.5mg/dL and his PTH level reduced to 109 pg/ml likely due to improvements in calcium level. On discharge, calcium level was 7.8 mg/dl with an ionized calcium of 1.27 mmol/L and 25-OH vitamin D level was at 13ng/ml. He was placed on 2,000 units of cholecalciferol at discharge.

Conclusion: The clinical significance of this case is that it demonstrates the importance of magnesium and its effect on the parathyroid gland. This man’s magnesium deficiency prevented adequate response of parathyroid glands to hypocalcaemia and once magnesium was repleted, calcium level improved well before we could observe the effects of routine calcium and calcitriol replacement suggesting PTH effect on bone to mobilize calcium. In order to adequately address the requirements of treatment for hypocalcaemia, a magnesium level must be determined and if low–replete.

Abstract #619

LOOKING BEYOND OSTEOPOROSIS: DIAGNOSING X-LINKED HYPOPHOSPHATEMIC RICKETS IN A 60-YEAR OLD FEMALE

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Objective: This case was described to emphasize the need to recognize less common metabolic bone diseases despite the initial diagnosis of osteoporosis.

Methods: The information on the clinical case and the condition was obtained by chart and literature review.

Case Presentation: A 60-year old female was referred for osteoporosis diagnosed over 10 years ago by a “bone scan”. She reported being chronically ill in childhood and always limping, without any known trauma. Her first traumatic fracture was at age 18 years on her left leg. At 32 years old, she had bilateral hip replacements for hip dysplasia and osteoarthritis, requiring multiple revisions on each side, afterwards becoming wheelchair-bound. She had 3 atraumatic fractures of her left femur from the age of 55 years. She has had poor dentition her entire life. Her mother had rickets as a child, her sister had hip dysplasia with avascular necrosis, and her grandmother had a hip fracture. She had high alkaline phosphatase levels (alk phos) since 2006, as well as low serum phosphate levels. Other work-up including calcium and magnesium as well as the renal function tests and other components of the liver function tests, PTH, 24-hr urine calcium, 25-OH and 1,25-(OH)2 vitamin D levels were normal. Her bone alk phos was found to be high at 79% (28-66%); bone turnover markers CTx and NTx were also elevated. Her FGF-23 was elevated at 400 RU/ml (<180). An octreotide scan and FDG-18 PET-CT did not reveal any suspicious masses. Genetic testing of the PHEX gene revealed somatic mosaicism for the W456R variant, which has not been reported in the literature. The patient was then diagnosed with X-linked hypophosphatemic rickets and treated with phosphorus supplementation and calcitriol, with some improvement in energy and pain, and normalization of alk phos levels. She has not had another fracture since.

Discussion: In patients with a history of multiple fractures or surgical revisions, causes of bone fragility other than osteoporosis should be suspected. Alk phos and serum phosphate levels are important clues in evaluating for other disorders of bone mineralization. Although uncommonly diagnosed in adults, X-linked hypophosphatemic rickets (reported in 1 of 20,000 births) can still be present and treated. Medical therapy has not yet been proven to cause bone strengthening, but newer therapies- like the FGF-23 antibody- may provide better outcomes in the future.

Conclusion: Less common metabolic bone disease like X-linked hypophosphatemic rickets should be suspected in adult patients with a history of multiple fractures and with abnormal alk phos levels.
**Abstract #620**

**WHY IS THE CALCIUM SO HIGH?**

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**Objective:** Hypercalcemia is a very common reason for a patient to be referred to endocrinology. However the differential can be very vast and includes some very rare causes.

**Case Presentation:** A 78 year old female with a history of fallopian tube malignancy in 2007 which was cured was sent to endocrine due to hypercalcemia of undetermined etiology. The patient was on multiple supplements for a long time but stopped them all about one year back. The patient received a dose of pamidronate IV prior to the endocrine referral, which helped in lowering the calcium levels. She had no obvious complaints. The physical exam was unremarkable.

Significant labs were a serum calcium level of 15.6 mg/dL (8.4-10.6), albumin 4.1 g/dl (3.2-5.5), creatinine 1.91 mg/dL (0.44-1.03), PTH 7.9 pg/mL (12-88), ACE level 91 U/L (9-67), Vitamin D being normal at 32 ng/mL, 1,25 Vitamin D >190 pg/mL (15-75), and PTHrp was 2.9 pmol/L (0.0 - 3.4 ). The DXA was normal.

With the above labs, no clear etiology could be discerned for the hypercalcemia but the differential included vitamin D toxicity vs sarcoidosis vs undetermined malignancy. Hence she underwent a bone marrow biopsy which showed Large B-cell lymphoma, with extensive involvement (80%) of the bone marrow cellularity. Based on the above results she received chemotherapy with cyclophosphamide, doxorubicin, rituxan and vincristine. The patient responded well to treatment and on the most recent labs the renal function and calcium levels normalized.

**Discussion:** This case demonstrates the rare occurrence of hypercalcemia with a B cell lymphoma. There are only a few cases reported in the literature and hypercalcemia was usually associated with poorer prognosis although this patient has done well.

**Conclusion:** Thorough work up for hypercalcemia is always necessary to identify rare causes.

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**Abstract #621**

**PRIMARY HYPERPARATHYROIDISM ON THE TEXAS-MEXICO BORDER: WHAT IS THE MOST COMMON PRESENTATION?**

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Texas Tech University Health Sciences Campus

**Objective:** In most of the developed world, primary hyperparathyroidism has evolved from a disease of “bones, stones and groans” to a disorder than is asymptomatic in most patients. In most published studies, approximately 20% of patients undergoing surgery for primary hyperparathyroidism presented with symptoms such as nephrolithiasis, osteitis fibrous cystic and fragility fractures, and abdominal pain. The more common presentation of modern primary hyperparathyroidism is that of an incidentally noted lab abnormality. This study was undertaken to describe the clinical presentation of primary hyperparathyroidism in a county hospital in El Paso, Texas.

**Methods:** Retrospective review of a prospectively maintained database was performed. All patients who underwent surgery for primary hyperparathyroidism by a single surgeon between October 2013 and October 2015 were included in analysis. Information on clinical presentation, biochemistry including calcium, PTH and vitamin D, radiologic localization and pathology findings were recorded.

**Results:** Fourteen consecutive patients with primary hyperparathyroidism underwent surgery over the 2-year period. The mean age at presentation was 51.9±12.1 years and 85% of patients were female. A majority (92%) of patients presented with at least one symptom (nephrolithiasis, fragility fracture or abdominal pain). Fifty percent of patients had depression. The only patient that presented without symptoms was found to have MEN1 syndrome. Mean calcium levels was 12.0±1.27 mg/dl range 10.7-14.7 mg/dl (normal 8.5-10.1) and mean parathyroid hormone (PTH) level was 197.3+/-14.2 pg/mL, range 81.6-604 pg/mL (normal 14-72 pg/mL). Ninety-two percent of patients had preoperative localization by ultrasound and sestamibi scan that was confirmed operatively. Intraoperative and pathologic findings showed 78% (11/14) of patients had a single adenoma, 14% (2/14) of patients had hyperplasia (including one patient with MEN1) and 1 patient had a double adenoma. No biochemically persistent disease was detected on post-operative follow up and no recurrences have been detected, although not all patients have been followed for more than 6 months.
**Discussion:** A large proportion of patients undergoing surgery for primary hyperparathyroidism may present with symptoms of nephrolithiasis, abdominal pain, and/or bone disease in some populations. **Conclusion:** Further investigation is warranted to determine that factors that contribute to the preponderance of patients presenting with symptomatic primary hyperparathyroidism in the study population, which is no longer the typical presentation in most contemporary series in the literature.

**Abstract #622**

**UNRECOGNIZED MILD PRIMARY HYPER-PARATHYROIDISM AS A CAUSE OF NEONATAL HYPOCALCEMIA**

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Cooper University Hospital

**Objective:** To present a case of unrecognized mild primary hyperparathyroidism (PHPT) that led to neonatal hypocalcemia. **Case Presentation:** A 34-year-old obese female with history of insulin-requiring gestational diabetes during her pregnancy 1 year prior presented for concerns of feeling unwell. She complained of feeling shaky, weak, and dizzy after eating. She had no history of renal stones, abdominal pain, bone pain or fractures. Her physical exam was normal and all vital signs were stable. Laboratory evaluation showed a calcium of 10.3 mg/dL. In reviewing labs with the patient, she reported her baby had seizures in the first 5 days of life and was readmitted and treated for hypocalcemia. Further laboratory evaluation revealed repeat calcium of 10.3 mg/dL, parathyroid hormone (PTH) of 78 pg/mL, and 24 hour urine calcium of 618.5 mg/24 hours. A parathyroid sestamibi scan and ultrasound did not localize a parathyroid adenoma but exploratory parathyroid surgery identified a left inferior parathyroid adenoma which was removed. Her intraoperative PTH levels dropped by >50% following removal of the adenoma, calcium levels normalized post-operatively, and clinical symptoms resolved. **Discussion:** PHPT, a rare condition during pregnancy, is most commonly caused by a single parathyroid adenoma. As much as 50% of PHPT in this population is frequently undiagnosed and associated with high rates of serious maternal (67%) and fetal (80%) complications. Most patients remain asymptomatic due to early disease, decreased total serum calcium levels due to utilization by the developing fetus, and the physiologic hyperalbuminemia of pregnancy. The fetus is maintained at a hypercalcemic state relative to the mother which inhibits development of the fetal parathyroid glands. When calcium efflux stops after delivery, the newborn may develop hypocalcemia due to hypoparathyroidism, usually presenting 5–14 days after delivery as seizures or tetany. In most cases of neonatal hypoparathyroidism caused by maternal PHPT, mothers have mild unrecognized hypercalcemia. In those with symptoms, clinical expression varies and signs may be nonspecific and misinterpreted as related to pregnancy. Once diagnosed, parathyroidectomy is the only recommended and definitive therapy for these patients. **Conclusion:** Neonatal hypoparathyroidism can be the first clue to detecting maternal PHPT and should prompt investigation of hypercalcemia in the mother as even mild PHPT can cause serious hypocalcemia in the neonate. This is important to prevent complications during future pregnancies. Approaching the case in a multidisciplinary fashion can be beneficial.

**Abstract #623**

**UTILIZATION AND COST OF ANTI-OSTEOPOROSIS THERAPY AMONG US MEDICARE BENEFICIARIES (2013)**

Smita Jha, MD, Timothy Bhattacharyya, MD

NIH

**Objective:** Osteoporosis is a major global problem with osteoporotic fractures posing a potentially avoidable burden on our already constrained healthcare resources. Given the availability of diagnostic tools and effective therapy to treat osteoporosis and prevent fractures, there is increasing emphasis on its early diagnosis and treatment. We studied the utilization and cost of anti-osteoporotic therapy to help understand the prescription practices of such therapy using the Part D Prescriber Public Use File produced by the Centers for Medicare & Medicaid Services with information on prescription drug events (PDEs) incurred by Medicare beneficiaries with a Part D prescription drug plan for the year 2013. **Methods:** Descriptive data were produced from Microsoft Excel and SPSS. **Results:** Our results showed that primary care providers account for over seventy-five percent of the prescriptions for anti-osteoporotic therapy with participation from physicians from several specialties like oncology, gynecology, orthopedic surgery, rheumatology and endocrinology engaged in care of patients with osteoporosis. Bisphosphonates particularly alendronate were the maximally utilized drugs despite the availability of several recently approved drugs in the market for the treatment of osteoporosis. In terms of cost, Medicare spent over 610 million dollars on anti-osteoporotic drugs in 2013.
with majority of the cost being accounted for by a small number of brand name drugs. We noted that orthopedic surgeons and gynecologists were more likely to prescribe brand name drugs unlike primary care doctors who mostly prescribed generic drugs. 

**Conclusion:** Our study shows that Primary Care Doctors are the largest prescribers of anti-osteoporotic therapy reinforcing need for continuing medical education and training to improve the identification and management of osteoporosis. Alendronate is the maximally utilized anti-osteoporotic therapy likely because of its low cost. A small number of prescriptions for brand name drugs account for majority of the cost of anti-osteoporotic therapy. Participation from physicians from multiple other specialties in the management of osteoporosis is duly noted though the appropriateness of these prescriptions needs to be further studied.

**Abstract #624**

**SEVERE REFRACTORY HYPOCALCEMIA FOLLOWING ADMINISTRATION OF DENOSUMAB IN METASTATIC PROSTATE CANCER**

Natalia Chaar Tirado, Sandeep Dhindsa, MD

TTUHSC

**Objective:** We present a case of severe refractory hypocalcemia following administration of a single dose of denosumab in a patient with metastatic prostate cancer. 

**Case Presentation:** 64 y/o Caucasian male diagnosed 1 year ago with metastatic prostate cancer s/p prostectomy (Gleason score 7) was admitted with congestive heart failure and hypocalcemia. He complained of muscle weakness and paresthesia of hands and feet. Chvostek’s and Trousseau’s signs were negative. EKG showed QT interval prolongation. Corrected calcium on admission was 6.0mg/dl (8.5-10.1), creatinine 2.3mg/dl (0.6-1.3), magnesium 2.7mg/dl (1.8-2.5), and phosphorous 3.4mg/dl (2.3-7). Four days prior to admission, patient had been seen by his oncologist who started him on leuprolide and denosumab for osteoblastic bone metastasis, after pretreatment with bicalutamide. Laboratory results prior to denosumab administration: corrected calcium 8.6mg/dL, creatinine 1.9mg/dL, alkaline phosphatase 286U/L (46-116U/L) and PSA 59.6ng/mL (0.0-4.0ng/mL). On the 11th day of hospitalization, endocrinology was consulted due to refractory hypocalcemia inspite of intravenous and oral calcium replacement. Laboratory results showed corrected calcium 6.4mg/dL, ionized calcium 0.79mmol/L (1.1 – 1.3), creatinine 1.6mg/dL, magnesium 2.3mg/dL, phosphorus 2.5mg/dL, PTH 442pg/mL (12-88), vitamin D 24ng/dL (30-100), and urine calcium less than 1.0mg/dL.

Intravenous calcium gluconate and oral calcium carbonate were progressively increased and calcitriol 0.25 mcg oral twice a day was added. Cholecalciferol 50,000 units daily for 3 days and magnesium oxide 400 mg PO twice a day were also given. After 22 days patient was discharged home on calcitriol 0.5 mcg twice a day and calcium carbonate 4 g four times a day. His corrected calcium was 9.2mg/dl, ionized calcium 1.09mmol/L, creatinine 2.1mg/dl and PTH 361pg/mL. Magnesium and phosphorous were normal.

**Discussion:** Denosumab administration can cause severe hypocalcemia in patients with metastatic prostate cancer. This usually occurs in the setting of renal failure or vitamin D deficiency. The degree of hypocalcemia has also been linked to severity of the tumor burden, reflected by alkaline phosphatase and PSA levels. The cause of hypocalcemia in our patient was likely suppression of osteolysis by denosumab in the setting of advanced osteoblastic metastatic disease.

**Conclusion:** This is the first case report of severe hypocalcemia following a single dose of denosumab administration in a patient with metastatic prostate cancer without the presence of renal failure or vitamin D deficiency. Aggressive calcium and vitamin D intake may be necessary with denosumab therapy in patients with advanced metastatic prostate cancer.

**Abstract #625**

**IMPLICATIONS OF DELAYED SURGICAL INTERVENTION OF HIP FRACTURES ON MORBIDITY AND IN-HOSPITAL MORTALITY: A RETROSPECTIVE OBSERVATIONAL STUDY**

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Eastern Virginia Medical School

**Objective:** Hip fractures in the elderly are associated with significantly diminished and often permanently decreased quality of life as well as increased mortality. Although most patients require surgery, it remains controversial as to timing of the procedure. Surgeons in favor of immediate repair believe the decreased bed rest minimizes associated complications. Those favoring delayed procedures argue that it allows for optimization of the patient prior to surgery. Current guidelines from the American Association of Orthopedic Surgeons favor repair within the first 48 hours of injury. Due to the varied opinions and evidence, the objective of this study is to determine the impact of delayed repair beyond 48 hours on morbidity and mortality in the population of Southeast Virginia.

**Methods:** De-identified data was obtained through Virginia Health Information (VHI) and included 7,398 patients.
admitted with a diagnosis of hip fracture or osteoporotic hip fracture based on ICD-9 codes that were treated at 1 of 19 hospital locations in Southeastern Virginia from 2008 to 2014. Parameters examined include demographics, admission information, type of fracture and repair, cost of care, and outcomes including in-hospital mortality rates and average length of hospital stay (LOS) of patients that were repaired within 48 hours of presentation compared to those with delayed surgical repair after 48 hours.

**Results:** Of those who underwent surgical repair for a hip fracture (n=7,203), 77.2% (n=5,558) received surgery within 48hrs. Early surgical intervention was associated with a 1.8% mortality rate (n=100). Whereas those that received delayed repair of their fracture greater than 48 hours(n=1645) had a 4.1% mortality rate. Fisher exact testing revealed a statistically significant difference with a p-value < 0.0001. In addition patients that received their surgery within 48 hours averaged a LOS of 4.88+/-.0.4 days vs. those with delayed repair had a hospital stay of 7.81+/-.0.13 days (p<0.0001). Financial implications of delayed repair included an average cost of USS46,084+/-.758 vs. an average cost of USS37,573 +/- 408 if repaired in the first 48 hours (p<0.0001).

**Conclusion:** Delayed surgical intervention for hip fractures beyond 48 hours is associated with significant increases in length of hospital stay, cost of care, and a 2.3X increased risk of mortality. While this study is unable to ascertain whether surgery was delayed because of patient or surgeon preference, the patient’s medical conditions or to optimize the patient for surgery, nevertheless there was a significant difference among many variables including age, cost of care, LOS and mortality emphasizing need for early surgical intervention.

**Abstract #626**

**SEVERE HYPERCALCEMIA AS A RARE COMPLICATION OF BUTTOCK AUGMENTATION**

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**Case Presentation:** The overwhelming majority of patients with hypercalcemia present with one of the three major causes of elevated calcium: hyperparathyroidism, malignancy or medications. Hypercalcemia due to granulomatous reaction is a more rare complication, but an important differential in diagnosis. Calcitriol induced hypercalcemia secondary to granuloma formation is a well-known entity in sarcoidosis, tuberculosis and some fungal infections. Reactions to silicone implants used in cosmetic surgery can also cause a granulomatous reaction and lead to hypercalcemia, particularly in setting of renal compromise. Foreign objects (mostly silicone implants) used for cosmetic breast and buttock enhancements can often elicit granulomatous reaction many years after initial surgery. The macrophages residing in the granulomas produce 1 alpha hydroxylase which converts 25-hydroxy vitamin D to 1, 25-hydroxy vitaminD3 leading to hypercalcemia.

A 43 year old female presented with severe hypercalcemia with calcium levels of 14-15mg/dl (normal <10.2 mg/dl) incidentally found during clinic visit. She was completely asymptomatic and was admitted on multiple occasions with hypercalcemia and responded to fluids and pamidronate. Workup revealed a parathyroid independent process of unclear etiology. She did not take any calcium containing supplements or medication. The degree of hypercalcemia led to suspicion of malignancy, but mammogram, Computer Tomography (CT) neck, bone marrow biopsy and bone survey did not show any abnormalities. Laboratory analysis revealed an elevated 1,25-hydroxy vitamin D level, with low 25-hydroxy vitamin D , low angiotensin converting enzyme along with a suppressed parathyroid hormone. A high normal parathyroid hormone related peptide led to further imaging and an abdomen pelvic CT scan showed multiple granulomatous reactions in the buttocks. The patient was asked about previous surgery and patient explained she had multiple injections of silicone into the buttocks 10 years prior.

**Conclusion:** This case demonstrates persistent hypercalcemia from granulomatous reaction to foreign body implants years ago in asymptomatic woman with no local complications. In view of increasing use of augmentation surgeries for cosmetic purposes, surgical history in regards to cosmetic procedures is important in the evaluation of rare causes of hypercalcemia.

**Abstract #627**

**RISK OF FALL-RELATED HIP FRACTURE IN DIABETES**

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Eastern Virginia Medical School

**Objective:** Hip fractures are among the important preventable causes of morbidity and mortality in the elderly population. The most important preventable risk factors of hip fractures include falls and osteoporosis. Despite having a higher bone density, patients with diabetes have higher risk of hip and proximal humerus fractures. This study examines the direct cost, morbidity and mortality of hip fractures and the risk of fall-related hip fractures in the diabetic population. The proximal femur is the third most
common location associated with osteoporosis, comprising 14% of the total osteoporotic fractures. Despite that, they represent 72% of the estimated 72 billion dollars of total medical care costs for pathologic osteoporotic fractures. Hip fractures have been associated with a 1-year mortality rate approaching 30% and significant morbidity and loss of function.

**Methods:** A total of 7398 de-identified discharge records from 2008 through 2014 were obtained from Virginia Health Information database. The data included those admitted with a diagnosis of hip fracture or osteoporotic hip fracture and comorbid conditions based on International Classification of Diseases-9 (ICD-9) codes admitted to 19 hospitals in Southeastern Virginia. Parameters examined include basic demographics, admission details, type of fracture and repair, pre-operative length of stay (LOS), mortality overall and in relation to pre-op LOS, cost of care, and disposition. We did not collect laboratory or bone densitometry data.

**Results:** Of the 7398 patients with hip fractures, 6079 (82%) were elderly. 67.7% (n=5011) were female and 32.3% (n=2387) were male, with 80.1% of the population being Caucasian. 5556 (75%) total patients developed fractures as the result of falls and 4972 (89%) of falls were in patients 65 years old or older. The average total cost of care per patient in the 19 locations was $36,973.93. 67.3% (n=4981) were discharge to a skilled nursing facility and overall mortality rate in patients ≥ 65 years old was 2.96%. Diabetes was present in 23.2% (n=1717) of the population. The relative risk of fall related hip fracture in diabetes was 1.97 (p<0.0001) at the 95% confidence interval (1.683 to 2.3264)

**Conclusion:** Osteoporotic hip fractures pose a serious health concern for the elderly and a huge financial burden on healthcare systems. With a progressive increase incidence of diabetes and related complications, fall related fractures become an important issue to contend with. Furthermore, the notion that diabetes related complications are limited to macro and microvascular pathology needs to be dispelled. This study highlights the need to direct more efforts to prevent hip fracture particularly in diabetics.

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**Abstract #628**

**HIGH INTAKE OF CARBONATED DRINKS AND FRAGILITY FRACTURES**

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**Objective:** We present a 37-year-old premenopausal woman who had suffered multiple fragility fractures. Her fractures included fracture of left 5th metatarsal bone in 2014 and right 5th metatarsal bone in 2000 occurring after trivial trauma.

**Case Presentation:** This patient was referred to us following her second fracture. Her past medical history was significant for mild bronchial asthma managed on salbutamol inhaler, hypertension and schizoaffective disorder. Her medications included Clonazepam, Duloxetine, Asenapine, Sodium valproate, Pantoprazole, Ramipril and Trazodone. She had never been on oral or inhaled corticosteroids. She had no history of other fragility fractures, epilepsy, cushing’s syndrome, height loss, back pain, secondary amenorrhea, malabsorption, hyperthyroidism, renal stones, rheumatoid arthritis, renal or liver failure. Her mother had fracture of metatarsal bone. She did not smoke or drink alcohol and denied using excess caffeine. She however, drank 6 bottles of diet coke (710 ml each) daily and this amounts to 4.2 liters of diet coke per day. Her dietary calcium intake was adequate.

On examination, there was mild kyphosis but no scoliosis or spinal tenderness were noted. Spinal movements were normal. The occiput to wall distance was 4 cm and rib-pelvic distance 4 fingers. Gait and balance were normal. There was no evidence of thyrotoxicosis. Systemic examination was unremarkable.

On laboratory work up, her calcium level was 2.35 mmol/L (2.15-2.60), serum phosphate 1.35 mmol/L (0.8-1.52), iPTH 5.4 pmol/L (1.2-8.2), 25-OH-vitamin D low at 45 nmol/L (75-250), TSH 1.70 mu /L (0.3-4.0), prolactin 18 mcg/L (4-24) and FSH was 5 IU/L (2-11). Liver and renal function tests were normal. Bone mineral density was normal with an Z score of +1.0 at the lumbar spine and +2.4 at the femoral neck.

**Discussion:** This patient was assessed with regard to fragility fractures. Her bone mineral density was normal. The following things may have contributed to the fractures. 1) Vitamin D insufficiency which was corrected 2) Use of sodium valproate and pantoprazole - started recently. 3) However, excessive use of carbonated drinks, 4.2 L/day stood out. Excess cola consumption is linked to osteoporotic fractures and low BMD. Potential causes of fractures include hypercalciuria, excess caffeine,
high phosphorus content and increased phosphorus bioavailability. Our report highlights the occurrence of fragility fractures possibly due to cola intake in a premenopausal woman with normal BMD.

Conclusion: We report a potential causal association between excess intake of carbonated drinks and fragility fractures in premenopausal women.

Abstract #629

HYPOPARATHYROIDISM AS A CAUSE OF SEVERE HYPOCALCEMIA IN A MALE NIGERIAN: NEED FOR MULTI-DISCIPLINARY APPROACH

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Objective: To highlight a rare finding of severe hypocalcaemia due to Hypoparathyroidism following extended laryngectomy; need for multidisciplinary approach.

Case Presentation: Patient is Mr A.M, a 50 year old Nigerian male muslim artisan, a known patient of the ear, nose and throat (ENT) unit previously managed for hoarseness but defaulted clinic 2 years ago. He represented to emergency department with worsening hoarseness of voice and recurrent difficulty with breathing of two months duration. Full workup done Shows transglottic tumour involving the right hemilarynx on CT scan and samples taken after laryngoscopy for histology showed squamous papilloma. Extended laryngectomy (total thyroidectomy and parathyroidectomy) was done.

Four days post operation, he complained of general discomfort and tingling in all the limbs. Due to worsening of symptoms, the endocrine unit was invited to review after ten days post-op. General examination revealed restless man, chvostek’s and trousseau’s sign positive. Investigation revealed anaemia (PCV 21%), leucocytosis with Neutrophilia and lymphopenia, hypokalaemia (2.2mmol/l), hypocalcaemia (ranges from 3.9-7.6mg/dL), hypoalbuminemia (20g/l), ECG shows prolonged QT interval.

A diagnosis of severe hypocalcaemia due to Hypoparathyroidism following laryngectomy was made. He was treated with multiple intravenous calcium and magnesium, oral calcium, and calciotrol. He received oral thyroxine and eventually had about 25 sections of radiotherapy.

Discussion: Surgery (total laryngectomy) is one of the causes of hypoparathyroidism which is preventable. Early preoperative work and multidisciplinary involvement will most likely prevent life threatening severe hypocalcaemia seen in this index patient. There is the possibility that this patient had a prior hungry bone syndrome due to osteoblastic effects of the metastasis which cannot be substantiated.

Conclusion: Severe hypocalcaemia in a hypoparathyroid person is preventable if this complication is anticipated with involvement of different expertises.

Abstract #630

PRIMARY HYPERPARATHYROIDISM PRESENTING WITH SECONDARY HYPOKALEMIC PERIODIC PARALYSIS AND SEVERE MULTIPLE LIFE THREATENING DYSELECTROLYTEMIA [HYPERPARATHYROID CRISIS]

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Objective: Challenging rare presentation of primary hyperparathyroidism with secondary hypokalemic periodic paralysis and life threatening multiple dyselectrolytemia, fully reversed with curative parathyroid adenomectomy.

Methods: 40 y male, 7 day fever, rapid weakness, inability to walk, slow irrelevant speech, drowsiness, disorientation, PR 110, BP 130/70, proximal and distal muscle weakness, ECG U waves, S potassium 2.4 mEq/L, S sodium 139, S creatinine 1.3 mg/dl, MRI brain-spine, CSF normal; S Calcium 22.1 mg/dl, S Phosphorus 1.9, S Alkphos 497 U/L[53-128], S PTH 2323 pg/ml[15-65], S magnesium 1.8, S 25OH Vitamin D 10 ng/ml. Complications: a. cardiac arrhythmia[PSVT]; b. bradycardia, hypotension, AV dissociation; c. severe hypernatremia [S Sodium 164]; d. S Creatinine 1.9; d. rhabdomyolysis S CPK 884 U/L(0-226)]. US: Mass right thyroid lobe 30x26x48 mm.

Case Presentation: Treatment: IV fluids, potassium, bisphosphonate, glucocorticoid, furosemide, magnesium. Surgery: Right hemithyroidectomy, parathyroid adenectomy, neck dissection; HPE:Parathyroid adenoma, no capsular vascular invasion, lymph nodes no metastasis. Post-op day 4: S Calcium 8.4, S Phosphorus 2.3, S Sodium 144, S Potassium 3.0, S Magnesium 1.8,
S Creatinine 1.4. Tc99mMDP Bone scan: Diffuse uptake calvarium, mandible, long bones upper/lower limbs, ribs, right iliac crest. PET CT Ga68 Dotanoc: 32X17 mm lytic lesion right iliac bone brown tumor; no metastases. 7 months: S Calcium 10.1, S Phosphorus 3.9, S PTH 35, S Sodium 141, S Potassium 3.9, S Creatinine 0.9. US: Bilateral renal calculi; BMD Z Scores: Improvement ++.

Discussion: Besides hypercalcemia and hypophosphatemia, other fluid and electrolyte abnormalities in primary hyperparathyroidism include hypokalemia [acquired renal tubular acidosis and renal potassium wasting secondary to hypercalcemic nephropathy] and, hypomagnesemia [with critical cardiac arrhythmias], nephrogenic diabetes insipidus [due to hypercalcemia, aggravated by hypokalemia], hyponatremia etc.

Conclusion: Hypokalemia is a potentially life-threatening abnormality in patients with hypercalcemia. [Prevalence of hypokalemia in hypercalcemia [no renal dysfunction/drugs]: Overall 32%; malignancy hypercalcemia 52%; primary hyperparathyroidism 17%, with degree and frequency of hypokalemia greatest at the higher serum calcium levels; Ann Intern Med. 1977 Nov;87(5):571-3]. The presence of hypokalemia must be considered when treating severe hypercalcemia; otherwise, vigorous use of diuretics may result in profound hypokalemia and tachyarrhythmias. Whether our patient has an underlying subclinical periodic paralysis associated [sodium / calcium] channelopathy, needs to be investigated?

Abstract #631

THE INCIDENCE AND RECOGNITION OF PRIMARY HYPERPARATHYROIDISM IN PATIENTS REFERRED FOR BONE MASS DENSITOMETRY.

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Objective: The diagnosis of primary hyperparathyroidism (PHPT) is under-recognized the general population. We explored the incidence and recognition of PHPT in patients who undergo bone mass densitometry (BMD), a population we hypothesized is at higher risk.

Methods: Patients with available outpatient laboratory studies who underwent BMD in 2012 within a tertiary care hospital system were sampled randomly. Classic PHPT was defined as calcium level ≥10.5 along with parathyroid hormone level (PTH) ≥60. Additional patients were defined as having hypercalcemia when calcium was ≥10.2 and were felt to have suspicion for PHPT if concomitant PTH was ≥40. Medical records were reviewed for data to support or refute the diagnosis of PHPT and for documentation of surgical referral. Bone loss was defined as osteopenia or osteoporosis based on World Health Organization BMD criteria. Statistical analysis was performed with JMP Pro 10.

Results: The sample included 757 patients, median age was 65 (range 17-96), and 90% were female. Of the 15% of patients found to have hypercalcemia, only 48% had a PTH measured. In these patients, the incidence of classic PHPT was 4.4%, with an additional 4.4% having suspicion for PHPT. Excluding the patients with classic PHPT, medications that could interfere with the diagnosis of PHPT were present in 50% of patients with suspicion for PHPT and 36% of patients with hypercalcemia. Susicion for PHPT was present in 5.2% of patients with bone loss compared to 2.7% of patients with normal BMD. Twenty-two patients with twice-documented hypercalcemia did not undergo PTH testing even though 59% had bone loss. Furthermore, classic PHPT was present in 1.4% of patients with normal BMD, 2.5% with osteopenia, and 3% with osteoporosis (p=0.5). On logistic regression analysis, decreasing T-scores of the spine, hip, and femur were associated with an increased risk of classic PHPT (all sites p<0.05). Only 25% of patients with classic PHPT were referred to a surgeon (median age was 65; bone loss was present in 75%), and no patient with suspicion for PHPT or hypercalcemia was referred.

Discussion: The population of patients referred for BMD is at high risk for PHPT and the risk increases with worsening bone loss. The incidence of PHPT is suspected to be even higher considering that many patients had incomplete investigations and/or were taking medications that potentially mitigated lab values.

Conclusion: These findings suggest that screening serum calcium should be recommended in all patients undergoing BMD. If discovered, hypercalcemia warrants a comprehensive investigation into PHPT including medications that affect the diagnosis and delay surgical consultation.
Screening for Bariatric Surgery: Are We Doing a Good Job?

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Objective: To raise awareness over the necessity to discuss Bariatric Surgery with patients having a Body Mass Index (BMI), between 35 and 40 with hypertension, diabetes, hyperlipidemia, or obstructive sleep apnea (OSA), or a BMI ≥40, regardless of other comorbidities.

Methods: Using HERON database, we created a search query of patients who met the screening criteria for bariatric surgery from the outpatient clinic during the year 2014. Our independent variables included predisposing characteristics: sex, age, race, and marital status, enabling characteristics: being seen by Family Medicine or Internal Medicine Physicians. These variables were then analyzed through RedCap database.

Results: Among 42710 patients with BMI>40, 1013 (2.3%) were screened for Bariatric Surgery. Among 34,283 patients with BMI between 35 and 40 who were eligible for screening, 5400 patients (15.8%) were screened by an Internal Medicine Physician as compared to 1281 patients (3.7%) screened by a Family Medicine Physician. 66% were females; the mean age was 57 years old. Among those screened, 72% were Caucasians and 58% were married.

In regards to co-morbidities with 35≤BMI<40, 613 patients out of 30459 patients (2%) with hypertension were screened. Only 87 patients out of 4497 patients (1.9%) with hyperlipidemia were screened. 350 patients out of 15502 patients (2.25%) with DM were screened. 350 patients out of 3496 patients (10%) with OSA were screened.

Discussion: Only 16.15% of the patients who were eligible for Bariatric Surgery were actually screened, it appears that there is an inadequate awareness over the importance of Bariatric Surgery which could be influenced by various factors such as age, sex, marital status, race, co-morbidities, financial status, or insurance issues.

Females constituted the majority of those screened which could be related to their increased health awareness, better overall compliance, and concern for body habitus; Caucasians were also more likely to be screened: factors such as insurance, financial situation and compliance could be playing a role. In addition, middle-aged people had higher chances to be screened possibly because they are more likely to benefit from surgery as compared to the younger population, who should focus on lifestyle changes, and the older population where the risks of Bariatric surgery outweigh its benefits. Married patients are probably more concerned about weight related problems as compared to single patients.

Conclusion: Screening for Bariatric Surgery among those who satisfy the screening criteria should improve with raising the necessary awareness among Primary Care Physicians. This important issue can greatly reduce morbidities and mortalities among our patients.

A Retrospective Analysis of the Impact of Weight Loss on Renal Function

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Objective: Approximately 66% of Americans are overweight with approximately half classified as obese. Obesity is associated with increased morbidity and mortality and is an independent risk factor for the progression of chronic kidney disease. Weight loss is correlated with improved renal function and reductions in obesity related glomerulonephropathy. This study investigated the effect of a medically supervised weight loss program on renal function among program participants at baseline and following 12 weeks of therapy.

Methods: This study was a retrospective analysis of adult patients voluntarily enrolled in a physician-directed community-based weight management program from 2009 to 2014. Patients consumed at least 800 kilocalories per day, attended weekly behavioral education classes, and expended approximately 300 kilocalories per day in physical activity. The primary outcome of improved renal function was assessed by comparing weight loss and GFR. Secondary outcomes included changes in fasting blood sugar, HbA1c, total cholesterol, LDL, HDL, triglycerides, systolic blood pressure, and the number of diabetic and anti-hypertensive medications.

Results: A total of 71 patients with an average weight of 286 pounds, BMI of 53, and baseline GFR of 29 were included. Following 12 weeks of therapy, 80% of participants improved in stage, 19% remained within the same stage, and 1% progressed to a higher stage (p=0.017). Analysis revealed a positive correlation of 0.29 between weight loss and GFR (p=0.029). Approximately 64% of patients required fewer anti-hypertensive medications and 83% of patients required fewer diabetic medications.

Discussion: Results obtained from this study indicate that weight loss is associated with improved renal function and increased GFR. The majority of patients within the program experienced improvements in chronic kidney disease stage. Analysis of secondary outcomes resulted in improvements in HbA1c, blood pressure, LDL, total cholesterol, and triglycerides. The majority of patients within the study
required fewer diabetic and antihypertensive medications following weight loss.

**Conclusion:** Organized weight loss programs are a viable treatment modality for prevention of co-morbid disease progression. This study indicated a positive correlation between weight loss and improved renal function, with the majority of participants exhibiting an improvement in chronic kidney disease stage. When controlling for both diabetes and hypertension, the effect of improved renal function with weight loss persisted.

**Abstract #702**

**EFFECTS OF HELICOBACTER PYLORI ERADICATION ON INSULIN RESISTANCE, ANTHROPOMETRIC, AND METABOLIC PARAMETERS: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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**Objective:** Helicobacter pylori (Hp) infection is shown to contribute to atherosclerosis and cardiovascular disease. Moreover, many studies have revealed a close relationship between Hp, insulin resistance, and altered metabolic parameters. However, studies that assessed effect of Hp eradication on those conditions revealed conflicting results. Thus, we conducted a systematic review and meta-analysis to evaluate the impact of Hp eradication on insulin resistance, anthropometric measurement, and metabolic parameters.

**Methods:** A comprehensive search of the databases of the Cochrane Central Register of Controlled Trials, MEDLINE and EMBASE was performed from their dates of inception to November 2015. The inclusion criterion was the interventional trials’ assessment of the impact of Hp eradication in Hp-infected adults. Primary outcome was homeostatic assessment of insulin resistance (HOMA-IR) comparing between the treatment group versus Hp infected controls who did not receive eradication. Secondary outcome was change in body weight (BW), body mass index (BMI), lipid profiles, and fasting blood glucose (FBG) after treatment. We reported the pooled mean difference and its 95% confidence interval (CI) of a change in outcome using a fixed effects model if I²<50% and a random effects model if I²≥50%. The between-study heterogeneity of effect-size was quantified using the Q statistic and I².

**Results:** The initial search yielded 331 articles. Ten articles underwent full-length review and data was extracted from six prospective interventional studies. Follow-up duration after Hp eradication ranged from 3 weeks to 1 year. There was no difference of HOMA-IR after Hp eradication with pooled MD of -0.52 (95% CI -1.47 to 0.42, I²=97%) in treatment group comparing to controls. Hp eradication significantly increased BMI (MD=0.36, 95% CI 0.11 to 0.60, I²=71%) and BW (MD=1.1, 95% CI 0.8 to 1.5, I²=23%). However, no significant changes of TG (MD=−5.0, 95%CI -23.8 to 13.9, I²=89%), LDL-cholesterol (MD=−4.5, 95% CI -11.3 to 2.2, I²=91%), HDL-cholesterol (MD=1.1, 95%CI -0.9 to 3.1, I²=87%), and FBG (MD=−0.2, 95% CI -2.7 to 2.4, I²=92%) were observed.

**Discussion:** Although Helicobacter pylori is associated with insulin resistance and change in metabolic parameters, its eradication does not improve insulin resistance, lipid profiles, or blood glucose. In fact, higher BW and BMI was also observed in treatment group.

**Conclusion:** The effect of Helicobacter pylori eradication on the prevention of cardiovascular diseases and metabolic syndrome still remains inconclusive. More studies investigating these associations are needed.

**Abstract #703**

**GREATER METABOLIC RESPONSE TO EXERCISE IN SEDENTARY AGING VETERANS COMPARED TO OLDER VETERANS. THE POTENTIAL ROLE FOR INFLAMMATION.**

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**Objective:** The high prevalence of sedentary lifestyle is related to increasing trends in obesity, diabetes, metabolic syndrome, and cardiovascular disease, which can improve after intentional weight loss through improvements in lifestyle, physical activity and exercise. Our prior findings showed improvements in physical function and quality of life. However, analysis had not compared metabolic results based on age and inflammatory markers.

**Methods:** In a prospective quasiexperimental design, Veterans age 55 and older with overweight/obesity were offered participation in an evidence-based supervised exercise program (Enhance Fitness), who received standard of care management (MOVE Weight Management program). Participants received exercise interventions delivered by certified instructors, for one hour, three times per week. Physical and metabolic assessments were performed at baseline and 12 weeks after the intervention. This is a post-hoc analysis of 184 subjects who completed follow up. We censored 30 subjects with high-sensitivity C-reactive protein values above 10mg/L, likely consistent with acute inflammation. We hypothesized that obesity, inflammation, according to age and race/ethnicity, would
impact anthropometric and metabolic outcomes at follow up.

**Results:** The analysis included 154 subjects, 97.4% males, age 67.2±5.9 years, 41% white non-Hispanics, 35% African American, and 23% Hispanics. Their weight was 237.2±44.3lb, BMI 35.0±6.3kg/m². Comorbidities: type 2 diabetes (T2D) 60%, coronary artery disease 25%, Chronic Obstructive Pulmonary Disease 16%, prior stroke 8%, osteoarthritis 36%. Baseline hemoglobin A1c was 6.7± 1.1%, total cholesterol 172.4±40.9mg/dl, high-density lipoprotein (HDL) 44.9±11.0mg/dl, low-density lipoprotein (LDL) 99.7±34.9mg/dl, 25(OH) vitamin D 30.8±9.9mg/dl, thyroid stimulating hormone 2.2±1.4µIU/mL, Free T4 1.1±0.2mcg/dl, high-sensitivity C-reactive protein (hsCRP) 3.9±2.6mg/L. We found no differences according to weight/BMI, hsCRP or race/ethnicity, but found statistically significant greater improvement in HbA1c in participants age 55-64 (-0.34±0.2%) compared to older than 65 (-0.06±0.1%).

**Discussion:** There were no statistical differences in anthropometrics or cholesterol panel. The presence of inflammation in older adults may hinder potential benefits from exercise programs, while it may not impair benefits in aging Veterans.

**Conclusion:** Greater improvements in Hemoglobin A1c were found in aging veterans compared with older Veterans, upon addressing obesity, inflammation, and race/ethnicity. Further studies are required to address the impact from inflammation in the response to exercise programs in these populations.

**Abstract #704**

**IMPROVEMENT OF METABOLIC PARAMETERS OCCUR BEFORE OBTAINED FOR WEIGHT LOSS IN BEHAVIORAL AND NUTRITIONAL INTERVENTION AMONG FACTORY WORKERS**

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**Objective:** Overweight and obesity are problems of growing importance. Also in factory workers, an increase in the incidence of overweight and obesity has been observed. Therefore, a study to assess the effectiveness of a life style intervention program was conducted among factory workers.

**Methods:** Twentytwo employees, 15 men (68.2%) and 7 women (31.8%), were included in the 6 month study. Baseline characteristics: mean age 32.9 years, mean weight 76.2 kg, BMI 28.35 kg/m², blood pressure 115/79 mmHg, abdominal circumference 95.4 cm, fasting blood glucose 90.9 mg/dl, LDL cholesterol level 134.9 mg/dl, HDL cholesterol 47.41 mg/dl.

Group education was performed every two months, accompanied by individualized nutritional intervention using food records and carbohydrate counting. Added to this was physical activity in terms of aerobic exercise three times a week. Real-time consultation related to food intake and physical activity was provided using a whatsapp application.

**Results:** Regarding overweight and obesity, no significant improvements were achieved. A mean weight loss of 1.92 kg (p = 0.02), a decrease in the mean body mass index of 0.487 kg/m² (p = 0.25), a decrease in waist circumference of 0.63 cm (p = 0.423) were observed. Laboratory data, however, showed a decrease in mean fasting blood glucose (-3.7 mg / dl [p = 0.032]) and LDL (-6.81 mg/dl [p = 0.001]), and an increase in HDL (+1.41 mg/dl [p 0.047]).

**Discussion:** We argue that there are other influential factors such as the external environment outside the workplace which contributed to the significant parameter is not overweight and obesity before and after intervention. Some studies show the influence of spouses and family life within the parameters of the success of the repair is overweight and obesity. Behavioral interventions and nutrition conducted in groups with individual approach coupled with the modification of the work environment does not affect the grouping of overweight and obesity in general but found a decrease in mean body weight, body mass index, and waist circumference are also some improvements metabolic parameters such as fasting blood glucose levels, LDL cholesterol and HDL cholesterol. Some studies that have been done previously illustrate a significant reduction of all parameters of overweight and obesity.

**Conclusion:** Interventions were conducted in groups with individual approach in the workplace does not significantly improve the parameters of overweight and obesity but can improve metabolic parameters such as fasting blood glucose, HDL cholesterol and LDL cholesterol. We think that the improvement of metabolic parameters occur before obtained for weight loss.
Abstract #705

DRUGS CAUSING WEIGHT GAIN IN ADULTS REFERRED FOR WEIGHT MANAGEMENT: IMPLICATIONS OF THE 2015 AACE COMPREHENSIVE DIABETES MANAGEMENT ALGORITHM AND THE ENDOCRINE SOCIETY 2015 PHARMACOLOGICAL MANAGEMENT OF OBESITY GUIDELINE

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Objective: The 2015 AACE Comprehensive Diabetes Management Algorithm and the Endocrine Society 2015 Pharmacological Management of Obesity Guideline emphasize the use of antihyperglycemics which do not cause weight gain in obese adults with type 2 diabetes (T2D). Both guidelines also recommend considering weight effects when choosing medications to treat obesity-related co-morbidities. The goal of this study was to determine the prevalence of weight-gaining medication use in obese adults referred for weight management at a university hospital in Bangkok, Thailand.

Methods: In this cross-sectional study, anthropometry, co-morbidities, medication use, and laboratory data was recorded at each patient’s initial clinic visit between 2007-2014. Medications reviewed included antihyperglycemics, antihypertensives, antidepressants, antipsychotics, antiepileptics, systemic corticosteroids, and sex steroids.

Results: Of 529 patients (67.9% female, age 41.4±15.2 years, BMI 39.6±8.9 kg/m2), 60% (314/529) had a BMI 25-40 kg/m2, 28.2% had a BMI 41-50 kg/m2, and 12.5% had a BMI >50 kg/m2. A third had T2D (171/529) with HbA1c of 7.6±1.6% (n=115) and FPG of 160.3±50.3 mg/dL (n=149). One-third (60/171) of T2D patients received lifestyle modification alone while two-thirds (111/171) received medications for diabetes. Among T2D patients who received any diabetes medications, weight-gaining oral hypoglycemic agents (WGOHAs, i.e. sulfonylureas, pioglitazone, or both) were used in 42.3% (47/111). As for weight-neutral and weight-losing hypoglycemic agents, metformin was used in 83.8% (93/111), GLP-1 agonists in 3 patients (2.7%) and DPP-IV inhibitor in one patient (0.9%). Insulin was used in 18.9% (21/111), with 8.1% (9/111) receiving insulin in combination with WGOHAs and 11.7% (13/111) in combination with metformin. BMI did not differ between T2D patients who did or did not receive WGOHAs (p=0.13) or insulin (p=0.54), however FPG and HbA1c were significantly higher in those who received either WGOHAs (200.6±68.7 vs. 154.1±43.9 mg/dL, p=0.008 and 9.0±1.9 vs. 7.4±1.4%, p=0.002) or insulin (177.9±49.8 vs. 152.9±48.9 mg/dL, p=0.006 and 8.1±1.6 vs. 7.3±1.5%, p=0.01). Weight-gaining medications other than antihyperglycemics were prescribed in 13.6% (72/529) of the cohort, including beta-adrenergic blockers in 10.2% (54/529), systemic corticosteroids in 1.9% (10/529), tricyclic antidepressants in 1.1% (6/529), antipsychotics in 0.4% (2/529), and benzodiazepines in 0.4% (2/529).

Conclusion: In obese adults seeking obesity treatment, WGOHAs and other weight-gaining drugs were commonly used. Medication-related weight gain is an important contributor of obesity, thus the AACE Algorithm and the Endocrine Society Guideline are highly relevant in this setting.

Abstract #706

IMC IS STILL A VALID ADIPOSITY INDEX FOR CLASSIFICATION OF OBESITY IN THE WORLD-WIDE POPULATION OF THE XXI CENTURY?

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Objective: Obesity is defined as excess adipose tissue and body mass index (BMI) is one of the most used methods for diagnosis, however, it fails to differentiate between fat and lean mass. Recently a new entity was named to Normal Weight Obesity (NWO), defined as a BMI in the normal range associated with an increase in body fat. In this regard, recent studies consider the need to set new reference values cutoffs for the traditional BMI for early detection of overweight and / or obese. The objective of this study was improved the cutoffs points of the traditional classification of BMI for nutritional status and overweight/obesity in a Brazilian sample.

Methods: A cross sectional study was conducted with 1000 individuals, of both genders, aged between 18 and 60 years. The subjects underwent measurement of weight, height so that they can later be proposed new BMI cutoffs for detection overweight / obesity. For statistical analysis regarding will be used simple linear regression analysis and it will use the SAS software, version 9, and p <0.05 accepted as statistically significant.

Results: These results are preliminary with a sample so far 700 individuals (30.1% women and 69.9% men), mean age of 48.3 ± 14.8 years, weight 70.9 ± 17.0 kg, height 162.8 ± 9.3 cm, BMI 26.8 ± 6.0 kg/m2. As expected lower cutoffs were found for BMI than classic reference points traditionally adopted by WHO for the classification of
Obesity, 26.93 kg/m² and 27.41 kg/m² for obesity for men and women, respectively.

**Discussion:** Previous studies of this same research group with smaller sample sizes have suggested the adoption of cutoffs below 26.11 kg/m² and 25.3 kg/m² for men and women of the United States. Guptap and Kapoor (2012) proposed 22.9 kg/m² and 28.8 kg/m² for men and women of North India. While Ambrozi-Gómez et al. (2012) concluded that 29.0 kg/m² and 27.0 kg/m², respectively, would be more accurate cut points for men and women in Spain.

**Conclusion:** This study corroborates other studies in the literature, which converge in the sense of reducing the BMI cutoff points for classification of obesity. It is not that BMI is a useless index, but the nutritional status of the population has changed substantially from the time when it was developed to nowadays and it is necessary a review of its cut-off points for a larger number of individuals is contemplated in the obesity diagnosis respecting ethnic differences among populations.

Abstract #707

**DEPRESSION AMONG SECONDARY AND HIGH SCHOOLS STUDENTS AND ITS RELATIONSHIP TO BODY MASS INDEX**

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**Objective:** Several studies from different countries have shown an increase prevalence of obesity in the last recent years. In USA, data from 2003-2006 showed that the prevalence of obesity was 11.3% and that 31.9% were overweight among children aged 2-19 years. Childhood depression was associated with increased BMI percentiles in recent study.

**Methods:** A cross-sectional study that includes students from 14 different Secondary and High schools located in Taif city, Saudi Arabia between April 2014 and June 2015. 2 private and 12 public schools were included. Each student’s waist circumference (WC), height, and weight were measured by the researchers and body mass index (BMI) was calculated. We excluded any students with any chronic medical illness, existing psychiatric disorders and those with learning disabilities. Data about smoking and exercise were self-reported.

To screen for depression we used the validated Arabic Patient Health Questionnaire-9 (PHQ-9). We categorized them according to the PHQ-9 total score, <5 normal, 5-9 mild, 10-14 moderate, 15-19 moderately severe, and > 20 severe depression.

The primary outcome of the study is to assess the prevalence of depression among the participants as well as to assess the relationship between lifestyle habits and depression.

**Results:** Total of 450 students were included, 74.2% were male and 25.8% were female, mean age 15.28 years old (SD 1.62), mean BMI of 22.8 kg/m² (SD 6.14), mean WC 81.4 cm (SD 15), and the mean PHQ-9 score is 8.15 (SD 4.8).

27.1% of the students are underweight, 41.8% are normal weight, 18.7% are overweight, and 12.4% are obese. 7.4% were active smokers and 40.6% reports sedentary lifestyle. According to the PHQ-9; 21.6% are considered to be normal, 43.8% have mild depression, 25.5% have moderate depression, 5.7% have moderately severe depression, and 3.4% have severe depression.

Those who screened negative for depression have mean BMI of 23.7, compared to BMI of 22.53 for those with mild depression, compared to BMI of 22.1 for those with moderate depression, BMI of 23.23 for those with moderately severe, and BMI of 23.74 for those with severe depression (trend p 0.92).

When adjusting for age, type of school, grade, gender, WC and BMI, there was a significant negative partial correlation between depression diagnosis and smoking (r -.1, p 0.022), and between depression diagnosis and exercise (r -.083, p 0.046).

**Conclusion:** 43.8% of the students screened positive for mild depression and 34.6% screened positive for moderate/severe depression. No significant relation between BMI and depression were found. Significant negative partial correlation between the exercise and depression diagnosis.

Abstract #708

**RELATIONSHIP BETWEEN ANXIETY AND BODY MASS INDEX IN SECONDARY AND HIGH SCHOOLS**

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**Objective:** According to WHO in 2013, the number of overweight children under the age of 5 is estimated to be 42 million. As the prevalence of obesity increased, so did the prevalence of the comorbidities associated with it. Recent studies suggested that increased weight is significantly correlated with anxiety symptoms among adolescents. Few studies advised that obesity and emotional disorders may be more frequent in females.
**Methods:** A cross-sectional study that involves students from 15 different Secondary and High schools located in Taif city, Saudi Arabia between April 2014 and June 2015. 13 public and 2 private schools were included. Each student’s waist circumference (WC), height, and weight were measured by the researchers and body mass index (BMI) was calculated. We excluded any students with any chronic medical illness, existing psychiatric disorders and those with learning disabilities.

To screen for anxiety we used the validated Arabic Generalized Anxiety Disorder 7-item (GAD-7) scale. We categorized them according to the total score; <5 normal, 5-9 mild anxiety, 10-14 moderate anxiety, and >15 severe anxiety. The primary outcome of the study was to assess the prevalence of anxiety among the participated students as well as to assess the relationship between BMI and waist circumference and the GAD-7 score.

**Results:** Total of 511 students were participated, 77.3% were boys and 22.7% were girls, mean age 15.23 years old (SD 1.612), mean BMI of 22.1 kg/m² (SD 6.16), mean WC 79.4 cm (SD 15.5), the mean GAD-7 score is 5.79 (SD 4.4). 35.6% of the students are underweight, 36.8% are normal weight, 16.4% are overweight, and 11.2% are obese. According to the GAD-7 categories; 43.6% are considered to be normal, 38.6% have mild anxiety, 11.5% have moderate anxiety, and 5.1% have severe anxiety. 20.7% of the girls compared to 15.9% of the boys were considered to have moderate-severing anxiety (p 0.01).

Those who screened negative for anxiety have mean BMI of 21.3, compared to BMI of 22.7 for those with mild anxiety, compared to BMI of 22.6 for those with moderate anxiety, and BMI of 23.1 for those with severe anxiety (trend p 0.02).

Partial correlation between anxiety diagnosis/GAD-7 score and the waist circumference when adjusting for age, type of school, grade, gender and BMI showed non-significant negative correlation (for GAD-7 score r -.017, p 0.712) and (for anxiety diagnosis r -.036, p 0.428).

**Conclusion:** 55.2% of the students screened positive for anxiety, majority of them were mild. Those with higher BMI even at normal range were at higher risk of anxiety. Non-significant negative partial correlation between the waist circumference and anxiety.

**Abstract #709**

**OBESITY AWARENESS ASSESSMENT AMONG SECONDARY AND HIGH SCHOOLS STUDENTS.**

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**Objective:** Obesity is considered one of the fastest growing health problems in the modern world. In USA, 21-24% of American children and adolescents are overweight and another 16-18% is obese. A study that aims to identify parent’s awareness of obesity and overweight in their children, only 25% of them recognized their children overweight or obesity. Previous studies have demonstrated that in different developed countries, the majority of persons reveal limited data concerning obesity co-morbidities.

**Methods:** A cross-sectional study between April 2014 and June 2015, that includes students from 12 different Secondary and High schools located in Taif, Saudi Arabia. 1 private and 11 public schools were included. Each student’s waist circumference (WC), height, and weight were measured by the researchers and body mass index (BMI) was calculated. We excluded any students with chronic illness and those with learning disabilities. Dietary and lifestyle habits data were self-reported by the participants.

To assess the obesity awareness, we used the Obesity Risk Knowledge (ORK-10) Scale. Each of the 10 multiple choices questions that is answered correctly on the ORK-10 scale is equal to 1 point, the minimum score is 0 and the maximum score is 10. Those answered >5 questions correctly were considered to be aware.

The primary outcome of the study is to assess the prevalence of overweight and obesity among the participants, also to assess the relationship between the awareness level and BMI.

**Results:** Total of 528 students were included, 82.6% were male and 17.4% were female, mean age 15.58 years old (SD 1.8), mean BMI of 22.5 kg/m² (SD 6.75), mean WC 79.8 cm (SD 14.9), and the mean ORK-10 score was 6.92 out of 10. 83.3% of the students considered obesity as a disease. 33.5% of the students are underweight, 38.8% are normal weight, 15.5% are overweight, and 12.2% are obese. 32.7% reports drinking soda daily, 28.65% play video games daily, and 37.62% reports sedentary lifestyle (p 0.31).

According to the ORK-10, 25% were considered to be aware compared to 75% were considered to be unaware. Those who are aware have a BMI of 22.39 (SD 6.1) compared to BMI of 22.52 (SD 6.95) in those who are unaware (p 0.85). Compared to those who are unaware,
Abstract #710

LONG TERM OUTCOMES OF BARIATRIC SURGERY ON BONE DENSITY IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Objective: Previously, we have reported reduced total hip bone density in patients two years post-bariatric surgery related primarily to weight loss. We now report the long term (> 4 years) changes in bone mineral density (BMD) in patient with T2DM randomized to bariatric surgery (Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG)) from a randomized controlled trial.

Methods: Ten subjects (6F, mean BMI: 36.1 ± 2.5 kg/m², mean age: 46 ±7 years) with type 2 diabetes (T2DM) (mean baseline HbA1C: 9.7 ± 1.3%) were randomized to RYGB (n= 7) or SG (n=3). These patients underwent bone densitometry at the same institution for BMD at the total hip and lumbar spine at baseline, 1, 2, and at >4 years (median 6.5 years) following surgery.

Case Presentation: Mean BMI at the final follow up time point was 29.3 ± 2.5 kg/m2, with a mean total body weight loss of 21.9 ± 8 kg (~21%) from baseline. However, 4.8 ± 11 kg (~6%) weight regain was noted for the cohort between the 2 year post-surgical follow-up and the final DXA. Average HbA1C at follow-up was 6.5 ± 0.6%, with a mean reduction of 3.2 ± 1.5% from baseline. Significant decreases in total hip BMD were seen between all time points (all p<0.001), with a reduction of ~16% from baseline on the final DXA compared to a reduction of 11% from baseline seen at 2 year follow-up. The only significant changes in spine BMD were seen ~4 years after surgery (p= 0.009), with an average decrease in BMD of 7% at this site. Two of the 10 patients progressed to osteopenia 8 years following intervention, and one patient who had osteopenia at baseline progressed to osteoporosis on 2-year DXA. One patient who had osteopenia on their 2 year post-surgical DXA did not progress on DXA at 4 years. None of the patients experienced new fragility fractures after the start of weight loss intervention.

Conclusion: Reductions in both total hip and lumbar spine BMD after bariatric surgery appear to persist and may worsen beyond 4 years post-intervention, despite modest weight regain. Moreover, reduction in spine BMD may not be appreciated in the short term following intervention. The decline in BMD over long term follow-up was associated with progression to osteopenia and osteoporosis.

Abstract #711

MASSIVE ENLARGEMENT OF THE ABDOMEN AND MEDIASTINUM

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NIH

Objective: 1. To understand the concept of severe lipomatosis
2. To understand the complications of severe lipomatosis

Methods: A case review of a patient with severe lipomatosis. We described his clinical presentation and all the complications that he had.

Case Presentation: We report a case of a 58 year old morbidly obese male (BMI: 46 kg/m2) with past medical history of hypertension, hyperlipidemia, CAD s/p stent placement (9 years prior), diabetes mellitus type 2 and sleep apnea that was brought into emergency room (ER) for worsening shortness of breath. In the ER, he was having oxygen saturation of 65% and required intubation. Patient was afebrile, with a blood pressure of 115/64 mm Hg and a heart rate of 74 beats per minute. Labs from admission revealed a respiratory acidosis with normal renal and liver function. Trans-thoracic echocardiogram revealed normal ejection fraction and normal pulmonary pressure with no wall motion abnormality. CXR showed no infiltration or consolidation. CT angiogram (CTA) was done to rule out pulmonary embolism (PE). Though CTA was negative for PE, it was notable for large deposits of fat involving the abdomen and thorax, with invasion into the mediastinum and the space between the liver and diaphragm. Tissue was biopsied, which confirmed the diagnosis of fatty invasion.

Discussion: Isolated lipomatosis of the abdomen is a variant of an entity called Multiple Symmetrical Lipomatosis (MSL). MSL affects white men between 25 and 60 years old and is characterized by a collection of large non-encapsulated lipomas mainly located in the subcutaneous tissues of the cervical, deltoid, thoracic, abdominal and pelvic areas. MSL is also associated with dyslipidemia, impaired glucose tolerance, hyperuricemia, macrocytic anemia and peripheral neuropathy. Some theories mentioned that the fat deposition in the abdominal area could be somehow related to defective lipid mobilization in lipomatoses. Abdominal
Lipomatosis may involve small intestine, colon or arise in the mesentery. Pelvic lipomatosis has been reported more commonly in males. Symptoms include bladder dysfunction, constipation, vague abdominal discomfort or edema of the lower extremities.

**Conclusion:** Mediastinal lipomatosis is a benign cause of mediastinal widening. CT and MRI of the abdomen are very helpful in the diagnosis but tissue biopsy is what makes the final diagnosis. There is no definitive treatment; the recommendations are a healthy life style including low fat diet, abstinence from alcohol and exercise. In severe cases, surgery is recommended.

**Abstract #712**

**EFFECT OF TREATMENT WITH DEXTROAMPHETAMINE SULFATE UP TO 5 YEARS ON WEIGHT LOSS IN WOMEN UNABLE TO LOSE WEIGHT BY DIETING**

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**Objective:** One explanation for inability to lose weight despite proper eating habits may be fluid retention. There is evidence that an abnormality leading to increased capillary permeability, either related to an intrinsic capillary defect and/or hypofunction of the sympathetic nervous system, may lead to the development of edema. This seems to be related to the inability to adequately decrease capillary permeability related to the increase in hydrostatic pressure in the erect position. Dextroamphetamine sulfate, by stimulating the release of dopamine from sympathetic nerve fibers, diminishes cellular permeability. Studies have shown benefit of this treatment in causing weight loss in diet refractory patients. Most studies have been limited to a maximum duration of treatment of 1 year. The purpose of this study was to evaluate the effects of this treatment up to 5 years.

**Methods:** Women seeking help for inability to lose weight by dieting were started with 15mg dextroamphetamine sulfate extended release capsules as long as thyroid, adrenal, cardiac, renal, and hepatic etiologies were excluded. The dosage could be increased to up to 60mg/day.

**Results:** 45 were patients initially recruited; 6 months – 3 lost no weight but stayed in study because weight gain ceased. The remainder lost weight indicated as percentage of initial weight as follows: 1-4% - 8 (11.7%), 5-9% - 14 (31.1%), 10-19% - 20 (44.4%), 20-29% - 0. One year as follows – no weight loss – 3%, 1-4% – 13.3%, 5-9% - 15.6%, 10-19% - 51.0%, 20-29% - 15.5, 30-39% - 0%.

Two years – 0% - 2.2%, 1-4% - 13.0%, 5-9% - 28%, 10-19% - 31%, 20-29% - 15%, 30-39% - 2%. Three years – 0% - 2.2%, 1-4% - 8%, 5-9% - 26%, 10-19% - 46%, 20-29% - 15%, 30-39% - 0%, 40-49% - 2.2%. Four years – 0% - 8.1%, 1-4% - 10%, 5-9% - 18.9%, 10-19% - 43%, 20-29% - 13%, 30-39% - 0%, 40-49% - 2% (8 patients ceased coming). Five years – 0% - 6.9%, 1-4% - 13%, 5-9% - 20%, 10-19% - 34%, 20-29% - 6%, 30-39% - 2%, 40-49% - 0%.

**Discussion:** Most treatments for weight loss seems to fail after a period of time. With dextroamphetamine sulfate 44% lost at least 10% of their initial body weight at 6 months. There were still 42% losing at least 10% of their body weight at 5 years. If one considers those who lost at least 20% of their weight initially, whereas 17% were in this category at 6 months, there was only 8% still losing this much at 5 years.

**Conclusion:** The effect of dextroamphetamine sulfate in inhibiting edema, and thus allowing weight loss, does not seem to be transient but relatively long lasting.

**Abstract #713**

**AGE DEPENDENT RELATIONSHIP BETWEEN BODY MASS INDEX AND FASTING PLASMA GLUCOSE IN SOUTH-WESTERN NIGERIA**

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**Objective:** Overweight and obesity represent a rapidly growing threat to the health of populations in an increasing number of countries. Several reports have linked obesity with diabetes mellitus. General obesity has been implicated in the development of diabetes mellitus. In a study, body mass index was the dominant risk factor for diabetes, increasing the risk of developing diabetes by 11-fold after adjustment for age. Literature is very scanty on the association of obesity and plasma glucose in Nigeria. This study evaluated the relationship between fasting plasma glucose (FPG) and body mass index (BMI) in south-west Nigeria.

**Methods:** This is a cross-sectional study involving five hundred and twenty one (521) adult participants comprising of 134 (25.7%) males and 387 (74.3%) females. Body mass index (BMI) was determined by standard protocol. The BMI was classified as follows: < 25.0kg/m2, non-obese; ≥25.0kg/m2, overweight/obese. Plasma glucose was determined by glucose oxidase method. Data were analysed using the statistical package for social sciences (SPSS) version 20.0. Pearson correlation between FPG
and BMI was determined. Student’s t-test was employed to compare the FPG of the obese and non-obese participants. A p-value of <0.05 was taken to be significant.

**Results:** Compared with men, women were significantly older (50.1±15.3 years vs 44.2±16.9 years, p<0.001), and had higher mean BMI (25.1±5.8 kg/m² vs 22.8±3.7 kg/m², p<0.001). The correlation coefficient between FPG and BMI in men and women were 0.241, (p=0.005) and 0.047, (p>0.05) respectively. The mean FPG of obese and non-obese men were 91.4±23.4 mg% and 80.5±12.4 mg% respectively, p= 0.013. As a whole, the mean FPG of obese and non-obese women were 86.8±27.9 mg% and 82.1±16.6 mg%, p = 0.056. In the fifth and sixth decades, the FPG of obese versus non-obese women were 81.93±11.6 mg% vs 75.3±8.2 mg%, (p=0.025) and 97.6±4.7 mg% vs 78.4±8.8 mg% (p=0.013), respectively.

**Discussion:** There was a positive but weak correlation between fasting plasma glucose and BMI in men, whereas there was no significant correlation in women. As a whole the mean FPG of obese men were significantly higher than those who were not obese, but it was not significant among women. However, among the women FPG was significantly higher in those with obesity compared to those who were not obese in the fifth and sixth decades.

**Conclusion:** Body mass index positively associated with fasting plasma glucose in men. Depending on the age, women with obesity had higher mean fasting plasma glucose compared with those who were not obese. Given the relationship between obesity and plasma glucose, concerted efforts should be made to achieve normal weight through lifestyle modification.

**Abstract #714**

**RELATIONSHIP BETWEEN ANTHROPOMETRIC INDICES AND BODY FAT IN SOUTH-WESTERN NIGERIAN WOMEN**

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**Objective:** Obesity may be defined based on percentage body fat. Because of the difficulty in measuring body fat in routine clinical practice, a number of surrogates have been proposed. These include body mass index (BMI), waist circumference (WC), waist to hip ratio (WHR) and waist-to-height ratio (WHtR). These surrogates have been shown to correlate with body fat by authors from other countries. But reports from our environment are scanty. Furthermore, the predictive ability of these indices with respect to body fat in our environment is unknown. The study aimed at determining the correlation between obesity indices and body fat, and the predictive ability of these indices to identify obesity defined as %body fat among women in Ekiti State, Nigeria.

**Methods:** Seventy nine (79) women who participated in health screening during the World Diabetes Day celebration in Ekiti State were included in the study. The BMI, WC, WHtR, and blood pressure (BP) of the participants were determined by standard protocols. Percentage body fat (%BF) and visceral fat (%VF) were measured by bioelectrical impedance analysis (BIA). Blood glucose (BG) was determined with glucose meter. Obesity was defined as %BF>33. Pearson correlation between percentage body fat and the obesity indices was determined. The area under curve (AUC) on the ROC was used to determine the best anthropometric index which identifies individuals with obesity, defined as %BF.

**Results:** The participant’s mean age was 42.4±9.1 years. Their mean Wt, BMI, WC, WHtR, %BF, %VF, BG, SBP and DBP were 73.8±16.3 kg, 30.5±6.1 kg/m², 88.2±13.8 cm, 0.57±0.08, 43.6±10.7%, 9.9±5.6% and 129.2±29.5 mmHg, 73.8±13.1 mmHg respectively. 84.8% participants were obese. The correlation between %BF vs Wt, %BF vs BMI, %BF vs WC, and %BF vs WHtR were 0.561, 0.601, 0.411, and 0.403 respectively, (p<0.001). The correlation between %VF vs Wt, %BF vs BMI, %BF vs WC, and %BF vs WHtR were 0.444, 0.481, 0.410, and 0.432 respectively, (p<0.001). The AUC on the ROC for BMI, WC, and WHtR, respectively were 0.831 (95% CI 0.669-0.993, p<0.001), 0.780 (95% CI 0.627-0.933, p=0.002), and 0.725 (95% CI 0.571-0.880, p=0.013).

**Discussion:** Consistent with previous studies, there was a significant positive correlation between percentage body fat and the three anthropometric indices. However, the correlation was best with BMI. Although BMI was not included in most criteria for diagnosis of metabolic syndrome, ROC showed that it identified obesity defined as %BF fat better than WC and WHtR.

**Conclusion:** BMI is better than WC and WHtR in identifying individuals with obesity and its use as obesity index should not be abandoned. BIA may be a good tool for obesity epidemiological survey in Nigeria.
Abstract #715

NECK CIRCUMFERENCE AS A MARKER OF OVERWEIGHT AND OBESITY: CUT-OFF VALUES FOR BANGLADESHI MEN AND WOMEN.

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Objective: To evaluate neck circumference as marker of overweight and obesity and to find out respective cutoff values for Bangladeshi male and female subjects.

Methods: Cross-section observational study (BADAS-ERC/EC/13/00134) was conducted [July 2013- June 2014] among randomly selected 871 Bangladeshi subjects [male=56.9%, female=43.1%, aged >18 years] who visited OPD of United Hospital, BIRDEM, Primary health centers of Dhaka, Gazipur and among healthy subjects of respective centers. Those having cystic or mass lesion, anatomical abnormality of neck, intra- or extra-abdominal mass-organomegaly-ascites, kyphosis, scoliosis, anatomical abnormality of waist-hip, pregnant, severe co-morbid conditions were excluded. Primary outcome: mean neck circumference (NC) in cm and its correlation with body mass index [BMI (kg/m2)], waist circumference (WC), waist hip ratio (WHR). NC measured (nearest 1 mm) with plastic tape at a horizontal plane, just below the larynx (thyroid cartilage) perpendicular to the long axis of neck. As specified by WPRO of WHO, BMI ≥23 defined overweight and ≥27.5 defined obesity. WC>90 cm, WHR>.9 in male and WC>80, WHR>.8 cm for female defined abdominal obesity. With informed consent, data were collected in pre-formed record form; analyzed with IBM SSPS for Windows ver 20.

Results: As mean± SD, men (n=496) had BMI (kg/m2): 22.17±3.23, WC (cm): 82.32±7.87, WHR: 0.91±0.05 and NC (cm): 34.16±1.95 and women (n=375) had BMI (kg/m2): 23.42±3.70, WC (cm): 81.62±9.20, WHR: 0.90±0.065 and NC (cm): 32.50±2.20. Significant positive correlation between NC and 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 ), WHR (men, r=0.22; women, r=0.18; each p <0.0001 ) were found.

ROC analysis: NC ≥34.75cm (Men, AUC: 0.77; p<0.001), ≥31.75cm (women, AUC: 0.62; p>0.001) were the best cutoff value for BMI≥23. NC ≥35.25cm (men, AUC: 0.82; p<0.001), ≥34.25cm in (women, AUC: 0.76; p<0.001) were the best cutoff value for BMI≥27.5. NC ≥35.25cm (male, AUC: 0.83; p<0.001), ≥31.25 cm in (women, AUC: 0.65, p<0.001) were the best cutoff value for WC>90cm in men & ≥80cm in women. NC ≥34.45 cm (male, AUC: 0.59; p 0.001), ≥31.25 cm (women, AUC: 0.66, p 0.008) were the best cutoff value for WHR>0.9 in men & ≥0.8 in women.

Discussion: Upper-body subcutaneous adipose tissue distribution is positively co-related components of metabolic syndrome and cardiovascular risk. NC can be a simple, potentially useful initial screening tool for overweight and obesity.

Conclusion: For overweight, NC ≥34.75cm (men) & ≥31.75cm (women) and for obesity, NC ≥35.25cm (men) & ≥34.25cm (women) can be considered as the cutoff values. Further population based study is required in this field.

Abstract #716

PREVALENCE OF NONALCOHOLIC FATTY LIVER DISEASE AMONG METABOLIC SYNDROME SUBJECTS & ITS RELATION WITH CENTRAL OBESITY: A HOSPITAL BASED STUDY.

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Objective: The aim of this study was to investigate the prevalence of nonalcoholic fatty liver disease (NAFLD) among metabolic syndrome (MS) subjects. We intended to establish a clinical association between NAFLD with central obesity.

Methods: This cross sectional observational study conducted with ethical permission, April 2015-September2015, among randomly collected Bangladeshi male=48(29.1%), female=117(70.9%), had MS & aged >18 years, who visited OPD of MARKS Medical College & Hospital. In our study ATP III criteria was used to diagnose MS.Those having history of alcohol intake, acute or chronic liver disease, kyphosis, scoliosis, pregnant, severe co-morbid conditions were excluded. Weight, height, waist circumference (WC), hip circumference (HC), blood pressure, and abdominal ultrasonography were performed to detect the presence of fatty infiltration in the liver. Primary outcome included WC, HC, BMI, and WHR. WC measurement was performed with the patient in a standing position with abdomen relaxed, arms at the sides, and feet together, using a non extensible tape measure. The tape involved the individual in the largest abdominal diameter. The measurement was carried out at the completion of the patient's normal expiration. BMI ≥ 25, overweight and BMI ≥30, obesity [WHO criteria]. HC ≥90 cm (male) and ≥80 cm (female) defined abdominal obesity. Serum triglyceride, total cholesterol, high density lipoprotein cholesterol and fasting plasma glucose level were measured.Data were collected in pre-formed record form; analyzed with IBM SSPS for Windows ver 20.
form, analyzed with IBM SSPS for Windows ver16.

Results: A total of 165 subjects having MS were included in this analysis and among them 42 had NAFLD in ultrasonography. The prevalence of NAFLD was 25.5% among MS subjects. 34.54% (men= 37.5%, women= 33.33%) were overweight and 21.81% (men=8.33%, women=27.35%) were obese. As per WC, 17.7% men and 82.2% women had abdominal obesity. As mean± SD, men had age (yrs): 51.52±10.57, height (m): 1.63±.66, weight (kg): 64.95±9.58, BMI (kg/m2): 24.53±3.53, SBP (mmHg): 133.44±1.07, DBP (mmHg): 83.64±8.16, WC (cm): 88.89±8/83, HC (cm): 91.81±1.00, WHR: 0.95±0.03. As mean± SD, women had age (yrs): 48.70±10.18, height (m):1.53±.07,weight(kg):64.23±1.03,BMI(kg/m2):26.96±4.47,SBP(mmHg):129.66±1.54,DBP(mmHg):85.20±9.26, WC(cm):92.83±1.32 ,HC(cm):94.38±1.08, WHR:0.94±0.04.

69.04% of NAFLD subjects had central obesity. Pearson Chi-Square test indicated significant positive association between NAFLD and central obesity (p<0.05).

Discussion: NAFLD was strongly associated with MS. We found a strong relationship between central obesity in patients with NAFLD.

Conclusion: These findings suggest that the cluster of MS components might be the predictor in NAFLD.

Abstract #717

OBESITY IN SECONDARY AND HIGH SCHOOLS AND ITS RELATION TO MEDIA CONSUMPTION AND DAILY BREAKFAST EATING: A CROSS SECTIONAL STUDY IN TAIF, SAUDI ARABIA

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Objective: Obesity is considered to be one of the major growing health problems globally. Internationally, studies showed that >30% of adolescents were either obese or overweight. In Saudi Arabia, obesity affects 39.9% and 30.4% of the adolescent boys and girls, respectively. Recent study showed that ownership of a television significantly increases the odd of being obese (OR 1.39). Shared family meals are significantly resulted in reduction in the odds for overweight among the adolescents.

Methods: A cross-sectional study that includes students from 19 different Secondary and High schools (2 private and 17 public) located in Taif city, Saudi Arabia between April 2014 and June 2015. Student’s height and weight were measured by the researchers and body mass index (BMI) was calculated. Data about eating habits and media consumption were self-reported. We excluded any students with any chronic medical illness and those with learning disabilities.

The primary outcome of the study is to assess the prevalence of underweight, normal weight, overweight and obesity as well as to assess the relationship between BMI and dietary habits, activity, gender, and media consumption.

Results: A total of 3025 students were participated, 2354 (77.8%) were male and 671 (22.2%) were female, mean age 15.39 years old (SD 1.67), mean weight of 62.21 kg (SD 55.42), mean BMI of 23.1 kg/m2 (SD 12.5), and mean WC 77.54 cm (SD 17.6).

34.8% of the students are underweight, 38.65% are normal weight, 13.72% are overweight, and 12.83% are obese. 34.44% of the girls are underweight compared to 35.2% of the boys. 36.79% of the girls are normal weight compared to 38.74% of the boys. 9.2% of the girls are overweight compared to 15.1% of the boys. 19.7% of the girls are obese compared to 10.96% of the boys (p 0.005).

Partial correlation adjusting for gender, grade and type of school; between BMI and watching TV while eating showed significant positive correlation (r 0.053, p 0.007), significant positive correlation between BMI and using electronic devices at the sleep time (r 0.094, p 0.000), non-significant negative correlation between BMI and daily breakfast eating (r -0.025, p 0.212), significant positive correlation between BMI and eating dinner/lunch with family (r 0.151, p 0.000), and non-significant negative correlation between BMI and playing sport (r -.002, p 0.94).

Conclusion: The prevalence of overweight/obesity around 25% and 1/3 of the students are underweight. Girls are more likely to be obese while boys more likely to be overweight. Significant positive partial correlation between the BMI and watching TV while eating, eating meals with family, and using electronic devices at bedtime.
Abstract #718

THE EFFECTIVENESS AND SAFETY OF WEIGHT LOSS SURGERIES TO INDUCE WEIGHT LOSS IN A SAUDI POPULATION

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Objective: To assess the effectiveness and safety of weight loss surgeries, namely laparoscopic sleeve gastrectomy (LSG), and laparoscopic gastric bypass (LGB) in reducing body weight in a Saudi population.

Methods: We recruited patients who underwent either LSG or LGB by a single surgeon between 2009 and 2013. Patients were then followed up for a period of 2 years to evaluate their weight and nutritional status.

Results: A total of 109 patients were recruited (56 females, and 53 males), age (33.2 years + 10.8, mean + SD). LSG was done in 74 patients (68%), and LGB was done in 35 patients (32%). LSG resulted in a reduction in BMI from 50.3 + 9.5 to 31 + 5.8 (P < 0.0001). LGB resulted in a reduction in BMI from 50.4 + 11.7 to 34 + 7.8 (P < 0.0001). No major complications were reported. About 1/3 of patients were not following the prescribed dietary program when evaluated 2 years after the surgery.

Discussion: We found that the LSG was performed more often in our center than LGB. Both LSG and LGB resulted in comparable statistically significant weight loss in accordance with previously published reports. We noticed that some patients in our cohort do not appreciate the importance of long term medical follow up after surgery, and this has to be stressed to them prior to the surgery to avoid nutritional deficiencies post-surgery.

Conclusion: LSG and LGB are considered as effective surgical treatment modalities in producing significant weight loss in Saudis. The importance of long term follow up for patients who undergo bariatric surgery should be highlighted to patients prior to the surgery. This is important to prevent weight regain and to treat any possible nutritional or vitamins deficiencies.

Abstract #719

WEIGHT REDUCTION WITH ONCE DAILY DOSE OF ORLISTAT AND METFORMIN

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Objective: To evaluate the efficacy of combination therapy with Metformin and once daily Orlistat in inducing weight loss in obese persons.

Methods: This is a retrospective study carried out at Diabetes and Obesity Centre, New Delhi, India. All non-diabetic obese patients who enrolled for weight loss during 6 months period and had follow up data of at least 3 months were included in the study. Patients were explained details of treatment strategy at the time of enrolment. All the patients were advised low calorie, high protein diets (1000-1200 kcal, 30% protein) and one hour of brisk walk or equivalent exercise, Metformin 1g/day (off label use), and Orlistat 120mg once daily to be taken before major meal. Metformin was give after dinner to reduce the possibility of gastritis. Patients were regularly followed up on weekly basis.

Results: Study population included 8 male and 28 female patients aged 15-66 years. Mean weight was 96.17(+19.19) kg and mean BMI 37.80(+6.25)kg/m2 (males 40.65+6.88kg/m2, females 36.98+5.94 kg/m2). After 3 months treatment mean weight loss was 8.46(+2.54)kg (8.97(+2.69)% of body weight), average weight loss in females was 8.19+2.39kg (9.22+2.74% of body weight) and in males was 9.39+2.99kg (8.1+2.47% of body weight). Of 36 patients, 34(94.44%) lost more than 5% body weight and 10(27.78%) lost more than 10% body weight. All patients tolerated orlistat and metformin well.

Discussion: Most weight loss drugs have been shown to induce a weight loss of 5-10% when used in conjunction with lifestyle changes. Metformin has been shown to cause modest weight loss in type 2 diabetes patient. Orlistat is the only approved drug available for weight loss in India. It is a weak agent and is expensive. However, there is no data on combination of Metformin and Orlistat. Though the study sample is small, our study shows that Metformin and once daily dose of Orlistat given before major meal in conjunction with lifestyle changes induce significant weight loss, with more than 90% patients losing more than 5% body weight at the end of 3 months.

Conclusion: Our observations show that combining a once daily dose of orlistat and metformin with intensive lifestyle modifications offers an effective and inexpensive alternative for weight loss.
Abstract #720

ECTOPIC ADIPOSEITY OF NON-ALCOHOLIC FATTY LIVER DISEASE IS A STRONG DETERMINANT OF POOR BONE HEALTH IN OBESITY

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Objective: Studies of bone health in obesity yielded conflicting results because of the complexities in defining obesity. We hypothesized that ectopic fat deposition in the liver as in non-alcoholic fatty liver disease (NAFLD) is responsible for poor bone health in obesity rather than BMI or fat mass.

Methods: 59 obese patients were recruited from our Obesity Clinic from July 2014 to June 2015. Obesity was diagnosed as per Indian criteria (overweight BMI ≥ 23 kg/m2; obese BMI ≥ 25 kg/m2). BMI and Waist Circumference (WC) were measured following standard guidelines. NAFLD was diagnosed and graded into 3 Grades based on ultrasonography by 2 blinded Radiologists. Bone Mineral Density (BMD) in gm/cm2, Bone Mineral Content (BMC) in grams and body composition were assessed by DXA. SAS 9.2 was used for statistical analysis. Comparison was done at baseline and after adjustment for confounders. ANOVA with post hoc Bonferroni method, Tukey’s test and ANCOVA were used to assess the effect of multiple cofactors affecting BMD. p<0.05 was considered significant.

Results: Out of 59 obese patients, 46 had NAFLD (Group A); 13 non-NAFLD served as controls (Group B). They were age and gender matched. No significant difference in BMI (Group A 34.1±5.2, Group B 31.6±3.2, p=0.11) or fat mass (g) (Group A 38789.4±11389.8, Group B 39293±15054.7, p=0.57) in two groups was seen. But WC (cm) was significantly higher (p=0.022) in Group A (108.9±10.5) than in Group B (103.4±6.1). BMD was significantly lower in Group A compared to Group B, persisting even after adjustment for confounders, at lumbar spine (1.07±0.15 vs 1.23±0.1, p=0.001), femur (1.04±0.15 vs 1.17±0.12, p=0.003) and whole body (1.18±0.13 vs 2.09±0.1, p <0.001). Total fat mass negatively correlated with BMD T-score and Z-score in NAFLD but not in non-NAFLD. Grades of NAFLD had no significant difference in BMI or fat mass. Increasing grades of NAFLD did not worsen BMD. Interestingly, negative correlation between triglyceride and BMD spine (r=-0.35, p=0.05) was seen.

Discussion: Results showed that for similar BMI and fat mass patients with NAFLD had worse bone health compared to non-NAFLD. Total fat mass had a neutral effect in non-NAFLD, while it negatively affected bone health in NAFLD (lower BMD T-score and Z-score). Mere presence of NAFLD rather than severity of NAFLD is sufficient to harm the bone as increasing grades did not further worsen bone health. High triglyceride is a marker of ectopic adiposity, explaining its negative correlation with BMD.

Conclusion: Poor bone health in obesity is explained by ectopic adiposity of NAFLD and not due to increase in fat mass per se. Research is needed to correctly identify the putative factors involved in liver-bone crosstalk.

Abstract #721

REAL WORLD PATIENT DATA OF EARLY EXTENDED-RELEASE NALTREXONE/BUPROPION COMBINATION THERAPY

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Objective: Extended-release naltrexone/bupropion (NB) tablets were approved by the FDA as an adjunct to a reduced-calorie diet and increased physical activity for chronic weight management in adults. This study describes real-world demographic and clinical characteristics of patients with early NB claims.

Methods: This retrospective cohort study used integrated claims and laboratory data from the HealthCore Integrated Research Environment. Patients with ≥1 pharmacy claim (first claim date is index date) for NB between September 1, 2014 and December 31, 2014, who were aged ≥18 years at the time of the index NB claim and were continuously enrolled during the 6 months prior to the index date, were included. Descriptive statistics were used to assess patient data.

Results: The study included 1,116 patients with NB claims: 79.6% were female, and the median age was 47 years [mean (SD), 46.3 (10.50)]. Family practitioners (31.8%), internists (18.3%), and endocrinologists (9.6%) were the top 3 prescribers of NB. During the 6 months prior to NB treatment, 44.9% of patients had ≥1 medical claim with a diagnosis for obesity, 38.4% for hypertension, 35.7% for hyperlipidemia, and 15.0% for type 2 diabetes. During the same period, 43.4% of patients had ≥1 pharmacy claim for antihypertensive medications, 24.8% for dyslipidemic medications, and 17.0% for antidiabetic medications. Although only 5.2% had a diagnosis for major depressive disorder, 37.8% of NB users had ≥1 pharmacy claim for antidepressants. Among study patients, 15.3% had laboratory results for total cholesterol [mean (SD), 191.4
mg/dL (39.12 mg/dL), and 15.2% for serum triglycerides [mean (SD), 169.4 mg/dL (165.66 mg/dL)], while 9.8% had glycosylated hemoglobin [mean (SD), 6.5% (1.53%)].

**Discussion:** This is the first real-world study to describe demographic and clinical characteristics of patients with NB claims. In the first 4 months of NB market availability, data show that 4 of 5 initiators were female. Family practitioners and internists prescribed over half of NB therapy, whereas endocrinologists prescribed < 10%. Antihypertensive and lipid lowering medications were commonly used among patients prescribed NB. Real-world NB patient demographics were similar to those observed in clinical trials.

**Conclusion:** These findings provide an overview of real-world users of NB. Further exploration is required to assess additional characteristics of NB patients and long-term outcomes associated with NB use.

**Abstract #722**

**IN HEALTHY MEN, CUSTOMARY MEASURES OF TOTAL AND ABDOMINAL FAT MASS ASSESSMENT ARE NOT STRONG DETERMINANTS OF COMPENSATORY MECHANISMS IN GLUCOSE/INSULIN HOMEOSTASIS**

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**Objective:** This study was intended to assess the sensitivity, and specificity of commonly used indicators of total and abdominal fat mass in prediction of glucose regulatory markers in healthy men.

**Methods:** 82 men aged 18-78 yrs with BMIs of 18-39 Kg/m2 were studied after an overnight fast and ingestion of 75 grams of dextrose solution. Sessions started at 0800-0900 hour and continued for 6.5 hours, with blood collected at 10-min intervals for the measurements of glucose, insulin, and C-peptide concentrations. Data from the first 2.5 hrs were used in this report. Total body fat was assessed by DXA and reported as fat mass index (FMI: Kg/m2). Tomovision software was applied to single-cut CT of abdomen to quantify total (TFA), visceral (VFA), and sub-cutaneous (SFA) abdominal fat masses. Considered as independent variable, fat mass indices (FMI,TFA, VFA, SFA) were correlated with (dependent variables) measures of post-dextrose glucose, insulin, and C-peptide concentrations. Data from the first 2.5 hrs were used in this report. Total body fat was assessed by DXA and reported as fat mass index (FMI: Kg/m2). Tomovision software was applied to single-cut CT of abdomen to quantify total (TFA), visceral (VFA), and sub-cutaneous (SFA) abdominal fat masses. Considered as independent variable, fat mass indices (FMI,TFA, VFA, SFA) were correlated with (dependent variables) measures of post-dextrose glucose, insulin, and C-peptide concentrations. Data from the first 2.5 hrs were used in this report. Total body fat was assessed by DXA and reported as fat mass index (FMI: Kg/m2). Tomovision software was applied to single-cut CT of abdomen to quantify total (TFA), visceral (VFA), and sub-cutaneous (SFA) abdominal fat masses. Considered as independent variable, fat mass indices (FMI,TFA, VFA, SFA) were correlated with (dependent variables) measures of post-dextrose glucose, insulin, and C-peptide concentrations.

**Results:** As the preferred predictors, SFA was correlated (r2:P) with HOMA-β% (0.13:0.001), HOMA-S% (0.19:<0.0001), HOMA-IR (0.15:0.0004), and insulinogenic index (0.13:0.0009), and FMI with Matsuda index (0.28:<0.0001), hepatic sensitivity (0.13:0.009), AUC glucose (0.24:<0.0001), insulin (0.23:<0.0001), and C-peptide(0.24:<0.0001), as well as peak insulin (0.19:<0.0001) and C-peptide (0.19:<0.0001) concentrations. Per ROC procedure, sensitivity for all outcome (dependent) variables was less than 47% with specificity at 90%, and higher end cut-off values for all predictor (independent) variables. Using median values as cut-off, sensitivity and specificity were at 70% or less.

**Conclusion:** Observed r2s in the range of 0.13-0.28 indicate that 13 to 28 % changes in glucose regulatory mechanisms are accounted by measures of total body and abdominal fat masses. This along with low levels of sensitivity at optimal specificity indicate that measures of total and abdominal fat are not sensitive in predicting observed dysregulation of glucose homeostasis with increasing body weight.

**Abstract #723**

**THE EFFECT OF LIRAGLUTIDE 3.0 MG FOR WEIGHT MANAGEMENT ON HRQOL, AS MEASURED BY SF-36: 3-YEAR DATA**

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**Objective:** Obesity has negative impacts on health-related quality of life (HRQoL), the degree of which is dependent upon the severity of obesity. This analysis investigated the effect of liraglutide 3.0 mg at 160 weeks, as an adjunct to diet and exercise, on HRQoL in patients with prediabetes and obesity (BMI ≥30 kg/m2) or overweight (BMI ≥27 kg/m2) with hypertension and/or dyslipidemia from the SCALE Obesity and Prediabetes 3-year clinical trial (NCT01272219).

**Methods:** Individuals 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=1505) or placebo (n=749). Physical and mental HRQoL outcomes, measured by Short-Form 36 v2 (SF-36) questionnaires, were assessed in subjects from countries
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with validated translations (73.6% of all randomized) over a period of 160 weeks. Data are reported as observed means and estimated treatment differences (ETD) [95% CI], derived using ANCOVA with LOCF.

**Results:** Mean baseline characteristics: 76.0% female, age 47.5 years, weight 107.6 kg, BMI 38.8 kg/m². Compared with placebo, individuals on liraglutide 3.0 mg had statistically significantly greater improvements from baseline on four SF-36 subscales: physical functioning (3.50 vs 2.48; ETD 1.47 [0.78;2.16]; p<0.0001), general health (2.25 vs 1.39; ETD 1.31 [0.54;2.08]; p=0.0009), vitality (1.84 vs 1.07; ETD 0.94 [0.06;1.82]; p=0.0368), and mental health (0.19 vs –0.81; ETD 1.27 [0.39;2.16]; p=0.0049). No significant differences were found for the role physical, bodily pain, social function and role emotional subscales. A statistically significant difference in favour of liraglutide 3.0 compared with placebo was also observed for the change in the physical component summary score (3.10 vs 2.61; ETD 0.87 [0.17;1.58]; p=0.0156) but not for the change in the mental component summary score (–0.46 vs –1.40; ETD 0.77 [–0.09;1.63]; p=0.0778). Liraglutide 3.0 mg was generally well tolerated.

**Discussion:** Use of liraglutide 3.0 mg, in addition to diet and exercise, was associated with improvements in HRQoL with the largest treatment effect observed on the physical functioning subscale. These results demonstrate the benefit of combining pharmacological treatments, such as liraglutide 3.0 mg, with diet and exercise.

**Conclusion:** At 160 weeks, treatment with liraglutide 3.0 mg was associated with significantly improved physical health components of quality of life in individuals with prediabetes who are overweight or have obesity, compared with placebo.

Abstract #724

**BARIATRIC SURGERY RESTORES BOTH CARDIAC AND SUDOMOTOR AUTONOMIC C-FIBER DYSFUNCTION TOWARDS NORMAL IN OBESE SUBJECTS WITH TYPE 2 DIABETES**

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**Objective:** Autonomic dysfunction has emerged as a major risk factor for the development of cardiovascular (CV) disease and diabetes (DM). Bariatric surgery is effective in inducing sustained weight loss, DM remission, reduction of CV events and mortality. However, the exact mechanisms by which these interventions induce long-term remission are still under debate. Cardiac and sudomotor autonomic dysfunction occur early in DM. 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 measurable using indices of heart rate variability (HRV).

The aim of this study was to evaluate the impact of bariatric surgery on cardiac and sudomotor autonomic C-fiber function in obese subjects with and without Type 2 diabetes (T2DM), using sudorimetry and measures of HRV.

**Methods:** Patients were evaluated at baseline, 4, 12 and 24 weeks after vertical sleeve gastrectomy (71 subjects) or Roux-en-Y gastric bypass (15 subjects). All subjects were assessed using SudoscanTM of hands and feet, time and frequency domain analysis of HRV, quantitative sensory tests (QST) for cold and warm perception thresholds and neurologic impairment scores (NIS-LL).

**Results:** Eighty six subjects completed 24-weeks of follow-up (28 non-T2DM, 34 pre-DM and 24 T2DM). ESC of feet improved significantly (MANOVA) in T2DM subjects by 12 and 24 weeks (Baseline=57.82±3.64 vs 12-weeks=64.05±3.02 vs 24-weeks=70.01±2.55, p<0.0005). HRV measures improved significantly in T2DM subjects (sdNN=33.35±3.63 vs 12-weeks=42.62±3.42 vs 24-weeks=46.09±4.63, p<0.005 and rmsSD=24.09±3.66 vs 12-weeks=36.95±4.28 vs 24-weeks=37.27±5.14, p<0.0005). Basal heart rate, weight, body mass index (BMI), percent body fat, waist circumference and HDL improved in all subjects. A1C, insulin and HOMA2-IR levels improved significantly in pre-DM and T2DM subjects. Multiple linear regression analysis showed that feet ESC improvement at 24 weeks was independently associated with baseline A1C, insulin and HOMA2-IR levels; after adjusting for age, gender and ethnicity; but it was not associated with baseline weight, BMI, body fat, triglycerides, or HDL. Similar results were found for improvements in heart rate and HRV measures.

**Discussion:** This report shows that bariatric surgery significantly improves sudomotor and cardiac autonomic function in obese subjects with diabetes, independent of baseline weight or body fat.

**Conclusion:** This is the first study to show that bariatric surgery can rapidly restore both sudomotor and cardiac autonomic dysfunction towards normal in subjects with T2DM, potentially impacting morbidity and mortality.
EVALUATION AND MANAGEMENT OF FABRY DISEASE

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1. SIU, 2. Carle

Case Presentation: A 14-year-old male was referred for possible metabolic causes of extremity pain and hypohidrosis. Onset of symptoms was age 7 years. Limb pain was exacerbated by cold exposure, and the patient’s parents reported hyperthermia with physical exertion and poor exercise tolerance. Angiokeratomas on the face and dorsum of the hand raised suspicion for Fabry disease, and plasma α-galactosidase (α-GAL A) activity was undetectable. No mutation was found on sequencing the α-GAL A gene. Enzyme replacement therapy (ERT) with the recombinant human α-GAL A preparation agalsidase beta (Fabrazyme) was started, and the patient noted improvement in extremity discomfort. During approximately 10 years of ERT, no renal dysfunction, cardiac abnormalities, or progression of neuropathy have occurred.

Discussion: Fabry disease is an X-linked inborn error of glycosphingolipid metabolism resulting in lysosomal accumulation of globotriaosylceramide (Gb3). The metabolic defect is deficiency of the lysosomal hydrolase α-GAL A that catalyzes hydrolytic cleavage of the terminal galactose from Gb3. Prevalence estimates range from as low as < 1:100,000 to as many as 1:20,000 Caucasian males. Several hundred α-GAL A mutations have been reported, though mutations are not discovered in all patients; in a survey of the Austrian national dialysis registry, only four of ten male patients with undetectable α-GAL A activity had mutations identified. There are numerous potential clinical manifestations including neuropathic limb pain, hypo- or anhidrosis, heat and exercise intolerance, lymphadenopathy, angiokeratomas, telangectasias, abdominal pain, diarrhea, renal abnormalities ranging from proteinuria to end-stage renal disease (ESRD), cardiac abnormalities (left ventricular hypertrophy, valvular heart disease, arrhythmias, and coronary disease), and stroke (at older ages). Diagnosis is made by measurement of α-GAL A activity in leukocytes or plasma. Gene sequencing is required to diagnosis atypically affected males (low α-GAL A activity) and female carriers. ERT is indicated in all classically affected males regardless of signs or symptoms and atypically affected males and female carriers if clinical manifestations occur.

Conclusion: Though typically a metabolic disease of childhood, adult endocrinologists need to be familiar with Fabry disease because presentation and diagnosis may be delayed to adolescence or early adulthood and adult patients require ERT. Data that ERT reduces major clinical events (e.g. ESRD) is limited, but ERT improves neuropathic pain and quality of life and should be started shortly after diagnosis. Once initiated, ERT is continued indefinitely.

PARAGANGLIOMA: A MANAGEMENT CONUNDRUM

Diana Denman, MD, Jagdeesh Ullal, MBBS, Donald Richardson, MD

Objective: Paragangliomas (PGL) are a rare neuroendocrine tumor that can be challenging to manage. In particular, distinguishing malignant from benign disease can be difficult, as histologically, both show pleomorphisms of the nucleus, mitosis, and some invasion. It is also important to distinguish between extraadrenal and intraadrenal paraganglioma (also called pheochromocytoma - PCC) as extraadrenal paraganglioma has a significantly higher risk of malignancy.

Case Presentation: A 38 year old man with no family history of hypertension or endocrine disorders was seen for a hepatic mass suspected to be a catecholamine secreting tumor. He was diagnosed with a left adrenal pheochromocytoma at age 15 when he developed sudden occipital headache and resistant hypertension that necessitated hospitalization and subsequent removal of the tumor. The patient reported that the tumor was on top of the adrenal gland and he did not require an adrenalectomy. His symptoms resolved until this summer when he experienced increased anxiety, hypertension, and occipital headaches that led him to present to the ER with a blood pressure of 197/93, when he was restarted on antihypertensives. He saw his primary doctor with continued hypertension. Urinary catecholamines were elevated: NE of 2395 ug/24hr and VMA of 33.3 mg/24hr. A CT of his abdomen showed a 4.4 x 4.7 cm mass in his liver concerning for metastasis. Interestingly, both adrenal glands were present on the scan. Fractionated plasma metanephrines returned with elevated normetanephrines at 2195 pg/mL. An octreoscan was done and revealed a somatostatin avid hepatic mass. He was started on phenoxybenzamine followed by propranolol prior to hepatic lobe resection but did not require antihypertensive medication after surgery. Pathology revealed metastatic paraganglioma with strong diffuse staining for synaptophysin and chromogranin. Ki-67 stain was positive for 2-3% of cells and the mitotic rate was 2 per 10 HPF. Genetic testing is underway.

Discussion: Paragangliomas have about a 20%-50% risk of malignancy. Due to this increased risk of malignancy and difficulty in distinguishing benign from malignant disease, annual evaluation is recommended for recurrence of disease. This can occur within 10 years of the initial diagnosis and up
to 20 years later. This patient who was lost to follow-up presented 23 years later, underlining the importance of annual long-term screening in these patients. Genetic testing for succinate dehydrogenase (SDH) and pathogenic MAX mutations is recommended for patients with PGL/PCC, especially for onset age less than 45 or recurrent tumors.

Conclusion: This patient underlines the importance of annual long-term screening for paragangliomas.

Abstract #802

A 60-YEAR-OLD WOMAN WITH SMALL FIBER PERIPHERAL NEUROPATHY RECOVERY ON OXYBUTYNIN

Diana Denman, MD, Aaron Vinik, MD, Tranettea Williams

EVMS

Objective: To present the first report of improvement in a patient’s small fiber peripheral neuropathy with oxybutynin.

Case Presentation: A 60-year-old woman presented with complaints of worsening numbness and tingling in her legs that she had not felt for years. She had clinical evidence of both large and small fiber neuropathy. Her total neuropathy scores (sensory, motor, and reflexes) ranged from 8 to 17 from 2008 (N=6) until 2011 when they decreased and plateaued at 5; Repeat testing in 2013 showed deficits in warm sensation (13.7 °C) and cold pain (27.4 °C) in the left great toe and also in warm sensation (14.4 °C) and cold pain (32.0 °C) in the right great toe. Measures of Quantitative Autonomic Function Testing using heart rate variability measures showed abnormal deep breathing and Valsalva responses. In the past, amitriptyline, nortriptyline, topiramate, and alpha-lipoic acid had been used to treat her neuropathy. She could not tolerate any of these medications. Interestingly, she had been on oxybutynin gel 10% since July 2011 for bladder spasms. She was seen at intervals and in October 2015 she volunteered that her neuropathy had improved in the past with reduction of the numbness and tingling in her legs and that she could now feel her legs for the first time in years. Her TNS fell to 5-7 with restoration of sensory, motor, reflexes and autonomic function tests towards normal. Two months prior to our visit, oxybutynin had been discontinued due to concern for its contribution to a recent hospitalization for altered mental status.

Discussion: It seems that adult peripheral neurons are under constant endogenous cholinergic constraint of axonal growth. Preclinical trials in rat models show oxybutynin promotes axonal growth from sensory neurons and also prevents loss of IENF. This patient has small fiber peripheral neuropathy as evidenced by her symptoms and abnormal sensory and autonomic testing. She was unable to tolerate any medications that may have helped her affliction. However, after she started oxybutynin gel, she had improvement in symptoms, intraepidermal nerve fiber density and autonomic testing.

Conclusion: After starting oxybutynin gel, our patient who was resistant to all forms of therapy showed amelioration in small fiber peripheral neuropathy showed amelioration in small fiber peripheral neuropathy findings. Trials in man are ongoing supported by the NIH.

Abstract #803

MILK ALKALI SYNDROME: MAKING A COMEBACK

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Baylor Scott and White

Objective: To describe a case of severe milk alkali syndrome and its multiple complications.

Case Presentation: A 66-year-old male presented with severe milk alkali syndrome complicated by acute encephalopathy, acute renal failure, metabolic alkalosis, hypomagnesemia, and acute pancreatitis. Prior to admission, the patient reported intermittent epigastric pain for several weeks that escalated over the last 7 days. He assumed the pain was from heartburn, and ingested two bottles containing 96 tablets of extra strength calcium carbonate 750 mg and bismuth subsalicylate. He also reported changes in taste, decreased urinary output, ataxia, constipation, nausea, and anorexia over four days. On admission, he was awake but confused. Labs were significant for total serum calcium 18.9 mg/dl, albumin 3.3 g/dl, ionized calcium 9.66 mg/dl, serum bicarbonate 31 mEq/L, blood urea nitrogen 53 mg/dl, creatinine 4.4 mg/dl, magnesium 1.5 mg/dl, phosphorus 3.8 mg/dl, arterial blood pH 7.54, 25-hydroxyvitamin D 23 ng/mL and parathyroid hormone 15 pg/mL. He was hydrated with normal saline, and given oral prednisone, intravenous calcitonin, and zoledronic acid. His total serum calcium improved over 4 days and despite gradual lowering of calcium, subsequently reached a nadir of 7.0 mg/dl. He required aggressive repletion of electrolytes before the total serum calcium returned to normal at 9.0 mg/dl on maintenance calcium carbonate 500 mg daily and cholecalciferol 2,000 international units daily. Parathyroid hormone rebounded to 248 pg/mL. His encephalopathy, acute renal failure and pancreatitis resolved with treatment of the hypercalcemia.

Discussion: Milk alkali syndrome is the third leading cause for hypercalcemia largely due to the availability of over-the-counter preparations of calcium. Previously, milk alkali syndrome accounted for <1% of hypercalcemia.
It can present with altered mental status, acute renal failure and hypomagnesemia. Our patient had a classic presentation along with multiple complications including acute pancreatitis. 

**Conclusion:** Clinicians should be aware of the presentation, complications, and treatment of milk alkali syndrome, as the incidence has increased over the last decade. Patients need to be educated about the potential dangers of using excessive over-the-counter vitamin and mineral supplements.

**Abstract #804**

**A RARE DISEASE WITH POOR INSURANCE: A PHYSICIAN’S DILEMMA**

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**Objective:** Multiple endocrine neoplasia type 2 (MEN2) is an autosomal dominant disorder with an estimated prevalence of 1 per 30,000 in general population. MEN 2a is characterized by Medullary Thyroid Carcinoma, Pheochromocytoma, and primary hyperparathyroidism. Diagnosing and treating such a complex disorder involves extensive and costly investigations, good patient compliance and involvement of the patient’s family as well. In the current healthcare system, treatment decisions are increasingly being dictated by health insurance corporations. We present a case of possible MEN 2a syndrome which left us feeling helpless in face of poor patient compliance and insurance issues.

**Case Presentation:** A fifty two year old female with history of hypertension, bipolar disorder, heroin abuse, multiple renal stones, and hemorrhagic stroke presented to emergency department with severe headache. Blood pressure was 234/124 mm Hg at admission. She mentioned having uncontrolled hypertension since her teens. Also gave history of intermittent headaches, tremors, and spells of anxiety. Her calcium and parathyroid hormone levels were also found to be high. Serum catecholamines and metanephrines were elevated and so was calcitonin. Thyroid ultrasound revealed bilateral nodules. Further questioning revealed several family member passing away from strokes and thyroid cancer, with her children having uncontrolled hypertension and strokes during their twenties. MEN 2a was strongly suspected. Meanwhile, records obtained from another hospital also showed the same diagnosis was suspected but she had left the against medical advice. The patient had little insight into the enormity of her disease likely due to her mental disease and poor educational status. Thyroid biopsy was planned in hospital, which she refused. Also, genetics team was consulted, to test for RET proto oncogene, essential to establish diagnosis and continue testing in family members. This could not be completed due to insurance guidelines stating it to be an outpatient consult. She was soon discharged with instructions to follow up in clinic which disappointingly never happened. Her children could not be tested as they were un insured.

**Discussion:** Early diagnosis via screening of “at-risk” family members in MEN2 kindreds is essential because medullary thyroid cancer is a life-threatening disease that can be cured or prevented by early thyroidectomy. With little compliance from patient or family, while following insurance protocols, this becomes difficult to achieve.

**Conclusion:** Physicians have to constantly walk a tight rope of balancing patient interests and expectations with their own academic curiosity which continues to get complicated by rising healthcare costs.

**Abstract #805**

**HYPOCALCEMIA AND PROFOUND VITAMIN D DEFICIENCY WITH INAPPROPRIATE PTH RESPONSE DUE TO HYPMAGNESEMIA**

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**Case Presentation:** 63 year old woman presented with paresthesias of proximal arms and legs bilaterally. She reported similar symptoms 2-3 months prior to current admission for which she was treated for hypocalcemia and hypomagnesemia at another facility. She did not continue the calcium and magnesium supplements after discharge. On admission, she was found to have hypocalcemia (corrected Ca 6.6 mg/dL) with inappropriately normal PTH (37.4 pg/mL). She was also noted to have severe hypomagnesemia (0.6 mg/dL). Further work-up also revealed significant vitamin D deficiency (25 OH Vit D < 4.2 ng/mL) and excess renal magnesium loss (FeMg++ 18.74%). She reported a history of alcohol abuse with poor oral intake for the last several years. Her past medical history was significant for psoriasis which was previously treated with UV therapy until 1 year ago. She had no other significant past medical history and was not taking any medications as an outpatient. Her family history was unremarkable. The patient’s paresthesias improved with calcium replacement. PTH became appropriately elevated (25 OH Vit D < 4.2 ng/mL) with replacement of her magnesium. Vitamin D replacement was initiated. She received counseling regarding alcohol intake prior to discharge, however, she did not attend any of her follow-up appointments with primary care or endocrinology.

**Discussion:** Hypocalcemia is commonly observed in
magnesium deficiency and in severe vitamin D deficiency. Previous studies have shown that hypomagnesemia leads to impaired PTH secretion and PTH resistance. Replacement of magnesium typically leads to rapid increase in PTH secretion and subsequent improvement in calcium. In our patient, improvement in serum calcium with correction of hypoparathyroidism secondary to magnesium deficiency was delayed due to profound vitamin D deficiency. Interestingly, she had discontinued UV therapy for her psoriasis approximately 1 year prior. The hypomagnesemia can possibly be attributed to alcohol-induced tubular dysfunction, which is a reversible cause of excessive urinary excretion of magnesium. Unfortunately, the patient did not attend her follow-up appointments to see if hypomagnesemia resolved with cessation of alcohol intake.

**Conclusion:** We describe a case of symptomatic hypocalcemia with profound vitamin D deficiency with inappropriate PTH response due to severe hypomagnesemia. The etiology is likely multifactorial, including excess renal magnesium excretion due to alcohol abuse and cessation of UV therapy for her psoriasis leading to vitamin D deficiency.

**Abstract #806**

**INTRATHYROIDAL PARATHYROID ADENOMA IN THE SETTING OF MULTINODULAR GOITER: A DIAGNOSTIC CHALLENGE**

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**Objective:** The estimated incidence of intrathyroidal parathyroid adenomas (ITPAs) varies from 0.7 to 6.7%. Preoperative localization is essential for successful minimally invasive parathyroidectomy (MIP). ITPAs may be mistaken for thyroid adenomas on Tc 99m-sestamibi scan. We report a case of a large ITPA that was reported as thyroid adenoma versus malignancy on sestamibi scan. But given the strong clinical suspicion for ITPA, patient underwent minimally invasive parathyroidectomy. An intrathyroidal parathyroid adenoma weighing 3.81 grams was resected. Intraoperative PTH declined from 231.4 pg/ml to 18.1 pg/ml. Post-operative calcium and ionized calcium levels normalized.

**Discussion:** Distinguishing an ITPA from a thyroid adenoma or malignancy may pose a diagnostic challenge, especially in a patient with multinodular goiter (MNG). There is significant histologic overlap between thyroid and parathyroid lesions. Increased uptake on sestamibi scan may also be seen with thyroid adenomas and thyroid cancers. In cases with primary hyperparathyroidism that show solitary increased uptake within a thyroid nodule on sestamibi scan, PTH analysis of the thyroid aspirate may help correctly diagnose an ITPA. Mazeh et al. reported that single ITPAs were significantly smaller than non-ITPAs (325 ± 47 vs 772 ± 61 mg). The ITPA in our patient was large and weighed 3.81 grams.

**Conclusion:** Strong clinical suspicion must guide the decision for surgery in patients with suspected intrathyroidal parathyroid adenoma and coexistent multinodular goiter.

**Abstract #807**

**SCLEROCHOROIDAL CALCIFICATION: PARA-THYROID CONNECTION**

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**Case Presentation:** 62 year old Caucasian male was referred to Endocrine section from ophthalmology for work up of possible secondary causes of an incidental finding of sclerochoroidal calcification noted on routine exam for diabetic retinopathy. The medical history is notable for type 2 diabetes since 2006, left nephrectomy for renal cell carcinoma, CAD, COPD, hypertension, hypothyroidism since childhood, and CKD stage 3. Ophthalmic exam noted all normal findings for pupillary reaction, extraocular motility, intra ocular pressures, and visual fields by confrontation test. Best corrected vision was 20/20 in both eyes and there was no evidence of diabetic retinopathy on dilated fundus exam. An incidental finding of an elevated round yellow lesion superior to the optic nerve head was noted on the fundus exam in the left eye. The lesion did not demonstrate any abnormal vasculature, pigmentation, or retinal fluid. The lesion was present in prior fundus photos from 2011 with no significant changes, indicating stability of the lesion over the last 4 years. Ophthalmic ultrasonography testing revealed hyper-reflectivity with acoustic shadowing behind
the lesion consistent with dense intra-lesional calcification. Spectral domain optical coherence tomography (SD-OCT) revealed marked sclerochoroidal elevation at the site of the lesion with absence of retinal fluid or neovascularization, normal pigment epithelium and neurosensory retina and intact overlying the lesion. Review of the medical record did reveal elevated calcium of 10.3 mg/dL with no simultaneous PTH 9 months prior to Endocrine clinic visit. Clinical exam was unremarkable with no additional significant findings. Laboratory work up revealed normal calcium and phosphorus levels with PTH intact of 124.9 pg/mL (Ref Range: 29.1 to 79.9), PTH intact was 115 pg/mL one month prior to the Endocrine visit, and eGFR of 47mL/min with serum creatinine of 1.6. Additionally, 25 (OH) vitamin D levels were 26.9 ng/mL with 24 hour urine calcium of < 140 mg/d. DEXA exam revealed a normal BMD and positive uptake in the inferior aspect of the right thyroid gland suggestive of parathyroid adenoma on parathyroid scan. With a clinical diagnosis of hyperparathyroidism (primary vs. secondary), we are awaiting the sonographic evaluation of thyroid and parathyroid.

**Conclusion:** Sclerochoroidal calcification is said to be an infrequent finding that occurs as a result of calcium deposit at the scleral and choroidal level. Though sclerochoroidal calcification can be idiopathic in most cases, clinicians need to rule out metabolic disorders such as abnormal calcium and phosphorous metabolism.

**Abstract #808**

**TRANSIENT HYPERPHOSPHATASEMIA (TH): RARE CAUSE OF ISOLATED ELEVATED ALKALINE PHOSPHATASE IN AN ADULT POST RENAL TRANSPLANT PATIENT**

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Ochsner Clinic Foundation

**Objective:** We present a case of isolated elevation of alkaline phosphatase (ALP) in a post renal transplant patient.

**Case Presentation:** Our patient is a 66 year old female with a history of a kidney transplant secondary to hypertension in 2009, new onset diabetes after transplant on chronic immunosuppressive therapy with mycophenolate and tacrolimus. Two years post-transplant the patient had stable allograft function. The patient was being followed by Endocrinology for diabetes when routine lab analysis revealed that her alkaline phosphatase (ALP) rose to 804 U/L, 6 fold increase from baseline (55-135 U/L). The patient had no symptoms of bone pain, gastrointestinal disease or ongoing infection. Vitamin D was found to be low at 19 ng/mL and was adequately replaced. Bone specific ALP was elevated 516 U/L (5-58 U/L) as was liver specific ALP 254 U/L (5-93 U/L). Gamma-glutamyl transferase (GGT), serum protein electrophoresis and parathyroid hormone (PTH) were normal. Serum C telopeptide (CTX), N telopeptide (NTX) and procollagen type 1 propeptide bone turnover markers were normal. The patient had a negative whole body bone scan. The patient had no evidence of lymphadenopathy or malignancy on physical examination or liver ultrasound. Based on asymptomatic presentation and no isolated source of alkaline phosphatase elevation, it was determined that the patient most likely had Transient Hyperphosphatasemia. A complete resolution of elevated ALP was seen in 16 months with continued normalization 3 years after resolution.

**Discussion:** TH of infancy and early childhood is characterized by marked elevation of serum ALP with elevated bone and liver isoenzymes (and rarely intestinal isoenzymes) without any detectable liver or bone disease. This benign condition occurs in children under 5 years of age, and is thought to be caused by a reduced clearance of ALP. This condition has been well documented in children but few cases have been reported in adults or transplant patients. The few adult cases reported had resolution time of 5 months or less. While our case follows the same pattern as others reported, the length of time for resolution was longer.

**Conclusion:** In an adult post renal transplant with isolated elevation of alkaline phosphatase after evaluation for other causes including bone involvement, liver disease, infection and malignancy the clinician should consider TH as the diagnosis of exclusion to prevent excessive unnecessary evaluation.

**Abstract #809**

**OBSCURE CAUSE OF HYPERCALCEMIA**

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**Case Presentation:** A 77 year old man was seen in the clinic for hypercalcemia. His wife reports confusion in the last 6 months. Recent intentional 15 lb loss was reported also. The patient has no neuromuscular, renal, skeletal or cardiac manifestation. Dietary history showed that he has been eating 2 pounds of cheese every 5 days for few years. He denied taking any anti-acid or excessive vitamin D. He was on Hydrochlorothiazide 12.5 mg a day since 1980s and Calcium 500mg BID. Few weeks before, he received intravenous hydration when calcium was 12.4 mg/dl (normal 8.4-10.4). No history of thyroid, parathyroid, Paget’s disease in the family. Blood tests showed hypercalcemia for the last 5 months. Calcium range was 10.6 to 12.4 mg/dl (normal 8.4-10.4) with normal albumin. PTH: 4 pg/ml (normal 14-64) when Calcium: 11.8 mg/dl. He has non-PTH mediated
hypercalcemia. Possible etiologies can be Granulomatous disease, excessive vitamin D intake, exogenous calcium intake, Milk-alkali syndrome, Hypervitaminosis A, Thyrotoxicosis, adrenal insufficiency or malignancy. In this case, given the excessive cheese intake with its high calcium content and Thiazide use, narrowed the differential diagnosis to these two etiologies. We preferred to correct the diet and hold Thiazide before doing extensive work up. The work up showed: PO4: 3.4 mg/dl (normal 2.7-4.5). 25-OH Vitamin D: 39.4 (normal 30-60). Vitamin D 1, 25 (OH)2 total: <8 pg/mL (normal 18-72 ). Vitamin D3,1,25 (OH)2: <8 pg/dL. Vitamin D2,1,25 (OH) 2: <8 pg/mL. TSH: 1.639 uU/mL (normal 0.5-5). ACTH stimulation test showed normal adrenal response. Vitamin A: 136 mcg/dL (normal 38-98). LDH: 122 U/L (normal 125-243). PTH- RP: 21pg/mL (normal 14-27). SPEP: normal. 24 hour urine calcium: mg/24HR (normal 100-300). Patient stopped taking Hydrochlorothiazide, Calcium, and cut down on cheese. Repeated calcium just after 5 days was 9.9 mg/dl. 24 hour urine calcium: 99 mg/24HR (normal 100-300). 5 months later, Calcium: 9 mg/dl and PTH intact: 64 pg/ml.

**Conclusion:** The patient was taking 2.7 gm of calcium a day, 1000 mg from calcium and 1700 mg dietary from cheese. Similar cases were reported in literature. Excessive cheese 2 kg a day in anorexic patient caused severe hypercalcemia. Thiazide-associated hypercalcemia is often discovered after years after initiation the medication. Milk-alkali syndrome can occur with minimum of 5-7 g of Calcium carbonate daily, which contain 2-3 grams of elemental calcium daily, for few weeks. Similar to Milk-alkali syndrome, our patient displayed a factitious Cheese-Thiazide syndrome with total of 2.7 gram of calcium daily leading to symptomatic hypercalcemia that required intravenous hydration at some point.

### Abstract #810

**INFLAMMATION, WEIGHT LOSS AND BMI AS PREDICTORS OF OUTCOMES IN COPD**

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**Objective:** Weight loss and inflammation are associated with poor prognosis in many chronic conditions including chronic obstructive pulmonary disease (COPD). Growth differentiation factor 15 (GDF15) is a novel inflammatory marker that has been associated with weight loss, smoking and poor prognosis in several conditions such as malignancy and congestive heart failure. However, its role in COPD and its relationship with weight loss in these patients have not been well characterized. In this study we examine the role of GDF 15 in COPD patients and its prognostic value in long survival.

**Methods:** We examined data collected prospectively in 221 well-characterized active and former smokers over the age of 40, with greater than 15-pack year history of smoking in the Longitudinal Exacerbation Study of COPD (LES COPD). Exclusion criteria included history of lung cancer, thoracic surgery or other lung diseases (e.g. asthma, sarcoidosis, fibrosis). Clinical assessment of COPD included, body weight and BMI change, pulmonary function tests (PFTs), and quantitative lung CT scans that were performed at baseline and at 3-5 years, annual 6 minute walk test, monthly documentation of upper and/or lower respiratory infections (URI/LRI).

**Results:** Among the 221 patients recruited, 138 (62.4%) subjects had emphysema based on CT criteria (Low Attenuation Area ≥ 7%). The mean age was 52.1±7.3, and 35% of the study participants were female. Baseline BMI was 27.9± 5.9 in COPD group and 29.8± 5.9 in non-COPD group. The percent change in BMI was -0.7% in the COPD group and 0.56% in the non-COPD group after 5 years (NS). At the end of the study period, 42 patients (30%) in COPD group and 5 patients (6%) in non-COPD group died. On Cox regression analysis, after adjusting for age, gender and baseline FEV1, baseline GDF 15 level was a significant predictor of survival (p=0.002, 95.0% CI of 1.68-9.41). Baseline BMI showed a trend (p=0.13), but weight loss and other inflammatory markers including IFN-γ, IL-6, IL-10, IL-13, and IL-17 and baseline 6-minute walk test distance did not predict survival.

**Conclusion:** Subjects with COPD had lower BMI than non-COPD subjects. However, over a 5 year period they did not experience significant weight loss. Baseline GDF 15 was a significant predictor of survival in COPD. These findings suggest a potential important role for GDF-15 in COPD pathophysiology. Further studies are needed to understand the role of GDF-15 as a biomarker in COPD patients.

### Abstract #811

**AN ORPHAN DISEASE DURING PREGNANCY**

**George Thott, MD, Karen Herbst, PhD, MD, Craig Stump, PhD, MD**

Banner University Medical Center

**Objective:** To describe calcium and vitamin D requirements during pregnancy in a patient with idiopathic hypoparathyroidism.

**Case Presentation:** Hypoparathyroidism is classified as an orphan disease affecting a limited number of people...
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worldwide. It is characterized by abnormally low levels of parathyroid hormone secretion which can lead to hypocalcemia and its related symptoms. Few published case reports exist on individuals with hypoparathyroidism during pregnancy. There are no established guidelines or therapeutic regimens for the treatment of hypoparathyroidism during pregnancy. Calcium and vitamin D homeostasis is subject to significant change during pregnancy. Therefore, the clinical course of a pregnant patient with hypoparathyroidism will differ substantially from the typical pregnancy.

CASE: A 31 year old female with history of idiopathic hypoparathyroidism was followed for the management of calcium homeostasis before and during her second pregnancy. Her first pregnancy was complicated by nephrolithiasis and hypercalcemia. During the second (current) pregnancy, the patient’s calcium and Vitamin D requirements increased steadily into the second trimester as evidenced by biweekly laboratory blood draws. This was supplemented with a 4 fold increase in calcitriol (0.25mcg daily to 1.0mcg daily), 2 fold increase in Vitamin D3 (2000 IU daily to 4000 IU daily), and additional increase in calcium from 1100mg to 1600mg daily. Currently, she remains asymptomatic in the second trimester of pregnancy and her endocrine care is still ongoing. Post-partum calcium and vitamin D status for the patient and newborn will also be evaluated, and compared to previous reports.

Conclusion: Our case of idiopathic hypoparathyroidism during pregnancy is a very rare occurrence without recognized treatment protocols or guidelines. We have demonstrated that calcium and calcitriol requirements increase during pregnancy. Moreover, with timely adjustment of calcium, Vitamin D-1-25, Vitamin D-25-OH supplementation calcium homeostasis can be maintained with minimal symptoms for the patient.

Abstract #812

CAUTION: WATCH ELECTROLYTES DURING HIGH-DOSE MGSO4 THERAPY

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Objective: Preeclampsia and eclampsia are severe obstetric disorders, the complications of which have dramatically been improved with the implementation of high-dose MgSO4 therapy. However, secondary complications may arise from MgSO4 therapy. The objective is to present an apparently overlooked biochemical complication of high-dose magnesium sulfate (MgSO4) therapy.

Methods: Case Presentation.

Case Presentation: A 34 year old male with history of MEN 2B presented to our hospital with abdominal pain and distention. Past medical history included total thyroidectomy for MTC (13 years old), bilateral adrenalectomy for pheochromocytomas (26 years old) and surgical removal of mucosal neuromas. There was no to the ER with witnessed seizure-like activity. She received 6-8 grams of intravenous magnesium sulfate (bolus-maintenance). Few hours after the infusion, she experienced epileptiform activity. Upon work up, serum calcium and ionized calcium were very low (6.14 mg/dL and 0.93 mg/dL, respectively). Initial calcium and magnesium were normal. Paradoxically, parathyroid hormone (PTH) was also low (9.2 pg/mL), which was perceived as counter-intuitive. While administering intravenous calcium as appropriate, the obstetricians ruled out eclampsia and thus MgSO4 was discontinued the following day. Subsequently, serum calcium and PTH gradually normalized.

Discussion: Hypocalcemia is a known complication of high-dose intravenous MgSO4 therapy, but it is our observation that this piece of knowledge is not conceivably recognized by obstetricians. Abnormal parathyroid hormone and calcitonin related protein levels have been seen in preeclampsia, which may in turn affect calcium homeostasis. There are no clear recommendations to monitor calcium levels with MgSO4 infusions. Both hypocalcemia and eclampsia can cause epileptiform activity, creating a challenge for clinicians managing these patients.

Conclusion: Pregnant women with preeclampsia should be monitored closely during and after MgSO4 infusion therapy. Seizures should prompt immediate evaluation for hypocalcemia, as first-line therapy for eclampsia-related seizures (magnesium sulfate) may worsen this electrolyte abnormality.

Abstract #813

MEGACOLON – AN UNDER RECOGNIZED COMPLICATION OF MULTIPLE ENDOCRINE NEOPLASIA (MEN) 2B

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Objective: To draw attention to the lesser known gastrointestinal (GI) manifestations of MEN 2B. MEN 2B is a rare disease characterized by an aggressive form of medullary thyroid cancer (MTC), neural mucosal gangliomas and pheochromocytomas. While association of Hirschsprung disease and megacolon in MEN 2A is a well-known phenomenon, association of GI manifestations in individuals with MEN 2B is not well recognized.

Methods: A case report and literature review.

Case Presentation: A 34 year old male with history of MEN 2B presented to our hospital with abdominal pain and distention. Past medical history included total thyroidectomy for MTC (13 years old), bilateral adrenalectomy for pheochromocytoma (26 years old) and surgical removal of mucosal neuromas. There was no
known family history of MEN 2B. For the past 3 years, he had been hospitalized multiple times for small bowel obstruction. He described long standing concerns with constipation, diarrhea, and feeling of gaseous distention of stomach which started at age 15 years. CT scan of the abdomen on admission showed markedly dilated ascending and transverse colon with no free air. Patient was conservatively managed in-hospital with subsequent reversal of his megacolon.

Discussion: GI manifestations are an important and commonly under recognized component of MEN 2B syndrome, however, reported to occur in 90% MEN 2B individuals. Symptoms often begin in the first months of life, before the diagnosis of MEN 2B. They include chronic constipation, intermittent diarrhea or both, flatulence, abdominal distention and pain, intestinal obstruction, ileus, megacolon, secondary diverticulosis and dysphagia. Colonic disorders tended to present earliest, followed by MTC and lastly, pheochromocytoma.

The mechanism of GI symptoms in MEN 2B is thought to be from diffuse transmural ganglioneuromatosis that may involve all or part of the GI tract. Neural proliferation is unassociated with fibrosis, allowing for easy distensibility of the bowel. The clinical picture can mimic Hirschsprung’s disease. However, enteric innervation and ganglia are absent in Hirschprung disease, while MEN 2B is characterized by hyperplasia and disorganized growth of ganglia, thereby prompting the terminology Pseudo-Hirschsprung’s disease in the literature.

Conclusion: MEN 2B is best known for its endocrine manifestations and typical phenotype. However, GI manifestations of MEN2B, particularly megacolon, are under recognized. Understanding the pathophysiology and association of colonic disorders in individuals with MEN2B can help clinicians achieve an early diagnosis and management plan.

Abstract #814

CALCIUM CORRECTION FOR ALBUMIN: A NEW USER FRIENDLY EQUATION

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Objective: It is very well recognised that serum calcium levels must be corrected for albumin in order to determine an accurate value of biologically important fraction of calcium. As ionized calcium lab measurement is not readily available and requires cumbersome sampling techniques, serum adjusted calcium formulae are commonly used to adjust for the difference in albumin concentration. We used a new easy formula to calculate corrected calcium and compared the results with the standard formula for calcium correction to determine the accuracy of our simpler equation.

Methods: The routinely accepted and frequently used equation to correct calcium for albumin is corrected calcium [mg/dL] = measured total calcium [mg/dL] + 0.8 (4.0-serum albumin [g/dL], where 4.0 represents the normal albumin level in g/dL. This equation is not easy to use and most providers often use apps or calculators to determine corrected calcium with this equation. We proposed a new convenient to use equation for corrected calcium: 4 + (Serum Calcium - Serum Albumin). We calculated corrected calcium using both equations on 100 patients to assess the accuracy of this new equation and compared the values with the standard and routinely accepted equation as described above.

Results: Using statistical analysis, including t-test, we find that there is no statistically significant difference between the corrected calcium values calculated by the two equations, with a p-value of 0.208, in a sample size of 100. Given that our equation provides results that are statistically the same as the more complicated, routinely used equation, the important implications of these results suggest that our new equation can be used as more user friendly norm for corrected calcium.

Conclusion: Our new easy to use and straightforward equation provides as accurate and comparable results to the current most commonly used complicated equation for corrected calcium. Given the ease of use of this new equation compared to current cumbersome formula, this new equation could prevent inconvenience and save time of medical professionals consumed to draw equally accurate results.

Abstract #815

A CASE OF PARATHYROID CANCER WITH MUTATIONS NF1 AND PTEN COEXISTING WITH RENAL CELL CARCINOMA: A VERY RARE OCCURRENCE

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Objective: To describe a case of coexisting parathyroid cancer and clear cell renal cancer.

Methods: Describe the clinical, laboratory, pathology and gene mutation findings in a patient with parathyroid cancer and clear cell renal carcinoma.

Case Presentation: A 52 years old female presented in 2010 for hypercalcemia and a rapidly enlarging neck mass
over 3 months. Physical exam included - a mass measuring 4cm in the right lobe of the thyroid gland. Neck sonogram showed a 3.3 cm complex nodule in the right lower lobe. Labs showed Ca 11.9 mg/dl, PTH 1047 pg/ml, TSH 2.22 mIU/L, FT4 0.69 ng/dl, BUN 6 mg/dl and Creatinine 0.6 mg/dl. Parathyroidectomy was done and pathology was consistent with right inferior parathyroid carcinoma. Postoperatively her calcium and PTH remained normal for 3 years and thereafter she was lost to follow up. In 2014, in preparation for a gastric banding surgery, labs were Ca 13.8 mg/dl, iPTH 281 pg/ml, 25OHD 32 ng/ml. Neck sonogram showed a 1.5 cm nodule adjacent to the right thyroid. Sestamibi scan revealed a focal area of uptake in the right neck, in the mid to lower portion of the thyroid lobe. She had a re-excision of the parathyroid tumor and the pathology report revealed parathyroid carcinoma. Six months later, patient went to ER for abdominal pain and labs showed Ca10.2 mg/dl, Vitamin D28.2 ng/ml. She had diagnostic work up including CT angiogram, which revealed a right renal mass. She underwent a partial nephrectomy and the pathology showed a clear cell carcinoma. Due to her history of multiple cancers, she was referred for genetic testing. The parathyroid tumors revealed 2 mutations NF1 (F1247fs*18) and PTEN (D92E) and the renal cancer tissue revealed a mutation in the von Hippel Lindau gene.

Discussion: Parathyroid cancer is a rare cause of primary hyperparathyroidism that can occur sporadically. Mutation of the HRPT2 plays a central role in the molecular pathogenesis of parathyroid carcinoma. NF1 and PTEN gene mutations have been linked to many different types of cancer but there association in parathyroid carcinoma with clear renal cell cancer remains unclear at present. There have not been any previously reported mutations of NF1 and PTEN in parathyroid carcinoma. Furthermore, there are no reports of parathyroid cancer and clear renal cell cancer occurring in a same patient.

Conclusion: To our knowledge, this is the first case report of recurrent parathyroid cancer with mutations coexisting with clear cell renal cancer. It is unclear if the two cancers are just coincidence or there is shared mutations between the two. Given that mutations in the PTEN and NF1 genes are associated with other forms of cancer, more surveillance is needed in parathyroid cancer patients with these mutations.

Abstract #816

A UNIQUE CASE OF A MALIGNANT, FUNCTIONAL, HEREDITARY PARAGANGLIOMA ASSOCIATED WITH A SDH-C GERMLINE MUTATION

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Objective: Approximately 30% of all paragangliomas are hereditary. Mutations in the genes encoding different subunits of the SDH enzyme complex have been linked to hereditary paragangliomas. There are five hereditary SDHx paraganglioma syndromes. Mutations most specifically in the SDH-C locus are rare and are usually benign, nonfunctional (parasympathetic) head and neck paragangliomas. Our case exemplifies a distinctive phenotypic variant.

Case Presentation: A 51-year-old woman presented in 2005 with hypertension and diarrhea. CT scan revealed a 4.4cm retroperitoneal mass. Complete resection was performed with pathology revealing characteristics of a paraganglioma without capsular invasion or angiolymphatic invasion. She underwent a series of scans in the following years without signs of relapse. However, patient developed recurrent hypertension, left sided flank pain, anxiety, and diarrhea in 2010. CT scan of the abdomen/pelvis revealed new retroperitoneal para aortic and para vena caval lymphadenopathy, dilation of the right ureteral pelvis, and a new lytic lesion of L1 measuring 2.5x2.2 cm. Her hypertension was improved with initiation of prazosin, then labetalol. 24-hour urine catecholamines were as follows: norepinephrine 2770 ug/24hr (nl. 0-140ug/24hr), dopamine 3083 ug/24hr (nl. 65-610ug/24hr ), epinephrine 7 ug/24hr (nl. 0-32ug/24hr). MIBG was unexpectedly negative while the octreotide scan showed foci of radiotracer activity within the L1 vertebral body and right ileum. Patient underwent exploratory laparotomy but was found to have unresectable disease due to extensive involvement of the para aortic region. Genetic testing was positive for a heterozygous c.43C>T (p.R15.x) mutation detected with SDH-C sequencing – the exact mutation found in genetic testing of her daughter later on. Patient underwent a series of different treatment regimens including radiation and chemotherapy. Her disease unfortunately progressed despite treatment and she eventually expired in 2012.

Conclusion: Our case is rare in that our patient had a SDH-C germ line mutation with metastatic paraganglioma that was functional (sympathetic). To our knowledge, no such case has been reported in the literature. Like SDH-B related paraganglioma, false negative MIBG scan may be encountered in SDH-C related paraganglioma.
Abstract #817

HYPERCALCEMIA OF IDIOPATHIC ELEVATED 1, 25 DIHYDROXYVITAMIN D

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Objective: Hypercalcemia is a relatively common problem with primary hyperparathyroidism and malignancy accounting for 80-90% of all cases. Elevated, 1,25-dihydroxyvitamin D [1,25(OH)2D], due to activation of extra renal 1α-hydroxylase in chronic granulomatous disorders, is a rare cause of hypercalcemia. We present a case of hypercalcemia due to elevated 1,25(OH)2D with unidentified etiology, with response to denosumab treatment after stopping glucocorticoids.

Case Presentation: An 86-year-old woman was admitted to the hospital with worsening shortness of breath, she was found to have left lung consolidation and large pleural effusion. Review of systems revealed occasional palpitations and constipation. Her past medical history included atrial fibrillation, congestive heart failure, chronic kidney disease and osteoporosis. Physical examination was remarkable for decreased air entry and coarse crepitations on the left lung base. Initial work up showed elevated calcium of 14.2 mg/dL (8.5-10.5 mg/dL). Work up for hypercalcemia revealed elevated 1,25(OH)2D of 182 pg/ml (normal 20-79 pg/ml) with low PTH, 25 Vitamin D and PTHrP. She underwent diagnostic and therapeutic thoracentesis along with work up for secondary causes of elevated 1,25(OH)2D which was unremarkable. Bone marrow biopsy and myeloma work up were unremarkable. Imaging studies were only remarkable for perisplenic hematoma. Hypercalcemia responded to treatment with prednisone. However patient could not tolerate its side effects so prednisone was tapered off. Serum calcium increased, so she was given one dose of denosumab to treat osteoporosis as well as hypercalcemia. Calcium level stayed normal after administration and 1,25(OH)2D level decreased to 106 pg/ml.

Discussion: Elevated 1,25(OH)2D in granulomatous, neoplastic, and other diseases is increasingly implicated as a cause of hypercalcemia. Increased levels of 1,25(OH)2D may be induced by direct intake of this metabolite, extra renal production in granulomatous diseases or lymphoma, or increased renal production that can be induced by primary hyperparathyroidism. Activity of 1α-hydroxylase appears to be sensitive to corticosteroids as shown by normalization of calcium level with steroid treatment. Our patient responded to steroid as well as to denosumab suggesting effectiveness of denosumab in patient with hypercalcemia and elevated 1,25(OH)2D.

Conclusion: In patients with elevated 1,25(OH)2D, a systematic search for occult malignancy and bone marrow granulomas is indicated when no other cause is apparent. Denosumab appears to have a promise in the treatment for patients with hypercalcemia and elevated 1,25(OH)2D.
for treatment of hypocalcemia in hypoparathyroidism. With adequate supplementation patients usually remain asymptomatic. Product solubility, dosage and timing, concomitant medications and food intake, affect calcium bioavailability. Absorption of calcium carbonate, one of the more commonly used preparations of calcium salt, requires an acidic environment. Calcium citrate, because of its absorption in low gastric acid states, is the calcium supplement of choice when treatments that reduce gastric acidity are implemented.

Conclusion: Clinicians should be aware of the multiple factors that affect absorption of calcium supplements, particularly in patients at risk of severe hypocalcemia.

Abstract #819

SALUD AL PASITO: SMALL STEPS TOWARDS BETTER HEALTH

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Objective: The mission of Salud al Pasito is to create an environment where participants can relay their health concerns to healthcare professionals and students so that they feel empowered to make healthier choices.

Methods: Salud al Pasito hosts free walking events throughout the year which feature walking activities, exercise/nutrition counseling, and free health screenings where participants are encouraged to interact with volunteers including healthcare professionals. Participants’ health knowledge is assessed through pre-walk and post-walk surveys and the “Wall of Issues,” a poster where participants indicate their top three health concerns. Through the surveys, participants are polled on health-related habits such as obstacles faced with initiating habitual exercise and more.

Results: A total of 1,201 responses have been recorded on the “Wall of Issues” from September 2013 to March 2015. Most respondents were aged between 41-64 years (41.63%). For all age groups, top health concerns were diabetes (17.74%) and obesity (17.48%). Within age groups, the top concerns for those aged 0-17 years was smoking/lung disease (16.95%), obesity for 18-40 (23.95%), and diabetes for those 41-64 and over 65 (20.00% and 22.90%, respectively). For frequency of speaking with healthcare professionals, 1% of participants exercise more than 46 minutes/week, 20% exercise 31-45 minutes/week, and 20% exercise less than 15 minutes/week, 30% exercise 16-30 minutes/week, 20% exercise 16-30 minutes/week, 20% exercise 31-45 minutes/week, and 20% exercise 16-30 minutes/week.

Discussion: The city in which this research is conducted has a high prevalence of chronic diseases, and although the etiology of these diseases such as diabetes and obesity are complex, exercise and nutrition are known ways to combat these health complications. Salud al Pasito is an organization which seeks to motivate the community to pursue healthier lifestyle choices to reduce the burden of these diseases.

Conclusion: Diabetes and obesity are top health concerns for adults, while smoking was most concerning to adolescents in our study. We strive to motivate the community to visit healthcare providers and include habitual exercise routines. Our organization will involve local schools to reach out to the youth and their families. Finally, information gathered from our events will be used to educate healthcare professionals and students to be aware of the most pressing health concerns of this community.

Abstract #820

NEUROPROTECTIVE ROLE OF 17B ESTRADIOL AGAINST AMYLOID BETA NEUROTOXICITY IN SYNPATOSOMES OF AGING FEMALE RATS

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Objective: Neurodegenerative disorders are characterized by the formation of distinct pathological changes in the brain, including extracellular protein deposits, cellular inclusions and changes in cell morphology. Alzheimer’s disease (AD) is the most common form of dementia in the elderly. AD is characterized by the presence of amyloid plaques which are formed from deposits of β-amyloid protein (Ab). Accumulation of oligomeric Ab in the brain contributes to neuronal dysfunction and ultimately leads to neurodegeneration. These changes increase during menopausal condition in females when the level of estradiol is decreased.

The aim of the present study was to determine the effect of neuropeptide, neurokinin B (NKB) and amyloid beta fragment Aβ (25-35) on 17β estradiol (E2) treated aging female rat brain of 3 months (young), 12 months (adult) and 24 months (old) age groups.

Methods: The aged rats (12 and 24 months old) (n=8 for each group) were given subcutaneous injection of 17b-estradiol (0.1 µg/g body weight) daily for one month. After 30 days of hormone treatment, experimental animals of all the groups were sacrificed and brains were isolated for further study. Synaptosomes were incubated
with NKB, Aβ (25–35) and NKB+ Aβ (25–35) in a microfuge tubes at 37°C for one hour in a shaking water bath with 0.1, 1 and 5 µM concentration of each of the peptides in all age groups of control and estradiol treated rats. Aging brain function were assayed by measuring the activities of antioxidant enzymes, monoamine oxidase (MAO), membrane bound ATPases, intracellular calcium levels and lipid peroxidation in presence of neuropeptides.

**Results:** The results obtained in the present work revealed that increased activities of antioxidant enzymes, membrane bound ATPases and decrease in level of calcium levels, MAO activity and lipid peroxidation in presence of NKB and combined NKB and Aβ in vivo estradiol (E2) treated aging rat brain. NKB treatment reversed the beneficial in preventing some of the age related changes in the brain.

**Discussion:** An in vitro incubation of E2 treated synaptosomes with Aβ showed toxic effects on all the parameters, while NKB showed stimulating effects and the combined NKB and Aβ showed a partial effects as compared to Aβ (25-35) and NKB alone.

**Conclusion:** Present study elucidates an antioxidant, neuromodulatory and neuroprotective role of tachykinin peptide NKB against the beta amyloid induced toxicity in E2 treated female rats. NKB treatment reversed the beneficial in preventing some of the age related changes in the brain.

Abstract #821

**TESTING THE EFFECTIVENESS OF SOYBEAN EXTRACT AS A SOURCE OF ISOFLAVONOID TO REPAIR ACUTE MYOCARDIAL INFARCTION AT INDUCED RAT**

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Andalas University

**Objective:** Soybeans contain phytoestrogens that act as isoflavonoids. Researchers interested in knowing the effectiveness of soy as a source of isoflavonoids when compared to estrogen in repair damaged cardiomyocytes. **Methods:** This was an experimental study design post test only. Each group was induced acute myocardial infarction. Where were divided into a control group, estrogen group, and the group given the extract of soya isoflavonoids. Then it will be seen repair heart muscle cells occurs through histopathological examination.

**Results:** From the results, the average score of 4,5 to control group, 2 to estrogen group, and 1,5 to isoflavonoids group. Where the group with the smallest score shows the best group and with p = 0.342.

**Discussion:** Isoflavone group be the best group in repairing cardiomyocytes at IMA. Extract Soy isoflavonoids as 17β-estradiol in the body, in addition to triggering proliferation and differentiation of stem cells, especially MSC heading into cardiomyocytes, 17β-estradiol was also instrumental activate paracrine signals Akt and SDF-1, which will accelerate the pace and keberikatan MSC with receptors on the heart that experienced IMA.

**Conclusion:** Isoflavonoids derived from soy extract is able to provide a better repair than cardiomyocytes estrogen or a control group.

Abstract #822

**A NOVEL PHENOTYPE OF MEN1 SYNDROME ASSOCIATED WITH PARATHYROID, PITUITARY AND ENTERO-PANCREATIC TUMORS, LIPOMAS AND AN ABDOMINAL WALL MYXOMA**

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**Objective:** We describe a novel phenotype of Multiple Endocrine Neoplasia (MEN) 1, associated with an abdominal wall myxoma, rather than the traditional non-endocrine tumors associated with MEN1: collagenomas, facial angiofibromas, lipomas and leiomyomas.

**Case Presentation:** A 46 year old Caucasian female presented to our clinic for ongoing management of her MEN 1 syndrome. She had an enlarging right abdominal wall mass, which measured 7.0 x 6.4 x 1.8cm on ultrasound. She previously had excision of four benign subcutaneous lipomas. She also had a history of breast cancer treated with lumpectomy, radiation therapy and Tamoxifen. She was genetically diagnosed with MEN 1 (age 24) when she presented with fatigue and was noted to be hypercalcemic due to hyperparathyroidism. She was subsequently found to have five parathyroid glands and underwent two surgical resections for treatment. She had a 9mm Pituitary Adenoma (Prolactinoma, age 28), treated for a decade with a dopamine agonist therapy which was discontinued when Prolactin levels normalized. In addition she has a history of hypergastrinemia with pancreatic and duodenal tumours (age 37), which are followed with serial imaging MRI’s (no change in size since 2012, largest lesion 1.2 cm islet cell, 1.6cm duodenal mass) on Omeprazole (20mg od) therapy for GERD symptom relief. She has primary hypothyroidism (on Levothyroxine 88 mcg od) and a 1.9cm right thyroid nodule that has been stable on ultrasound since 2009 and FNA biopsy suspicious for a follicular neoplasm. She has 2 children, one of whom has been diagnosed with MEN1 (female, age 15).
Her father had MEN 1 with primary hyperparathyroidism, Zollinger Ellison Syndrome and bronchial carcinoid. An ultrasound guided biopsy of the right abdominal wall mass showed it to be a benign myxoma. As the mass was starting to cause discomfort, she was advised to have the mass resected. Although abdominal wall myxoma is a benign tumor with no risk for malignant transformation elective resection is advised to relieve mass effect symptoms and to confirm the diagnosis, as sampling error may misdiagnose a more aggressive tumor such as liposarcoma with myxoid changes. There is a 5% recurrence rate after resection.

**Conclusion:** MEN1 has both functioning and nonfunctioning tumors (and hyperplasia) of the pituitary gland, parathyroid glands, and pancreatic islet cells. In addition, MEN1 patients can have adrenal or thyroid tumors and non-endocrine tumors, such as lipomas, angiofibromas, and leiomyomas. This case demonstrates a previously undescribed phenotype of MEN 1 syndrome associated with parathyroid, pituitary and entero-pancreatic tumors, lipomas and an abdominal wall myxoma.

**Abstract #823**

**BILATERAL CATARACTS REVEALING POST-THYROIDECTOMY HYPOPARATHYROIDISM: CASE REPORT**

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**Objective:** The common symptoms of hypocalcaemia resulting from hypoparathyroidism include tetany, confusion, weakness and paraesthesiae. However chronic hypocalcaemia is associated with mild neuromuscular irritability and may be asymptomatic. In this report, we present a case of profound hypocalcaemia that presented 1 year after thyroidectomy and was diagnosed during the management of bilateral cataracts.

**Case Presentation:** A 17 Y.O adolescent was admitted to the ophthalmology department for the management of bilateral cataracts. The patient medical history was significant for a total thyroidectomy 12 months ago for a multinodular goiter, she subsequently developed bilateral cataracts. On questioning, the patient reported muscle cramps and fasciculation that occurred 5 months ago. On examination, shvostek’s sign was negative. Routine lab investigations found a low calcium level (1.14 mmol/l (2.10-2.60)). Albumin level was normal (42g/dl(30-60)). The patient was biochemically euthyroid. PTH levels were indetectable. The patient underwent cataract surgery and received calcium and vitamin D substitution.

**Conclusion:** Lens abnormalities caused by hypocalcaemia are usually bilateral and consist of punctuate, iridescent opacities of the anterior and posterior cortex. The opacities may remain stable or progress to a complete cortical cataract as was the case in our patient. Young patients presented with bilateral cataracts should have calcium levels checked in order to rule out a chronic hypocalcaemia

**Abstract #824**

**VITAMIN D STATUS AMONG WOMEN LIVING IN A SUNNY REGION: MARRAKESH STUDY**

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**Objective:** Background: Hypovitaminosis D is associated with poor dietary intake and inadequate sunshine exposure. It is common worldwide. However, just few studies were undertaken in the sunny regions of the globe.

**Objective:** We undertook this study to determine the specific prevalence of hypovitaminosis and its relationship to metabolic parameters in pre-menopausal women living in a sunny region.

**Methods:** The group studied included 105 patients aged from 18 to 45 years. Between March and July, we assessed socio-demographic parameters, metabolic parameters and associated pathologies as well as risk factors for hypovitaminosis. 25 OH Vitamin D, serum calcium, phosphorus and lipid panels were measured. Hypovitaminosis was defined for the values below 75 nmol/l.

**Results:** All the patients have hypovitaminosis with a mean value of 10.20 +/- 8.3 nmol/l. 78.1% had a vitamin D value under 25 nmol/l while 21.9% had insufficiency. Calcium and phosphorus were normal. The hypovitaminosis severity was not correlated to the metabolic parameters (BMI, Lipids, FG, HbA1c).

**Conclusion:** Our results show that hypovitaminosis is common among young Moroccan women even if they are living in a sunny region. In the absence of precise information regarding the vitamin D intake and the time spent outdoors, this should emphasize the need for evaluation of vitamin D status in every women. Prevention strategies should be initiated by governments regarding the enhancement of vitamin D intake.
Abstract #825

PTHrP-INDUCED HYPERCALCEMIA AND RESPONSE TO TYROSINE KINASE INHIBITOR

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Objective: To describe an unusual case of Renal Cell Carcinoma (RCC) with Parathyroid Hormone-related Protein (PTHrP) induced hypercalcemia that resolved with Sunitinib.

Case Presentation: RCC is the most common type of kidney cancer in adults. RCC may remain clinically occult for most of its course. Only 10% of patients present with the classic triad of flank pain, hematuria, and flank mass. PTHrP plays crucial roles not only in development and in various physiological events associated with normal life, but also in a number of pathological conditions such as cancer and appears as the major causative agent in humoral hypercalcemia of malignancy associated to a broad range of tumors such as RCC. This patient is a 67-year-old male who had been complaining of chronic constipation for years, so he had basic labs that were significant for iron deficiency anemia, calcium of 11.5, and creatinine of 1.38. Workup was significant for PTH of 2; therefore, the patient was referred to Endocrinology for further management. On further tests, the patient had an elevated PTHrP at 3.1, with normal Vitamin D and TSH levels as well as normal protein electrophoresis and 24 hour urine collection for sodium, calcium and creatinine. CT chest/abdomen/pelvis demonstrated multiple bilateral renal lesions consistent with renal carcinoma in addition to left upper lobe pulmonary nodule. Further investigation included renal mass biopsy that confirmed renal cell carcinoma, eosinophilic variant of clear cell type. He was later determined to have Stage IV RCC after following with Oncology. After this diagnosis, the patient was started on Sunitinib.

Discussion: Hypercalcemia resolved while the patient was on Sunitinib, last level was 8.5, and his creatinine is now down to 1.15.

Conclusion: This case highlights the potential role of PTHrP in the regulation of tumor growth and invasion and, thus, the therapeutic potential of PTHrP-targeting strategies in human cancer including RCC.

Abstract #826

ALCOHOLIC KETOACIDOSIS MASQUERADING AS DIABETIC KETOACIDOSIS

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Objective: Describe a case of alcoholic ketoacidosis and the challenge of making the correct diagnosis. Alcoholic ketoacidosis is an important diagnosis to consider in patients with chronic alcohol use who presents with a high anion gap metabolic acidosis and hyperglycemia.

Case Presentation: 34-year-old female with no past medical history, presented with a five-day history of vomiting and abdominal pain. She reported a prolonged daily use of alcohol, with a recent binge six days previously. She denied any alcohol use since that time. The patient denied fever, polydipsia, or polyuria. She was afebrile, tachycardic, normotensive and physical exam was notable for lethargy, dry mucous membranes and abdominal tenderness. Initial laboratory studies showed glucose 231 mg/dL, bicarbonate 9 mmol/L, anion gap 30, HbA1c of 5.1%, lipase 3479 u/L, lactic acid 1.2 mmol/L, positive serum ketones, positive urine ketones and negative serum ethanol. The patient was kept NPO and started on intravenous normal saline with dextrose, thiamine 100mg IM daily and lorazepam 2mg IV every 2 hours as needed. Gastroenterology was consulted, and an abdominal ultrasound was performed and was negative. On hospital day two, the anion gap decreased to 17, lipase decreased to 1840 u/L and she was started on a clear diet. Hospital day three, the anion gap improved to 5, lipase improved to 1048 u/L. Intravenous fluids were discontinued, and she was started on thiamine 100mg by mouth and her diet was advanced. The patient was subsequently discharged home.

Discussion: Ketoacidosis with hyperglycemia is generally identified with diabetic ketoacidosis. However, alcoholic ketoacidosis should be considered in the differential diagnosis when there is a lack of symptoms associated with chronic hyperglycemia in conjunction with a history of heavy alcohol use. The case illustrated the importance of differentiating alcoholic from diabetic ketoacidosis so that there is no inappropriate use of insulin therapy.

Conclusion: Alcoholic ketoacidosis must be considered in the differential diagnosis of a patient presenting with high anion gap, hyperglycemia, and history of alcohol use.
Abstract #827

A CASE OF HASHIMOTO'S ENCEPHALOPATHY REQUIRING INTRAVENOUS IMMUNOGLOBULIN TREATMENT

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Case Presentation: Introduction: Hashimoto’s encephalopathy is a rare disorder with an unknown etiology and incomplete understanding of the pathophysiology. It presents with a wide range of symptoms and is almost always responsive to high dose steroids; however, a small number of steroid unresponsive cases have been reported. We present a case of Hashimoto’s encephalitis which was partially steroid responsive, with a full response to steroids + IVIG.

Case: An 82 year old man with a history of hypothyroidism, mild dementia, and hypertension presented with worsening mental status x 6 weeks. 2 weeks prior to admission he was brought to the ED by family as they noticed he was depressed and not taking his medications. TSH was 14.9 and levothyroxine 75mcg was restarted. On the day prior to admission he expressed suicidal ideation, auditory hallucinations and was refusing all oral intake. A ROS was unable to be obtained as he was altered.

Exam was remarkable for a confused, elderly man with brisk hyperreflexia throughout, and positive babinski reflexes bilaterally.

TSH was 8.7, FT4 1.28, T3 112, thyroxine 11.1. Synthroid 75 mcg/day was continued. CT head found mild generalized atrophy with an old lacunar infarct. Lumbar puncture showed: glucose 84, protein 43, 3 WBC. HSV, lyme, CMV, cryptococcal antibodies were negative. EEG showed increased activity over both temporal lobes. MRI brain w/ gadolinium showed no acute changes. Repeat EEG showed mild diffuse background attenuation and slowing. Mental status continued to decline over the next few days prompting an endocrinology consult.

Anti-TPO antibody was 223 and free thyroxine by direct dialysis was 3.0. The patient received 3 days of prednisolone 500mg IV BID with mild improvement. He was then transitioned to PO prednisone but had no further progress. IVIG 400mg/kg/day was initiated, and after a 5-day course, he returned to his baseline. Repeat anti-TPO antibody was 115. AM cortisol was 28 and steroids were safely stopped prior to discharge.

Discussion: Our final diagnosis was Hashimoto’s encephalopathy, and responded to systemic steroids, confirming the diagnosis. Interestingly, this patient only partially responded to steroids then made a dramatic improvement after IVIG therapy.

Conclusion: Hashimoto’s encephalopathy is a complex, poorly understood disease that has a wide variation in its presentation as well as responsiveness to therapy. Our patient required both steroids and IVIG for an adequate response.

Abstract #828

EXERCISING LEADING TO TEMPORARY PARALYSIS: A CASE OF FAMILIAL HYPOKALEMIC PERIODIC PARALYSIS

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Objective: The regulation of total body potassium is a complex process that is tightly regulated through a variety of mechanisms. It has a normal extracellular range outside of which patients can have a variety of symptoms. We present a case of symptomatic paralysis from hypokalemia caused by familial hypokalemic periodic paralysis syndrome (FHPP).

Case Presentation: A 24 year-old male with a history of FHPP presented with weakness and increasing paralysis after strenuously exercising the night before. On arrival he was no longer able to move at all and had a potassium level of 1.2. With replacement his potassium normalized and his symptoms resolved after several hours. He has had multiple admissions to the hospital since childhood for transient episodes of paralysis during which he was areflexic. Every time these episodes had occurred after he had eaten large meals or had undergone strenuous exercise and would present with hypokalemia. His mother also had a similar history of episodes. He had undergone extensive testing to distinguish his symptoms from other causes of periodic paralysis (PP) including thyrotoxicosis, Anderson syndrome and myasthenia gravis. He and his mother had genetic testing after several admissions that verified that they had the most common calcium channel mutation for FHPP. He was ultimately discharged home after being educated to avoid triggers of potassium shifts and to seek prompt medical attention at the onset of symptoms.

Discussion: FHPP is the most common cause of PP. Accurate diagnosis with genetic testing is important, since patient education on the disease can prevent future episodes. FHPP is a disorder which is an incompletely penetrant, autosomal dominant disease with defects in skeletal muscle ion channels that facilitate intracellular shifting of potassium. Precipitants for attacks are activities...
that cause a surge in catecholamines or in insulin. Symptoms typically start as attacks with generalized weakness progressing to complete paralysis.

**Conclusion:** This case illustrates a common presentation for a very rare disease and cause of transient paralysis. Careful management of these episodes of paralysis is important. One has to take care when correcting a patient’s potassium with this disorder with overall normal total body potassium, as it is easy to over correct. Education of the patient regarding avoidance of triggers of intracellular shifts (especially strenuous exercise or high carbohydrate loads) is important to avoid further episodes. This disease is a lifelong disorder but through diligence by the physician and the patient the impact on the patient’s life can be minimized.

**Abstract #829**

**EFFECT OF BODY MASS INDEX (BMI) AND LIPIDS ON NON-SMALL CELL LUNG CANCER (NSCLC) SURVIVAL**

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**Objective:** Obesity is a known risk factor for numerous types of cancer. There is evidence that proteins secreted by adipose tissue affect progression of malignant cells and overall survival. The effect of obesity in non-small cell lung cancer however remains unclear. The aim of this study was to investigate the effect of BMI and lipids in the survival of patients with NSCLC.

**Methods:** We retrospectively reviewed the records of all patients diagnosed with (NSCLC) at our cancer center from 2010 to 2013. Data analyzed included: demographics, tumor characteristics, lipid profiles and BMI at diagnosis, at the time of surgery and before chemotherapy. Kaplan-Meier was used for survival analysis and Cox regression for univariate and multivariate analyses.

**Results:** There were 730 patients; median age at diagnosis was 70 years. There was an equal distribution of females and males. The median BMI at diagnosis was 26 kg/m² (range: 15.2-44.7 kg/m²), at the time of surgery was 24 kg/m² (15.46 kg/m²) and before chemotherapy was 22 kg/m² (13.8-41.3 kg/m²). At diagnosis, median LDL of 90 mg/dL (25-189 mg/dL), HDL 44mg/dL (14-98 mg/dL), and triglycerides 105 (42-371 mg/dL). Of the comorbidities reviewed, 38% of patients (n=274) had hyperlipidemia and 20%(n= 144) diabetes mellitus. Regarding treatment, 39.7% (n=290) underwent surgery, 71.5% (n=522) received chemotherapy and 31.6%(n=231) radiation. Overall median survival was 26.8 months (95%CI: 17.5-31.6).

There was a significant difference in overall median survival between patients with a BMI<20 kg/m² compared to a BMI>20 kg/m² at the time of chemotherapy, 16.7 months (95%CI: 9.2-21.1) vs. 27 months (95%CI: 24.2-31.8) (p<0.01). At the time of surgery patient’s with a BMI>30 kg/m² had lower survival 18.3 months (95%CI: 10.2-21.0) when compared to patients with a BMI<30 kg/m² 26.9 months,( 95%CI: 19.4-30.1) (p<0.03). History of hyperlipidemia or HDL<50 mg/dL was not a predictor of survival by univariate or multivariate analysis.

**Discussion:** In the past, studies have been inconclusive about the effect of BMI on survival and complications post-surgical resection. Our data suggests an elevated BMI at time of surgery was shown to have a decreased survival, and lower BMI prior to chemotherapy was associated with decreased survival. The later observation has not been detected previously. The effect BMI has on survival may influence type of treatment provided by clinicians but also clinical trials for treatment options. If survival is known to be affected by BMI, patient selection may be altered.

**Conclusion:** The effect of BMI on survival in NSCLC varied depending on the type of cancer treatment. There was no effect shown in this study between hyperlipidemia or low HDL on survival.

**Abstract #830**

**RARE CASE OF SEVERE HYPERCALCEMIA: GAUCHERS DISEASE**

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**Objective:** Hypercalcemia is one of the frequently encountered medical problems. Though most commonly caused by primary hyperparathyroidism or malignancy, a number of other conditions can lead to hypercalcemia. We report a case of Gaucher’s disease causing hypercalcemia which has sparingly been reported in the past

**Case Presentation:** 53 year old female with PMH significant for Gauchers disease, DM-2, systolic CHF, CAD, CKD III and chronic osteomyelitis of bilateral lower extremities was referred to the ED for a calcium level of 14.9. On further questioning, patient reported chronic hypercalcemia with a baseline of 11 since the diagnosis of Gaucher’s disease. Patient had chronic diarrhea, otherwise was asymptomatic. She denied any symptoms of hypercalcemia. Vitals were stable. Physical examination was unremarkable. Lab work in the hospital was significant for Calcium of 15.9 (corrected calcium of 15.98), Phosphorous 4.7mg/dl (2.8-4.9mg/dl), Intact PTH 13pg/ml (20 – 85pg/ml), 25 hydroxy Vitamin
ABSTRACTS – Other

D 21.6 ng/ml (normal 30-100 ng/ml), 1-25 Vitamin D 61.2 (19.9-79.3 pg/ml), PTHrp 28 pg/ml (normal: 14-27 pg/ml), BUN 44, Creatinine 1.8 (baseline 2), CRP 0.123 (0.02-1.20 mg/dl), ESR 35 (0-30 mm/hr), SPEP / UPEP was normal with no spikes, TSH 0.75 mIU/mL (0.76-4.60 MCIU/ML). CT scan with and without contrast of chest, abdomen and pelvis showed hepatomgaly with cirrhosis, cholelithiasis, abdominal and pelvic adenopathy unchanged from 2012. Patient was treated with IV fluids, Calcitonin and IV bisphosphonate, improving the calcium to 11.1. Patient was discharged with recommendation to follow up at the endocrine clinic. The cause of her hypercalcemia was determined to be from Gaucher disease after ruling out other causes of hypercalcemia with the above mentioned workup.

**Discussion:** Gauchers Disease is an autosomal recessive lysosomal storage disease, caused by deficiency of glucocerebrosidase leading to accumulation of glucocerebroside in lysosomal cells. The exact mechanism of hypercalcemia in Gaucher’s is not known but is postulated to be from pathological activation of osteoclasts due to proinflammatory cytokines. Circulatory Pro inflammatory cytokines and cathepsins, especially IL-6 and IL 10 are significantly elevated in GD. IL-6 is associated with osteolysis in multiple myeloma and in the development of post-menopausal osteoporosis. High levels of IL 6 thus mark the development of bone disorders and are also the markers of associated lympho-proliferative disorders.

**Conclusion:** Rare causes of hypercalcemia including Gaucher’s disease, Pheochromocyotoma, adrenal insufficiency for which the mechanism of action is poorly understood should always be ruled out when managing a patient with hypercalcemia of unknown etiology.

**Abstract #831**

**A CASE OF KETOACIDOSIS IN A BREASTFEEDING PATIENT ON THE PALEO DIET**

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**Objective:** Ketoacidosis is a life-threatening clinical condition that is usually thought of as a complication of diabetes mellitus, starvation, alcoholism, ingestion of medications, ethylene glycol or methanol. We discuss a rarely reported case of lactation ketoacidosis in humans.

**Case Presentation:** 31-year-old gravida 2, para 2, 16-weeks postpartum, lactating female presented with a 2-day history of shortness of breath, vomiting, and weakness. History was remarkable for an intentional 20-lb weight loss on the “Paleolithic diet” which was recommended by her dermatologist for eczema treatment. In addition, she was breastfeeding her newborn child, producing 70 oz of milk per day on average with excess to store.

On presentation, respiratory rate was 24 breaths/min, but physical exam was otherwise unremarkable. Lab results were significant for an arterial blood gas with pH of 7.1, pCO2 11.7, pO2 142.3, HCO3 3.7. Anion gap was 26 with lactic acid of 1.9, Beta-hydroxybutarate was elevated over 7.96, and Hemoglobin A1c of 4.5. A drug screen was negative. Insulin level was suppressed and cortisol level appropriate. Chest radiograph and CT Angiography were normal.

The patient was transferred to the ICU and treated with aggressive fluid resuscitation with 150 mEq of NaHCO3 in D5W at 150 cc/hr for 24 hours. Regular diet was started and breastfeeding stopped. Her symptoms and acidosis improved within 24 hours of admission. Anion gap closed and beta-hydroxybutarate normalized within 48 hours. Patient was discharged from the hospital on Day 4 with instructions to stop breast-feeding and dieting.

**Discussion:** Lactation ketoacidosis is a recognized disorder in cows known as “Bovine ketosis.” The rate of hepatic gluconeogenesis doubles to meet the demands of lactation without an increase in their dietary glucose supply. Lactating women rely on gluconeogenesis as well for milk production. The energy cost of breastfeeding is an additional 500 kcal/day. The average lactating woman produces 30 oz of milk daily while our patient was producing 2.5 times that quantity. Dieting lactating women are at risk to develop a more profound metabolic acidosis, especially those consuming a low carbohydrate diet. The nutritional requirements needed to support lactation are significant and therefore active weight loss should not be undertaken during breastfeeding.

**Conclusion:** Similar to prior reports, our patient was under the stress of lactation but the degree of her acidosis, a serum pH of 7.0, has rarely been reported. In her case, the Paleolithic diet and weight loss precipitated ketoacidosis while the increased metabolic demands of lactation produced a life-threatening acidosis.
Abstract #832

PRIMARY HYPERPARATHYROIDISM PRESENTING AS HAEMORRHAGIC STROKE IN A YOUNG FEMALE

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Objective: To present a case of haemorrhagic stroke in a young female suffering from primary hyperparathyroidism.

Case Presentation: A 39-year-old young female suffering from primary hyperparathyroidism presented with weakness of left side of the body, sudden onset progressed rapidly over two hours and was barely able to move her left arm or leg. History of slurring of speech, deviation of angle of mouth to right side, no history of diplopia, blurring of vision, seizures, prior transient ischemic events, sensory complaints, bladder bowel involvement. No history of hypertension, diabetes mellitus, and tuberculosis, high risk behaviour in the past. No family history of hypertension. On examination medium built woman adequate hydration and nutrition. Pulse 82/mnt regular; BP 200/110 mm Hg right arm equal in all limbs. She had palsy no icterus, cyanosis, clubbing, lymphadenopathy, neck swelling or edema. JVP not raised. CNS examination left hemiparesis with upper motor type of facial nerve palsy, rest of the systemic examination was normal. CT head intraparenchymal bleed in right external capsule and putamen measuring 4.3X1.7 cm. Hb 8.6g/dl(12.0-14.5), TLC 4600/cu mm (4000-11000), platelet 160000/cu mm (150000-400000), bilirubin-0.9mg/dl(0.2-1.2), AST/ALT 24/17U/l(15-50), blood glucose-93mg/dl(75-100), serum calcium-12.1mg/dl(8.5-10.5), phosphate-4.3g/dl(3.5-5.5), albumin 4.3g/dl(3.5-5.5), globulin 3.2g/dl(1.5-3.5), Serum calcium was 12.0,12.1mg/dl (8.5-10.5),phosphate 2.6mg/dl(2.5-5.5), T cholesterol 154.0mg/dl(150-250), triglyceride 107mg/dl(50.0-200). ANA, APLA antibody Negative. Carotid Doppler, 2D Echo, USG abdomen was normal. Vitamin D3 21.5ng/ml (30-56), Serum PTH level was 272 pg/ml (14-75). 2D Echo RML, carotid Doppler showed no AVM formation or aneurysm. CECT neck 18X8X7 mm hypodense nodule in inferior pole of right thyroid suggestive of parathyroid adenoma. Hospital stay: patient’s weakness improved over next few weeks, was discharged on bisphosphonates, antihypertensive and physiotherapy. Patient was submitted for planned surgery at a later date.

Conclusion: Hypertension in our opinion was secondary to hyperparathyroidism. Cerebral infarction due to hypercalcaemia & Hyperparathyroidism has been reported in very few occasions. This case is unique because CVA was haemorrhagic in hypercalcaemia due to parathyroid adenoma instead of ischemic.

Abstract #833

RURAL-URBAN DIFFERENCE IN LEVELS OF PHYSICAL ACTIVITY AMONG HAUSA-FULANI OF NORTH-WESTERN NIGERIA

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Objective: The objective of this study was to determine the level of physical activity among the Hausa-Fulani of Sokoto, Nigeria and to compare physical activity levels between rural and urban Hausa-Fulani of Nigeria.

Methods: This was a cross-sectional study conducted in Sokoto State in Northern Nigeria using multistage sampling design. Seven hundred and eighty two participants were recruited. Using the WHO STEP wise approach to surveillance (STEPS) instrument, information on socio-demographic, physical activity and anthropometric data was obtained. Being physically active was defined as participating in 30 or more minutes of moderate or vigorous activity per day for at least 5 days in a week.

Results: The mean (SD) age of the study population was 38.9 (36.6) years. Four hundred and sixty two (59.0%) subjects were physically active comprising of 182 (46.8%) and 280 (71.2%) from the urban and rural locations respectively. The male subjects (64.1%) were significantly more physically active than the females (53.6%) p=0.002. Occurrence of physical inactivity in the Hausa-Fulani increases with increased age and Body mass index.

Discussion: Physical inactivity is common among the Hausa-Fulani ethnic group of North-Western Nigeria. It is commoner in the urban compared to the rural dwellers. This may be due to the fact that rural subjects mostly live a subsistence economy where they farm and rear cattle. Much of their physical activity is occupational in nature and related to providing food and subsistence to their families. In contrast, the urban subjects have adopted Western lifestyle with low level of occupational physical activity.

Conclusion: There is therefore the need for public health
interventions to improve physical activity so as to reduce the risk of non-communucable diseases associated with physical inactivity.

Abstract #834

HIRSUTISM: EXPERIENCE WITH STEREOTYPE TREATMENT

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Objective: Hirsutism is an embarrassing problem particularly for unmarried females in a country like Bangladesh, where there is limited scope for cosmetic care. The prevalence is increasing due to increasing trend of obesity and PCOS. Evaluation to find out the causes like PCOS, Idiopathic or Familial, androgen producing tumor of Ovaries or Adrenals, Drugs, Cushing’s Syndrome etc sometimes not done properly. In many cases drug treatment and weight management is not feasible due to socio-cultural barriers.

Methods: Unmarried 75 cases of Hirsutism either Idiopathic or PCOS were analysed. Exclusion criteria was high Total Testosterone (> 25 % From Upper Limit), Glucose Intolerance or suspected other causes of Hirsutism. All cases are advised for low dose O(Oral Contraceptive Pill containing Ethinylestradiol 0.030 mg & Drospirenone 3 mg or Ethinyl Estradiol 0.03 & Desogestre 0.15 mg) and Spiranolactone 25 mg twice daily. Unstructured exercise and weight management was encouraged with Dietary modifications. Metformin or no other drugs were prescribed. All patients were followed for six months to one year. After initiation of treatment .Clinical ( Hirsutism , weight, BMI, BP) were recorded and Biochemical(Na, K, FPG) were investigated.

Results: All the cases(N=75) were analyzed. Age 22±07 years. BMI 26.2±2.2 Kg/M2. Hirsutism Grade 3-4(F-G) . Irregular menstruation was in 68 (90 %) cases. Per abdomen USG showed Enlarged Ovary in 31 %, Multiple cyst in 46% and nothing significant in rest 26 %. Total Testosterone were normal 58 (77%). Mild elevated( Upto 25% more than upper limit) in rest 23%. After treatment BMI 25±2.8 kg/M2 in 35 % subjects, increased weight 2-5 Kg among 75%. Hirsutism was improved in six months among 56 (75%) cases. Treatment satisfaction was 72 (96%). Irregular menstruation or other minor side-effect was noted and discontinued treatment in 3 (4%) cases only. No electrolytes imbalance (Na, K) were found to stop treatment. FPG were not significantly during study period. Dropout rate up to 12 months was 19(25 %).

Discussion: Hirsutism is not an uncommon problem but due to lack of awareness, patients presents late and sometimes shy to be exposed. For resource constrained society where cosmetic treatment is costly and limited scope, straight forward medical treatment is considered specially up to premarital stage. Socio-cultural perspective urges simpler but cost effective improvement of Hirsutism.

Conclusion: Significant (75%) improvement of Hirsutism and Menstrual Regulation with physical well being was observed in 96 % cases. The treatment (OCP +Spiranolactone) is very safe and effective .No Electrolytes imbalance was observed. Only 4% patient discontinued due to side-effects.

Abstract #835

VITAMIN D AS PROGNOSTIC MARKER IN SEPSIS

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Objective: To measure vitamin D levels in sepsis patients and to compare it with various mortality indicators used in critically ill patients in sepsis like SAPS II score, Charlson Comorbidity Index, procalcitonin and to find any association vitamin D levels and severity of sepsis calculated by mortality, ICU and hospital length of stay and duration of mechanical ventilation and to match them with vitamin D levels of age and sex matched healthy patients

Methods: Prospective observational study in tertiary care referral hospital attached to Medical college & university

Results: The mean age of the cases was 55.47 yrs, for the surviving group was 52,79 years & the non surviving 58.15 years. 58.33% were males and 26.04% had diabetes and 36.46% had cardiovascular risk factors. . The average vitamin D level in patients with sepsis in our study was 15.33 ng/dl and that of controls was 41.11ng/dl. Correlation of vitamin D with age, procalcitonin levels, ICU length of stay (LOS), Hospital LOS and mortality showed a negative correlation. Although mortality was not significantly contributed by vitamin D levels, the cut off for vitamin D was 23.83 ng/dl to predict patients of primary outcome (Mortality at 28 days) and had a sensitivity of 90.6% and a specificity of 77.1% with a good accuracy (Area under ROC curve 0.899). Survival was not significantly different between the deficient and insufficient groups or between the insufficient and sufficient groups of vitamin D although 71% of the cases had vitamin deficiency and mortality was more among the deficient (50.7%) and insufficient (41.7%) than among the sufficient group (14.6%) (p 0.809). Kaplan-Meyer survival plot showed increased hospital stay in vitamin D deficient then insufficient followed by normal vitamin D groups while a Hazard function showed more morbidity in
the deficient than in the insufficient and sufficient groups.

**Discussion:** Vitamin D stimulates innate immunity by activation of TLRs in the leucocytes and induction of peptides, β defensin 2 and cathelicidin that kills the organism, including M.tb. Vitamin D acts as an immunomodulator and its deficiency has been reported in patients of sepsis and may contribute to multi-organ dysfunction and nosocomial infections seen in them. Our studies correlate with various studies of vitamin D in critically ill.

**Conclusion:** This is the first prospective cohort carried out in this part of the world, near the tropics. Deficient levels of vitamin D has a possible role in sepsis. Further interventional RCTs with larger sample size and supplementation of vitamin D is required to substantiate the findings.

Abstract #836

**PREVALENCE OF NONALCOHOLIC FATTY LIVER DISEASE AND LIVER FUNCTION TEST ABNORMALITIES IN PATIENTS WITH TYPE 2 DIABETES MELLITUS**

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**Objective:** Nonalcoholic fatty liver disease (NAFLD) represents a spectrum of conditions and includes both nonalcoholic fatty liver and nonalcoholic steatohepatitis (NASH) with or without varying degrees of fibrosis and cirrhosis. A substantial proportion of the mortality in patients with type 2 diabetes mellitus (T2DM) is related to NAFLD and its complications. 10-75% of NAFLD patients have T2DM and 21-72% of patients with diabetes are reported to have NAFLD. We aimed to study the prevalence of NAFLD among T2DM patients and its relation with glycaemic status and metabolic factors like obesity and dyslipidaemia.

**Methods:** Total 100 patients with T2DM attending outpatient Diabetic clinic of semiurban multispeciality hospital of Feni, Bangladesh from January 2015 to September 2015 underwent abdominal ultrasonography to detect fatty Livers and evaluated. Patients who have secondary aetiology to cause fatty liver were excluded from study. Clinical data was obtained from each patients using a well structured questionnaire after obtaining informed written consent. Data was analyzed using the SPSS statistics 21 software.

**Results:** Out of 100 patients, 61 were male, 39 was female. Abdominal ultrasonography of study groups revealed 43 (43%) have fatty liver and 57 (57%) have normal ultrasound. Among fatty liver groups, 27 (62.7%) have Grade 1 fatty liver, 11 (25.5%) have grade 2 fatty liver and rest 5 (11.6%) have Grade 3 fatty liver and 9 patients (21%) presented with elevated liver enzymes. BMI (Body mass index) and triglyceride levels in the fatty liver group were significantly higher than patients with normal livers (p= 0.003 and 0.004 respectively) but glycaemic status (HbA1C) shown not to have significant association fatty liver.

**Discussion:** In this study we examined Diabetic patients attending at outpatient clinic to find out the prevalence of NAFLD by abdominal ultrasonography. In this study, average BMI of fatty liver group is 27.4±7 kg/m2 which is statistically significant. Although mild to moderate elevations of serum aminotransferase are common in NAFLD, In this study, 9 patients (21% of fatty liver group) presented with elevated liver enzymes. Dyslipidemia is common with NAFLD. In this study, triglyceride levels in the fatty liver group (average 227.4±106.8 mg/dL) were significantly higher than patients with normal livers (average 178.5±109.6 mg/dL) but glycaemic status (HbA1C) shown not to have significant association with fatty liver.

**Conclusion:** We conclude that the prevalence of NAFLD is high amongst T2DM patients and considering the increased liver mortality among these patients, NAFLD should be actively sought out and treated in patients with Diabetes.

Abstract #837

**LIFE THREATENING HYponatraEMIA Due To SYNDrome OF INAPPROPRIATE SECREtion OF ANtiDiuretic HORMone REVEALING A LUNG CANCER**

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**Objective:** Paraneoplastic hyponatraemia (plasma Na+ < 135 mmol/l) is a common finding in small cell lung cancer (10-25%); syndrome of inappropriate secretion of antidiuretic hormone (SIADH) accounts for about 60% of cases. Hyponatremia was also reported to be a prognostic marker in non small cell lung cancer, malignant pleural mesothelioma and a predictive marker of treatment efficacy.

**Methods:** TSH, Ft4, calcitonin were measured by chemiluminesce, plasma cortisol and ACTH by
electrochemiluminescence, chromogranin A (CgA) and neuron specific enolase (NSE) by ELISA.

**Case Presentation:** A 53 years old man presented with vertigo, postural instability, headache, incoherent speech. Biochemical data revealed severe, life-threatening hyponatraemia (plasma Na+ at admission= 110 mmol/l). Initial treatment consisted of administration of hypertonic saline, which lead to improvement of patient’s neurological status. There were no renal insufficiency, congestive heart failure, liver insufficiency, volume depletion. Further work-up showed syndrome of inappropriate secretion of antidiuretic hormone: low levels of serum uric acid, serum hypo-osmolality (271 mosm/kg) associated with an inappropriate high urinary osmolality (735 mosm/24 h) and urinary Na+ > 30 mmol/l (141.7 mmol/24h). Hormonal assessment found normal thyroid function (TSH=1.32 mIU/l, FT4=15.8 pmol/l, total T3=102 ng/ml), normal glucocorticoid axis (serum 8 a.m. cortisol=15.76 mg/dl, serum 8 a.m. ACTH=31.42 pg/ml, free-urinary cortisol=63.18 mg/24 hours). Neuron specific enolase (NSE) was markedly increased (59.7 ng/ml), while calcitonin (8.14 pg/ml) and chromogranin A (67 ng/ml) were normal. Computed tomography revealed right lower lobe lung tumor stage IIIb (T4 N3 M1a) with regional invasion and lung metastases, right pleural effusion, pericarditis. Evolution was favorable under oncologic treatment.

**Discussion:** Proper biochemical and endocrine work-up are mandatory for diagnosis of syndrome of inappropriate secretion of antidiuretic hormone. Identification of the etiology of SIADH, early diagnosis and correction of hyponatraemia can improve the prognosis of the case.

**Conclusion:** This clinical case highlights the possibility of severe hyponatraemia revealing a lung cancer.

Abstract #838

A CASE OF PARATHYROID ADENOMA WITH NORMAL PTH LEVEL: A SPECIAL ENTITY FOR PRIMARY HYPERPARATHYROIDISM

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**Objective:** Primary hyperparathyroidism (PHP) is the most common cause of hypercalcemia in outpatient based clinic. PHP consists of high intact parathyroid hormone (iPTH) level and hypercalcemia. Normocalcemic PHP is also known as a phenotype of PHP. However, hypercalcemia with normal iPTH levels on a PHP context is not well known.

**Case Presentation:** A thirty-six year-old woman who have type 2 diabetes mellitus was admitted to the hospital with the diagnosis of acute pancreatitis caused by hypertriglyceridemia. On laboratory examination; calcium level was 8.0 mg/dL (8.8-10.2), iPTH level was 28.8 pg/ml (12-88) and 25 hydroxy vitamin D level was 6.5 ng/ml. In her past medical history, hypothyroidism was present. So that, thyroid ultrasonography was performed. There was a 17x6 mm sized lesion outside the thyroid capsule at the bottom of right thyroid lobe defined as parathyroid adenoma. On Tc 99m MIBI scintigraphy, a lesion was demonstrated as parathyroid adenoma. On follow-up, serum Ca and iPTH levels were as follows: 10.6, 10.7, 10.9 mg/dl and 28.8, 33.3, 31.7 pg/ml, respectively. Twenty-four hour calcium excretion was above 400 mg/day. iPTH measurement was repeated in a accredited laboratory. iPTH was measured as 27 pg/ml in this laboratory also. iPTH was measured also by using dilution technique and obtained as 38 pg/ml. Hidration and furosemide treatment were performed, but the Ca levels was still high, which was 11.4 mg/dl. With the findings of hypercalcemia, hypercalciuria and positive sonographic and scintigraphic images, operation was performed with the diagnosis of PHP. Besides, we thought that hypercalcemia could precipitate the episodes of pancreatitis. During operation, PTH level was measured through right jugular vein as 634 pg/ml. Histopathological examination revealed as parathyroid adenoma. Postoperative hypocalcemia didn’t occur. Postoperative calcium levels were normal.

**Conclusion:** There are a few case in the literature showing hypercalcemia with normal PTH level in PHP. High intraoperative jugular PTH levels with normal peripheral PTH levels could be explained by rapid clearance of PTH or an issue of binding with antibodies. We think that this case will be important for the literature and clinicians who should keep such a case of PHP in their mind.

Abstract #839

CARDIOMETABOLIC RISKS AND INCIDENCE OF METABOLIC SYNDROME AMONG WOMEN WITH POLYCYSTIC OVARY SYNDROME

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**Objective:** It was a cross sectional and observational study of 75 women with PCOS, diagnosed on basis of the 2003 Rotterdam consensus criteria. Metabolic syndrome was defined according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III 2001) definition and WHO Criteria 1998. All collected data
were entered on Microsoft Office Excel 2007 for analysis. Statistical analysis was done using SPSS version 17.0. The study protocol was approved by the Institutional Review Board, and women were enrolled for the study only after an informed written consent. Patients aged <18 years were enrolled after taking consent of their parents.

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Results: According to NCEP ATP III 2001 and WHO 1998, the incidences of metabolic syndrome among PCOS women were 29.3% (n=22) and 4% (n=3) respectively. Total 23 (30.7%) out 75 PCOS women were diagnosed as metabolic syndrome by any definition. After adjusting the covariates, FBS (p=0.03), LDL (p= 0.05) and triglyceride (p=0.02) were found as predictor for metabolic syndrome among women with PCOS.

Discussion: Incidence of metabolic syndrome among PCOS women was 30.7%. Some other studies also showed similar high prevalence. Conversely, a relatively low prevalence, 14.5%, was reported in a Korean study as well as 8% to 16% among Italian women with PCOS, suggesting a modifying effect of racial and/or cultural differences. FBS, LDL and triglyceride were the key biochemical assessor for metabolic syndrome among women with PCOS.

Conclusion: Among the women with PCOS, the incidence of metabolic syndrome is high. Screening of blood sugar and lipid profile of PCOS women is necessary to identify metabolic syndrome along with other parameters.

Abstract #840

NATIONAL BURDEN OF NON-COMMUNICABLE DISEASE RISK FACTORS IN BANGLADESH

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Objective: Non-communicable diseases (NCDs) are now a serious public health issue in Bangladesh. In 2007, NCDs were reported to represent the highest cause-specific mortality burden among adults in Bangladesh. To date, a comprehensive nationally representative data are lacking on the NCDs using the full protocol of WHO-STEP approach to describe the NCDs risk factors in Bangladesh. The objectives of this study were to describe the prevalence of selected NCD risk factors in Bangladesh through a nationwide analysis.

Methods: After cleaning of data, finally 20039 from whole Bangladesh was used for final analysis. The target population for this survey includes all men and women aged 15 years or older who consider Bangladesh to be their primary place of residence excluding those who were in military base or group quarters (e.g. a dormitory) and who were institutionalized. The study uses the World Health Organization’s STEPS approach (modified), which entails a stepwise collection of the risk factor data based on standardized questionnaires covering demographic characteristics, somatic illnesses, somatic and mental symptoms, medications, life style, and health-related behavior (step 1), basic physical measures (step 2) and basic biochemical investigations (step 3).

Case Presentation: In Bangladeshi population the total prevalence of selected risk factors are as follows: smoking (21.7%), smokeless tobacco (30.8%), low intake of fruits and vegetables per day (86.9%), inadequate physical activity (41.4%), alcohol consumption (0.7%), raised blood pressure (23.8%), diabetes (10.6%), overweight and obesity (24.1%), abdominal obesity (19.7%), raised total cholesterol (28.0%), hypertriglyceridemia (33.8%),
low HDL level (65.7%). Nearly half of the participants use any types of tobacco, 17.8% reported were diagnosed with high blood pressure, and 6.5% reported having diabetes. Overweight, abdominal obesity, physical inactivity, low intake of fruits and vegetables per day, smokeless tobacco, raised cholesterol and raised blood pressure (BP) were more common in females than males, 25.5% vs 22.7%, 31.1 vs 8.3, 60.1% vs 22.6%, 93.1% vs 80.6%, 31.9 vs 29.6, 30.7% vs 25.3% and 26.6% vs 21.0%. A total of 5.07% of the teenagers had one risk behaviour, 20.74% had two, 28.57% had three, and 43.37% presented all the investigated risk behaviors. Only 2.25% did not display any of the analysed risk behaviours.

Conclusion: Diabetes, high BP, high TG, low HDL, and obesity are a public health concerns in Bangladesh. Adequate and continuous monitoring of NCD risk factors in Bangladesh is needed, and the surveillance findings should be used in health promotion and disease prevention activities.

Abstract #841
ASSOCIATION OF DEPRESSION WITH TYPE 2 DIABETES IN BANGLADESHI ADULTS- A CASE CONTROL STUDY

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1. Bangabandhu Sheikh Mujib Medical University, 2. Sadar Hospital, 3. Medical College for Womens

Objective: The purpose of this study was to describe the association of depression among diabetic patients in tertiary care hospitals of Bangladesh compared with people without diabetes.

Methods: We conducted a case-control study in Bangabandhu Shiekh Mujib Medical University to assess the study objective. We identified 121 cases of type 2 diabetes based on diagnostic criteria and prescription records for individuals had the evidence of least one year treatment irrespective of their sex. For each case subject, one control subjects were randomly selected from the non diabetic population during the same index period. Since the cases and controls are at first screened and confirmed by trained medical officer and specialist psychiatrics of BSMMU using HADS and DSM-IV questionnaire respectively. Simple and multivariate logistic regression analysis was used to estimate the odds ratio (OR) and 95% CIs, after adjusting for age, sex.

Results: According to DSM-IV, 68(56.2%) of Diabetics had depression while 30(24.8%) of control having depression, so that association of depression was almost double in diabetics than control population. The risk of developing depression among diabetic was around seven fold higher than people without diabetes [OR 7.005 95% CI 3.44-14.284, p= .000]. we found higher WHR and higher income were found to be associated with depression but this association was no longer significant at the multivariate level when controlling for other demographic and clinical variables [BMI[OR 0.43 95% CI 0.17-1.01, p=0.08], Income p=0.388]. high prevalence of depression among female [OR 4.27 95% CI 2.06-8.87 p=0.000] even after controlling for potential confounding factors, gender remained as the strongest risk factor for depressive symptoms, with nearly a fivefold increase risk in females compared with males.

Conclusion: Significantly higher association of depression in patient with diabetic had been found in our study. So diabetes may be a risk factor for developing depression and vice versa. But the causal relationship between diabetes and depression is still unexplored.

Abstract #842
NOVEL ACTION OF SAROGLITAZAR IN PATIENTS WITH DIABETIC DYSLIPIDEMIA – AN OBSERVATIONAL STUDY.

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Objective: To evaluate the safety and efficacy of saroglitazar in patients with diabetic dyslipidemia, not controlled by statin and with elevated liver enzymes

Methods: This is a single centre, observational study of saroglitazar in Indian diabetic patients who were on statin and metformin. Total 50 patients (58% male), with a mean age of 49.62 years were included. All patients were on stable doses of metformin (mean dose 1070 mg/d) and statin (atorvastatin 5-20 mg/d or rosuvastatin 5-10 mg/d). The mean baseline HbA1c, TG, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were 7.51%, 272 mg/dL, 68.84 U/L and 65.04 U/L respectively. All patients were prescribed saroglitazar 4mg once daily for 12 weeks without changing the doses of on-going metformin and statin therapy. Patients were evaluated for change in lipid parameters, glycemic parameters and liver enzyme at 12 week follow up. The changes in laboratory parameters from baseline to 12 week follow up were statistically evaluated using paired “t” test

Results: At 12 week follow up, there were significant improvements in lipids [reduction in TG from 272 to 119.66 mg/dL (p=0.0001), LDL-C from 88.84 to 84.68 mg/dL (p=0.004), total cholesterol from 159.98 to 147.50 mg/dL (p=0.0005)]; increase in HDL-C from 39.34
to 40.40 mg/dL (p=0.046]) and glycemic parameters (reduction in HbA1c from 7.51 to 7.21%, p=0.0001). Significant reductions were observed in ALT (from 68.84 to 22.68 U/L; p=0.0001) and AST (from 65.04 to 22.80 U/L; p<0.0001). There was no significant change in serum creatinine level (from 0.72 to 0.74 mg/dL). No major adverse event reported during follow up.

Discussion: Saroglitazar is a dual peroxisome proliferator-activated receptor (α/γ) agonist, approved in India for the treatment of hypertriglyceridemia in type 2 diabetes not controlled with statin. Nonalcoholic fatty liver disease (NAFLD) is strongly associated with obesity, dyslipidemia, type 2 diabetes mellitus, and cardiovascular disease. Saroglitazar improves insulin sensitivity and is a potent agent for controlling hypertriglyceridemia. The results of this study indicate that 12 week saroglitazar treatment is associated with significant improvement in liver enzymes in patients with type 2 diabetes and dyslipidemia.

Conclusion: 12 week treatment with saroglitazar 4 mg once daily significantly improves liver enzymes along with lipids and glycemic parameters in patients with type 2 diabetes and hypertriglyceridemia. This assumes significance in the treatment of Metabolic Syndrome where fatty liver is an important component often difficult to manage.

Abstract #843

STATUS OF GLYCEMIC CONTROL OF ADULT TYPE 2 BANGLADESHI DIABETIC PATIENTS

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Objective: The aim of the study was to determine the frequency and status of glycemic control among adult type 2 diabetic (T2DM) people in Bangladesh.

Methods: This cross sectional study was conducted in the outpatient departments of diabetes care centers of Dhaka, Bangladesh during January 2013 to December 2014. The randomly selected adult type 2 diabetes, upon fulfilling the informed written consent form, were recruited for the study. A semi-structured questionnaire containing items to elicit socio-demographic information and relevant information about co-occurring physical illnesses was used. Diabetes related information were collected from the patient’s guide book provided by the hospital. Three milliliter of venous blood was taken for estimation of HbA1C.

Results: Total 5140 adult T2DM patients were included in the study and 32.99% of them were aged between 40-49 years and 33.54% were aged between 50 - 59 years. Most of the respondents (64.05%) came from urban background. About 27.12% T2DM patients studied up to primary level and 57.47% up to college level. About 51.46% were male and most of them were house wife. Around 19% were smoker and 27.1% were smokeless tobacco consumer.

About 10.2% of the respondents were on medical nutrition therapy, 27.8% on secretagogue, 50.3% were on one or other OADs AND 21.4% patients took insulin of any form as their current modality of diabetes treatment.

Glycated hemoglobin (HbA1c) level was measured to determine the glycemic control status and 18.8% have their diabetes controlled, mean (i) is 8.78 . Level of education and family income seem to have significant relation with diabetes control status. HbA1c (P<0.01) showed to have better control with increasing educational attainment and higher level of family income among the diabetes patients, however family size doesn’t seem to have significant relation with diabetes control status.

Conclusion: Only 18.8% of Bangladeshi T2DM have their glycemic status controlled. Diabetes controlled seems to increase with higher age. Sex in general seems to be unrelated with HbA1C. HbA1c showed to have better control with increasing educational attainment and higher level of family income among the diabetes patients, however family size doesn’t seem to have significant relation with diabetes control status.

Abstract #844

CAN B-LYMPHOCYTE STIMULATOR (BLYS) BE A SEROLOGICAL PROGNOSTIC MARKER IN PATIENTS WITH NEUROENDOCRINE TUMORS?

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Objective: To evaluate the potential prognostic role of the cytokine B-Lymphocyte Stimulator (BLyS) in the follow-up of a large population of patients with neuroendocrine tumors (NET).

Methods: The study included 124 consecutive unselected patients (48.4% male, mean age 63.4 ± 12.9 years; disease duration 5.9 ± 4.4 years) with a diagnosis of NET: 36 patients with lung NET (24 typical carcinoid, 11 atypical, 1 large cell neuroendocrine carcinoma), 47 with gastrointestinal NET (GE-NET) and 41 with pancreatic lesions (30 nonfunctioning and 11 functioning: 9 insulinomas, 2
glucagonomas). In 23 cases BLyS was repeatedly assessed during the follow-up (within 1 to 4 years from the first evaluation), and the disease was monitored (progression, stabilization or remission) according to the RECIST definitions. Patients were compared with a group of 77 healthy blood donors, matched for age and sex. Serum levels of BLyS and Chromogranin A (CgA) were analyzed using ELISA.

**Results:** NET patients generally present BLyS serum levels significantly higher than controls (1274 ± 808.6 pg/ml versus 666.5 ± 240.3 pg/ml; p <0.0001). A cut-off value, obtained from the ROC curve analysis, of 932 pg/ml discriminates between patients and controls with a sensitivity of 96% and a specificity of 67% (AUC: 0.9003; 95% CI = 0.8562-0.944). The levels of BLyS showed a significant but weak correlation with CgA (r=0.19 and p=0.035), while no correlation was found with Ki67, grading (G1 vs. G2/G3), or NET site. In patients with sustained remission after surgery, BLyS levels showed a gradual reduction over time (1478 ± 1398 pg/ml within 6 months vs. 1043 ± 514.5 pg/ml after 6 months; p=0.08). Patients with metastases tended to show higher levels of BLyS compared to those without (p=0.052). Patients with stable disease disclosed lower levels of BLyS compared to patients with progressing disease (1177 ± 365.6 pg/ml vs 1521 ± 680.9 pg/ml; p = 0.046). However, more elevated BLyS levels at baseline (diagnosis, before surgery and therapy) did not predict progressing disease in the follow-up.

**Conclusion:** Increased levels of BLyS are significantly associated with the presence of NET. They do not seem to have prognostic value at baseline, but they may identify a more severe disease in the follow-up, which is progressing despite treatment.

**Abstract #845**

**SINGLE HISTRELIN IMPLANT SUPPRESSES PUBERTY FOR FOUR YEARS**

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**Objective:** To report a case of a patient with persistent hypothalamic-pituitary-gonadal axis suppression after 4 years of Histrelin implant.

**Case Presentation:** Patient had initial endocrine evaluation at the age of 9 years. She presented with minimal vaginal bleeding. Breast development was at Tanner stage III. Tests disclosed pubertal LH 0.37, FSH 5.01 and estradiol 21 pg/ml. Bone age was 13 years. She received the Histrelin implant. Patient missed several appointments due to maternal mental health issues. Patient returned for implant removal after 4 years. Breast development was still at stage III. Patient had no menstrual bleeding while on the implant. Tests showed suppression of HPG axis (LH 0.12, FSH 1.3 and estradiol 6.4). Bone age was at 15 years. There was difficulty in removing the implant. The implant had severely deteriorated and had amalgamated with the surrounding tissue.

**Discussion:** Histrelin implant is only FDA approved for 12-month use, containing 50 mg of Histrelin acetate and delivers approximately 65 mcg Histrelin acetate per day (approximately 24 mg/year). Hypothalamic-pituitary-gonadal axis suppression with the implant left for 2 years had been previously described. This case demonstrates that the implant can suppress the hypothalamic-pituitary-gonadal axis beyond 2 years.

**Conclusion:** This case and other studies involving the use of a single Histrelin implant beyond 12 months may be cost-effective for treatment of precocious puberty. However, scarring may make it difficult to remove the implant when left beyond 12 months.

**Abstract #846**

**THE DETECT STUDY: VITAMIN D DETERMINATIONS IN TWO CONSECUTIVE YEARS ARE CLOSELY CORRELATED IN AN EPIDEMIOLOGIC GERMAN STUDY (DIABETES CARDIOVASCULAR RISK EVALUATION TARGETS AND ESSENTIAL DATA FOR COMMITMENT OF TREATMENT)**

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**Objective:** Vitamin D deficiency is a risk factor for increased mortality and morbidity, including cardio- and cerebrovascular events, cancer, infectious and autoimmune diseases. Epidemiological data on Vitamin D are mainly derived from studies with a single determination of 25-hydroxyvitamin D (25(OH)D). The DETECT study is a cross-sectional, prospective, epidemiological, primary care-based study in Germany, with two determinations of 25(OH)D in September 2003 and 2004. We evaluated the association of baseline 25(OH)D with follow-up levels after one year and the prevalence of Vitamin D deficiency.

**Methods:** We included 2454 non-smoking participants of DETECT with a complete set of Vitamin D from September 2003 and 2004. Samples were immediately deep-frozen at -70°C and analyzed in 2010. We performed
Pearson correlation analyses between 25(OH)D levels in 2003 and 2004 and analysis of variance (ANOVA) for continuous variables and Chi Square/Fischer exact test for categorical data.

**Results:** Mean age of patients was 59.7±13.8 years with 72% females. Vitamin D deficiency, defined as 25(OH)D<20 ng/mL was demonstrated in 16.6% of subjects in 2003 and 28.9% in 2004. The Pearson coefficient between 25(OH)D for the consecutive years was 0.61 (P<0.001). The correlation is present in age-and sex-stratified analyses. Vitamin D deficiency was significantly associated with older age, female sex and higher BMI.

**Discussion:** DETECT is the first study tracking 25(OH)D in a large cohort of primary care patients in Germany with two visits in an interval of 12 months, minimizing the impact of seasonality. Vitamin D levels of two consecutive years are well comparable, even though 2003 was an exceptionally hot and UV-intensive year. One may speculate that Vitamin D levels in modern, Western societies are much more influenced by lifestyle than by climate, geographical and weather conditions. We found a high prevalence of Vitamin D deficiency of almost 25% of the population; although we assume that in our study Vitamin D deficiency in Germany may be underestimated due to the collection time in late summer and to the selection of non-smokers and inclusion of Vitamin D treated and untreated subjects. Further in-depth investigations of our results are needed to translate our findings into clinical routine.

**Conclusion:** 25(OH)D levels in two consecutive years with extreme weather and UV differences are very well comparable. Vitamin D deficiency has a significantly high prevalence in primary care patients in Germany even in a very UV intense year and should be considered to be highly influenced by lifestyle and/or age and BMI.
showed hyponatremia (Na)-131 mmol/L, potassium of 7 mmol/L, bicarbonate 19.8 mmol/L and elevated blood urea nitrogen (BUN) of 22 mg/dl and a creatinine level of 1.7 mg/dl from a baseline of 1.4 mg/dl. The patient was hospitalized for hyperkalemia likely related to an acute on chronic kidney injury. She received intravenous hydration, insulin and sodium polystyrene for hyperkalemia. The patient continued to have hyperkalemia and elevated creatinine despite treatment. Given her history of CKD, hyperkalemia and metabolic acidosis hyporeninemic hypoaldosteronism was considered as a possible differential. Her aldosterone levels were low (less than 4 ng/dl) with high renin activity despite adequate hydration. The patient was noted to have hyponatremia, hyperkalemia, metabolic acidosis, borderline low blood pressure and low glucose levels; adrenal insufficiency became apparent. A serum cosynotropin test was done to confirm primary adrenal insufficiency.

The patient also had thyroid hormone resistance syndrome with TR beta gene mutation and was on high doses of levothyroxine. She tested positive for thyroperoxidase, thyroglobulin and 21 alpha hydroxylase antibody. Also, the patient was noted to have vitiligo. Connecting all the pieces together (primary adrenal insufficiency, autoimmune polyendocrine syndrome, and thyroid hormone resistance), a diagnosis of polyglandular autoimmune type II was made. Later, the patient provided further history of similar conditions in her daughter and granddaughter. The patient was started on fludrocortisone with hydrocortisone and the levothyroxine dose was further increased. The patient improved with treatment and was discharged with a close follow up.

Conclusion: Thyroid hormone resistance (RTH) is rare autosomal dominant with TR beta gene mutation. Over 1000 cases have been reported since 1967. We report a very rare occurrence of concomitant autoimmune polyendocrine syndrome and resistance to thyroid hormone (RTH) with TR beta gene mutation in codon 317. Similar mutation was found in patient’s daughter also. Here clinical presentation was not typical for RTH due to presence of autoimmune polyendocrine syndrome. Treatment is challenging as TSH is not a reliable indicator for the response. When a disorder like Addison’s disease is present, it is important to identify other disorders like hypothyroidism where glucocorticoid replacement should be preceded by thyroxine replacement.

Abstract #849

PRIMARY HYPERPARATHYROIDISM (PHPT) ASSOCIATED BARLOW’S MITRAL VALVE DISEASE (BMV)

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Objective: Serum ionized calcium concentrations are normally maintained within very narrow range that is required for optimal intra/extra-cellular activity and is tightly regulated by calcium-parathyroid hormone (PTH) homeostatic system. Some pathological conditions associated with PHPT include Adenoma (85% of cases), glandular hyperplasia and carcinoma. Some rare manifestations of PHPT are mitral valve Regurgitation with BMV.

Case Presentation: A 65 years old male with history of arthritis presented with a 12 month period of increasing generalized bone pains and fatigue. Physical examination at presentation was significant for grade II/VI non-radiating holosystolic apical murmur. Laboratory work up showed: Calcium 11.4 mg/dl, Parathyroid hormone (PTH) 243.8 pg/ml. Patient mentioned having an elevated calcium level for about a year and denied having a history of renal calculi. Outpatient work up revealed a DEXA scan that showed lumbar spine t score of -4.0 and Femoral neck or total hip t score of -2.2. Echocardiogram revealed severe mitral valve regurgitation, type II P2 and mitral annular calcifications (MAC), which was confirmed by trans-esophageal echocardiogram and coronary angiogram. Further work up included: parathyroid with SPECT/ CT Scan showing parathyroid adenoma inferior to the lower pole of the left lobe of the thyroid gland. During treatment course, the patient underwent parathyroidectomy. Intraoperative PTH was 427 pg/ml and postoperative PTH was 23.7 pg/ml consistent with successful procedure. Then, he underwent endoscopic robotic mitral valve repair during which a globally myxoid mitral valve with excess tissue was seen consistent with BMV disease. Eventually, the patient was discharged home with close outpatient follow up.

Conclusion: Mitral annular calcifications are reported in few case reports and stabilization of calcifications has been noticed after Para thyroidectomy. However it is important to diagnose hyperparathyroidism to avoid progression of cardiac disease, as seen in this case report.
COMPARISON OF PRIMARY HYPERPARATHYROIDISM PATIENTS WITH DIFFERENT INTACT-PTH LEVELS

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Objective: To compare primary hyperparathyroidism (PHPT) patients with different iPTH levels for serum calcium levels and other laboratory values.

Methods: In this retrospective study, charts of 182 PHPT patients who presented at Robert Wood Johnson University Hospital were reviewed. Patients were divided into two groups according to their serum intact parathyroid hormone (iPTH) levels. Student t-tests are used to compare the two groups for differences in age, body mass index (BMI) and laboratory test values, which included serum calcium, intact parathyroid hormone (iPTH), 25-hydroxyvitamin D (25OHD) and the lipid panel. Pearson’s correlation coefficients are used to assess the relationships. A P value < 0.05 was considered significant.

Results: Of the 182 PHPT patients, 88 (14 males and 74 females) who had serum iPTH below 140 pg/ml (101 ± 22.4) were classified as m-iPTH group, whereas 94 patients (20 males and 74 females) with serum iPTH above 140 pg/ml (248 ± 126) were classified as h-iPTH group. h-iPTH patients are younger than m-iPTH patients (58 ± 13 yo vs 62 ± 12yo, P <0.05). No statistic significant differences in BMI, total cholesterol TG and 25OHD levels were found between the m-iPTH group and the h-iPTH group ( P> 0.05). h-iPTH patients, compared with m-iPTH patients, had slightly but significantly higher calcium (11.3±0.71 mg/dl vs 11.0 ± 0.47 mg/dl P <0.05) and lower HDL (53.2±14 mg/dl vs 58.9± 20 mg/dl P<0.05). Additionally, we found iPTH was positive correlated with serum calcium (r=0.3, P<0.001), BMI (r=0.161, P <0.05) and triglyceride (TG) level (r = 0.127, P<0.05), and negatively correlated with HDL (r= -0.18, P <0.05). iPTH levels did not correlate with the total cholesterol levels (P>0.05).

Discussion: Finding from our analyses is consistent with previous studies suggesting iPTH levels correlated metabolic syndrome. Additionally, our results suggest that h-iPTH patients tend to be younger ones with lower HDL. While the underlying mechanisms for these changes are unclear, we speculate that the elevated iPTH levels might decrease HDL directly or indirectly though increasing insulin resistance.

Conclusion: Our study supports the notion that iPTH levels are an important factor to contribute in the management of PHPT patients. iPTH levels, lipid panel in addition to the calcium levels might also need to be considered in the therapeutic decision for PHPT patients.

A THOUSAND INSULIN UNITS DAILY FOR A 50 KG WOMAN? NOT YOUR TYPICAL DIABETES CASES.

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1. Louis A Weiss Memorial Hospital, 2. Hospital Nacional Arzobispo Loayza

Objective: We present two Latino patients with severe insulin resistance diagnosed and treated in Peru.

Methods: We reviewed literature, clinical characteristics, laboratories and treatment of the patients.

Case Presentation: First patient: A 42 year-old female with a history of RA, SLE and hashimoto thyroiditis presented with severe hyperglycemia. Her exam was remarkable for BMI:18 kg/m2, acanthosis nigricans, high testosterone, hirsutism and synovitis in wrists. Her laboratories showed negative anti-insulin antibodies, high HDL, high ESR, and negative HIV. Blood glucose levels ranged between 400 to 700 mg/dl, despite Insulin with up to total daily dose of 1000 IU. Diagnosis of type B insulin resistance autoimmune nature was made and immunosuppressive therapy was initiated. The patient received 8 pulses of 1 g cyclophosphamide monthly and prednisone 20 mg daily. One year later the patient was asymptomatic with BMI 24 kg/m2, HbA1C was 5.6% without therapy.

Second patient: A 42 year-old female presented with polyuria, polydipsia and hyperglycemia. She had BMI:18.2 kg/m2 with acanthosis nigricans and hirsutism. Blood glucose ranged between 500-700 mg/dl and was difficult to control despite high insulin doses (500 IU/d). Her laboratories showed negative GAD antibodies, high anti-RNP antibodies, high free testosterone, positive HTLV-1-2 and negative HIV. No immunosuppressive treatment was implemented. Slowly over time, insulin requirements diminished and two years later she did not require any insulin (HbA1C was 5.6%). She was asymptomatic, and she gained weight.

Discussion: To date, there are six published cases of Latino patients diagnosed with type B insulin resistance. The pathophysiology is explained by the presence of anti-insulin IgG receptor antibodies (anti-IRAB), which acts as partial agonists of the insulin receptor. Our patients presented with severe hyperglycemia, cachexia, achantosis nigricans, high testosterone, absence of anti-insulin antibodies or GAD antibodies. Our diagnoses were based solely on a clinical presentation and course. Confirmatory commercial anti-IRAB are not available in the region. Treatment of these patients could be challenging as well. An extra-large volume of insulin could be managed by using Insulin U-500 instead of U-100. Our first patient
achieved complete remission of the disease after receiving pulsed cyclophosphamide along with prednisone. Other regimens (e.g. rituximab) have shown promising results. Our second case presented a spontaneous remission and this is the first case reported in a Latino patient; however this self-limiting course remains unpredictable.

**Conclusion:** Anti-IRAB are not available in developing countries.
High clinical suspicion is recommended to establish diagnosis and treatment.

**Abstract #852**

**SYMPATHOMIMETIC AMINE THERAPY RESULTS IN TREMENDOUS RELIEF OF SYMPTOMS OF SCLEROSING MESENTERITIS**

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¹. Cooper Medical School of Rowan University, 2. Cooper Institute for Reproductive Hormonal Disorders, P.C.

**Objective:** The reproductive endocrinologist will frequently treat pelvic pain medically instead of surgically. The most effective medical treatment of pelvic pain is the sympathomimetic amine dextroamphetamine sulfate. The mechanism of pain relief is believed to be related to causing a release of dopamine from sympathetic nerve fibers which, in turn, decreases cellular permeability. The increased cellular permeability theoretically allows the absorption of unwanted chemicals or other toxic material leading to inflammation and pain. This therapy has successfully treated various types of inflammatory bowel disease, helping both pain and diarrhea. The objective of this study was to determine if dextroamphetamine sulfate could relieve the severe abdominal pain with eating in a 47 year old male related to sclerosing mesenteritis. Also, he would vomit at least 20 times per day.

**Methods:** Dextroamphetamine sulfate 15mg extended release capsules were prescribed. He was evaluated 1 month later.

**Case Presentation:** When evaluated 1 month after therapy he stated that within the first couple days of treatment his severe stabbing and shooting pain with eating was completely gone. His vomiting was reduced from over 20 times per day to 1 or 2. He did not get any relief from his joint pain related to psoriatic arthritis. He was asked if he wanted to raise the dosage to see if the joint pain could be ameliorated. He decided to stay at the same dosage because of side effects of dry mouth (common) and a rare side effect of diminished libido. His abdominal symptoms have remained markedly improved now for 4 months. He has not had one day of relief of symptoms prior to treating with dextroamphetamine sulfate in 4 years.

**Discussion:** This man had been to several highly regarded university centers. His diagnosis of sclerosing mesenteritis was biopsy proven. They explained that his pain with eating was related to the food causing increased blood supply to his stomach and thus stealing blood supply from the compromised mesenteric arteries leading to ischemia and pain.

**Conclusion:** Since the main beneficial effect on pain syndromes with dextroamphetamine sulfate seems to be related to correcting permeability defects, possibly increased cellular permeability leads to deposits of unwanted material in the mesenteric arteries leading eventually to sclerosis. Relief of symptoms may be provided by correcting the permeability defect. Testing excluded gastroparesis as the cause of his abdominal symptoms. Prior studies showed that both gastroparesis and pseudointestinal obstruction have been helped by sympathomimetic amine therapy.

**Abstract #853**

**EXTREMELY SEVERE UNEXPLAINED LEG EDEMA RESOLVED WITH TREATMENT WITH DEXTROAMPHETAMINE SULFATE**

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**Objective:** To evaluate the efficacy of treatment with dextroamphetamine sulfate for severe treatment refractory edema of the lower extremities.

**Methods:** A 39 year old man who weighed 460 pounds and was 85 inches tall noticed edema of his lower extremities. This progressed to such a severe degree that by age 44 he became disabled and was hospitalized. Though he was evaluated by vascular specialists, cardiologists, nephrologists, and endocrinologists that the etiology of his severe edema of his entire legs and feet and severe staging dermatitis remained unknown. He did not respond to conventional diuretics including furosemide. Following his discharge after being hospitalized for 1 ½ months he sought another opinion. He was started on 20mg dextroamphetamine sulfate extended release capsules. For insurance reasons he was switched eventually to 30mg immediate release amphetamine salts immediate release tablets twice a day.

**Case Presentation:** Within 2 months his edema completely resolved. He has remained edema free for 4 years while taking 30mg amphetamine salts immediate release tablets twice a day.

**Discussion:** This case demonstrates a few important points. First his condition without the existence of thyroid,
heart, kidney or liver disease or vascular abnormalities in idiopathic edema. Second, though idiopathic edema is more often seen in females, severe edema from this etiology can be found in men as evidenced by this case. Third, though the treatment with dextroamphetamine sulfate has been known for over 50 years, this therapy is not known to most treating physicians. In fact a very recent expert update on idiopathic edema was published and the treatment with dextroamphetamine sulfate was not emphasized at all despite the fact it is by far the most effective and least toxic therapy for this condition. The mechanism of action of dextroamphetamine sulfate is believed to stimulate sympathetic nerve fibers to make dopamine. The action of dopamine is to decrease capillary permeability which in this case, is to decrease capillary permeability. A decrease in capillary permeability is needed to prevent leakage of fluid from the intravascular to extravascular site in response to the increase in hydrostatic pressure which occurs when humans are in the erect position.

**Conclusion:** Severe idiopathic edema can be present in males. Dextroamphetamine sulfate should be considered as first line therapy not merely because of this case but a long history of successfully treating women with this treatment.

**Abstract #854**

**USE OF A BEHAVIORAL ENGAGEMENT MODEL TO IMPROVE PATIENT-PROVIDER COMMUNICATIONS: A PILOT STUDY OF A REAL LIFE APPLICATION IN AN ENDOCRINE PRACTICE**

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**Objective:** Effective communication is the basis of productive patient-provider relationship. Today’s patient-centered care environment calls for a behavior change model that improves provider communication-skills to effectively engage and empower patients for sustained behavior change, improved satisfaction, compliance and outcomes. This study explores the effects of Behavioral Engagement with Pure PresenceTM (BEPP) on patients’ satisfaction.

**Methods:** This one-group pretest-posttest study recruited 40 adult patients at a high-volume private endocrine practice, utilizing the Consultation and Relational Empathy (CARE) Measure Survey, pre- and post-intervention. An endocrinologist was trained to apply the intervention (BEPP). Paired-samples t-test were conducted on dependent variables against exposure to the intervention, the independent variable. Patient demographic and medical information were tested as covariates. Provider pre- and post-intervention Work Satisfaction Survey results on BEPP’s effect on provider satisfaction in the patient-provider relationship and workplace were reported.

**Results:** Paired-samples t-test showed statistical significance (p ≤ .05) on each dependent variable measured. Patient report on relational empathy in the patient-provider relationship increased through improved provider communication skills after applying BEPP. The endocrinologist reported favorable changes in workplace satisfaction (e.g., reduced stress, improved productivity, more time with patient).

**Discussion:** This pilot study confirmed that utilizing BEPP significantly improved patient-provider relationship. BEPP is a behavioral change model that applies an integrated approach to interpersonal communication engaging patients and providers, placing the whole patient at the center of care. Providers can learn a communication skill-set that would facilitate emotional shifting in patients altering subconscious brain state essential to sustained behavior change. New patients only participated in the study, to eliminate potential bias from established relationships with provider. The seasoned endocrinologist reported that he further developed communication skills improving empathy in the patient-provider relationship.

**Conclusion:** Results of this pilot study demonstrate the effects of BEPP to improve patient-provider communications for implementation in clinical practice. Future research is warranted to evaluate the effect of behavior modification models, such as BEPP, on disease outcomes in patients with chronic diseases such as diabetes, prediabetes and obesity. The success of management of such diseases is contingent on motivational interviewing, and effective providers’ communication skills.

**Abstract #855**

**COMPARING REGIONS OF BEST AND WORST LIVER FUNCTION INCREASES SENSITIVITY TO DETECT LIVER DISEASE IN INSULIN RESISTANT PATIENTS**

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**Objective:** Analyze relationships between best and worst areas of liver function and liver disease severity in insulin resistant patients.

**Methods:** SPECT liver-spleen scans used a Siemens Ecam, iterative reconstruction and low dose, < 0.4 mCi Tc-99m-sulfur colloid/L extracellular fluid, ECF in L = (Ht in m) (SQRT(Wt in kg)). Modified fractal analysis, extrapolated LN(A/M) vs. LN(V), for A=average counts in an isocontour
I of volume V, and M, either peak (for best function) liver counts, or minimum (for worst function), to define fractal slopes, Sb for the best, and Sw for the worst, areas of liver function, both normalized for BMI, ECF, and indices of liver and spleen size. Liver function categories were assigned using ultrasound, serum transaminases, a calculated hepatic fibrosis index, abdominal CT and liver biopsy. Montreal Cognitive impairment monitored cognition.

**Results:** Among 79 patients, Sb slopes were all positive and found in the liver right lobe. Whether calculated directly or from a quotient of the average and best slopes, the Sw slopes were all negative and found in the liver left lobe. Spleen Sb was between liver Sb and Sw, except for splenectomy or sickle cell patients. Sb and Sw are insensitive to image smoothing, variation usually < 15% for Gaussian filters from 5 mm to 10 mm using a 7 mm resolution collimator. Among many ways to normalize fractal slopes, the best used ECF/15; BMI/25; liver vertical span, L1/17, Liver AP diameter L2/12 and spleen vertical span/12. Near normal patients (n = 11) had HbA1c (5.9±0.6)%, Sb 0.49±0.04 and Sw -1.43±0.033; NAFL patients (n = 22) had Sb 0.60±0.09, Sw -2.12±0.67; hepatic steatosis patients (n = 20) had Sb 0.66±0.08, Sw 2.76±1.03; liver fibrosis patients (n = 25) had Sb 0.75±0.09, Sw -3.49±0.86. Patients (n = 23) with high HbA1c (11.1±1.2)% had Sb 0.75±0.11, Sw -3.52±0.92 similar to fibrosis patients. Liver disease severity and S values trended to correlate directly with overall complications of insulin resistance, including cognitive impairment, excluding brain injured patients and Cushing’s patients.

**Discussion:** Quantitative measure of liver function is increasingly important. The difference between Sb and Sw increases as liver disease progresses. Use of Sw increases sensitivity for early disease but Sw is more prone to attenuation artifacts and noise due to Poisson error at low count rates, which is reduced somewhat by adjusting tracer dose to ECF.

**Conclusion:** Abnormal liver function is fundamental to insulin resistance. Early liver disease is more sensitively detected by Sw, derived from the areas of worst liver function, or the ratio of Sb to average liver function.
ACROMEGALY WITH EMPTY SELLA IN A 43 YEARS OLD MALE

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Objective: The objective of this report is to describe a patient of acromegaly with empty sella and secondary adrenal insufficiency and hypogonadism.

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

Case Presentation: A 43 years old male was referred to the BIRDEM due to coarse facial features and visceromegaly which were noted incidentally during work-up for his chronic low back pain. He has been diagnosed as diabetes mellitus, hypertension and low back pain due to lumbar spondylosis since last 5 years but paid little attention to the facial features which was of same duration but not progressive. There was no history of headache, visual disturbance or excessive sweating. On examination he had prominent supraorbital ridges, enlarged nose and tongue and prognathism, deep and hollow voice, and spade like fingers and toes. Blood pressure was 160/100 mm Hg. Our provisional diagnosis was acromegaly with secondary diabetes mellitus, hypertension and lumbar spondylosis. Endocrine evaluation revealed raised serum basal growth hormone (10.2 ng/ml) and prolactin (543 mIU/L). Serum cortisol level was decreased (Basal-152 nmol/L, 30 min & 60 min after rapid ACTH stimulation- 441 nmol/L and 386 nmol/L respectively), but serum ACTH level was inappropriately normal (46.1 pg/ml). Serum testosterone (13.54 pg/ml), LH (2.81 mIU/ml) and FSH (4.68 mIU/ml) were also diminished. FT4 (15.10 pmol/L) and TSH (0.39 μIU/ml) were normal. X-ray skull lateral view showed enlarged sella, but interestingly MRI of sella with contrast revealed a partially empty sella. He was diagnosed as a case of burned out acromegaly with empty sella, secondary adrenal insufficiency, hypogonadotrophic hypogonadism, diabetes mellitus, hypertension and lumbar spondylosis. Glucocorticoid and testosterone replacement was started. On follow-up visits patient had sense of improved well being and no clinical sign of active acromegaly.

Discussion: Acromegaly with empty sella is not a common entity. Previously it was thought to be due to spontaneous remission of the growth hormone secreting adenoma, but recent evidences suggest that there may be coexisting growth hormone secreting microadenoma or ectopic growth hormone secreting adenoma. In one series of acromegaly patients with microadenomas, 20.3% had presurgical evidence of empty sella. Ectopic growth hormone secreting tumours are rare, with 38 case reports till date, only 6 of them presenting with empty sella.

Conclusion: Presence of an empty sella does not exclude active acromegaly in an appropriate clinical setting. It is imperative to follow-up the patient for an extended period of time for signs of an active tumour both clinically and biochemically.

PREGNANCY AFTER A DECADE OF AMENORRHEA IN A CASE OF HYPERPROLACTINEMIA WITH PARTIALLY EMPTY SELLA

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Objective: Most cases of secondary amenorrhea and primary infertility with hyperprolactinemia are due to prolactinoma. We report a case of secondary amenorrhea and primary infertility with hyperprolactinemia associated with partially empty sella.

Case Presentation: 34 year old lady presented with secondary amenorrhea and primary infertility for 10 years. She did not take medical advice as she believed she had reached early menopause. Noticing intermittent galactorrhoea for 1 year she visited our clinic 2 years back. She had no headache or visual symptoms. Drug history was negative. Vitals and visual fields were normal. There was galactorrhoea without regression of secondary sexual characters. Biochemistry showed normal thyroid function and prolactin of 470μg/l. Other anterior pituitary hormones were normal, MRI of the hypothalamo-pituitary region revealed partially empty sella. Signal in the compressed pituitary was normal.

She was given cabergoline 0.5 mg twice weekly. After 4 months prolactin was 18μg/l. After 4th dose of cabergoline galactorrhoea stopped and in 3rd month of therapy menstruation resumed. She was advised to monitor her cycles and use barrier contraception so that she may be shifted to bromocriptine with planned pregnancy. In 8th month of therapy she developed amenorrhea without galactorrhoea. Urine for pregnancy test was positive. Ultrasonography showed 7 weeks gestation. Cabergoline was stopped and bromocriptine 1.25 mg daily started. She is being monitored for pituitary growth with monthly visual field monitoring and for development of signs of raised intra-cranial tension. Fetal profile on imaging is normal. Expected date of delivery is 27th January 2016.

Discussion: Her diagnosis was missed for almost a decade as she had amenorrhea without galactorrhoea. This calls for awareness especially among peri-menopausal women (our patient was much younger) as amenorrhea could be falsely
attributed to early menopause. Empty sella may be associated with hyperprolactinemia but levels are usually <100μg/l. We believe the hyperprolactinemia in our patient was not due to stalk compression as level was very high. We hypothesized she had an adenoma which partially regressed due to micro-infarcts with the surrounding rim of pituitary still hyperfunctioning. Thus we felt the need to monitor the pituitary for increase in size during pregnancy.

**Conclusion:** Hyperprolactinemia (from any cause) may present with amenorrhea without galactorrhea. It is important not to miss the diagnosis especially in perimenopausal women. Surrounding pituitary rim in partially empty sella could be hyperfunctioning and needs to be treated and monitored for growth during pregnancy.

**Abstract #902**

**PITUITARY METASTASIS SECONDARY TO occult BREAST MALIGNANCY: A CASE REPORT**

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**Objective:** Pituitary metastases are rare and account for 1-2% of sellar masses. Breast and lung cancers are the most common diseases to metastasize to the pituitary gland. We report an individual with pituitary metastasis secondary to occult breast malignancy.

**Case Presentation:** A 56 year-old post-menopausal female presented with one month of weight loss and decreased appetite. She had no headaches, increased thirst or visual symptoms. Systemic review was unremarkable. Physical examination revealed right supraclavicular and axillary lymphadenopathy. Visual fields were normal. Computed tomography of the body and brain showed a mass in the cecum, suprasellar, and extensive intramuscular, bone, lung, lymph nodes and cerebellar deposits. Axillary lymph node biopsy revealed poorly differentiated adenocarcinoma that stained positive for human epidermal growth factor receptor 2 and estrogen receptor. Endoscopic biopsy of the cecal mass revealed similar histology. She was diagnosed to have occult breast malignancy with extensive metastases.

Magnetic resonance imaging of the pituitary fossa showed a 1.3 x 0.9 cm suprasellar mass inseparable from the pituitary stalk. The pituitary gland was normal. Her biochemistries showed panhypopituitarism: ACTH 5.3 (0-10.2 pmol/L), cortisol 79 nmol/L, Free Thyroxine 6 (8-21 pmol/L), Thyroid Stimulating Hormone 0.81 (0.34-5.60 mIU/L), Insulin-like GF 1 42 (81-225 ug/L), Prolactin 274 (73-478 mIU/L), FSH 3 (17-114 IU/L), Luteinizing Hormone < 1 (11-59 IU/L). Intravenous dexamethasone was replaced before thyroxine to avoid precipitating an Addisonian crisis. Expectedly, after glucocorticoid therapy, she developed new onset polydipsia and polyuria. The laboratories obtained showed: serum sodium 144 (135-145 mmol/L), serum osmolality 312 (275-305 mmol/kg), urine osmolality 133 mmol/kg, urine sodium 37 mmol/L. Central diabetes insipidus was diagnosed and regular intranasal desmopressin was used, with improvement of polyuria.

She was commenced on chemotherapy and brain radiation therapy. Unfortunately, four weeks later, she passed away from cecal perforation and peritonitis.

**Conclusion:** This patient had pituitary metastasis based on the radiological presence of pituitary stalk invasion, panhypopituitarism and central diabetes insipidus, on a background of metastatic breast malignancy. Although the pituitary gland was normal, interruption of pituitary portal vessels by the tumor can cause loss of stimulation of the pituitary hormones, with ensuing hypopituitarism. During glucocorticoid replacement, the patient’s fluid status must be monitored as diabetes insipidus can be unmasked. Those with pituitary metastasis have poor prognosis as it reflects severe and high disease burden.

**Abstract #903**

**CUSHING’S DISEASE RECURRENCE PREDICTIVE FACTORS: OUTCOME ANALYSIS OF PATIENTS IN VANCOUVER OVER 30 YEARS**

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**Objective:** There are currently no established guidelines to effectively risk-stratify Cushing’s Disease (CD) patients following initial transphenoidal surgery (TSS), and epidemiology data on CD in Canada is limited. The purpose of this study was to characterize the management and outcomes of patients with CD in the Vancouver region over a 30 years period and to investigate the predictive factors in CD recurrence.

**Methods:** We retrospectively reviewed the clinical charts from most endocrinologists in Vancouver who have agreed to participate in the research. A total of 48 patients diagnosed with CD since 1985 were identified and included in the analysis.

**Results:** All 48 patients received initial TSS. The mean follow-up time was 11.73 (+6.98) years. Twenty-six patients (54.2%) remained in remission, and 22 patients (45.8%) received subsequent interventions due to disease.
ABSTRACTS – Pituitary Disorders/Neuroendocrinology

ACTH-PRODUCING TUMOUR OF THE LIVER. CASE REPORT PRESENTATION.

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Objective: We report the clinical presentation, immunohistochemistry, imaging, histopathology, treatment and outcome of a patient with ACTH-Secreting tumour of liver.

Case Presentation: Cushing’s Syndrome due to ectopic ACTH production is uncommon and due to neuroendocrine tumour of liver is extremely rare. We discuss the case of a 27-year-old female who initially presented with vague, non-specific symptoms, such as general and muscle weakness, weight gain, hirsutism, increase in fasting blood glucose, in which an ACTH-secreting tumor found to be the cause of her clinical presentation. At admission: Height 166 cm, Weight 70 kg, normosthenic constitution, diffusely hyperpigmented skin, darkened skin around elbows, striae on the stomach. Laboratory showed AM cortisol of 1750 mmol/l, PM cortisol more than 1750 mmol/l, 24-hour urinary free cortisol more than 6700 nmol/day, AM ACTH level of 211.2 mg/ml, PM ACTH level of 148.0 mg/ml and non-suppression of cortisol with overnight dexamethasone suppression test (1 mg and 8 mg). Brain MRI showed no pathological changes. CT scan showed tumor of the right lobe of the liver (7.5 x 6.8 x 5.8 cm, density 40H). Selective sampling of the lower sinuses showed no gradient. Because of severity of the condition for health reasons she had bilateral adrenalectomy Clinical and laboratory signs of hypercortisolism disappeared after surgery, but ACTH level was very high. In 2 months she had right-sided hemihepatectomy. ACTH level next day after surgery was 1 mg/ml. Immunohistochemistry showed primary neuroendocrine tumour, Grade 2. We still observe her 1 year and 8 months and during this period she felt fine and she has a laboratory and clinical remission.

Conclusion: Despite numerous guidelines in diagnosis and treatment of hypercortisolism, there are still diagnosis and treatment mistakes due to rarity and complexity of clinical presentation in ACTH-ectopic syndrome. So, we need to improve the guidelines for diagnosis and treatment of ACTH-ectopic tumors.

Abstract #905

SHORT STATURE: WHAT IS THE CAUSE IN OUR POPULATION?

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Objective: Globally children and adolescents with growth failure are referred to specialized units for evaluation and management. We designed this study is to determine the cause of short stature in children and adolescents referred to our endocrine unit for evaluation and further management.

Methods: This descriptive cross sectional study was performed in the Department of Endocrine, Diabetes and Metabolic Diseases, Hayatabad Medical Complex, Peshawar. All children and adolescents between 2-20 years of age with height below 2SDS or less then 3rd percentile for their age and gender with reference population were included while those with contractures, kyphoscoliosis, thalassemia major, diabetes mellitus type 1 and those who were on renal replacement therapy were excluded. Detailed history was taken, standard deviation scores and mid-parental height were calculated. Complete physical examination including examination for stigmata of genetic syndromes associated with short stature was performed followed by a pre-set penal of investigations.

Results: A total of 73 children with mean chronological age of 11.75 ± 4.06 years, 41 (56.31%) boys and 32 (43.83%) girls (p<0.05) were included. Mean height was 117.28 ± 17.55 cm, which was -4.23 ± 2.06 SDS below for this population age group. Mean parental height was 156.87 ± 11.82 cm, mean bone age was 8.56 ± 4.03 years, 41 (56.31%) girls (p<0.05) were included. Mean height was 117.28 ± 17.55 cm, which was -4.23 ± 2.06 SDS below for this population age group. Mean parental height was 156.87 ± 11.82 cm, mean bone age was 8.56 ± 4.03 years while mean bone age delay was 3.23 ± 1.94 years.

Most common causes found were variants of normal growth present in 38.35%. Constitutional Delay of Growth and Puberty (CDGP) was found in 10 (13.7%), Familial Short Stature (FSS) in 8 (11.0%) while
overlapping features of both CDGP and FSS were found in other 10 (13.7%). Among the endocrine causes the most common pathologies found were isolated Growth Hormone Deficiency (CHD) found in 17 (23.3%) children followed by primary hypothyroidism in 5 (9.6%) and pan-hypopituitarism in 2 (2.7%) children. Common non endocrine causes of short stature were Turner’s syndrome found in 5 (6.8%), rickets in 4 (5.4%), chronic anemia and bronchial asthma in 3 children (4.10%) each and achondroplasia in 2 (2.7%).

**Conclusion:** Isolated GHD, idiopathic short stature (CDGP and FSS), primary hypothyroidism and Turners’s syndrome are the most common causes of short stature in our set up. Pathological cause are more likely to be found in our population compared to Western reports.

**Abstract #906**

**SQUAMOUS CELL CARCINOMA OF THE PITUITARY STALK, A PRIMARY CANCER**

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**Case Presentation:** Case of a 74 year-old female with past medical history of type 2 diabetes mellitus, hypothyroidism, arterial hypertension, and dyslipidemia that was evaluated by neuro-ophthalmology service due to a 4 month history of visual changes. The patient was found with homonymous hemianopsia and loss of visual acuity. Because of this, a Brain MRI was obtained, showing thickening of the pituitary stalk and tuber cinereum measuring 1.4 cm transverse by 1.4 cm AP by 2.4 cm craniocaudally. Inflammatory workup and spinal tap were done to rule out lymphoma, but results were negative. A recent mammography was also available, which was negative for malignancy. Chest, abdomen, and pelvis CT scan were performed, but failed to reveal any primary or metastatic disease. Patient underwent right pterional craniotomy and lesion excisional biopsy. Pathology was remarkable for squamous cell carcinoma with positive immunohistochemistry for Cytokeratin (CK) 7, Cytokeratin high molecular weight (CKHMW), and p63, supporting the diagnosis. The tumor was subsequently irradiated. The patient developed panhypopituitarism that was treated accordingly. The patient condition has remained stable.

**Discussion:** Pituitary adenomas are the most common pituitary tumors. Pituitary carcinomas represent only 0.1-0.2% of these tumors. They typically presents with mass effect causing visual field impairment, headaches, diplopia, or other neurological deficits. Intracranial squamous cell carcinomas are usually the result of metastasis from a primary site outside the brain or can result from direct extension from the cranial base. Treatment options include surgical resection, hormonal therapy, radiotherapy and/or chemotherapy. Prognosis is poor and the mean survival time is usually less than five years.

**Conclusion:** This illustrates a strange case of primary pituitary squamous cell carcinoma without metastasis showing a common presentation of mass effect.

**Abstract #907**

**MEDICAL THERAPY WITH PASIREOTIDE IN RECURRENT CUSHING’S DISEASE—SINGLE-CENTER EXPERIENCE OF PATIENTS TREATED FOR AT LEAST 1 YEAR**

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OHSU

**Objective:** Pasireotide subcutaneous (SC) injection is a somatostatin analog approved for the treatment of adults with Cushing’s disease (CD) for whom pituitary surgery was unsuccessful or not an option. There are few reports of long-term pasireotide SC treatment, especially in a non-research setting. We highlight the symptomatic and biochemical improvement of 6 patients with recurrent CD treated with pasireotide SC for at least 1 year at a single center.

**Methods:** Patients were treated either through commercial use (n=5) or as part of the phase 3 trial (n=1; ClinicalTrials.gov identifier, NCT00434148; study number, B2305).

**Results:** Most patients (n=5) were female, and mean age at diagnosis was 35.8 years. Mean disease duration was 12 years (range, 3–25 years). Symptoms most commonly included abnormal weight gain, fatigue, cushingoid face, and ecchymosis. All patients underwent surgery, and median time to recurrence after surgery was approximately 3 years (range, 5 months to 22 years). Pasireotide SC 600 µg twice daily (BID) (n=5) or 300 µg BID (n=1) was initiated in 2 patients naive to medical therapy (ketoconazole and mifepristone or ketoconazole and cabergoline). Pasireotide was used in combination with cabergoline (dose: 1.0–1.5 mg twice weekly) in 2 patients. Mean treatment duration was 18 months (range, 12–31 years). All patients demonstrated biochemical control at 1 year of treatment. Three of 6 patients remain on pasireotide SC and are controlled, and 1 patient was controlled at the end of the B2305 study. One patient had persistent urinary-free cortisol elevations and gallstones requiring drug cessation. The other patient exhibited an unrelated brain tumor and received high dexamethasone
Objective: Central diabetes insipidus (CDI) is a disorder characterized by inability to maximally concentrate urine secondary to deficiency or impairment of antidiuretic hormone. Diabetes insipidus secondary to neurosarcoidosis (NS) is a rare but serious disorder. We present a case of CDI secondary to NS.

Case Presentation: A 61 year old female with adenocarcinoma of the colon was admitted for hemicolectomy. She had baseline sodium of 140-145 meq/l. She was started on D51/2 NS +20 Kcl and nothing by mouth (NPO) for the surgery. The patient’s sodium next morning was found to be 162 meq/L. She did not have any insensible fluid losses. She reported feeling very thirsty but was NPO. Fluid balance revealed a significant urine output of 4L/day despite being NPO. Urine osmolality was 60 mosm/kg and specific gravity -1.002. On further questioning she reported having polydipsia and polyuria for the last 2-3 months. A water deprivation test was done. Urine osmolality increased to 578mOsm/Kg after administration of 1 mcg of Desmopressin. Patient was diagnosed with CDI & desmopressin was started with improvement in urine output, serum sodium and clinical symptoms. CT Thorax done prior to surgery to evaluate for metastasis showed biapical spiculated nodularities, mediastinal lymph nodes. MRI brain revealed homogeneously enhancing, rounded pituitary gland with thickened, enhancing infundibulum and mild hypothalamic enhancement. Bronchoscopy with endobronchial biopsy of lymph nodes showed non-necrotizing granulomas. Anterior pituitary hormonal evaluation showed central hypothyroidism.

Discussion: CNS involvement of sarcoidosis is relatively rare, 5–16%. Posterior pituitary involvement is more common than anterior pituitary dysfunction with isolated hormonal deficits or panhypopituirturism. Initial investigation includes endocrine assessment and MRI of the pituitary .In most cases of DI caused by sarcoidosis, there is a clear evidence of it being found elsewhere in the body. Direct biopsy of pituitary lesions is difficult, PET-CT can be used to identify lymph node involvement. Biopsy typically reveals caseation, which is focal, small and centrally located within the granuloma. MRI with gadolinium can reveal infundibular-hypothalamus involvement, pituitary stalk thickening, pituitary gland enlargement or lesions situated in other areas of the brain. Absence of posterior pituitary bright spot on T1 weighted images is indicative of an infiltrative process. Mainstay of treatment is steroids, however DI is permanent in most cases.

Conclusion: CDI is a rare manifestation of NS. Early recognition and evaluation with endocrine assessment and MRI of pituitary is warranted in suspected patients.
necrosis and viable cells stained positive for ACTH. He has developed adrenal insufficiency post operatively and was started on hydrocortisone. 16 weeks post operative cortisol stimulation test still revealed adrenal insufficiency. His vision and bilateral ptosis has resolved.

**Discussion:** Incidence of ACTH secreting macroadenoma is 5-10% of patient with Cushing’s disease. Pituitary apoplexy in patient with ACTH secreting macroadenoma is rare, accounting for <5% of pituitary apoplexy. Here, we present a patient with pituitary apoplexy in an ACTH secreting macroadenoma. ACTH secreting macroadenomas has low rate of remission and high rate of recurrence. Data from previous reports indicate that pituitary apoplexy in ACTH secreting macroadenoma leads to higher rate of remission after transsphenoidal surgery.

**Conclusion:** This patient demonstrates that high index of suspicion is necessary to diagnosis Cushing’s disease. Early treatment with transsphenoidal surgery in case of pituitary apoplexy with ACTH secreting macroadenoma leads to better outcome.

**Abstract #910**

**PROLACTIN-SECRETING PITUITARY CARCINOMA: A CASE REPORT**

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**Case Presentation:** A 50-year-old man with vision problems since 10 years ago. MRI showed a pituitary adenoma measuring 2.7-cm and compressing the optic chiasm. Prolactin level was 541 ng/mL. He was started on cabergoline. After 5 weeks, his vision was unchanged, prolactin dropped to 141 ng/mL, but the size of the tumor remained the same. He had transsphenoidal surgery. Over the next 2 years, his tumor progressed and he had another surgery plus radiation. Three years ago he started complaining of a headache, an MRI showed progression of the tumor with suprasellar extension and right cavernous sinus involvement. The cabergoline dose was increased with no response. He had a right craniotomy for debulking and vision protection. He did well until 4 months after surgery, when he had worsening headache and vision problems. MRI showed a recurrent pituitary tumor compressing the optic chiasm and bigger in size. A redo right craniotomy was done and he had Cyberknife. Pathology was consistent with pituitary prolactinoma. After 14 months, he came with loss of consciousness. MRIs showed multiple, extra-axial masses and spine lesions concerning for metastases. It was recommended to obtain a biopsy. The lesion was compatible with a blue cell tumor. Pathology showed sparsely granulated lactotrophs with numerous mitotic figures. DNA repair mismatch protein (MSH6) activity was elevated while O-6-methylguanine-DNA methyltransferase (MGMT) was low. The patient was recommended treatment with temozolamide along with craniospinal radiation. The patient began treatment with some intolerance due to gastrointestinal side effects. Temozolamide was held on the third week of treatment due to thrombocytopenia. His radiation therapy now focused on the brain and cervical spine area to reduce gastrointestinal effects. After the platelet level increased, he was restarted on temozolamide and continued on it for 12 months. MRI, 11 months after radiation and temozolamide, showed no lesions in the spine and a stable, 2.1-cm sellar lesion with right cavernous sinus involvement and slight optic chiasm displacement. Four months after, a new MRI was done and no pituitary lesion was noted. MRI was repeated 2 months after that, when he complained of vision problems and had the left visual field affected. MRI showed a developing, enhancing lesion in the sella involving the optic chiasm and measuring 1.2 cm. Current MRI shows a lesion with no recurrence or enlargement. His prolactin is normal; it was in the 3,000s just prior to receiving temozolamide and radiation therapy. This is the rare case of a prolactin-secreting pituitary carcinoma which eventually responded well to a combination of temozolamide and radiation.

**Abstract #911**

**CASE REPORT OF MACROPROLACTINEMIA: A NEW DIAGNOSTIC CONSIDERATION**

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**Case Presentation:** Approximately 25% of patients with hyperprolactinemia may present with the condition of macroprolactinemia. We present a unique case of a 28 year old female who presented to the clinic for evaluation of menstrual irregularities and bilateral galactorrhea. Her initial prolactin level was elevated at 320 ng/mL (4.8-23.3 ng/mL) and a pituitary MRI with contrast demonstrated a 4 mm pituitary microadenoma. She had no risk factors for secondary hyperprolactinemia. She was briefly started on treatment with cabergoline, but she did not tolerate this medication and it was discontinued on her own volition. Her galactorrhea and menstrual irregularities resolved over the next year without any treatment. She was lost to follow up until two years later. A repeat prolactin level was still elevated at 411 ng/mL and a repeat MRI pituitary now demonstrated no pathology. Macโปรlactin and prolactin were checked with the prolactin level being 379 ng/mL,
which was confirmed by 1:100 dilution. The monomeric prolactin level was 198 ng/mL and prolactin recovery percentage by polyethylene glycol (PEG) precipitation was 48%. Although the assay is considered indeterminate at percentages between 40-50%, this patient’s clinical presentation is suggestive of macroprolactinemia. In light of the patient having no symptoms of hyperprolactinemia and a normal MRI, she was not started on any medications and levels were followed serially.

**Discussion:** The determination of hyperprolactinemia due to macroprolactinemia is clinically significant as a macroprolactin has low biological activity and does not require treatment. Macroprolactinemia is diagnosed when the concentration of macroprolactin exceeds 50% of the total serum prolactin concentration determined by PEG precipitation. It is considered a benign condition with low incidence of clinical symptoms; hormonal and imaging investigations as well as medical or surgical treatment are unnecessary. When results are indeterminate, confirmatory testing should be performed with gel filtration chromatography after screening with PEG precipitation. However, in the case of our patient, our clinical suspicion and macroprolactin percentage were high enough that further testing with gel filtration chromatography was not considered necessary to make the diagnosis as it would not change her management.

**Conclusion:** This case raises a question of whether intermediate results for macroprolactinemia should be treated as a macroprolactinemia in patients without symptoms and whether the level of elevation of the macroprolactin is useful in that decision. There are no controlled studies in the literature and ultimately, the decision to treat is individualized.

**Abstract #912**

**NINE YEAR FOLLOW UP OF A 45 YEAR OLD FEMALE WITH IDIOPATHIC GRANULOMATOUS HYPOPHYSITIS MAINTAINING NORMAL PITUITARY FUNCTION**

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**Objective:** Granulomatous hypophysitis is a histological variant of hypophysitis and is a rare inflammatory disorder of the pituitary gland. It can present as a primary pituitary disease or as a part of systemic illness. We present a very interesting case of idiopathic granulomatosus hypophysitis that initially presented as migraine headache, amenorrhea and hyperprolactinemia who has maintained normal pituitary function on long term follow up.

**Case Presentation:** The patient is a 44-year-old female who initially presented to obstetrics in 2005 with complaints of menstrual irregularities and migraine headaches and was found to have elevated prolactin levels. Her MRI brain showed diffusely enlarged pituitary gland. She was put on cabergoline which brought about the drop in prolactin and resumption of menses. However, over time, the pituitary gradually enlarged to the point where it was beginning to abut and compress the optic nerve. As a result, she had surgery in November 2009 when gland was explored and no tumor found as such pituitary biopsy taken instead. The pathology report showed granulomatous infiltration of the pituitary. It was subsequent to that that Endocrinology became involved in her care. She received a course of prednisone 40 mg daily shortly after that initial surgery and continued as a tapering course for 3 months. She also had evaluation for any rheumatologic disorder or infective disorder and this was negative. In 2011, she received a course of methyl prednisone started at 128 mg daily for 2 weeks followed by tapering course. This brought about only minimal shrinkage on MRI and was accompanied by some symptoms from the steroids which lead to stop steroids after the short course and repeat follow up MRI showed return to previous size. Throughout this, she has had maintained normal pituitary function. Patient care was extensively discussed and ultimately pituitary saving course was adopted with serial visual field testing and follow up MRIs. She was closely followed for 3 years with 3 to 6 month MRIs and visual field exams. After 3 years of stable size and pituitary function, a decision was made to lengthen the follow up time period. The patient is now followed on yearly basis and at last follow up in November 6 2015, she had retained normal pituitary function, MRI showed mild shrinkage of size and clinically asymptomatic.

**Conclusion:** Granulomatous hypophysitis is a rare pituitary disease and in certain selected cases close monitoring can be a safe option for management as long as long term pituitary function and the underlying process remain stable.

**Abstract #913**

**HEREDITARY PARAGANGLIOMA SYNDROME WITH SDHB MUTATION - THE BAD KIND OF MUTATION.**

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University of Wisconsin - Madison

**Objective:** Paragangliomas are rare neuroendocrine tumors that arise in sympathetic and parasympathetic paraganglia and are derived from neural crest cells.

**Case Presentation:** A 44 y/o male was referred to the endocrine clinic by Urology for evaluation for possible...
recurrence of paraganglioma in 2012. The patient had history of a bladder mass removed surgically 11 yrs ago. This was found on abdominal CT done for hematuria, dysuria and headache with urination. At the time of our initial evaluation, those surgical specimen records were not available. He did have significant family history of his sister’s daughter with paraganglioma who had had bilateral adrenalectomy and unilateral nephrectomy. His father passed away from “renal cancer” at age 75. He mentioned he did well for 9 years however in 2010 once again started experiencing similar symptoms. Evaluation performed at that time showed a 1cm bladder mass, which was removed. In 2012, he was found to have a 10cm mass in the left wall of the bladder on imaging done for symptom recurrence. Urology planned surgery and referred to endocrine first, given his concerning history. Plasma and urine metanephrines were elevated consistent with recurrence. He underwent surgical debulking after treatment with alpha blocker. Genetic testing confirmed succinate dehydrogenase Type B mutation. He had routine surveillance labs and imaging after establishing with endocrine and over the next few months was found to have new lesions on the right side of the bladder, inguinal area and right lung on whole-body PET/CT. He underwent a second surgical debulking, with pathology consistent with malignant paraganglioma. He subsequently met with Oncology to discuss palliative chemotherapy and received 4 out of 6 cycles of Cytoxan, Dacarbazine and Vincristine. Repeat imaging showed improvement in tumor burden hence he elected to monitor with imaging and labs. Follow-up imaging now shows new metastasis in the liver, rectus abdominis muscle and right obturator adenopathy along the right lateral pelvic sidewall. He remains on 4 anti-hypertensives and has reasonable blood pressure control. He is now agreeable to completion of palliative chemotherapy. He continues to be closely monitored. His 5 siblings and 8 offsprings are undergoing genetic screening.

Conclusion: Malignant paragangliomas are extremely rare. An estimated incidence in 2002 was 93 cases per 400 million people. Surgical debulking of primary tumor is recommended. Chemotherapy is reserved for more advanced disease. Genetic screening is mandatory for all immediate family members of patients with hereditary paraganglioma syndromes.

Abstract #914

PANHYPOPITUITARISM ASSOCIATED WITH GIANT PARASELLAR CAROTID ARTERY ANEURYSM

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Objective: The prevalence of hypopituitarism is estimated to be approximately 1 in 2200. Annual incidence of hypopituitarism is 4.2/100,000. Hypopituitarism is most commonly caused by pituitary adenomas and their treatment (hypophysectomy or radiation therapy), or by hypothalamic or paraseellar tumors or metastatic carcinoma; together, these tumors account for approximately 90% of cases. We present a case and MRI images of a giant internal carotid artery (ICA) aneurysm with findings of panhypopituitarism.

Case Presentation: A 50 y/o obese female with PMH of post-surgical hypothyroidism for symptomatic goiter in 1990 presented to her ophthalmologist with diplopia due to left 6th cranial nerve palsy and blurry vision, and was placed on prednisone 20 mg daily for presumed Graves’ ophthalmopathy. Her visual symptoms did not improve and in the following 2 months she developed headache, nausea/vomiting and dizziness. She was admitted to hospital where she was found to have a 26 mm unruptured left giant ICA aneurysm in the cavernous segment. High dose dexamethasone was started and she underwent successful Pipeline Device insertion. She was discharged the following day on 2 weeks steroid taper. Three weeks after discharge she was readmitted with DVT and PE. She developed shock, requiring transfer to ICU. A cosyntropin stimulation-test was abnormal, with baseline cortisol 5.2 mcg/dL and peak 8.8 mcg/dL at 60 min. The patient clinically improved on stress dose hydrocortisone. She was discharged on hydrocortisone 20 mg in am and 10 mg in pm, but had to be readmitted to hospital with recurrent adrenal crisis after she was taken off hydrocortisone by her doctor. While off hydrocortisone and on thyroxine, her pituitary testing was consistent with panhypopituitarism with a random cortisol 1.2 ug/dL, ACTH <5 pg/mL, TSH <0.02 uIU/mL, free T4 1.23 ng/mL, prolactin <0.7 ng/mL, FSH 1.4 mIU/ mL, estradiol 13 pg/mL, and IGF-I <16 ng/mL. The patient responded well to re-initiation of corticosteroid treatment and has continued to do well since.

Discussion: Cerebral aneurysm is a rare cause of panhypopituitarism, responsible for less than 0.2% of cases. There are only 40 reported cases in the literature to date. Patients usually manifest neurological and visual defects. Pituitary dysfunction due to an ICA most frequently involves the pituitary-gonadal axis (67.5 %) followed by pituitary-adrenal (48.6%) and pituitary-gonadal (48.6%)...
thoracic axis (40.5%). Diabetes insipidus and pituitary stalk effect are very rare.

**Conclusion:** Pituitary endocrine disorders in the presence of supra- or para-sellar carotid artery aneurysm should always be suspected, especially when accompanied by neurological and visual defects.

**Abstract #915**

**NELSON’S SYNDROME IN A PATIENT WITH ADDISON’S DISEASE**

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**Objective:** We describe a patient with an ACTH-secreting pituitary adenoma that developed 40 years after a diagnosis of Addison’s disease.

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

**Case Presentation:** A 76 year-old woman was diagnosed with Addison’s disease at 35 years of age, with fatigue, weight loss, salt craving and hyperpigmentation. Treatment with hydrocortisone and fludrocortisone led to improvement of her symptoms. In June 2015, development of hyperpigmentation prompted further investigation; ACTH level prior to hydrocortisone dosing was 40,304 pg/mL (6-50) with cortisol level of <0.16 mcg/dL. MRI pituitary with/without contrast revealed a 1.8 x 1.9 x 1.9 cm macroadenoma that did not compress the optic chiasm. Increasing the hydrocortisone from 20 to 30 mg daily did not lessen the hyperpigmentation. Four hours after administering hydrocortisone 10 mg, cortisol level increased from 8.1 to 17 mcg/dL, and her ACTH concomitantly dropped from 17740 pg/mL [8-42] to 8758 pg/mL. Random beta-MSH was 5,903 pg/mL [<150]. Other investigations: FSH 1.7 mU/mL and LH 0.4 mU/mL confirming secondary hypogonadism; prolactin elevated, 40.5 ng/mL [2.0-17.4]; IGF1 normal - 140 ng/mL (29-215); TSH <0.015 mU/L with normal free T4 level of 1.42 ng/dL on levothyroxine 125 mcg daily. Thyroid peroxidase antibodies were positive, confirming autoimmune hypothyroidism.

**Discussion:** Primary hypoadrenalism in Addison’s disease is characterized by excess ACTH due to the negative feedback to the pituitary, and hyperpigmentation that largely resolves after steroid treatment. Patients receiving adequate treatment with currently available steroids inevitably have periods when cortisol levels are low, with elevated ACTH. This intermittent stimulation of the corticotrophs may lead to pituitary hyperplasia, and occasionally adenoma formation. The latter is a rare event; review of the literature shows cases with ACTH levels as high as 4,000 pg/mL. There is no reason to believe that our patient was not compliant with her medication, or that she had an ectopic tumor secreting ACTH. The development of a corticotroph adenoma in a patient with Addison’s disease could be likened to Nelson’s syndrome - continuing enlargement of a pituitary adenoma after bilateral adrenalectomy in Cushing’s disease - though in our patient there is no reason to suspect a pre-existing pituitary adenoma.

**Conclusion:** To our knowledge, the ACTH levels in our patient are unprecedented in the published literature. Worsening hyperpigmentation in a patient with Addison’s disease receiving adequate steroids replacement with elevated ACTH levels may portend pituitary tumor formation, and further investigations should be undertaken.

**Abstract #916**

**A CASE OF FLUSHING IN A YOUNG MAN WITH HISTORY OF CARCINOID TUMOR: THE ESSENCE OF THOROUGHNESS IN CLINICAL MEDICINE**

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**Objective:** Vigilance and thoroughness are essential principles in clinical medicine. Diseases do not always feature the textbook description; sometimes disease presentations can be misleading. This case presentation illustrates how a serious and life-threatening condition could have been missed. The objective is to present an intriguing case illustrating the essence of clinical vigilance.

**Methods:** Case Presentation.

**Case Presentation:** A 26 year old male with a remote history of appendiceal carcinoid tumor found in a ruptured appendix, presented with facial flushing and hot flashes for 3 months. Laboratory markers for carcinoid syndrome were negative. Pursuing other etiologies for hot flashes, testosterone level was measured (despite absence of hypogonadal symptoms), revealing total testosterone of 127 ng/dL. This led to hypogonadal diagnostic work up, revealing elevated prolactin of 196 ng/dL with low gonadotropins. Subsequent MRI revealed a large pituitary tumor with central hemorrhage compatible with pituitary apoplexy (PA), albeit absence of symptoms. The patient underwent a successful, emergent surgical resection of the hemorrhagic tumor.

**Discussion:** PA, a hemorrhagic infarction in large pituitary tumors, is a life-threatening endocrinological emergency. The commonest presenting symptoms are headache and vomiting (95% and 70%, respectively). While PA's presentation is often catastrophic, it can be
asymptomatic (2-10%). Over 80% of patients sustain generalized hypopituitarism, including hypothyroidism and hypocortisolism. In this case, the misleading patient’s presentation suggested recurrent carcinoid tumor. When the latter was ruled out, it was the vigilance and thoroughness of the managing physicians that led to the uncovering of an unexpected, totally asymptomatic PA, which even surprised the patient and his wife, both being a happy newly married couple.

**Conclusion:** This case underscores the importance of thoroughness in clinical medicine. While it is a rule of thumb to focus on the “elephant in the room”, it is prudent to keep the “zebra” in the back of mind. While this patient was solely referred to endocrinology to rule out a recurrence of carcinoid tumor, it was the thoroughness of the endocrinologist to include androgen levels in the initial lab, suspecting andropause in an otherwise asymptomatic young man. Or was that test just a matter of a strike of luck?! Either way, this was a life-saver in this case.

**Abstract #917**

**IPILIMUMAB INDUCED HYPOPHYSITIS IN A PATIENT WITH METASTATIC MELANOMA**

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**Objective:** Ipilimumab is approved for the treatment of unresectable or metastatic melanoma and is under investigation for other types of solid tumors. It is a humanized immunoglobulin (lg)G1 monoclonal antibody that blocks cytotoxic T-lymphocyte antigen-4 (CTLA-4). One of the most common immune related adverse events of this therapy is hypophysitis. The presentation can be insidious but life-threatening. Early diagnosis and treatment can result in clinical improvement, radiological resolution of pituitary masses, and variable normalization of pituitary function.

**Methods:** We present a case of ipilimumab-induced hypophysitis in a patient with metastatic melanoma.

**Case Presentation:** The patient is a 68 year old male with history of metastatic melanoma treated with four cycles of ipilimumab over a two month span. Following the fourth dose, he was admitted with extreme fatigue, somnolence, emotional lability, retro-orbital headaches, constipation, anorexia and nausea. Biochemical findings confirmed central hypocortisolism, central hypothyroidism, and hypogonadotropic hypogonadism. Magnetic resonance imaging (MRI) revealed globular enlargement of the pituitary gland with mild infundibular thickening and diffuse contrast enhancement, suggestive of hypophysitis. He did not have evidence of diabetes insipidus (DI). The acute onset, clinical presentation, and imaging features suggested hypophysitis, so the patient was started on 50mg oral prednisone twice daily for 2 weeks, and levothyroxine (T4) replacement at 125μg daily. He achieved remarkable symptomatic improvement and the prednisone was tapered to 5mg daily over 6 weeks. Two months after initial presentation, a repeat MRI showed a significant reduction in size of the pituitary gland. Repeat thyroid function testing indicated adequately replaced central hypothyroidism. He is currently on 125 mcg of levothyroxine and 5 mg of prednisone, with a plan to taper off completely and repeat an 8am cortisol and ACTH with an ACTH stimulation test. His melanoma disease burden remains stable thus far.

**Discussion:** Hypophysitis is a common complication of ipilimumab therapy, occurring in up to 17% of patients in one series. Hormonal deficiencies are common with central hypothyroidism and hypocortisolism predominating and DI being a rare manifestation. The mechanism of hypopituitarism is likely from ipilimumab’s immunomodulatory effect on activating T-cells, resulting in a lymphocytic hypophysitis.

**Conclusion:** It is important that endocrinologists, internists, and oncologists become familiar with ipilimumab-induced hypophysitis, a common and potentially life-threatening manifestation of an agent being used with increasing frequency to treat metastatic melanoma.

**Abstract #918**

**ROLE OF RADIOSURGERY IN MANAGEMENT OF PITUITARY ADENOMA-THE BNI EXPERIENCE**

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Barrow Neurological Institute

**Objective:** To determine the efficacy of stereotactic radiosurgery with CyberKnife in the treatment of recurrent pituitary adenoma.

**Methods:** This is a retrospective study involving review of patients who underwent cyberKnife radiosurgery for recurrent or residual pituitary adenoma at Barrow Neurological Institute. Forty eight patients with recurrent pituitary adenomas received stereotactic radiosurgery with cyberKnife and were followed for average of 44 months. Patient population consisted of 33 with non-functioning adenomas, 10 with acromegaly, and 5 with Cushing’s disease. The change in tumor size, hormonal function, and complication of therapy was analyzed in each case.

**Results:** All patients underwent tumor resection operation through either transsphenoidal or transcranial approach
prior to cyberknife treatment. All patients had either recurrence or residual mass in the cavernous sinus before cyberknife treatment. The total irradiation dose ranged from 2100-4000 cGy in average of 3-5 fractions. 26 patients (54.2%) had smaller tumors at follow up. 22 patients (45.8%) had stable tumors. Visual acuity remained unchanged post treatment. 1 patient developed radiation induced temporal lobe necrosis. 4 patients (8.3%) had panhypopituitarism requiring hormonal replacement. Hormonal function improved in 12 out of 15 patients with functioning adenoma. Treatment failure was seen in 1 patient with acromegaly, 2 patients with Cushing’s disease, and 1 patient with nonfunctioning adenoma.

Discussion: Transsphenoidal or transcranial surgery is the gold standard for treatment of sellar lesions. It provides immediate decompression of the optic apparatus, the advantage of pathological confirmation, and rapid reduction in hormone oversecretion. Functioning tumors have higher failure rate after surgical resection and has higher recurrence rate. Surgery alone may not be curative due to incomplete tumor resection resulting from local invasion into the cavernous sinus and proximity to critical neurovascular structures. Radiosurgery is indicated in such cases to achieve both growth control and hormonal remission with minimal neurological complications. Radiosurgery with CyberKnife have shown to be fairly effective in our experience and has lower rate of cranial neuropathies and endocrinopathies.

Conclusion: Stereotactic radiosurgery with CyberKnife is effective and relatively safe compared to conventional radiotherapy in treating recurrent/residual pituitary adenomas. Longer follow up is needed to evaluate for therapeutic efficacy in patients with functioning pituitary adenomas.

Abstract #919

A HOT THYROID NODULE IN AN ACROMEGALY PATIENT

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Case Presentation: 29 year old female with no past medical history was referred for evaluation of a pituitary macroadenoma found on MRI brain, which was done for severe headaches and acute blurry vision. Review of systems was negative for change in shoe size, menstrual irregularities or arthralgia. On exam patient did not have thyromegaly, palpable thyroid nodules, hirsutism, acromegalic or cushingoid features. Initial labs revealed IGF-1 536 (63-373 ng/mL) and TSH 0.78 (0.55-4.78 IU/mL). Patient underwent transphenoidal surgery and pathology stained positive for growth hormone (GH). 10 months post-operatively, IGF-1 remained elevated (728 ng/mL), with unsuppressed GH (3.6 ng/mL) after glucose load. At this time, patient was noted to have suppressed TSH (0.09), normal free T4 and T3 and elevated thyroid antibodies (thyroid peroxidase antibody 381; thyroglobulin antibody 62). Ultrasound of the thyroid showed multiple bilateral solid nodules, and 24 hour radioactive scan demonstrated hyperfunctioning left nodule suppressing the remainder of the thyroid (uptake 28%). Patient underwent a second surgery, after which IGF-1 reduced to 553 and TSH increased to 0.629. However, IGF-1 failed to normalize after four months, and patient was started on Sandostatin LAR for persistently elevated IGF-1 levels. During this time, TSH reduced to 0.148. After 2 doses of Sandostatin LAR, IGF-1 reduced to 388, and TSH increased slightly, to 0.283.

Discussion: Acromegaly is associated with a spectrum of thyroid pathologies, the most common being nodular goiter (55%), presumably due to chronic GH secretion. The majority of these goiters are diffuse and non-functioning. Only 14% of goiters in acromegaly patients display areas of hyperactivity. TSH physiology in acromegaly patients is complex, with regulation by TRH, T3 and T4 as well as IGF-1, leptin and the autonomic nervous system. Our patient presented with subclinical hyperthyroidism due to toxic multinodular goiter. Studies show that thyroid size is increased in active acromegaly, and thyroid size can be reduced after treatment. Treatment of acromegaly, with surgery or somatostatin analog, also presumably treats concurrent thyroid dysfunction. In our patient, treatment with Sandostatin resulted in a decrease in IGF-1 and an increase in TSH.

Conclusion: Acromegaly is frequently associated with thyroid diseases. Thus, it is reasonable to evaluate hormonal and imaging evaluation of the thyroid once diagnosis of acromegaly is established. The role of IGF-1 and TSH on goiter pathogenesis in patients with acromegaly is not well understood. Our case suggests that nodule autonomy may correlate with IGF-1 levels.
**Abstract #920**

**A PLASMACYTOMA PRESENTING AS A PARASELLAR MASS AND CRANIAL NERVE DEFICITS**

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**Objective:** We discuss a rare case of a plasmacytoma presenting as a parasellar lesion with cranial nerve deficits.

**Case Presentation:** A 48-year-old female presented with several months of progressive diplopia, tongue spasms, dysphagia, and a right-sided facial droop. Her physical exam was notable for numerous cranial nerve deficits including impaired abduction of the left eye, right-sided facial asymmetry, and rightward deviations of her uvula and tongue. MRI showed a large, invasive mass in the central skull base, measuring 4.1x3.4x3.4 cm, completely replacing the clivus. The pituitary was displaced superiorly, but her pituitary function was normal except for a mildly elevated prolactin (65 ng/mL). The patient underwent endonasal trans-sphenoidal biopsy with pathology consistent with a lambda light chain restricted plasmacytoma. Subsequent hematologic evaluation revealed an abnormal monoclonal band on serum and urine immunofixation, elevated lambda free light chain count, 15% plasma cells on bone marrow biopsy, and multiple lytic lesions on skeletal imaging, confirming the diagnosis of lambda light chain multiple myeloma. The patient was treated with external beam radiation, dexamethasone, velcade and revlimid and has achieved shrinkage of the sellar mass as well as serological remission.

**Discussion:** Plasmacytomas are malignant plasma cell tumors that may present as a solitary lesion or as a manifestation of multiple myeloma. Sellar plasmacytomas are rare with only about 30 cases reported. Unlike other sellar lesions, plasmacytomas often present with cranial nerve involvement, especially of ocular palsies. Our patient also presented with painful tongue spasms which have not previously been reported with plasmacytomas but have been observed in patients who have other structures exerting mass effect on the hypoglossal nerve. Despite the aggressive nature of sellar plasmacytomas, patients typically have relatively preserved anterior pituitary function, likely because the tumor originates outside the pituitary fossa. On MRI, plasmacytomas can be difficult to distinguish from adenomas or chondrosarcomas so the diagnosis is often made only after trans-sphenoidal resection. However, radiation therapy is the treatment of choice for these highly radiosensitive tumors.

**Conclusion:** The differential for parasellar lesions is broad and includes rare entities such as plasmacytoma. As the treatment for this lesion is distinct from other more common sellar masses, maintaining a high index of suspicion is paramount when evaluating a patient with any parasellar tumor presenting with cranial nerve deficits.

**Abstract #921**

**ECTOPIC GROWTH HORMONE SECRETING PITUITARY ADENOMA PRESENTING AS CHRONIC SINUSITIS**

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Westchester Medical Center

**Objective:** Ectopic growth hormone secreting pituitary adenoma, involving the sphenoid sinus is a very rare entity. We present a case report of an unusual presentation of a pituitary adenoma in a female with chronic sinusitis, discovered to have an infrasellar mass, which on pathology was found to be a growth hormone producing pituitary adenoma.

**Methods:** A 62 year-old female presented with a complaint of chronic nasal congestion and severe sinusitis for over 5 years. She was concurrently treated for asthma and allergic rhinitis but her upper respiratory symptoms persisted. Eventually a CT scan of her sinuses revealed a large soft tissue mass with opacification in the sphenoid sinus extending to the ethmoid sinuses with partial bony dehiscence of the sellar floor. MRI brain revealed a mass in the sphenoid sinus with a normal pituitary gland.

**Case Presentation:** Due to the abnormality of the sella turcica on imaging, laboratory workup by her primary care physician revealed normal anterior pituitary function except for an elevated IGF1 of 550ng/mL, which was 0.8 standard deviations above normal. She had undergone bilateral carpal tunnel surgery one year prior. On review of systems, she reported an increase in shoe size, approximately 3 shoe sizes over 30 years, and noted that she had always had large hands with some swelling. Her husband complained that she snored frequently. She denied any galactorrhea. Physical exam was notable for a prominent lower jaw, underbite and arthritic changes of the distal interphalangeal joints of her hands without soft tissue swelling. No skin tags were seen.

**Discussion:** After resection of the sinus tumor, she had a normal endocrine profile. Pathology confirmed sparsely granulated somatotroph adenoma with immunostain CD34 positive, consistent with growth hormone secreting adenoma. She was evaluated post surgery in the neuroendocrine clinic where she reported less swelling of her hands and her husband reported that she no longer snored. Growth hormone suppression testing confirmed curative resection of the tumor.
Conclusion: This is a rare case of ectopic growth hormone producing pituitary adenoma presenting in the sphenoid sinus with a normal pituitary gland. Pituitary adenoma should always be considered in the differential in patients presenting with chronic sinusitis and sphenoid sinus tumor, in order to help prevent surgical or endocrine complications.

Abstract #922

CORTICOTROPIN-SECRETING PITUITARY TUMOR WITH CLINICAL ADRENAL INSUFFICIENCY: A CASE REPORT

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University of Utah

Objective: The authors describe a unique case of a corticotropin-secreting pituitary tumor with low serum cortisol and clinical adrenal insufficiency.

Case Presentation: 77-year-old male presented with recurrent pituitary tumor, first resected five years prior and identified as a nonfunctioning pituitary adenoma at that time. No hormonal staining was performed after initial resection, and we have no ACTH or cortisol evaluation. MRI five years after initial resection revealed 2.1 x 3.9 x 2.3 cm sellar mass with extension into sphenoid sinus and right cavernous sinus. Therefore, he underwent repeat transphenoidal resection, followed by radiation to the cavernous sinus portion for 6 weeks. Pre-operative labs revealed elevated ACTH and normal cortisol. Pathology specimen stained diffusely positive for ACTH. He had persistently elevated ACTH post-operatively, with borderline low or low serum cortisol. He received high dose cosyntropin stimulation, to which he demonstrated a partial adrenal response with cortisol 16.0 micrograms/dL at 30 minutes. He then underwent metyrapone stimulation test which successfully suppressed his cortisol to 0.9 micrograms/dL, and ACTH remained elevated (104 pg/mL as compared to previous level of 78 pg/mL). Again, he demonstrated a partial adrenal response, with 11-deoxycorticisol value 2,940 ng/dL. Clinically, the patient had severe fatigue, orthostasis, and slight pallor, with low normal blood pressure. He was initiated on hydrocortisone 20mg in the morning and 10mg in the afternoon, with marked improvement in symptoms.

Discussion: This is a rare case of secretion of an inactive corticotropin, demonstrated by his lack of response to the high endogenous ACTH levels, but more positive response to IV cosyntropin. Corticotroph adenomas of the pituitary are generally reported to have a high tendency to “transform” and may be functioning or “silent”, with normal serum ACTH. However, it is rarely reported that an elevated serum ACTH is coexistent with adrenal insufficiency. Corticotropin-secreting adenoma is also reported to be a more aggressive tumor, and this case is consistent with that, with elevated serum ACTH despite treatment with both surgery and radiation.

Conclusion: This case demonstrates that high serum ACTH in the setting of corticotroph pituitary adenoma does not rule out clinical adrenal insufficiency. Stimulatory hormones secreted by pituitary tumors may be nonfunctional. Therefore, both ACTH and cortisol should routinely be evaluated in assessment of potential corticotroph adenomas.

Abstract #923

RESPONSE TO PASIREOTIDE LAR BY AN OCTREOTIDE RESISTANT SOMATOLACTOTROPH TUMOR WITH RARE NEURONAL METAPLASIA

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Objective: We report the first case of neuronal metaplastic transformation in a mixed somatotroph-lactotroph pituitary adenoma which had a poor response to octreotide (Oct). Only partial biochemical response was achieved with high dose cabergoline (Cab). Pasireotide is a newly approved somatostatin receptor (SSTR) ligand (SRL) targeting both SSTR2 and 5, while Oct mainly targets SSTR2. In this patient, the addition of pasireotide LAR resulted in GH<1 ng/ml.

Case Presentation: A 54 y.o Caucasian female presented with increased ring and shoe size, changing features, and arthralgias over 10 years associated with type 2 diabetes requiring insulin, carpal tunnel syndrome and obstructive sleep apnea. MRI of the brain revealed a 3.0 x 2.6 x 3.1 cm sellar mass extending to the sphenoid sinus and clivus. Compression of the optic chiasm was noted but visual fields were normal. Growth hormone (GH) was 25.7 ng/ml (normal 0.05-4.0 ng/mL) and IGF-1 level was 834 ng/ml (normal 48-187) or 4.5x upper limit of normal (ULN). Transphenoidal resection was complicated by involvement of vascular structures. Tumor stained for GH and prolactin (PRL) with the rare finding of neuronal metaplasia (Cam 5.2, Pan-cytokeratin, Neurofilament+). One week post-op, GH was 20.9 ng/ml. Treatment was started at 1 month with Oct LAR 20 mg q28 days and 3 month GH and IGF-1 were 11 and 4.8xULN. After 3 months on 30 mg, GH was 8.77 and IGF-1 was 4.9xULN. Cab was added at 0.5 mg thrice weekly (GH 6.3 and IGF-1 3.28xULN at 3 months) and then titrated up to 0.5 mg daily. At 1 year post-op, the residual mass remained unchanged and GH was still elevated at 3.27 with IGF-1 2.5xULN. She was switched to pasireotide LAR 40 mg q28 days with the Cab. 6 months
later, GH was 0.99 and IGF-1 level was 1.4xULN with stable residual tumor. She has been titrated to pasireotide 60 mg in the hope of biochemical remission and tumor shrinkage. During the course of her therapy on pasireotide, she required down-titration of her insulin doses as her GH levels became controlled.

**Discussion:** Metaplastic transformation of PRL, ACTH or GH secreting adenoma cells to a neuronal phenotype is exceedingly rare and the clinical implications are not well understood: does this contribute to resistance of medical therapy? In our case, the biochemical response of IGF-1 was non-existent and was most marked using Cab with pasireotide LAR.

**Conclusion:** There are no reported cases of neuronal metaplasia in the background of somato-lactotroph pituitary adenoma. Although resistant to initial Oct LAR, this tumor responded biochemically to pasireotide LAR, which should be considered as a therapy for resistant tumors.

**Abstract #924**

**HYPERCALCEMIA CAUSED BY LARGE MEDIASTINAL PARATHYROID ADENOMA IN A PATIENT WITH FAMILIAL MEN1 - MOYAMOYA DISEASE ASSOCIATION**

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**Case Presentation:** A 28 year-old Caucasian man presented with seven days of headache, generalized weakness, and paresthesias. He had hypercalcemia (13.3 mg/dL). Family history included his mother, brother (deceased) and two uncles with Moyamoya Disease (MMD) and Multiple Endocrine Neoplasia 1 syndrome (MEN1). Parathyroid hormone (PTH)(580pg/mL), prolactin (1098ng/mL) and gastrin were also elevated. Imaging showed an enhancing 2.3cm-pituitary mass and a 3.5cm-medial mass. Incidental findings included stenosis of the right middle cerebral artery, internal carotids and posterior vessels (Classic MMD features), and two small pancreatic masses. Sestamibi and octreotide scans showed uptake in the mediastinum. Medical therapy failed to control hypercalcemia and thus, parathyroidectomy was attempted. Three hyperplastic parathyroid glands were resected (a fourth was not found). Calcium and PTH remained unchanged. Adrenal, thyroid, and growth hormone axes were normal. Visual field testing confirmed bitemporal hemianopsia. Though endorsing new headaches, his symptoms were not consistent with apoplexy. Coexistence of prolactinoma and RCC was considered. Instead of surgery, he was started on cabergoline, titrated to 2 mg weekly. A month later, his visual fields and headaches improved significantly. There was no significant change in the MRI

**Abstract #925**

**NONSURGICAL MANAGEMENT OF CYSTIC MACROPROLACTINOMA LEADING TO NEAR RESOLUTION OF CYSTIC COMPONENT**

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**Case Presentation:** A 32 year old male was evaluated by ophthalmology for visual field loss. MRI revealed a 2.9 x 2.1 x 2.3 cm cystic sellar mass without solid nodular component causing mass effect on the optic chiasm and hypothalamus – considered to be likely a Rathke’s cleft cyst (RCC) versus hemorrhagic adenoma or craniopharyngioma. He was referred to Neurosurgery and scheduled for transphenoidal cyst fenestration. At our evaluation, serum prolactin (PRL) was 730 ng/mL (4.04 – 15.2) and free testosterone was 54.9 pg/mL (35 – 155) – but he did not endorse specific symptoms of hypogonadism. Adrenal, thyroid, and growth hormone axes were normal. Visual field testing confirmed bitemporal hemianopsia. Though endorsing new headaches, his symptoms were not consistent with apoplexy. Coexistence of prolactinoma and RCC was considered. Instead of surgery, he was started on cabergoline, titrated to 2 mg weekly. A month later, his visual fields and headaches improved significantly. There was no significant change in the MRI
but the report favored apoplexy due to a fluid-fluid level. 5 months into therapy, his PRL was 15.6 ng/mL and MRI revealed marked decrease in tumor size, near complete collapse of the cystic region, and resolution of the mass effect on the optic chiasm. Visual field testing was normal and free testosterone improved to 112 pg/mL. He reported increased libido. 8 months into therapy, his PRL was 8.9 ng/mL and the tumor measured 0.9 x 0.9 x 1.2 cm. The initial tumor volume, estimated by (height x length x width)/2, was 7.0 cm3 and shrunk to 0.49 cm3 – a 93% reduction. He is asymptomatic and tolerating dopamine agonist (DA) therapy well.

**Discussion:** Prolactinomas typically present in premenopausal females but macroprolactinomas are more frequent in males. Cystic macroprolactinomas (CP) present commonly in males between their third and fourth decade. Formation of the cystic regions can result from intratumoral hemorrhage, misplaced exocytosis, trauma, angiography, coughing, pregnancy, radiation, anticoagulants, steroids, or DA. First-line treatment of prolactinomas is DA; surgery is reserved for nonresponse/intolerance to DA, CSF fistula, apoplexy, and patient preference. Although CPs are not believed to respond adequately to DA therapy and several published reports and guidelines recommend surgery, our patient appears to be an exception, as evidenced by his excellent response to cabergoline.

**Conclusion:** Cystic macroprolactinomas are an unusual variety of a common pituitary tumor and are usually treated surgically. This case adds to the growing number of patients in the literature managed successfully with medical therapy alone.

**Abstract #926**

**CEREBELLOPONTINE ANGLE LYMPHOMA AS ETIOLOGY OF CENTRAL DIABETES INSIPIDUS**

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SIU School of Medicine

**Case Presentation:** A 71 year old female presented with abrupt onset headache, right facial droop, diplopia, and ataxia. She reported polyuria and drinking large volumes of fluid shortly before admission. Brain MRI confirmed a heterogeneously enhancing 2.9 cm right cerebellopontine angle (CPA) lesion with mass effect on the brainstem, right cerebellum, and right vertebral artery. Serum sodium concentration was modestly elevated on admission and rose rapidly (peak 165 mM hospital day 3) in the setting of inappropriately dilute urine (256 mOsm/kg). Central diabetes insipidus (DI) was suspected, and treatment with desmopressin quickly resolved polyuria and allowed restoration of eunatremia. Retromastoid craniotomy was performed on hospital day 6, and postsurgical pathology revealed a diffuse non-Hodgkin B-cell lymphoma. No other foci of lymphoma were apparent on subsequent staging. DI persisted after surgery, but no anterior pituitary deficits occurred.

**Discussion:** Central DI occurs when injury or dysfunction of the supraoptic or paraventricular nuclei of the hypothalamus or the proximal supraopticohypophyseal tract causes failure of antidiuretic hormone (ADH) release to osmotic stimuli. Craniopharyngiomas, suprasellar germinomas, and pinealomas are primary central nervous system (CNS) tumors most likely to occur in the hypothalamic-pituitary area and present with central DI. Central DI due to metastatic involvement of the hypothalamus or pituitary (e.g. lung cancer) and granulomatous disorders (e.g. sarcoidosis) are also well described, though presence of disease in other organ systems and characteristic findings on CNS imaging are usually present. CNS lymphoma is more common due to the increased rate of lymphoproliferative disorders in immunosuppressive conditions such as HIV/AIDS and hepatitis C and may cause central DI, though primary CNS lymphoma still accounts for < 1% of extranodal non-Hodgkin lymphoma cases. Further, CPA angle tumor is a rare presentation of CNS lymphoma. Intracranial lymphomas can extensively infiltrate the CNS, and central DI in this case implies subradiographic extension into the middle fossa. There is at least one report of apparent left CPA angle lymphoma later discovered with diffuse subarachnoid and leptomeningeal extension into the pituitary on autopsy.

**Conclusion:** Primary CNS lymphoma should be considered in the differential diagnosis of central DI along with established etiologies such as craniopharyngiomas and neurosarcoidosis. This case is unusual because of the location of the patient’s tumor and immunocompetent status.
Abstract #927

THYROTROPIN ADENOMAS: RARE, SILENT, AND PLURIHOROMONAL, OH MY!

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Objective: Thyrotropinomas (TSHomas) account for less than 2% of all functioning pituitary tumors and less than 1% of all cases of hyperthyroidism. The aim of this research was to characterize the biochemical and clinical characteristics of this rare entity.

Methods: A retrospective chart review was conducted on histopathologically-proven TSHomas surgically resected between 1999-2015 at Cleveland Clinic. Patients were divided into two groups: functional tumors, defined as having an elevated level of free T4 in the setting of a normal or elevated TSH level (central hyperthyroidism); and silent tumors, defined as diffuse tumor staining with TSH without biochemical evidence of central hyperthyroidism.

Results: Among 1,065 operated pituitary adenomas, 32 (3.0%) stained diffusely with TSH antibodies. 66% of patients were male; the median [range] age was 49 [20-77] years. Tumor size was 20 mm [2-37]. There were 7 microadenomas (22%), of which 2 were biochemically active. Only 8 (25%) TSHomas stained for TSH alone, the rest were plurihormonal (75%, diffuse staining): growth hormone (47%), gonadotropins (19%), prolactin (16%), ACTH (9%). 5 adenomas (16%) stained diffusely with 3 hormones, including TSH. Among patients with GH and ACTH staining, 13/15 and 1/3 had Acromegaly and Cushing disease, respectively.

Functional tumors (n=5, 16%) had a median [range] TSH 3.69 uU/mL [1.2-6.2] and Free T4 2.3 ng/dL [2.2-3.4] at diagnosis. Median tumor size was 10 [5-21] mm. Among functional tumors, 2 were microadenomas (40%). Two patients had a goiter. Two patients had symptoms of hyperthyroidism (one of them had symptoms of acromegaly as well), 2 were diagnosed incidentally, and 1 patient was incorrectly diagnosed with hypothyroidism and 6 years later was found to have a 6 mm TSHoma. All patients were treated surgically, 4 were cured (biochemical normalization of thyroid function tests).

Silent tumors (n=27, 84%) had a median [range] TSH 1.2 uU/mL [0.5-4.6] with Free T4 1.2 ng/dL [0.6-1.6] at diagnosis. Median tumor size was 20 [2-37] mm. 19% were microadenomas. 5 patients had a goiter. 13 had acromegaly, 1 had prolactinoma, 1 had Cushing’s disease, and 12 had non-functional adenoma. The majority co-stained with GH (52%). Only 5 patients stained for TSH alone.

Conclusion: Historically TSHomas have been characterized as being large and invasive, in this series, 22% of them were a microadenoma. The vast majority of TSHomas are silent and plurihormonal, with co-secretion of GH being most common. Most active tumors do not present with clinical hyperthyroidism.

Abstract #928

NOT YOUR TYPICAL SINUS INFECTION: INVASIVE GIANT PROLACTINOMA WITH NASAL OBSTRUCTION

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Objective: Giant prolactinomas are larger than four centimeters with no other hormone co-secretion. They are six to nine times more common in men. Extrasellar extension is common, but orbital invasion and presentation as a nasal mass are rarely reported. We present a case with these features, as well as sinus obstruction and infection.

Methods: We describe the patient’s presentation, workup, and management, along with literature review.

Case Presentation: A forty year old man with a history of prolactinoma and noncompliance presented with purulent nasal drainage, fevers, progressive nasal obstruction, and right eye bulging. He was diagnosed seven years prior, when he presented with headaches and epistaxis and had a 6.9cm pituitary mass with prolactin of 17,000 (normal 4-18 ng/mL). Other hormones were normal except for hypogonadotrophic hypogonadism. He originally responded well to cabergoline, with reduction in size and prolactin down to 211 after four months. Unfortunately he was noncompliant with appointments and cabergoline and experienced recurrent sinus infections.

On current exam he had a nasal voice, right eye proptosis, and a pink mass protruding out the right nare with purulent material blocking the left nare. Labs revealed leukocytosis and a prolactin of 23,300. MRI showed growth of the mass up to 9cm in diameter, extending into the maxillary and ethmoid sinuses, with retained secretions in the frontal and maxillary sinuses. The mass invaded the right lateral orbital wall.

Due to sinus obstruction, otolaryngology performed a debulking surgery, in addition to giving antibiotics. Pathology confirmed a prolactin-staining pituitary adenoma. Although he reported taking cabergoline and
denied side effects, his compliance was questioned due to lack of follow-up in the past year and pharmacy fill history. We restarted 0.5mg daily to treat the significant amount of remaining tumor.

**Discussion:** Orbital invasion is the least common form of extrasellar extension for giant prolactinomas, with only one case report found on literature search. Nasopharynx invasion is also uncommon, with two case reports found with diagnosis by biopsy of a nasal mass. First-line treatment is cabergoline, with meta-analyses showing doses up to 12mg/week. Resistance to cabergoline is often quoted as 10%, but varies depending on how high the dose was raised. Other treatments include surgery, radiation, and temozolomide.

**Conclusion:** We present a man with nasal obstruction, recurrent sinus infection, and orbital invasion secondary to a giant prolactoma, visible at the nares. Although cabergoline remains first-line treatment, surgical debulking was used to relieve nasal obstruction and allow resolution of post-obstructive sinus infection.

**Abstract #929**

**GIANT PROLACTINOMA PRESENTING AS SKULL BASE TUMOR CAUSING INSTABILITY OF THE CRANIOVERTEBRAL JUNCTION**

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**Case Presentation:** 52 y/o Male with 5 years’ history of worsening sharp occipital headaches with radiation to the upper neck and intensity of 8/10. He described lancinating neck pain when he moves his head down and when he turns to look back feels his head is about to “fall off.” He denied double or blurry vision, muscle weakness or paresthesias. He also denied history of head or neck trauma. His brain MRI revealed a large sellar mass of 5.6 x 4.5 X 3.0 cm without suprasellar extension but with extension into both cavernous sinuses and encircling the internal carotid arteries bilaterally. The mass extended inferiorly through the clivus and was eroding the occipital condyles. The initial impression was a meningioma. Pituitary hormonal work up was remarkable for a prolactin level of > 8000 ng/mL, ACTH: 6 pg/ML, cortisol: <1.0 µg/dL. The patient was diagnosed with a Giant prolactoma causing instability of the craniovertebral junction and secondary adrenal insufficiency. Neurosurgery recommended hard collar and surgical fixation. The patient was started on 1 mg cabergoline twice weekly and over 4 days the prolactin level decreased to 422 ng/mL and he developed lancinating neck pain and tingling and numbness on both arms. He required an urgent occipital C2 fusion with internal fixation and bone grafting. After surgery his neck pain and paresthesias resolved and he was prescribed 0.5 mg of cabergoline twice weekly. 3 months later the prolactin level was < 5.0 ng/mL, ACTH: 39 pg/ML, cortisol: 12 µg/dL and the tumor decreased 40 % in size.

**Discussion:** Giant prolactomas comprise 2% of all prolactinomas and are defined as ≥ 40mm in diameter with extrasellar extension, and with prolactin levels ≥ 1000 ng/mL, requiring determination with serial dilution to avoid the hook effect. Their most common extension is suprasellar, however several cases of invasion to the skull base have been reported. The posterior and inferior extension causing craniovertebral junction instability is very infrequent, we conducted a literature review finding only two similar cases previously reported. Giant prolactinomas represent a diagnostic challenge as they have atypical clinical presentations and can potentially cause serious neurological complications.

**Conclusion:** Giant prolactinomas are very sensitive to dopamine agonists, medical therapy is the first line of treatment even in the presence neurological complications. The rapid recognition and treatment of a craniovertebral junction instability is essential to prevent permanent paralysis or death. Surgical fixation must be done before medical therapy, as illustrated in this case a rapid tumor shrinkage worsened the neck instability causing acute myelopathy.

**Abstract #930**

**IBD WITH A SIDE OF CARCINOID**

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**Objective:** This case serves as an uncommon presentation of carcinoid tumor diagnosed in a patient with history of Ulcerative Colitis. To date, only 50 cases of carcinoid tumor with IBD have been reported since 1942, with only two were diagnosed pre-operatively.

**Methods:** This case is based on an extensive literature review involving minimal case reports and case series.

**Case Presentation:** A 46-year old man with long standing history of ulcerative colitis developed refractory disease and underwent total proctocolectomy with ileo-anal–J pouch. Three years after the surgery, he presented with symptoms of fatigue, dizziness and dyspnea on exertion lasting one week. He also reported melonatic stools and pica. Hemoglobin on presentation was 7.7g/dl, despite previous normal values. He underwent an EGD showing a 2 cm submucosal nodule...
in the duodenal bulb, and later EUS with biopsy. Both
pathologic specimens were positive for well-differentiated
neuroendocrine tumor (carcinoid), and IHC stains were
positive for gastrin, but negative for Somatostatin. The
tumor stains were also positive for Chromogranin and
Synaptophysin. The patient then underwent pouchoscopy
and capsule endoscopy which found mild ulceration in the
distal bowel. The imaging studies, including CT abdomen
as well as an Octreotide scan, did not reveal evidence of
metastases. He subsequently underwent resection of the
tumor with pathology confirming a stage II-A, low-grade
neuroendocrine carcinoid tumor with a proliferative index
Ki-67 of 1%. Hemoglobin levels returned to baseline within
two months and the patient continues to do well clinically.

Discussion: We are reporting a rare presentation of a
carcinoid tumor diagnosed pre-operatively by biopsy in a
patient with Inflammatory Bowel Disease. In IBD, enterо-
endocrine cells can be hyper-stimulated by inflammation to
cause hyperplasia and neoplasia, although the time period
from conversion of enterо-chromaffin like cell (ECL)
hyperplasia to ECL like Carcinoids is unclear. Interestingly,
most of the case reports in the literature have documented
Carcinoid tumors in the un-inflamed intestine. While this
inflammatory mechanism is a theoretically justifiable
concern, aberrant endocrine cells have not been definitively
linked to the presence of carcinoid tumors. Therefore, the
association of carcinoid and IBD awaits confirmation.

Conclusion: Based on literature review, there have been
only two other cases involving diagnosis of a carcinoid
tumor pre-operatively. With these case reports it is difficult
to determine if the association between them is fortuitous,
or if in fact IBD is really a risk factor for the tumor. More
studies are needed to known if ECL like hyperplasia plays
any role to Carcinoid tumor with IBD.

Abstract #931
A CASE OF GASTRIC NEUROENDOCRINE TUMOR IN A PATIENT WITH PERNICIOUS ANEMIA

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Objective: To describe the association between gastric
neuroendocrine tumor and pernicious anemia.

Case Presentation: 64 year-old African American female
with a history of type 1 diabetes mellitus, hypertension,
pernicious anemia and Hashimoto thyroiditis presented
complaining of mild abdominal pain and persistent
dyspepsia. An upper endoscopy revealed an atrophic
gastric mucosa and multiple small subcentimeter polyps
in the body of the stomach. Histopathological analysis
of the polyps was consistent with well differentiated
neuroendocrine tumors neuroendocrine tumor (carcinoid)
while the biopsy of the gastric mucosa confirmed the
atrophic gastritis, mucosal atrophy, intestinal metaplasia
and Enterochromaffin-like (ECL) cells hyperplasia.

Laboratory tests showed low hemoglobin levels (10.5
gm/dL, hematocrit 30.8%), low vitamin B12 level
(131 pg/mL; N 200 to 950 pg/mL), a normal serum
5-hydroxyindoleacetic acid level (2.2 mg/dL; N < 6 mg/
dl) a markedly increased level of fasting serum gastrin
(1701 pg/mL; N < 100 pg/mL) and a positive intrinsic
factor and parietal cell antibodies.

On the basis of these findings, a diagnosis of autoimmune
atrophic gastritis leading to hypergastrinemia and ECL
proliferation with type 1 variety of gastric neuroendocrine
tumors (NETs) formation was made. MRI of the abdomen
and pelvis did not reveal any abnormal masses.
Repeat upper endoscopy failed to identify any residual
carcinoid tumors and long term endoscopic surveillance
was planned.

Discussion: Discussion: There are four types of gastric
NETs varying by tumor characteristics, histology,
association with hypergastrinemia, as well as their
biological behavior. In autoimmune atrophic gastritis, loss
of parietal cells decreases acid production. As a result,
gastrin secretion from antral G cells increases and directly
stimulates parietal cells to secrete more acid. In addition,
gastrin is trophic to ECL cells. Thus, chronic antral
enterochromaffin cell hyperplasia progresses to type 1
gastric NETs. Type 1 gastric carcinoid tumors are typically
small, multifocal, and located in the gastric fundus. Type
2 gastric NETs are also multiple small nodular lesions
usually associated with Multiple Endocrine Neoplasia
type1 syndrome, or Zollinger-Ellison syndrome. Type
3 NETs are solitary polypoid tumors with tendency for
angio-invasion and lymph nodes and liver metastases. Type
4 NETs are solitary, poorly differentiated neuroendocrine
carcinomas typically accompanied by vascular invasion
and metastases.

Conclusion: Physicians should be aware of the association
of gastric carcinoids with chronic autoimmune atrophic
gastritis. Endoscopic surveillance is mandatory due to the
associated risk of developing of gastric adenocarcinoma.
Abstract #932

SEVERE HYPERTHYROIDISM PRECIPITATING ADRENAL CRISIS: A CASE OF UNRECOGNIZED POSTPARTUM HYPOPITUITARISM

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Objective: Patients with multiple endocrinopathies can present a diagnostic challenge given common symptoms shared by multiple disorders. We present a case of secondary adrenal insufficiency (2ºAI) precipitated by Graves’s disease (GD).

Case Presentation: A 39-year-old woman was evaluated for hyperthyroidism. The patient reported a three week history of decreased appetite with episodes of nausea, vomiting, and diarrhea. Of note, 10 months prior to admission, she required an emergent cesarean section due to preeclampsia but no hypotension, hemorrhage, or transfusion occurred. She breast fed for 3 months and amenorrhea persisted. She had a 30 pound weight loss over 6 months. Physical exam included T 97.2 °, BP 91/49, P 138, a thin, anxious woman, no exophthalmos, and palpable diffusely enlarged thyroid gland. Laboratory tests revealed TSH 0.007 IU/mL, free T4 5.14 ng/dL, and free T3 >20 pg/mL. The patient was started on methimazole and a beta blocker. Within hours of admission, the patient developed extreme lethargy. Thyroid storm was considered and stress dose IV glucocorticoid caused rapid resolution in what was 2ºAI. Intensification of management with IV hydrocortisone and Lugol’s solution were initiated with rapid clinical improvement. The pre-treatment cortisol level was found to be <0.2 ug/dL. Additional testing confirmed GD with thyroid stimulating immunoglobulin of 398%. 2ºAI was confirmed by ACTH <5 pg/mL and additional lab assessment included prolactin <0.2 ng/mL, LH 3.1 mIU/mL, FSH 5.3 mIU/mL, and estradiol 11 pg/mL. Post discharge the patient has been euthyroid on methimazole and a beta blocker.

Discussion: Our patient with severe hyperthyroidism as a result of GD was initially thought to progress to thyroid storm. Intensification of management with IV glucocorticoid caused rapid resolution in what was 2ºAI in crisis. There is an overlap of symptoms in these entities. In this case, the childbirth history was important and we believe the patient had postpartum hypopituitarism due to Sheehan’s syndrome, as pituitary imaging did not suggest lymphocytic hypophysitis. Although the patient developed symptoms of hypopituitarism months prior to her admission, it was onset of GD that precipitated her episode of AI resulting in the diagnosis.

Conclusion: Relative adrenal insufficiency can often be seen in severe hyperthyroidism. GD and concomitant primary AI have been well documented, as seen in autoimmune polyglandular syndrome. However, GD combined with 2ºAI with panhypopituitarism is an exceedingly rare occurrence. Our literature search revealed only one other documented case.

Abstract #933

PREGNANCY IN MENOPAUSE: IS IT TRUE?

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University at Buffalo

Objective: To report a rare case of elevated hCG levels in a menopausal female.

Case Presentation: 54 year old G10L7A3 menopausal female was incidentally found to have elevated hCG levels during a preoperative evaluation for back surgery. She reported some intermittent nausea and vomiting, similar to her morning sickness experienced during pregnancy. She denied any postmenopausal symptoms, visual disturbances, or menstrual irregularities since her menopause 7 years ago. Physical exam was unremarkable. Lab tests over the past 9 months revealed: 6 separate measurements of persistently elevated quantitative hCG ranging 15-20mIU/mL(<10mIU/mL in menopause), indeterminate qualitative hCG assays, and negative urine hCG tests. Pelvic ultrasound did not reveal an ovarian or uterine mass. Repeat hCG levels remained elevated on a different laboratory assay and no interference by heterophile antibodies. MRI brain showed a 3mm pituitary lesion. She had normal cortisol, thyroid function tests, prolactin and IGF-1 levels with low estradiol 28pG/mL(menopause range <32pG/mL) and elevated FSH 146.6mIU/mL(menopause range 23.0-116.3mIU/mL) and LH 85.1mIU/mL(menopause range 10.0-54.7mIU/mL). With a preliminary diagnosis of hCG-secreting pituitary lesion, hormonal replacement therapy with combined estrogen and progesterone was tried but patient could not tolerate it due to mood swings.

Discussion: In this case with elevated hCG, pregnancy is excluded given her postmenopausal state, negative ultrasound with stable hCG levels. Furthermore, FSH >45 mIU/ML supports a non-placental hCG origin. With no recent pregnancies or prior gestational trophoblastic disease (GTD), a dormant GTD is unlikely. A false positive result due to lab error is unlikely as consistent elevation across two testing platforms. Antibody interference was also ruled out.
During menopause, reduction of ovarian synthesis of sex steroids reduces negative feedback to GnRH secretion, resulting in increased FSH and LH production with stimulation of pituitary release of hCG. With her age, a likely explanation is a pituitary source of hCG. Confirmation is by suppression with short course of estrogen and progesterone; however our patient did not tolerate it. In our case either a pituitary lesion or the pituitary gland is the source of excess hCG and this has been rarely reported.

**Conclusion:** Elevated hCG is generally believed to originate from pregnancy or GTD. This may have dire consequences with unnecessary investigations and harmful therapy if the source is not properly identified. Recognition of a pituitary source for elevated hCG will allow for more appropriate evaluation.

**Abstract #934**

**PITUITARY MASS IN THE THIRD TRIMESTER OF PREGNANCY**

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Heart of Lancaster Regional Medical Center

**Objective:** Describe a case of a pituitary mass in the third trimester of pregnancy whose symptoms were vision loss and headache. A pituitary mass that develops abruptly during pregnancy is within the realm of pituitary macroadenoma and lymphocytic hypophysitis.

**Case Presentation:** A 24-year-old primigravida at 28 weeks with a past medical history of bipolar and recent diagnosis of Lyme disease with an eight week history of intermittent migraines. On admission, she developed a severe headache and blurry vision. The patient denied slurred speech or gait disturbances. She was afebrile and physical exam was notable for symmetrical face, pupils were equal round and reactive to light, extraocular movements were intact, visual fields intact. The patient underwent a lumbar puncture with clear fluid WBC 0, glucose 65mg/dL, and protein 29mg/dL. She subsequently had a MRI of the brain without contrast that showed an intrasellar and suprasellar mass 2.4x1.9x1.0cm with mass effect on the optic chiasm and extension to the cavernous sinus. She was later discharged home. Two weeks after discharge, she presented with a sudden increase in her headache, along with peripheral visual field disturbances. Repeat MRI ruled out pituitary hemorrhage and no increase in pituitary size. Due to her progressive visual complaints, she was seen by a neuro-ophtalmologist. Formal visual field testing was completed and shown bitemporal mid-quadrantanopsia. She was started on Decadron 4mg/daily. Laboratory showed prolactin 25.3 ng/mL, IGF-1 192ng/mL, LH 0.6mIU/mL, FSH 0.6mIU/mL, TSH 0.75uIU/mL, FT4 0.56ng/mL. Levothyroxine daily was started. Patient was scheduled for c-section at 34 weeks with subsequent transphenoidal resection two weeks after delivery.

**Discussion:** Symptomatic pituitary masses provide a challenge in diagnosing and treating when they occur during pregnancy. The majority of pituitary masses that develop tend to be macroadenomas with the more rare instances being lymphocytic hypophysitis. MRI with and without gadolinium is the initial imaging modality, but is contraindicated during pregnancy. Conservative management with oral steroids is the initial treatment, and may be a bridge to transphenoidal surgery for a definitive diagnosis once pregnancy has come to term.

**Conclusion:** This case illustrates the diagnostic and therapeutic challenges that can arise with pituitary masses in pregnancy. Such a diagnosis must be considered in a pregnant patient presenting with sudden onset of headache and vision disturbances.

**Abstract #935**

**LANGERHANS CELL HISTIOCYTOSIS: THE CHALLENGE OF MAKING AN ACCURATE AND TIMELY DIAGNOSIS**

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Baylor College of Medicine

**Objective:** We present a case of Langerhans Cell Histiocytosis (LCH) in an adult with a pituitary stalk lesion and diabetes insipidus (DI) which evolved to panhypopituitarism. Without evidence of systemic involvement, confirmation of LCH and initiation of therapy was delayed by five years.

**Case Presentation:** A 31 year old woman presented with central DI. Diagnostic evaluation revealed hypogonadotrophic hypogonadism (LH <0.07 mIU/mL, FSH 2.13 mIU/mL), and low IGF-1 of 111 ng/dL (range: 115-307 ng/dL). Her prolactin was 26.6 ng/mL, thyroid function was preserved, and morning cortisol was 11.5 ug/dL with stimulation to 23.5 ug/dL after 1 mcg ACTH. Pituitary MRI showed a 6x5x5 mm nodular prominence of the stalk with equal enhancement to pituitary tissue, and an absent bright spot. LCH was...
A 59 year-old man presented with central adrenal insufficiency secondary to Ipilimumab. He was treated with high dose steroids followed by maintenance steroids with plan to taper off. Four years later (in August 2015), he self-tapered to hydrocortisone 5 mg every other day and noticed worsened above symptoms. Laboratory studies revealed ACTH <5 pg/ml, AM cortisol <0.5 ug/dl. Hydrocortisone was increased to 15 mg daily in divided doses with remarkable improvement in symptoms and resolution of memory gaps, leg swelling.

Discussion: There has been expanding use of immune checkpoint inhibitors in cancer treatment. A significant increase in immune-related adverse events (irAE) is seen with ipilimumab. AH is the most common endocrinopathy encountered in patients on CTLA-4 inhibitors, followed by thyroiditis/hypothyroidism. Hypothalamus-pituitary-adrenal axis (HPA) is the most common affected axis, which can be life threatening, if untreated. Due to non-specific symptoms, endocrinopathies often mask symptoms as non-specific conditions ascribed to other causes. Onset of hypophysitis is variable (weeks to months) after ipilimumab. A dose-dependent pattern is seen in some clinical studies. Although exact mechanism is unknown and no patient till date has had biopsy studied autoimmune hypophysitis, auto-immunity with antibodies directed against pituitary gland is postulated. High clinical suspicion, urgent hormonal evaluation and MRI imaging for prompt diagnosis and treatment with high dose steroids followed by maintenance steroids is advised. Recovery of thyroid and gonadal axis is seen in up to 50% patients but HPA axis recovery is rare. Majority of patients with AH require long-term/lifelong steroid replacement.

Conclusion: Autoimmune hypophysitis is the most frequently seen but underdiagnosed irAE endocrinopathy seen with Ipilimumab, most commonly affecting HPA axis. Increased awareness among physicians is necessary for prompt diagnosis and treatment. Persistent/permanent secondary adrenal insufficiency is common necessitating long-term treatment.

Abstract #936

PERSISTENT CENTRAL ADRENAL INSUFFICIENCY SEEN WITH CYTOTOXIC T-LYMPHOCYTE ASSOCIATED ANTIGEN-4 (CTLA-4) INHIBITOR (IPILIMUMAB) INDUCED HYPOPHYSITIS

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Objective: Cancer therapy has a new era with increased use of immune checkpoint inhibitors. Although classical hypophysitis is rare, Autoimmune hypophysitis (AH) is seen in 1–2% patients on Ipilimumab. We present a case of persistent central adrenal insufficiency secondary to Ipilimumab.

Case Presentation: A 59 year-old man presented with worsening fatigue, dizziness, memory loss and leg swelling. His medical history was significant for metastatic prostate cancer initially treated with ipilimumab (June 2011). After 2 doses of ipilimumab 10 mg/kg, he noticed severe fatigue, 30 lbs weight loss, headaches. AH was diagnosed based on ACTH <5 pg/ml, cortisol <0.2 ug/dl, low free T4 0.77 ng/dl, TSH 2.8, and hypoenhancement within central pituitary on MRI pituitary. He was treated with high dose steroids followed by maintenance steroids with plan to taper off. Four years later (in August 2015), he self-tapered to hydrocortisone 5 mg every other day and noticed worsened above symptoms. Laboratory studies revealed ACTH <5 pg/ml, AM cortisol <0.5 ug/dl. Hydrocortisone was increased to 15 mg daily in divided doses with remarkable improvement in symptoms and resolution of memory gaps, leg swelling.

Discussion: There has been expanding use of immune checkpoint inhibitors in cancer treatment. A significant increase in immune-related adverse events (irAE) is seen with ipilimumab. AH is the most common endocrinopathy encountered in patients on CTLA-4 inhibitors, followed by thyroiditis/hypothyroidism. Hypothalamus-pituitary-adrenal axis (HPA) is the most common affected axis, which can be life threatening, if untreated. Due to non-specific symptoms, endocrinopathies often masquerade as non-specific conditions ascribed to other causes. Onset of hypophysitis is variable (weeks to months) after ipilimumab. A dose-dependent pattern is seen in some clinical studies. Although exact mechanism is unknown and no patient till date has had biopsy studied autoimmune hypophysitis, auto-immunity with antibodies directed against pituitary gland is postulated. High clinical suspicion, urgent hormonal evaluation and MRI imaging for prompt diagnosis and treatment with high dose steroids followed by maintenance steroids is advised. Recovery of thyroid and gonadal axis is seen in up to 50% patients but HPA axis recovery is rare. Majority of patients with AH require long-term/lifelong steroid replacement.

Conclusion: Autoimmune hypophysitis is the most frequently seen but underdiagnosed irAE endocrinopathy seen with Ipilimumab, most commonly affecting HPA axis. Increased awareness among physicians is necessary for prompt diagnosis and treatment. Persistent/permanent secondary adrenal insufficiency is common necessitating long-term treatment.

Abstract #937

TREATMENT OF PASIREOTIDE LAR-ASSOCIATED HYPERGlyCEMIA IN A PATIENT WITH ACROMEGALY

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Objective: Hyperglycemia was noted in pasireotide long-acting release (PAS LAR)–treated patients with acromegaly during clinical trials. We describe a clinical approach to hyperglycemia in a patient with acromegaly and diabetes mellitus type 2 (DM2) during PAS LAR initiation and treatment.
**Methods:** Clinical response to PAS LAR, including self-monitored blood glucose (SMBG) levels, HbA1c, IGF-1, and adverse effects, was reported.

**Case Presentation:** A 44-year-old male was referred for consultation in 2007 owing to uncontrolled DM2 despite maximum metformin (MET) dose. Testing led to a biochemical diagnosis of acromegaly. An 8-mm pituitary adenoma was seen on MRI. Transsphenoidal pituitary adenoma resection was performed, but residual tumor remained. Postoperative IGF-1 levels were 394 ng/mL (age-normalized range, 75-216 ng/mL). Octreotide (OCT) therapy was initiated, switched to OCT LAR 20 mg monthly, increased to 40 mg monthly, and twice-weekly cabergoline (CAB) 0.5 mg was added; none of these treatments normalized IGF-1 or resolved symptoms. Change to either lanreotide or pegvisomant (PEG), combined with CAB, was also unsuccessful; IGF-1 levels were 364 ng/mL (age-normalized range, 61-200 ng/mL), FPG 174 mg/dL, and HbA1c 7.3%. Metformin was initially decreased postoperatively then re-optimized. Before switching from PEG to PAS LAR, SMBG frequency increased. Within 24 hours of PAS LAR initiation (and continuation of CAB), glucose levels increased to 200 to 300 mg/dL. Liraglutide (LIRA) was added, although severe nausea slowed titration, and glimepiride (GLIM) was added. After 6 weeks of PAS LAR, LIRA, GLIM, and MET, IGF-1 levels were reduced to 239 ng/mL, whereas glucose and HbA1c were 265 mg/dL and 7.9%, respectively. Frequency of SMBG remained consistent. Severe nausea improved upon increase to GLIM 8 mg daily and switch from LIRA to dulaglutide. Glucose levels slowly dropped to 150 to 160 mg/dL. Three months after PAS LAR initiation (and continuation of CAB), glucose levels increased to 200 to 300 mg/dL. Liraglutide (LIRA) was added, although severe nausea slowed titration, and glimepiride (GLIM) was added. After 6 weeks of PAS LAR, LIRA, GLIM, and MET, IGF-1 levels were reduced to 239 ng/mL, whereas glucose and HbA1c were 265 mg/dL and 7.9%, respectively. Frequency of SMBG remained consistent. Severe nausea improved upon increase to GLIM 8 mg daily and switch from LIRA to dulaglutide. Glucose levels slowly dropped to 150 to 160 mg/dL. Three months after PAS LAR initiation, IGF-1, glucose, and HbA1c were 274 ng/mL, 172 mg/dL, and 7.9%, respectively.

**Discussion:** PAS LAR resulted in IGF-1 reduction. Significant hyperglycemia occurred immediately after initiation and required rapid changes to DM2 medication. Following recommendations to increase SMBG, frequent medication adjustment, and addition of GLP-1 analogue in response to hyperglycemia returned SMBG levels to baseline, although HbA1c was predictably unchanged at 3 months.

**Conclusion:** Hyperglycemia is an expected adverse effect of PAS LAR. Vigilant SMBG and rapid response to hyperglycemia using GLP-1 analogues can be an effective option for treating patients with acromegaly and DM2 who are receiving PAS LAR, although more study is warranted.

**Abstract #938**

**MPOWERED: STUDY DESIGN OF A PHASE 3 HEAD-TO-HEAD TRIAL EVALUATING ORAL OCTREOTIDE CAPSULES VERSUS INJECTABLE SOMATOSTATIN ANALOGS IN PATIENTS WITH ACROMEGALY**

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**Objective:** While long-acting injectable somatostatin analog (SSA) injections are a mainstay of acromegaly medical therapy, a significant QoL burden and incomplete symptom regulation persist. In a baseline-controlled Ph 3 study, oral octreotide capsules (OOC) demonstrated sustained biochemical and clinical response through 13 mos in 77/91 patients (85%) who previously responded to SSA injections and successfully completed an OOC dose titration phase. Here we describe the design of a new Ph 3 trial, the Maintenance of acromegaly Patients with Octreotide capsules compared with injections – Evaluation of REsponse Durability (MPOWERED): an active-controlled evaluation of the safety and efficacy of OOC compared with standard of care SSA injections in patients with acromegaly who previously responded to both injectable and oral treatments.

**Methods:** This prospective, open-label study will include ~50 sites globally (target enrollment = 150). Eligible patients will have received a stable dose of an injectable SSA (octreotide LAR or lanreotide) for ≥4 mos and a biochemical response (IGF-1<1.3x ULN and integrated GH<2.5 ng/mL) at screening. Patients will enter a 26-wk run-in phase and receive OOC 40 mg qd and 36-wk phase until adequate response is achieved. Patients who respond to OOC will proceed to a 9-mos randomized controlled trial (RCT) phase; randomization will be 3:2 to continue OOC or revert to previous SSA injection regime. Patients with inadequate response during the RCT phase will revert to injectable SSA or, at selected sites, may elect to enter a 36-wk substudy to receive OOC 80 mg + cabergoline (<3.5 mg/wk). Patients who respond adequately or obtain significant treatment benefit upon core study completion (Run-in and RCT) may enter an extension to receive OOC (or OOC + cabergoline if treated in the combination substudy) until
approved product marketing or study termination.

**Results:** Primary endpoint is the proportion of patients with biochemical response during the RCT determined by time weighted average of IGF-1<1.3 ULN. Secondary endpoints include frequency and severity of acromegaly symptoms and proportion of patients with inadequate response to OOC who respond to OOC + cabergoline after 36 wks combined treatment.

**Conclusion:** The MPOWERED trial will assess maintenance of biochemical response with OOC compared to standard of care SSA injections in acromegaly patients who previously responded to both treatments. The OOC + cabergoline substudy will provide an important set of prospective data to date on combined SSA/dopamine receptor agonist therapy, and will be the first trial of an exclusively oral combination regimen in acromegaly.

**Abstract #939**

**CUSHING’S DISEASE IDENTIFIED POST-ADRENALECTOMY FOR ADRENAL NODULES**

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**Objective:** Cushing’s Disease (CD) with bilateral adrenal hyperplasia is the expected presentation; the association with nodular adrenal hyperplasia has been described. We report 2 cases of CD that were initially treated with adrenalectomy, one for a diagnosis of hyperaldosteronism, another for Cushing’s syndrome due to adrenal adenoma. **Case Presentation:** A 52 year old male presented with complaints of mood swings. He had right adrenalectomy for primary hyperaldosteronism in 2000 and gastric bypass surgery in 2011. Initial CT scan showed mildly enlarged bilateral adrenal glands with a 32 x 20 mm low attenuation right adrenal mass. Evaluations for pheochromocytoma and Cushing’s syndrome were reportedly negative. Pathology showed adrenal cortical hyperplasia with micro and macronodules of varying sizes. In our clinic, physical examination was unremarkable except for obesity. CT scans showed a nodular left adrenal with continued growth of the gland up to a benign-appearing 25 x 80 mm in 2014. Pheochromocytoma work up was negative; 24 hr urine free cortisol (UFC) was 65.3 mcg (nl<60). An 8 mg dexamethasone suppression test (DST) was positive with a corresponding plasma ACTH of 24 pg/ml. ACTH response to CRH stimulation was positive. MRI showed an 18 x 16x 18 mm enhancing pituitary adenoma with erosion into the clivus and remodeling of the sphenoid sinus, findings consistent with CD. Neurosurgery opted for initial conservative management given his normal visual fields and minimal symptoms. A 30 year old male we reported previously (AACE 4th Annual Meeting 1995) regarding his unique MEN1 syndrome with primary hyperparathyroidism, gastrinoma and CD, initially presented elsewhere with cushingoid features, elevated UFC, and a 30 mm left adrenal nodule. Left adrenalectomy revealed a benign 28 x 23 x 20mm adenoma. At age 33 he presented with persistent Cushing’s. Work-up included positive 8 mg DST, CRH stimulation, metyrapone test, CT abdomen with mild diffuse right adrenal enlargement and a 1 cm left sided pituitary lesion on MRI. Transsphenoidal resection documented a 1 cm ACTH- and prolactin- containing pituitary adenoma. Review of the previous adrenal tissue revealed an adenoma with hyperplasia of the adjacent cortical tissue. **Conclusion:** In both cases subsequently found to have CD, the dominant biochemical findings (increased aldosterone and cortisol) associated with obvious adrenal lesions led to unilateral adrenalectomy. This challenging presentation of CD has not been reported frequently. The presence of bilateral adrenal enlargement with evidence of excess hormonal function should prompt thorough evaluation to exclude pituitary Cushing’s.

**Abstract #940**

**CUSHING’S SYNDROME CAUSED BY NEURO-ENDOCRINE TUMOR**

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**Case Presentation:** Introduction

Cushing’s syndrome is caused by excess levels of cortisol with the most common etiology being iatrogenic glucocorticoid use. There are two classes of endogenous hypercortisolemia: adrenocorticotropic hormone (ACTH) dependent and ACTH independent. Hypercortisolemia caused by ACTH-secreting pituitary adenoma accounts for 80% while the remaining 20% are ectopic ACTH secreting tumors. The work up to differentiate the cause of hypercortisolemia can be challenging. We present a case of Cushing’s syndrome caused by neuroendocrine tumor of lung primary, likely ACTH producing. **Clinical Case Description**

63 year old male with past medical history of Parkinson’s disease, hypothyroidism, hypertension, and bipolar disease who was incidentally found to have bilateral adrenal nodules. Biochemical evaluation was performed with 24 hour urine collection for metanephrines and cortisol and serum aldosterone/rein which were within normal limits. A 1 mg dexamethasone suppression test was abnormal
(cortisol post 1mg dexamethasone was 5.9 ug/dL). This was followed by a high dose 8 mg dexamethasone suppression test which showed a cortisol level 35.8 ug/dL, revealing a lack of suppression, with inappropriately elevated ACTH 49 pg/mL. CT head was done which did not reveal pituitary mass (unable to obtain MRI was patient had pacemaker). He did not have any symptoms associated with hypercortisolemia.

He then presented with bilateral leg swelling and was found to have bilateral deep vein thromboses. CT abdomen showed liver lesions which were biopsied with pathology revealing neuroendocrine tumor of lung primary, likely ACTH producing. A whole body PET scan showed hypermetabolic activity in left upper lung lobe compatible with primary neoplasm and associated metastases to left hilar and mediastinal lymph nodes, liver, bones, right frontal lobe, and bilateral adrenals. He had rapid progression of his disease and unfortunately succumbed to his metastatic neuroendocrine stage IV lung cancer.

Conclusion: Ectopic ACTH secreting tumors account for 20% of ACTH-dependent Cushing’s syndrome cases. It is prudent to locate the source of ectopic ACTH secreting tumors as resection of the tumor can be curative. Although surgery is the first choice treatment for ACTH-secreting tumors, the localization of such lesions is rather difficult, and it needs a compelling work up as we have demonstrated in our case. In retrospect, pursuing aggressive medical treatment for hypercortisolemia while investigating for primary malignancy may have changed the outcome, and perhaps improved morbidity and mortality, for our patient.

Abstract #941

HYponatREMIA AS A PRESENTING SYMPTom IN PATIENTS HARBORING SEllAR LESIONS- HYponatREMIA AS A PRESENTING SYMPTOM IN PATIENTS HARBORING SEllAR LESIONS

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Objective: We aimed to review the long-term clinical outcomes in patients who presented pre-operatively with hyponatremia in the setting of a sellar lesion.

Methods: We retrospectively reviewed all patients undergoing transsphenoidal surgery with the senior author from April 2008 through August 2014.

Results: Of 554 patients, 15 (2.7%) presented with pre-operative hyponatremia. The mean age of these patients was 50.1 years (SD=18.0 years), 8 (53.3%) were men, and the mean follow up was 39 months (SD=25 months). Comorbidities included hypertension in 7 patients (46.6%), obesity in 7 (46.6%), smoking in 6 (40.0%), hyperlipidemia in 5 (33.3%), and diabetes in 3 (20%). No patients had a history of renal disease. Additional presenting complaints included headache in 9 patients (60.0%), vision problems in 8 (53.3%), hypopituitarism in 6 (40.0%), and apoplexy in 5 (33.3%). Of the 7 premenopausal women, 3 (42.9%) had dysmenorrhea.

On imaging, 14 patients (93.3%) harbored macroadenomas, and the mean tumor diameter was 2.25cm (range 0.8-3.7cm, SD=0.93cm). All patients underwent transsphenoidal resection. On pathology, 4 patients (26.7%) were found to have non-functioning adenomas, 4 (26.7%) were GH-staining, and 2 (13.3%) were ACTH-staining. Prolactinoma, Rathke cleft cyst, metastatic prostate cancer, silent gonadotroph adenoma, and silent ACTH-secreting adenoma were diagnosed in one patient each.

The mean pre-operative serum sodium concentration was 131.9 (range 127-134, SD=2.2). On POD1, the mean had risen to 137.3 (range 133-144, SD=2.9). Mean serum sodiums at POD2, POD3, POD7, POW6, POW12, POM6, and POM12 were each greater than 135. By POM6, no patient had biochemical evidence or clinical symptoms of hyponatremia.

The most common complications in these patients were transient diabetes insipidus, transient SIADH, and temporary visual field deficit in 2 patients (13.3%) each. One patient (6.7%) developed thyroid hormone deficiency, and one (6.7%) developed adrenal deficiency. One patient (6.7%) required readmission, and one (6.7%) required subsequent reoperation.

Discussion: Pre-operative hyponatremia in the setting of a sellar lesion is relatively uncommon. In this series, 2.7% of patients undergoing transsphenoidal resection over a 6-year period presented with hyponatremia, and none had a history of renal issues. Transsphenoidal resection is the standard of care for symptomatic patients with sellar lesions, and in those patients who present with hyponatremia, it is associated with long-term remission of sodium imbalance.

Conclusion: Lesional resection and proper peri-operative management of patients who present pre-operatively with hyponatremia is associated with durable normalization of serum sodium levels.
Abstract #942

A RARE CASE OF DOPAMINE SECRETING PARA-GANGLIOMA (PGL) IN A PATIENT WITH SDHB AND A VARIANT OF UNKNOWN SIGNIFICANCE IN TMEM127 GENE MUTATIONS

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Case Presentation: PPGL’s and pheochromocytomas are neuroendocrine tumors whose pathogenesis and progression are strongly influenced by genetics. Here we present a case of a dopamine secreting PPGL associated with an SDHB mutation coexisting with a variant of the TMEM127 gene.

A 60-year-old lady presented with headaches, palpitations, sweating and flushing. History was pertinent for anxiety, depression, chemotherapy for Non-Hodgkin’s lymphoma and surgical resection of meningioma and schwannoma. Genetic testing performed due to her personal history as well as history of a benign kidney tumor in her mother. This revealed SDHB specifically pI27S(c 380T>G) mutation and she was also heterogeneous for p. M85V variant of TMEM127 gene. Her son was found to have the same mutation and 2 other children were negative for any mutation.

She had a normal blood pressure and heart rate. She was found to have a significantly elevated 24 hour urinary dopamine levels at 3134mcg(0-510). MRI of the abdomen revealed a 1.4 cm hyperintense enhancing nodule adjacent to the right adrenal corresponding to the area of increased uptake on the I-123 MIBG scan. 24 hour urine studies were repeated which confirmed elevation in dopamine levels at 1379 mcg(52-480) and normal fractionated metanephrines. Chromogranin A was elevated at 27 ng/ml (1.9-15).

She underwent resection of PPGL and pathology confirmed a chromogranin A positive, Synaptophysin Positive PPGL. She improved clinically with the exception of anxiety.

Conclusion: Germline mutations in susceptibility genes have been identified in up to 40% of patients with pheochromocytoma and/or paraganglioma (PPGL). SDHB-related PPGLs are usually solitary, have a higher malignancy potential, secrete norepinephrine or both norepinephrine with dopamine but rarely produce dopamine exclusively. TMEM127-related PPGL are usually benign, almost exclusively adrenal, and not known to exclusively produce dopamine. Over 30 TMEM127-related mutations have been identified, however coexistence of with a SDHB has not been described. The significance of the TMEM 127 variant identified in this patient especially in regards of the PPGL phenotype is not known. We agree with the opinion suggesting genetic counseling for everyone with PPGL. Referring patients with positive mutations to large tertiary centers including the NIH should be considered to help expanding the database and subsequently the knowledge and experience regarding these mutations and the various phenotypes of associated PPGL.

Abstract #943

A RARE CAUSE OF LOW SODIUM

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Objective: Low sodium is very common in the inpatient setting. However rare causes also need to be kept in the differential.

Case Presentation: A 20-year-old male presented to the hospital with a history of multiple episodes of non-projectile vomiting, altered mental status and an episode of seizures. There was no prior medical history of significance and he was not on any medications. The patient was admitted to the ICU and underwent a very detailed work up. Physical examination was unremarkable except for some confusion.

CT brain was nonspecific, ECG showed left ventricular hypertrophy and labs revealed severe hyponatremia and hypomagnesemia, also the bilirubin was high and minor elevation of LFTs was noted. TSH was normal and CRP was high. Labs of significance – serum sodium at admission was 104 mmol/L (136-145 mmol/L), serum uric acid 2.3 mg/dL (3.5-7.2 mg/dL), serum creatinine 0.8mg/dL (0.8-1.3 mg/dL), urine osmolality 559 mosmol/kg and serum bilirubin 2.0 (>1.0 mg/dL).

With routine management of hyponatremia the sodium levels improved but no clear etiology was ascertained. Hence the patient had a whole body PET CT scan which showed nonspecific changes. Finally the patient had a urine porphobilinogen tested which was positive. The patient was diagnosed with acute intermittent porphyria and discharged in stable condition.

Discussion: Acute intermittent porphyria can cause hyponatremia, the presentation can be very similar to the usual causes of SIADH.

Conclusion: Acute intermittent porphyria should be considered in the differential when no clear etiology for hyponatremia can be ascertained.
Abstract #944

MULTIPLE ENDOCRINE NEOPLASIA 1 PRESENTING WITH THYMIC NEUROENDOCRINE CARCINOMA

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Objective: Multiple endocrine neoplasia (MEN)1 is a rare autosomal dominant endocrine cancer syndrome, characterized primarily by parathyroid gland tumor (95%), endocrine gastroenteropancreatic tumor (30-80%), anterior pituitary tumor (15-90%), and bronchial and thymic endocrine tumor (2-10%). Not completely understood, it is related to the production of menin, a primarily nuclear protein that functions as a tumor suppressor. Mutations in the menin gene may lead to its lack of activity and result in down regulation and uncontrolled cell growth.

Case Presentation: 34-year-old man with history of kidney stones presented to the Emergency room with severe intermittent abdominal pain in the right flank radiating to the back. Upon admission, the patient was found to have hypercalcemia at 12.6 mg/dl (8.5-10.2mg/dl). The PTH level was elevated at 119.9 pg/ml (10-55pg/ml) suggesting a diagnosis of primary hyperparathyroidism. Interestingly his family history was significant for nephrolithiasis in his mother and sister, and insulinoma in his mother. Computerized-tomography (CT) of the chest and abdomen revealed bilateral kidney stones, an anterior mediastinal mass of 10 cm as well as multiple subcentimeter pulmonary nodules and lymphadenopathy. Initial biopsy of the mass reported well differentiated neuroendocrine carcinoma. Subsequently, patient underwent surgical resection of the anterior mediastinal mass, debulking of lymph nodes, with right and left inferior parathyroidectomy. The final pathology of the mass showed neuroendocrine carcinoma of the thymus with positive chromogranin and CD56 stain, and negative serotonin, calcitonin and somastostatin stain. Pathology of parathyroid glands showed right and left inferior hyperplastic parathyroids. Metastatic disease was found in the left femoral neck, left posterior tibia, T5 and T10 vertebral bodies on MRI. Evaluation of pituitary and pancreas was performed. MRI of the brain did not show any mass and pituitary hormones were normal. Pancreatic neuroendocrine evaluation was relevant for negative octreotide scan, mild elevated chromogranin A 23 ng/ml (1.9-15ng/ml) and, normal gastrin and pancreatic polypeptide level. Genetic testing confirmed MEN-1 heterozygous disease causing nonsense mutation c781 C>T p.Gln261Ter (Q261X).

Conclusion: The worldwide prevalence of MEN1 has been reported to be up to 1 in 20000. Primary neuroendocrine carcinoma of the thymus is exceedingly rare and represents about 2-10% of all MEN1 cases. The largest retrospective study to date in Europe, Asia and North America mentions 205 cases from 1984 to 2012. Although this is a very aggressive tumor, its prompt diagnosis and excision can affect prognosis.

Abstract #945

WEST NILE VIRUS ENCEPHALITIS INDUCED CENTRAL DIABETES INSIPIDUS

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Objective: To highlight the endocrine complications of West Nile Virus encephalitis.

Case Presentation: 40-year-old female with history of HIV presented with fever and confusion. Neurological examination revealed altered mental status, areflexia and 4/5 lower extremities strength. Initial head CT was normal. Lumbar puncture was performed. Empiric antibiotics and acyclovir were commenced for possible infectious meningitis. Her mental status deteriorated rapidly and she was intubated for airway protection. CSF analysis revealed increased protein and lymphocytic pleocytosis. Brain MRI showed diffuse leptomeningeal enhancement, consistent with encephalitis. Electroencephalogram showed focal epileptiform activity. CSF serology revealed West Nile Virus (WNV) IgG titer of 2.2 and IgM titer of 4.40 consistent with acute viral infection. On day 5 of hospitalization she developed hyponatremia (serum sodium 156 mEq/L), with increased urine output (400 ml/hr). Serum osmolality was elevated (448 mOsm/kg H2O) and urine osmolality was below 200 mOsm/kg H2O. Administration of desmopressin resulted in a remarkable improvement of polyuria, normalization of urine osmolality and serum sodium. Her general condition improved and she was discharged after one month of hospitalization.

Discussion: Acute CNS infections can rarely disrupt hypothalamic-pituitary function and result in variable endocrinopathies such as central hypothyroidism, ACTH deficiency and hyperprolactinemia. Similarly, destruction of hypothalamic vasopressin producing neurons by the infection can result in Central Diabetes Insipidus (CDI). WNV is a flavivirus that can cause neuroinvasive syndromes such as meningitis, encephalitis and flaccid paralysis.
CDI usually presents with polyuria, polydipsia, and nocturia. However, patients with severe encephalitis are neurologically altered and have impaired thirst sensation. Therefore, profound polyuria is an essential clue for CDI diagnosis in these cases. Hypernatremia is usually the main biochemical abnormality seen. Documentation of urine concentrating ability in response to exogenous vasopressin is the best diagnostic approach to CDI. Searching for the underlying etiology of viral encephalitis, however, is important and can be suggested by imaging, and confirmed by the polymerase chain reaction test for the virus in the CSF.

The goal of CDI treatment is to maintain water balance and normalize plasma sodium. The drug of choice for CDI is desmopressin, however, remarkable improvement of CDI can occur with the resolution of encephalitis.

Conclusion: Central Diabetes Insipidus can result from hypothalamic-pituitary injury associated with WNV encephalitis. Prompt diagnosis and treatment can improve clinical outcomes.

Abstract #946

ASSESSMENT OF ACROMEGALY PATIENTS WITH AND WITHOUT DIABETES TREATED WITH LANREOTIDE DEPOT: 2-YEAR REAL WORLD DATA

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Objective: Diabetes mellitus (DM) is a common comorbidity in patients with acromegaly. Somatostatin analogs (SSAs) can exert variable effects on glucose metabolism with worsening due to inhibition of insulin secretion and improvement due to improved insulin sensitivity with improved acromegaly control. This report examined 2-year biochemical control among patients with and without DM from the SODA registry, a multi-center observational study of long-acting SSA lanreotide depot for acromegaly treatment.

Methods: Data on patients with and without DM at enrollment were collected, including demographics/baseline characteristics and biochemical efficacy assessed by growth hormone (GH) and insulin-like growth factor-1 (IGF-1) levels.

Results: In the studied cohort, 25% (61/241) had a diagnosis of DM at enrollment. Compared with non-DM patients, DM patients were older (55.3 vs 48.2 yr; p=0.0008), had higher body mass index (BMI) (34.3 vs 31.7 kg/m2, p=0.013), and greater prevalence of hypertension (67.2% vs 37.8%, p<0.0001) and statin use (50.8% vs 20%, p<0.0001). There were no differences between groups (DM vs non-DM) in the proportion of patients with GH≤2.5 ng/ml at 1 year (94.4% [17/18] vs 78.7% [37/47], p=0.05) and 2 years (82.4% [14/31], p=0.05), and in the proportion of patients with IGF-1 below upper normal limit (UNL) for age and gender at 1 year (67.6% [23/34] vs 72.6% [61/84], p=0.05). However, significantly less DM patients (38.3% [14/24]) vs non-DM patients (80.6% [50/62]) had IGF-1 levels<UNL at 2 years (p=0.033).

Discussion: The prevalence of DM among patients with acromegaly reported here (25%), as well as older age, higher BMI, and higher coexistence of hypertension and statin use in the DM group were similar to those reported in other registries. Overall, during the 2-year observational period in the SODA study, the majority of patients in both DM and non-DM groups achieved and maintained biochemical control assessed by either GH or IGF-1, with more patients with controlled IGF-1 in the non-DM vs DM group at 2 years.

Conclusion: Two years of lanreotide depot therapy in an acromegaly cohort from real world clinical practice was associated with consistent and similar biochemical control in the majority of patients both in the group without diabetes and in the group with diabetes.

Abstract #947

ECTOPIC GH-PITUITARY ADENOMA IN THE SPHENOID SINUS WITH EMPTY SELLA TURCA: DIAGNOSIS AND TREATMENT.

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Objective: To report an usual presentation of a patient with a GH-secreting pituitary adenoma in the sphenoid sinus with empty sella turcica.

Methods: We reviewed the clinical presentation, laboratories, imaging, treatment and follow-up of the reported patient.

Case Presentation: 54 years-old Peruvian patient with PMH of HTN and T2D, stated for the last 20-years a slowly thickening of face and extremities. 7-years-ago, he started to have headaches and he was diagnosed of Acromegaly based on a head CT, but the patient refused to take any treatment. 1-year-ago, he developed polyuria, polidypisia, hoarseness, tiredness and his headache became severe.
PE: BP:150/80, HR:89, RR:28, O2sat:98%, T:98°F. He presented with acanthosis negricans, thyroid was not palpable. Labs: Glucose:600mg/dl, Prolactin:44.3ng/ml, and normal ranges of the rest of hormones. The Acromegaly diagnosis was confirmed by IGF1:660ng/ml and an oral glucose tolerance test that revealed no suppression of GH values. MRI revealed an hyper-intense mass in the sphenoid sinus. The patient underwent a transsphenoidal surgery, an adenoma located in the sphenoid sinus was removed, the sellar floor and the duramater were not affected. Immunohistochemistry was positive for GH and negative for prolactin. 6 months after surgery, his IGF-1 level continued in normal ranges and remained asymptomatic.

Discussion: To our knowledge less than 15 cases of ectopic pituitary adenoma have been reported, mainly located in the sphenoidal sinus and clivus; most of them have remnants of the tumor in the sella turcica. However, just 5 cases of ectopic pituitary adenoma in the sphenoidal sinus with empty sella turcica have been reported, findings that makes us consider this presentation might have occurred through the migration of the Rathke’s pouch in the sphenoid sinus rather than invasive extension from the sella turcica into the sphenoid sinus. Transsphenoidal surgery has been used to confirm diagnosis and for therapeutic goals. No difference in the symptoms or laboratory parameters were found compared to non- ectopic acromegaly. Investigation revealed- Basal S. FSH- 0.45 mIU/mL, LH-0.04 mIU/mL, S. estradiol- 30 pg/mL & 1 hour after GnRH stimulation S. FSH- 32.4 mIU/mL, LH- 4.70 mIU/mL & S. estrogen- 67.5 pg/mL. Other investigations revealed- S. FT4- 11.19 pmol/L, S. TSH- 2.04 mIU/mL, S. Prolactin-11.50 ng/mL. Basal cortisol- 6.50 mg/dL, Plasma ACTH-35.77 pg/mL, GH- 0.82 ng/mL, DHEA SO4- 16.50 mg/dL, 17-OHP-1.12 ng/mL, USG- Normal both adrenal glands with early development of uterus and ovaries. Abdominal CT- Normal both adrenal glands with early development of uterus & adnexae, bone age 6-7 years, MRI of brain- pituitary microadenoma. Patient was diagnosed as a case to precocious puberty (central) on the basis of history, physical & biochemical findings. GnRH analogue injection triptorelin 3.75 mg (IM) was started on 30.06.2014 & 1 ampule per month. 18th dose of triptorelin is given on 8.12.15. Patient’s whitish P/V discharge is no longer present, breast changes are now static, height- 120 cm, weight- 24 kg, USG- infantile uterus otherwise normal study, LH-0.32 mIU/mL, FSH- 0.78 mIU/mL, estrogen- 16.50 pg/mL, MRI of brain- Normal findings of brain & pituitary gland. Discussion: Precocious puberty may occur due to central or peripheral cause. Central precocious puberty is considered when associated with abnormalities in hypothalamus or pituitary region causing increased GnRH or gonadotropins secretion. Hypersecretory cells may give false positive MRI result. Treatment with GnRH analogue may cause down regulation of GnRH receptors causing gradual shrinkage of tumor like lesion. Conclusion: Children with central precocious puberty are treated with GnRH analogues which down regulate pituitary GnRH receptors & decrease gonadotropin secretion.
Abstract #949

**CASE REPORT: OBESITY IN CUSHING’S DISEASE.**

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*Case Presentation:* Obesity is a substantial public health crisis world wide, and its prevalence is increasing in industrialized nations. Diet, exercise, and behavioral modification and other management strategies such as pharmacotherapy and bariatric surgery may be considered. However a small percentage of obese patients may have an underlying cause that may be overlooked by a non-suspecting practitioner. It is highly recommended to be prepared especially when a patient presents with cushing’s syndrome instead of plain obesity. When iatrogenic causes are excluded, the most common cause of Cushing’s syndrome is Cushing’s disease, accounting for approximately 70% of cases and majority of tumors are small microadenomas. A key biochemical hallmark of the disease is a relative resistance of ACTH secretion to normal glucocorticoid feedback inhibition due to a higher set point from the adenoma. The definitive management is pituitary surgery, from then obesity of a patient may be reversed from this perspective. 

*Case presentation:* A 61-year old female was referred for planned weight loss and nutritional counsel due to BMI 29.9. History revealed she had 20 lbs weight gain in 5 months without any increase in appetite. Review of systems were unremarkable, however, physical exam showed central obesity with buffalo hump, thinning of skin and round facial contour. Although she had a family history of diabetes mellitus, her medical history revealed only Hypertensive cardiovascular disease, Stable Angina (on Amlodipine, ASA and Isosorbide mononitrate) and some surgical procedures: spinal surgery in 2011 (herniated disc) and intraarticular injection in 2014 (Partial tear and tendinopathy supraspinatus/infraspinatus, left). Initial lab tests showed FBS 106.68 mg/dL FT4 20.890 TSH 0.810 and Cortisol 0800H 782.90 nmol/L. Eventually, patient had further endocrine work up which showed the ff: Overnight 1mg Dexamethasone Suppression Test of 475.01 nmol/l (from baseline: 545.47 nmol/L), ACTH: 71.803 pg/mL and an overnight High dose Dexamethasone Suppression Test of 73.76 nmol/L (from baseline: 752.45 nmol/L). MRI was then done revealing pituitary microadenoma 0.2cm. She underwent pituitary transphenoidal surgery thereafter and currently on physiologic dose of steroids. 

*Conclusion:* Delayed identification of Cushing’s Disease in obese patients results in possible progression, with the risk of irreversible complications. More often it is overlooked due to the prevalence and association of obesity in several clinical disease entities. It is therefore invaluable to do a thorough history and physical examination before initiating management for a patient even with a presentation of a simple obesity.

Abstract #950

**MALE WITH GIANT MACROPROLACTINOMA PRESENTING WITH IMPAIRED VISION DURING TREATMENT WITH CABERGOLINE.**

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*Objective:* Present a very rare complication of medical treatment of a macroprolactinoma.

*Methods:* We present the clinical characteristics and evolution.

*Case Presentation:* Male, 30 years. Refer a condition of three years of evolution characterized by retro-orbital and frontal headache of moderate intensity such oppressive sagging with painkillers. Subsequently decreased bilateral visual acuity predominantly left, went to another specialist center in January, 2013 where the study of MRI showed a pituitary macroadenoma of 47x40x50 mm with optic chiasm and commitment to both cavernous sinus extension is added. Analysis: PRL: 6470ng / ml, he received prednisone (5 mg / d) and LT4 (100 ug / d) for 10 months and Cabergoline 1.5mg / week for 12 months; during treatment with cabergoline had improved vision and headache; then meet so irregular taking cabergoline coming to suspend for more than three months, returning at times depending on the economy. Six months before admission he presents progressive deterioration of bilateral visual acuity associated with retro-left dominance headache returning cabergoline (1.5 mg / week) and go to our hospital with severe headache. MRI showed herniation of the left parietal lobe in sella. Analysis: PRL: 112ng / ml. He underwent craniotomy left posterior optic nerve decompression + + plasty of bone and sellar region; Findings: gyrus rectus herniation of the left parietal lobe inside sella generating marked and compression on the left optic nerve chiasm. Intraselar solid pituitary tumor with cystic degeneration. In the postoperative improvement in visual acuity is continuing evidence of hormone replacement therapy and cabergoline 1mg / week.

*Discussion:* CBG-treated patients experienced tumor regression of at least 50% during the first 6 months of treatment, but rarely has reported a sharp antitumor effect it causes, as in this case, herniation of brain tissue to sella or to brainstem depending on the pretreatment extension.

*Conclusion:* Use of CBG in the treatment of prolactinomas has proved very effective and safe, being accepted as a treatment of choice.
Abstract #951

SHEEHAN’S SYNDROME THE MOST CAUSE OF PANHYPOPITUITARISM IN SUB-HIMALAYAN REGION.

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Case Presentation: Panhypopituitarism is a rare disorder with varied clinical presentation having various etiologies. Pituitary tumors are the most common cause in adults in developed nations. Sheehan’s syndrome is decreasing in frequency worldwide and is a rare cause of panhypopituitarism in developed nations owing to advance in obstetric care. Long-standing pituitary damage is associated with increased mortality primarily due to increased cardiovascular and cerebrovascular mortality. We retrospectively investigated the etiological profile of panhypopituitarism patients at a territory care teaching hospital without having endocrinologist service in a sub-Himalayan region at an altitude of 7,200 feet. Total 12 patients of panhypopituitarism were diagnosed in the previous three years. Out of twelve, 33.33% were male and 66.66% were female with mean age of diagnosis 38.83±14.49 years. Sheehan’s syndrome was the most common cause of panhypopituitarism in 50%, followed by post surgery in 25% and empty sella, macroadenoma and lymphocytic hypophysitis in 8.33% respectively. Three fourth of women with panhypopituitarism had Sheehan’s syndrome with mean age of diagnosis 37.83±12.79 years. All women with Sheehan’s syndrome were from the rural (two of them from >9000 feet altitude) and low socioeconomic background. All except one had home conducted delivery. Generalized weakness and easy fatigability was the commonest mode of presentation with a mean duration of symptoms 2.39±1.54 years. However; history of post partum hemorrhage, failure of lactation and amenorrhea were present in all with a mean duration of 8.64±6.39 years. All patients were treated with oral hydrocortisone, levothyroxine. Except for two females (age>45) all were treated with oral contraceptive pills and only one male was treated with testosterone. Because of monitoring issue, only one male was treated with testosterone. On follow-up all were symptomatically and biochemically better. Growth hormone was not given because of cost, availability and storage problem.

Conclusion: Sheehan’s syndrome is common in developing countries, more so in rural areas, mostly remained unrecognized due to lack of awareness among primary care physicians coupled with non-availability of endocrine specialized investigations. High degree of clinical suspicion is of paramount important, as clinical features are most often subtle and many years may pass before diagnosis is suspected. History of post-partum hemorrhage, failure of lactation and amenorrhea are important clues for the early diagnosis and treatment of this unrecognized clinical syndrome to reduce the morbidity and mortality.

Abstract #952

REVIEW OF TEN PATIENTS OF HYPOPHYSITIS

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Case Presentation: Ten patients of hypophysitis were seen in a single center between 2007 and 2015. All were female mean age 34.8 years range: 22.2 - 54 years. Five had children prior to diagnosis, the age of the youngest being 3 years. There was no temporal relation of symptoms to childbirth. Headache was the presenting feature in all patients. Seven presented to the endocrinology unit with an enlarged pituitary. A presumptive diagnosis of hypophysitis was confirmed by separate neuroradiologist. Standard secondary causes of hypophysitis were excluded. Three patients presented to the neurology unit and went on to have pituitary surgery. The diagnosis of hypophysitis was established histologically and confirmed by a retrospective review of the neuroradiology images. Two out of seven patients were not given any treatment except for headache. Four recieved glucocorticoids. One patient was advised glucocorticoids but refused treatment. MRI of the head was done every 6 months and all 4 patients received dexamethasone for the first 12 months. This was switched to prednisolone in the second year when a attempt was made to taper and stop the treatment. Radiological improvement was seen from 6 months and all patients experienced symptom resolution by 2 years. All 4 patients had insulin tolerance test at the conclusion of treatment. Two were steroid dependent and were maintainiend on hydrocortisone. One had hyperprolactinemia and was treated with cabergoline. One patient developed features of polycystic ovary syndrome (PCOS). She was know to have PCOS earlier, had suppressed LH and FSH levels during treatment and went on to have typically elevated LH:FSH ratios post treatment.

Conclusion: Hypophysitis should be high on the list of diagnoses of a female patient who has headache with an enlarged pituitary. The condition is not always associated with childbirth and has a widely varying presentation. Some patients may merely need treatment for headache and do well on follow up. The condition usually resolves over two years. Contrary to earlier literature the majority of patients need not undergo surgery.
Abstract #953

**DUMBELL TUMOR CAUSING CATASTROPHIC CRISIS**

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**Objective:** To present a case of pituitary apoplexy

**Case Presentation:** A previously asymptomatic 62 years male presented to emergency with acute confusional state. He had bifrontal headache, vomiting and dizziness of 2 days duration. No seizures, motor weakness or diplopia. He was on treatment for hypertension since 1 year. No H/O diabetes, impotence, polyuria, fatigability, weight gain or symptoms suggestive of hypothyroidism. He did not have any addictions. Pulse 98/minute regular, BP 118/70 mmHg, temperature 100.0 F. Pupils normal size sluggishly reacting, bilateral gynaecomastia, sparse axillary and body hair and bilateral soft testes (12 ml each). CNS examination no focal neurological signs, neck rigidity or ophthalmoplegia. Bilateral planar withdrawal. Emergency CT showed a dumbbell shaped mass arising from sella extending into suprasellar region (8X10X6 cm) with presence of extensive intrasellar haemorrhage. Diagnosis of pituitary apoplexy was made. Investigations: Blood glucose (random) 123mg/dL, Sodium 135 meq/L (135-145), TSH: 0.093 mIU/ml (0.550-4.780), FT3 1.32pg/ml (2.3-4.2), FT4: 0.45ng/dl (0.89-1.76), FSH-0.50mIU/ml(1.40-18.0), LH 0.25mIU/ml (1.50-9.30), Testosterone 170.0ng/ml (300-827), Cortisol 6.93ug/dl (4.30-22.40), ACTH 15.30pg/ml (<46.0), GH 0.94ng/ml(<5.0), IGF-1 33.40 ng/mL (75-212). Patient was put on I/V Inj hydrocortisone and IV fluids. He became conscious, started recognising relatives over next 2 days. Eltroxin was added subsequently and he was discharged after 10 days on oral steroids and eltroxin. Testosterone and growth hormone replacement therapy was to be discussed subsequently. Neurosurgical consultation suggested for conservative management.

**Discussion:** Pituitary apoplexy presents as life threatening emergency because of either haemorrhage or infarction in preexisting adenoma. Our patient was largely asymptomatic for any mass effect or hormonal deficiency/excess. There were no eye signs in spite of marked suprasellar extension. Life threatening acute adrenal deficiency arose from acute onset panhypopituitarism & responded to early introduction of steroids and fluids unlike routine management of CVA where steroids do not find any role. Prompt recognition of this condition and treatment with steroids can be life saving.

**Conclusion:** Large dumbbell tumours of pituitary may remain asymptomatic for long periods of time & may present with catastrophic pituitary haemorrhage and life threatening consequences. Clinician may start with life saving steroids in such situations bringing dramatic recovery of the patient.

Abstract #954

**THYROID CANCER IN ACROMEGALY: PROPORTIONAL GENDER INVOLVEMENT AND ADVANCED STAGE AT PRESENTATION**

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**Objective:** To determine whether thyroid cancer in acromegaly exhibit distinctive clinical or epidemiological characteristics.

**Methods:** Retrospective chart review of 18 patients with acromegaly and thyroid cancer. Their demographic and clinical characteristics were compared with those of the entire ACRO-Canada database and with thyroid cancer patients from the general population as reported in Canadian (PHAC) and American (SEER) cancer registries.

**Results:** Thyroid cancer (TC) was the most common cancer in acromegaly patients from our series (31% of all cancers), compared with 2.5-3.8% of malignancies in the general population. Unlike the general population, the distribution of TC in acromegaly patients showed no specific gender preponderance (55% females compared with 75%). The mean age of TC diagnosis in acromegaly was 51, compared to 46 in TC registries. Mean IGF-1 (SD) at diagnosis for Acro-TC patients was 2.52 ± 0.99 x upper limit of normal range (ULN) compared to 3.12 ± 1.48 ULN in the entire database. All TC detected in the Acro-TC group were papillary thyroid cancer (PTC), while in general TC registries PTC represents 80%. Advanced stage (III-IV) represented at least 33.3% of patients in the Acro-TC, as compared to 15% in general TC registries.

**Discussion:** TC in acromegaly patients seems to have distinctive features. TC in patients with acromegaly appears to adopt distinctive features: higher occurrence than the general population, loss of female sex predominance, absolute predominance of the papillary subtype, and a tendency to present at later age, and at more advanced stages than in the general population.
**Conclusion:** Our findings need to be corroborated in larger series. Important implications for the management of TC in this population may derive from our analysis. Until more information becomes available TC in acromegalics may need to be treated as a more aggressive variant of TC.

**Abstract #955**

**SHEEHAN SYNDROME IN A JIZAN REGION OF SAUDI ARABIA.**

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**Objective:** Sheehan syndrome is hypopituitarism caused by ischemic necrosis due to blood loss and hypovolemic shock during or/and after childbirth. Sheehan syndrome (SS) remains an important cause of maternal morbidity in the developing world. Our study depicts the correlation between Sheehans Syndrome and Maternal morbidity in King Fahd Central Hospital of Giza city in Saudi Arabia. Located near the Red Sea about 1000 km south west of Riyadh, Giza region is inhabited by about 1 million people, a third of which are Bedouins. Despite a recent and rapid socio-economic progress and availability of free and efficient health services in Saudi Arabia, a proportion of deliveries in rural areas are domiciliary with frequent peri-partum complications.

**Methods:** Over 6 years, 30 patients (29 Saudis and 1 Yemeni) with SS were diagnosed in KFCH, Giza. The diagnosis was made on basis of clinical features and biochemical evidence of lack of one or more pituitary hormones. Levels of T3, T4, TSH, cortisol, LH, FSH, GH, prolactin and estradiol were obtained by standard radioimmunoassay. Metoclopramide and insulin stimulation tests obtained in 10 patients were abnormal. 1 patient presented with diabetes insipidus, a rare finding in SS.

**Results:** All patients had symptoms related to all aspects of target organ hormonal deficiencies. There was a significant delay in the diagnosis from symptom onset with 2 patients being diagnosed within a year and 20 having symptoms for >6 years. Although the delay can be attributed to late presentations in the hospital, some of the primary care physicians did not consider SS during the initial evaluation.

**Discussion:** The mean age of the patients was 38.5 yrs (range 23 and 60 yrs). 19 were < 40 yrs and 26 delivered at home. A history of significant post – partum hemorrhage requiring blood transfusion was noted in 29 patients and 3 had ruptured uterus. The interval between last delivery and diagnosis was < 5, 6 - 10 and more than 10 years in 10, 12 and 8 cases respectively. 22 had >5 children before diagnosis. CT Brain showed empty sellae. Metaclopramide and insulin stimulation tests obtained in 10 patients were abnormal. 1 patient presented with diabetes insipidus, a rare finding in SS.

**Conclusion:** Many patients were diagnosed around menopause or even in their 6th-7th decade. Many presented with shock after acute gastritis or some trivial illness. Quite a lot suffered from consequences of untreated hypopituitarism like infertility, sexual dysfunction, osteoporosis and ill health. For patients who have had p.p bleed or failure to lactate or secondary amenorrhea, the diagnosis of SS should be ruled out early in order to reduce significant morbidity. Improvement in obstetric care and education of primary care physicians may reduce the frequency of SS and associated suffering.

**Abstract #956**

**SUCCESSFUL DEBULKING OF PITUITARY MACROADENOMA WITH PASIREOTIDE LAR AND DOPAMINE AGONIST COMBINATION THEORY**

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**Objective:** Pasireotide long-acting release (LAR) is approved for the treatment of patients with acromegaly who have had an inadequate response to surgery and/or for whom surgery is not an option. Pasireotide LAR has been shown to reduce levels of growth hormone (GH) and insulin-like growth factor 1 (IGF-1) and shrink tumor volume. Here, we report successful preoperative use of pasireotide LAR in a patient who originally could not undergo surgery.

**Methods:** The patient was enrolled in the ACCESS pasireotide LAR safety monitoring trial (ClinicalTrials.gov identifier, NCT01995734) and was transitioned to commercially supplied pasireotide LAR 40 mg once monthly upon study completion.

**Results:** A 64-year-old male reported experiencing several years of sleep apnea, excessive sweating, osteoarthritis, low-grade headaches, and vertigo. MRI revealed a 3.6-cm\(^3\) left-sided pituitary adenoma with partial invasion of the left cavernous sinus and partial encapsulation of the left internal carotid artery with effacement of the chiasm, preventing surgical resection. Tumor size was unchanged after 2 months of cabergoline 250 μg twice weekly (BIW), which was then increased to 500 μg BIW. The presence of bilateral carpal tunnel syndrome, excessive sweating, and arthritis led to an evaluation for acromegaly, which
was diagnosed on the basis of GH and IGF-1 levels of 1.97 ng/mL and 198 ng/mL (reference range [RR], 35–190 ng/mL), respectively. Pasireotide LAR was initiated with enrollment into the ACCESS trial and, after 6 months of treatment, GH and IGF-1 levels were reduced to 0.02 ng/mL and 135 ng/mL (RR, 43–225 ng/mL), respectively, and glycemic levels were controlled (HbA1c, 5.9%). Tumor volume was unchanged at this time, so bromocriptine 2.5 mg once daily was added. Normal GH and IGF-1 levels were maintained through poststudy transition to commercially supplied pasireotide LAR. After 8 months of combination therapy, tumor volume was reduced to 1.7 cm³ with no encasement of the carotid artery. The patient underwent endoscopic endonasal resection of the pituitary tumor, and there was no evidence of residual tumor postsurgery, which allowed for discontinuation of pasireotide LAR and bromocriptine.

Discussion: Recent guidelines have discussed preoperative use of medical therapy (particularly somatostatin analogs) to reduce surgical risk from severe comorbidities and to relieve symptoms due to compressive mass effect, when surgery is not possible.

Conclusion: This case showed significant debulking of a large extrasellar tumor encasing the internal carotid artery using pasireotide LAR and bromocriptine. This debulking allowed for safe, uncomplicated, and complete tumor resection.

Abstract #957

SURGICAL OUTCOMES AND PROGNOSTIC FACTORS IN PATIENTS WITH PROLACTINOMAS: A SINGLE-CENTER CONSECUTIVE CASE SERIES

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Objective: Dopamine agonists (DA) have been the mainstay treatment for prolactinomas, with surgery performed for intolerance or resistance. Recently, more patients choose surgery to avoid taking longterm medications and potential side effects. As data are sparse on surgical outcomes and predictors of surgical remission, we ascertain these in patients operated over a span of 20 years by a single neurosurgeon.

Methods: Retrospective study of patients with clinical and histological diagnosis of prolactinoma operated between 1994-2014. Remission was defined as normoprolactinemia at 1-3 months postoperatively in absence of DA. We performed multivariate and Kaplan-Meier analyses and considered the following events after surgery: death, recurrence of hyperprolactinemia, reoperation and radiation.

Results: 77 patients (41 M) mean age 36±13 were operated via transsphenoidal (76) or transcranial approach (1). Surgical indications were patients’ preference (32), DA resistance (21), DA intolerance (11), vision loss (7), apoplexy (5), and unknown (1). Among patients who preferred surgery, 50% were operated after 2009. Maximal tumor diameter was 2.1±1.3 cm; median preoperative PRL 470 ng/mL (IQR 172-1520). DA were used in 48 patients preoperatively and yielded a median preoperative PRL of 108 ng/mL (IQR 23.5-310). Postoperative remission status was determined in 74 patients followed for a median of 28 months (1.3-157). Normal PRL was achieved in 12/15 microadenomas and 10/59 macroadenomas; 6/20 DA-resistant and 6/11 DA-intolerant patients. Female gender, younger age, no prior surgery, no cavernous sinus invasion, smaller tumor diameter, lower preoperative prolactin (PRL), and surgeon’s experience were predictors of remission by univariate analysis. A model including preoperative PRL and tumor diameter (cutoff 17 mm) best predicted postoperative remission (AUC 0.89). Preoperative PRL ≤586 ng/mL predicted remission with 100% sensitivity and 64% specificity. Postoperative day 1 PRL ≤19 ng/mL predicted remission with 95.4% sensitivity and 95.8% specificity (AUC 0.99). In patients treated with DA before surgery, event-free survival was higher if PRL while taking DA was ≤143 ng/mL (p 0.09).

Discussion: Patients’ preference has become increasingly prevalent as indication for surgery. Tumor diameter and preoperative PRL in absence of medical treatment are independent predictors of remission. Other factors that influence surgical outcomes are gender, response to DA and cavernous sinus invasion.

Conclusion: Remission after surgery by an expert neurosurgeon is expected in patients with preoperative PRL ≤586 ng/mL and diameter ≤17 mm.

Abstract #958

ISOLATED CRANIAL NERVE THREE PALSY SECONDARY TO HEAD TRAUMA: AN UNUSUAL PRESENTATION OF PITUITARY APOPLEXY

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Objective: Most cases of pituitary apoplexy are spontaneous. Here we describe an unusual presentation of pituitary apoplexy with partial pupil sparing CN III palsy caused by head trauma.

Case Presentation: A 56 year old African American male with a history of hypertension and HIV initially presented to ER with complaints of a headaches and
nausea after a fall which resulted in a minor head trauma. CT scan in the ER showed a small severe scalp contusion without skull fracture or hemorrhage and the patient was discharged home. He returned to the ER 2 days later with unresolved headaches and new onset left sided ptosis. On examination, he did not have any visual field deficits and his left pupil was noted to have a reduced response to light compared to the right pupil. Repeat CT scan was negative for hemorrhage. An MRI was done which showed a 1.2 X 2.5 cm hemorrhagic pituitary adenoma with left sided cavernous sinus invasion. Given the unique presentation, an MRA of the head and neck was performed to rule out aneurysm, AVM or ischemia. Neurosurgery and ophthalmology were consulted for surgical evaluation. The patient received 100 mg IV hydrocortisone and the hormonal workup showed a free T4 of 0.56 mcg/dL with a TSH 0.096 mIU/ml, a prolactin of 0.4 ng/ml, and a total testosterone of 4 ng/dL. The patient had a transphenoidal endoscopic resection with no immediate postoperative complications. He was able to partially open his left eye within 24 hours of surgery and had complete resolution of CN III palsy by discharge on day 4.

Discussion: The majority of pituitary apoplexy cases are due to a spontaneous hemorrhage with no identifiable cause but precipitating factors can be identified in 10-40% of cases. Most common causes include cardiac surgery and dynamic endocrine testing. Head trauma is a relatively rare cause of pituitary apoplexy and usually bleeding occurs within the first 24 hours but has been noted to occur up to a week later. Apoplexy episodes with neurological symptoms can be managed either surgically or conservatively depending on the stability of the patient. However surgery can result in diabetes insipidus which can be permanent as well as bleeding and infection, which must be taken into consideration when determining management. Time is an important factor with better outcomes if surgical decompression is completed within the first week.

Conclusion: Even though pituitary apoplexy is a rare condition compared to the number of head trauma patients seen daily in ER, it is critical to have a high index of suspicion to diagnose and treat pituitary apoplexy immediately as it is an endocrine emergency and can result in significant morbidity and mortality if diagnosis and treatment are delayed.

Abstract #959

OSTEOBLASTIC OSTEOSARCOMA IN A PATIENT WITH GIGANTO-ACROMEGALY

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Objective: To present a rare case of osteoblastic osteosarcoma in a male with giganto-acromegaly

Methods: We present the clinical and paraclinical characteristics of a young man with this rare association

Case Presentation: 20 year old male. No medical history. States that have high stature at age 14 compared to their other family members also presented growth of limbs and some acromegaly traits. Comes in for a condition of three months of evolution characterized by right knee pain and enlargement of bone parts so he was hospitalized. Analysis: GH: 32.9ng/ml; IGF1: 1325ng/ml, TSH: 0.967uUI/ml, FT4: 1.08ng/dl, FT3: 4.15pg/ml, PRL: 27.90ng/ml, ACTH: 49pg/ml, LH : 1.36mlU/ml; FSH: 1.78mlU/ml, free testosterone: 2 pg/ml. MRI of the pituitary: tumor of 30x20x18mm, compresses the optic chiasm with extension to right cavernous sinus. MRI knee bone expansion process large medial femoral distal, with distortion of cortical bone and soft tissue prominence over. He underwent arthroscopy + biopsy: Osteosarcoma locally advanced right distal femur, osteoblast-like. TEM chest and abdomen-pelvis (-). Octreotide-LAR 20mg/28d neoadjuvant chemotherapy (ifosfamide, doxorubicin, methotrexate and leucovorin) to the present indicated. Control post treatment (6 months) GH: 24.6ng/ml; IGF1: 1240ng/ml. Pituitary MRI: 28x16x16mm formation extending into the suprasellar region, infiltrates medial wall of the right cavernous sinus and extends the left as far as therapy was associated cabergoline 1.5mg/week. It is expected to complete the treatment of osteoblastic osteosarcoma and evaluate response to combination therapy for acromegaly in order to consider pituitary surgery.

Discussion: As the patient has other risk factors for osteosarcoma, the hypothesis that the rate of bone turnover and stimulation caused by long term exposure to high concentrations of GH and IGF-I could act as a predisposing factor for the development of this malignant bone tumor.

Conclusion: Only three cases reported in the literature describe the coexistence of acromegaly and osteosarcoma.
REPRODUCTIVE ENDOCRINOLOGY

Abstract #1000

OVARIAN HYPERTHECOSIS: A SECONDARY CAUSE OF DIABETES

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Objective: The objective of this presentation is to recognize the clinical presentation of Ovarian hyperthecosis (OHT) and to discuss the treatment options available for premenopausal patients as well as the associated risks.

Case Presentation: A 35-year old female presented to the endocrine clinic for evaluation of new onset diabetes. The patient was diagnosed four months prior to presentation after presenting with polyuria, fatigue and polydipsia. The patient had been managed by another endocrinologist since diagnoses but has had difficulty controlling her glucose despite a 55 lb weight loss, oral anti-hyperglycemic medications and insulin therapy. Despite compliance her glucose remained above 250 mg/dL. She had no family history of diabetes. Associated symptoms included worsening acanthosis nigricans, secondary amenorrhea and hirsutism. Physical examination was consistent with acanthosis nigricans and facial acne. A secondary work-up was normal with the exception of an elevated serum testosterone level of 296 ng/dL (normal range 9-55 ng/dL). An overnight 1 mg dexamethasone suppression test showed a normal suppression of serum cortisol and IGF-1 was not elevated. MRI of the ovaries and adrenals showed mildly enlarged, symmetrical ovaries measuring 4.3 x 2.7 x 5.3 cm on the left and 4.4 x 3.1 x 4.5 cm on the right, and no evidence of adrenal masses. In the absence of an identifiable ovarian or adrenal tumor, a diagnosis of ovarian hyperthecosis was entertained. The patient was started on spironolactone and oral contraceptive pills.

Discussion: OHT is a severe variant of Polycystic Ovarian Syndrome. The condition is characterized by non-neoplastic proliferation of ovarian stroma and stromal cell luteinisation. The severity of hyperthecosis correlates with the degree of insulin resistance. Because insulin and IGF-1 stimulation proliferation of thecal interstitial cells, hyperinsulinemia may be an important pathophysiological factor in the cause of hyperthecosis. Hirsutism is also another common clinical findings in OHT. These patients usually do not ovulate in response to traditional therapies. Bilateral oophorectomy should be a last resort, but may be necessary to control testosterone production in some of these patients. The main concern, apart from cosmetic issues, is the high association of endometrial cancer with ovarian stromal hyperplasia.

Conclusion: Endocrinologist should have a high index of suspicion for OHT in the setting of worsening insulin resistance with associated hirsutism and amenorrhea. These patients can be easily overlooked and labeled as uncontrolled diabetics thus delaying appropriate treatment. Effective treatment improves hirsutism and may reduce the risk of endometrial cancer.

Abstract #1001

CLASSIC EVOLVING AUTOIMMUNE POLYENDOCRINOPTHAPY

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Howard University Hospital

Objective: To present a case of a young female patient with Autoimmune polyglandular syndrome.

Methods: We present the case of a 34 year old African American female who was referred to us with an elevated TSH of 51 uIU/ml and a low free Thyroxine of 0.54 ng/dl. She had no symptoms of hypothyroidism. She had no prior neck surgery, thyroid radioiodine ablation, thyroiditis or any family history of thyroid disease or autoimmunity. Vital signs were normal. Examination findings did not reveal a goiter and were otherwise normal. She was commenced on levothyroxine while awaiting full investigative work up.

Case Presentation: She had a normal complete blood count with normal red cell indices. Her serum B12 was normal. She had normal metabolic panel. Her Thyroid peroxidase antibody was found to be elevated at 293 IU/ml confirming that she had Hashimotos.

Two years later, she complained of fatigue and irregular menstrual cycles. She was never pregnant though she desires to have children. She was no longer involved in competitive sports. FSH and LH were elevated at 87.7 mIU/ml and 49.3 mIU/ml respectively. Estradiol levels were very low. Serum Beta hCG was not elevated. 17 OH progesterone was low but DHEAS and androstenedione were normal. Karyotype analysis was normal. Antiovarian and antiadrenal antibodies were negative. Her hemoglobin A1c was 5.7% with a weak GAD 65 antibody titer.

A bone densitometry scan showed decreased bone mineral density. She was commenced on low dose estrogen and progesterone replacement.

A year later fatigue persisted despite normal thyroid function and a cosyntropin test was ordered which was negative.

Discussion: Autoimmune polyglandular syndromes (APS) can be classified as Type 1 or 2 but there can be considerable overlap. APS type 1 is autosomal recessive and associated with the AIRE mutation. It presents in early life with chronic mucocutaneous candidiasis, hypoparathyroidism and addisons disease. APS type 2 presents in late childhood or
In adult life without hypoparathyroidism or mucocutaneous candidiasis. It often presents with autoimmune thyroid disease, addisons, type 1 diabetes, pernicious anemia and there may also be gonadal failure.

Autoantibodies and organ dysfunctions can often be detected before the onset of symptoms in both syndromes. This is important so as to avoid preventable causes of death such as addisonian crisis.

**Conclusion:** Patients with APS benefit from early recognition of their variable organ dysfunctions and their appropriate treatment.

**Abstract #1002**

**PENILE GROWTH IN RESPONSE TO HORMONE TREATMENT IN AN ADULT WITH MICROPENIS AND KALLMAN SYNDROME**

Oscar Ruiz, MD, Margarita Ramirez-Vick, Miliette Alvarado, MD, Loida Gonzalez, MD, Dalitza Alvarez, MD, Anette Garces, MD, Viviana Ortiz, MD, Alex Gonzalez, MD

University of Puerto Rico

**Objective:** Report the effect of testosterone therapy on penile growth in a male with Kallmann syndrome (KS) and micropenis.

**Background:** Kallmann syndrome is a rare genetic disorder characterized by hypogonadotropic hypogonadism. The clinical hallmark of KS is the failure of onset of puberty in which micropenis is one of the presenting symptoms. The main goal of treatment in young men with KS is to restore serum androgen to normal levels by the use of testosterone or human chorionic gonadotropin (hCG), allowing virilization, penile growth, puberty and finally, to induce fertility.

**Case Presentation:** Case of a 26 year-old male with no past medical history that presented with absence of pubertal development, which was first noticed at 15 years of age. He had normal developmental milestones. Family history was unremarkable. On examination, the patient showed eunuchoid body proportion, micropenis (1cm), normal scrotum and palpable prepubertal testes bilaterally (<4ml), absence of facial and axillary hair, and sparse pubic hair, associated with decreased libido, anosmia, and high pitched voice. A normal karyotype (46XY) was documented. Hormonal workup was consistent with hypogonadotropic hypogonadism (FSH=1.27mIU/ml, LH=0.5mIU/ml, total testosterone=0.27ng/ml, free testosterone=0.007ng/ml, sex hormone binding globulin=13.7nmol/L). Other pituitary hormones were within normal levels. hCG stimulation test was performed, and plasma testosterone rose from 26 ng/dl to 69 ng/dl. MRI of the brain showed bilateral hypoplastic olfactory bulbs. DXA scan resulted in low bone mass for age at lumbar spine. (Z score -3.4). Testosterone Cypionate 100 mg intramuscular weekly was started with a goal of keeping testosterone levels within normal adult range. After three months of therapy, penile length showed a growth of 2cm.

**Discussion:** The most important concern in a patient with micropenis is whether he will have sufficient penile growth to allow sexual function. The etiology of micropenis in this condition has been commonly attributed to , the most common cause is failure of the hypothalamus to stimulate gonadotropins or hypophyseal dysfunction. Treatment of patients with KS should be individualized. Therapy with testosterone to achieve virilization is the treatment of choice whenever fertility is not currently wanted. Nevertheless if fertility is desired, treatment with hCG can be initiated.

**Conclusion:** Testosterone treatment seems to be effective in patients with KS and micropenis. It successfully increased serum testosterone level and resulted in a satisfactory gain in penile length. Thus, it may be the primary form of treatment for micropenis in adults with prepubertal characteristics.

**Abstract #1003**

**STROMAL LUTEOMA WITH POSTMENOPAUSAL VIRILISATION AND SUBSEQUENT HEPATOCELULAR CANCER**

Sowmya Chandra Reddy, MD, Monica Agarwal, MD

University of Alabama at Birmingham

**Objective:** We present an interesting case of microscopic stromal luteoma (steroid cell tumor) causing hyperandrogenism. Steroid cell tumors are very rare neoplasms that account for 0.1% of all ovarian tumors.

**Case Presentation:** 64-year-old postmenopausal woman with T2DM, steatohepatitis, and obesity (BMI 41) was referred to endocrinology clinic with 12-month history of excessive hair growth on face, chest, and extremities associated with male pattern baldness and temporal recession of hairline. The laboratory studies showed total testosterone of 638 ng/dL (2-45), free testosterone 56 pg/mL (0.1-6.4), FSH 60 mIU/mL (23-116), LH 35 mIU/mL (10-54), estradiol 51 pg/mL (postmenopausal < 31) and DHEA-S 27 mcg/dL (< 145). Sex hormone binding globulin was normal. There was adequate suppression of cortisol on dexamethasone suppression test. The laboratory studies showed total testosterone of 638 ng/dL (2-45), free testosterone 56 pg/mL (0.1-6.4), FSH 60 mIU/mL (23-116), LH 35 mIU/mL (10-54), estradiol 51 pg/mL (postmenopausal < 31) and DHEA-S 27 mcg/dL (< 145). Sex hormone binding globulin was normal. There was adequate suppression of cortisol on dexamethasone suppression test. Transvaginal ultrasound showed uterine leiomyoma but no adnexal masses. The CT scan showed normal adrenal glands, adnexe and 5 mm lesion in the right lobe of the liver. The MRI showed normal ovaries for postmenopausal state. The sub-centimeter hepatic lesion increased to 1.8 cm...
on subsequent CT scan 8 months after initial evaluation while there was persistent elevation in testosterone level. Patient underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy for suspected ovarian source of hyperandrogenism. Pathology revealed 2 mm stromal luteoma in the right ovary. The testosterone level normalized to 33 ng/dL one month after surgery and remained normal at one year. The core biopsy of the liver showed hepatocellular carcinoma (HCC) in the background of cirrhosis and started treatment for HCC.

Discussion: Stromal luteoma (SL) are small tumors confined to the ovarian cortex which have been classified as steroid cell tumors in the WHO 2014 classification for ovarian sex cord-stromal tumors. SL are usually benign and surgery is the definitive treatment. They mostly present with hyperestrogenism (abnormal uterine bleeding, endometrial hyperplasia) but a small percentage present with hyperandrogenism (hirsutism, acne, hoarse voice, male pattern baldness). It is unclear if hyperandrogenism had any role in subsequent development of HCC. The literature suggests that androgen mediated and non-androgen mediated signals stimulate the androgen receptor which is implicated in hepatocarcinogenesis. It is the expression of androgen receptor that affects initial tumor growth.

Conclusion: Hyperandrogenism should be investigated systematically to establish adrenal or ovarian source. Ovarian steroid cell tumors are uncommon cause of hyperandrogenism. Our case highlights that clinical history and hormonal analysis are important in making the diagnosis as imaging may be unremarkable.

Abstract #1004

A CASE OF VIRILIZATION IN A POSTMENOPAUSAL WOMAN

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Objective: Hirsutism is a common reason for consultation in endocrine practice. The development of frank virilization suggests androgen excess from an adrenal or ovarian tumor, and warrants immediate evaluation.

Case Presentation: A 49 year old postmenopausal African American woman presented to the endocrine clinic with progressive hirsutism and virilization. Gonadotropin and estradiol levels were in the postmenopausal range. Total and free testosterone levels were 429 and 66.1 ng/dL respectively. The DHEAS, 17-hydroxyprogesterone, prolactin and IGF-1 were within normal limits (90.7 mcg/dL, 149 ng/dL, 8.32 ng/mL and 107 ng/mL respectively; as was the cortisol after 1 mg dexamethasone suppression test (1.0 mcg/dL). An MRI with contrast and CT with contrast were negative for both ovarian and adrenal masses. Patient received a single dose of a gonadotropin-releasing hormone (GnRH) agonist, Lupron Depot 3.75mg IM. One month after the GnRH agonist administration, total testosterone was 9 ng/dL and free testosterone was 1.3 ng/dL. Then, a diagnosis of hyperandrogenism of ovarian origin was made and the patient underwent bilateral oophorectomy. Pathology was consistent with bilateral ovarian hyperthecosis. Four weeks after surgery, her androgen levels decreased to the normal female range.

Conclusion: The diagnosis of hyperandrogenism in postmenopausal women is challenging. Postmenopausal virilization may be associated with androgen-secreting ovarian and adrenal tumors or with benign conditions. In this case the GnRH suppression test was useful in determining the origin of hyperandrogenism. Oophorectomy established the final diagnosis of ovarian hyperthecosis, and allowed for normalization of her androgen levels.

Abstract #1005

LEYDIG CELL HYPERPLASIA OF THE OVARIES: A RARE CAUSE OF SEVERE HYPERANDROGENISM IN A POSTMENOPAUSAL WOMAN

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Drexel University College of Medicine

Objective: To report a rare case of Leydig cell hyperplasia as a cause of severe hirsutism in a postmenopausal woman.

Case Presentation: 63 year old postmenopausal female presented for consultation of elevated testosterone level drawn to evaluate worsening acne and androgen dependent hair growth for ten years. She noted increased hair growth in her face, arm, and chest. The facial hair was initially fine, but progressively became coarse and terminal resulting in a need to shave daily. She had menarche at age 13 with regular menstrual periods, conceived naturally and had one child. She had a history of total abdominal hysterectomy for uterine fibroids 22years ago, but the ovaries were not removed. Her mother had increased hair growth, but less severe than she. Her only medications were vitamin D3 and intramuscular triamcinolone injection monthly for eczema. On exam, she had temporal recession of hair and hair loss over the crown of her head. She had comedones and cystic acne over her face, back and arms. Coarse terminal hair was present over her face, back and chest. There were no physical findings suggestive of hypercortisolism. She underwent a partial evaluation one year prior to presentation. This included a total testosterone of 86 (2-
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45 ng/dl) and free testosterone of 9.6(0.1-6.4 ng/dl). An ovarian ultrasound had shown intact ovaries with follicles. We ordered labs to be drawn before the triamcinolone injection which demonstrated a total testosterone of 115 (2-45 ng/dl), free testosterone of 19.3 (1-6.4ng/dl), estradiol of 44 (<31), DHEAS of 24 (12-133 mcg/dl), androstenedione of 213(20-75 ng/dl), 17 hydroxyprogesterone of 55 (<45 ng/dl). An MRI of the pelvis was done due to clinical suspicion of an ovarian source, but showed no evidence of ovarian mass. She underwent laparoscopic bilateral salpingoophorectomy. Pathology showed leydig cell hyperplasia of both ovaries. She noted significant improvement in her acne following surgery and postoperatively the total testosterone was <1, estradiol was <15 (<=31 pg/ml) androstenedione was 14 (20-75 ng/dl).

Discussion: The differential diagnosis for postmenopausal hirsutism may range from PCOS, hypercortisolism, ovarian or adrenal tumors to leydig cell hyperplasia. After ruling out an adrenal source, imaging of the ovaries should be done. Leydig cell hyperplasia may pose a diagnostic challenge, as it may not be apparent on imaging. Few cases are currently reported in the literature. Bilateral salpingoophorectomy may be required to make a diagnosis on pathology.

Conclusion: Leydig cell hyperplasia as a cause of postmenopausal hirsutism is rare. It is important to have a high index of suspicion to diagnose it, as surgery is curative in these cases.

Abstract #1006

PRELIMINARY FINDINGS FROM A PROSPECTIVE STUDY OF THYROID STIMULATING HORMONE AND IN VITRO FERTILIZATION / EMBRYO TRANSFER OUTCOMES

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Objective: The effect of “high normal” thyroid stimulating hormone (TSH) levels on fertility and pregnancy outcomes is a topic of debate due to inconsistent results from retrospective studies. The American Association of Clinical Endocrinologists and the American Society for Reproductive Medicine have differing recommendations regarding TSH screening and treatment of TSH levels between 2.5 and 4.5mIU/L in infertilitry patients. This study explores the role of “high normal” TSH (HN-TSH) on in vitro fertilization (IVF) fresh and frozen embryo transfer (ET) outcomes using a prospective cohort.

Methods: TSH levels were prospectively collected from patients preparing for IVF/ET. Women 18-43 years at the time of ET were included. Exclusion criteria were uncontrolled hypo- or hyperthyroidism, lack of a pre-IVF TSH level, and change in thyroid medication without repeat TSH prior to IVF/ET. In this preliminary analysis, TSH and hCG results following IVF/ET were analyzed for 135 patients. The association between TSH level (normal vs. >2.5) and positive hCG test following IVF/ET was investigated with a generalized estimating equation (first order autoregressive correlation structure) to account for multiple embryo transfer attempts per patient. Presented are absolute pregnancy rates, odds ratios, and 95% confidence intervals.

Results: Of 135 women, 113 (84%) had a TSH<2.5 prior to IVF/ET versus 22 (16%) with HN-TSH. Patients were 34.9+4.5 years vs. 33.6+4.4 years (NS) in the “low normal” and HN-TSH groups, respectively. BMI, parity, number of IVF cycles, and previous pregnancy loss were not significantly different between groups. Neither embryo quality (defined by blastocyst development and embryos available to freeze) nor frozen versus fresh ET cycle differed significantly between groups. The percentage of patients with a positive hCG following IVF was 73% with TSH<2.5 vs 64% with HN-TSH. After adjusting for age, the odds ratio of positive hCG was 0.42(0.14, 1.27) in HN-TSH versus controls. Positive hCG was not associated with thyroid replacement status, parity, or frozen versus fresh ET cycle.

Discussion: Although presently underpowered, our preliminary findings suggest a negative association between HN-TSH levels and pregnancy rates after IVF/ET. Final results may add to our understanding of thyroid function in implantation and early pregnancy.

Conclusion: HN-TSH values may be associated with a decreased rate of positive hCG tests following IVF/ET in this preliminary analysis of a prospective cohort study. Data collection is ongoing to determine if this reduction is statistically significant in a larger sample and how other pregnancy outcomes (such as miscarriage rates) relate to TSH> 2.5mIU/L.
Abstract #1007

ANDROGEN SECRETING BENIGN OVARIAN TUMOR: A CASE REPORT AND REVIEW OF THE LITERATURE

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Objective: To describe a rare case of steroid cell tumor: a sex cord stromal tumor.
Methods: Clinical case presentation and review of literature.
Case Presentation: A 24-year-old female presented with scalp baldness, hirsutism, acne and oligomenorrhea for two years duration. She had her menarche at the age of 17. She denied use of any herbal supplement, or exposure to any kind of steroid preparation. Her physical examination was significant for male pattern baldness, and virilization with excess hair growth on chin, upper lips, sides of her face, back, chest, abdomen, and inner thighs. She had cliteromegaly and acanthosis nigricans. Laboratory studies revealed normal dehydroepiandrosterone (DHEA-S) and elevated testosterone levels: total testosterone 197ng/dl (reference range: 2-45), free testosterone 23.1pg/ml (0.2-5.0), and bioavailable testosterone 51.5ng/dl (0.5-8.5). Transvaginal ultrasound revealed hypervascular left adnexal mass. MRI of abdomen and pelvis showed solid enhancing left ovarian mass measuring 5.3 x 4.1 x 5.2 cm, and normal appearing right ovary and uterus. Laparoscopic left oophorectomy was performed, and final pathology was consistent with the steroid cell tumor, not otherwise specified (NOS). The pelvic washing was negative for any malignant cells. Three weeks after the surgery, she had significant clinical improvement and decreased testosterone levels.
Discussion: In most patients, hirsutism is either idiopathic or related to polycystic ovarian syndrome. It manifests with slowly progressive signs and symptoms of hyperandrogenism. We have to consider ovarian or adrenal androgen-secreting tumors as a cause of androgen excess, especially when there is abrupt onset and rapid progression of clinical signs and symptoms or there is presence of virilization. Testosterone level of more than 200 ng/dl suggests possibility of malignant adrenal disease. DHEA-S secreted by adrenals helps differentiating ovarian from adrenal tumors.
Conclusion: Steroid cell tumors are rare sex cord stromal cell tumors that account for less than 0.1% of all ovarian neoplasms. Majority of them (>75%) present with virilization due to excess steroid production, particularly testosterone. Steroid cell tumors are generally benign with excellent prognosis. The symptoms improve after surgery, but there is a risk of malignant transformation. Ovarian steroid cell tumors NOS variant accounts for 60% of all ovarian steroid cell tumors. Majority cases present with hyperandrogenic state with rapid onset of virilization. In these cases appropriate laboratory and radiological testing should be done for further evaluation. However, pathology report is essential for final diagnosis and exclusion of malignancy.

Abstract #1008

ENHANCED AROMATASE ACTIVITY PRESENTING WITH HYPERPROLACTINEMIA AND MALE HYPOGONADISM

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Objective: Male hypogonadism is a common condition physicians encounter. Often, patients are started on testosterone supplements before complete pituitary work-up. We present an elderly male with hypogonadism and hyperprolactinemia with no pituitary lesion, corrected with anastrozole and bromocriptine.
Case Presentation: A 64 y/o male with hypertension and hyperlipidemia was referred for low testosterone, impotence, fatigue, and gynecomastia. He had low testosterone for 3 years, treated with testosterone gel on and off for 2 years. On exam, bilateral gynecomastia was present, L>R. Genital exam was normal with 9cm penis and 20ml testicles bilaterally. The rest of the exam was normal. Labs showed low total and free testosterone 55, 2.5 (250-1100ng/dL, 46-224pg/mL), respectively, high prolactin 138.6 (2-18ng/mL), and high estradiol 57 (<39pg/mL). Pituitary MRI was normal, there was no adenoma. Medication effect, hypothyroidism, and renal disease were ruled out. No history of seizures. Tadalafil and testosterone gel did not improve his symptoms. Repeat labs showed low LH 0.9 (1.6-15.2mIU/mL), high cortisol 20.2 (4-22ug/dl) and higher prolactin 260.8. He was started on bromocriptine and anastrozole which decreased prolactin to 11.8 and increased total and free testosterone to 367 and 10.6, respectively, with improvement of symptoms.
Discussion: Men with hyperprolactinemia present with hypogonadism, impotence, or infertility. Causes are pituitary tumors, antipsychotics, hypothyroidism, renal disease, estrogen, and macroprolactinemia. Idiopathic hyperprolactinemia is diagnosed with normal pituitary MRI and no identified cause. Dopamine agonists are first line treatment of hyperprolactinemia. Testosterone therapy is considered in men with hypogonadism. The aromatase enzyme complex converts androgens into estrogens. It is found in the testes, adipose, and muscle tissue. Enhanced aromatization is associated with obesity, aging, liver disease, and thyrotoxicosis. This
causes increased estradiol which inhibits the secretion of gonadotropins. Aromatase inhibitors prevent conversion of androgens to estrogen and increase LH, FSH, and testosterone. Studies report successful use of aromatase inhibitors in infertility, andropause, and gynecomastia. In this case, hyperprolactinemia was likely caused by increased estradiol from enhanced aromatase activity associated with aging. Symptom improvement with anastrozole supports the role of these agents in such cases. **Conclusion:** Hypogonadism due to increased aromatase activity and elevated prolactin without a pituitary lesion is rare. Patients with hypogonadism should have complete work up done to rule out other causes before committing to long term testosterone replacement therapy.

**Abstract #1009**

**BENIGN CYSTADENOMA WITH VIRILIZATION IN A POSTMENOPAUSAL WOMAN**

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New York Methodist Hospital

**Objective:** Hyperandrogenism is characterized by excess production of androgens by the ovaries and or the adrenal glands. This is an unusual case of benign cystadenoma with virilization in a postmenopausal woman.

**Case Presentation:** 73-year-old female G6P6 presented with headache and visual disturbances was found to have pituitary tumor. Her pre-operative hormonal evaluation revealed gonadotrophins in the postmenopausal range, normal TSH, GH, and Cortisol, mild hyperprolactinemia (66.1 ng/mL) and elevated testosterone (142 ng/dL). She underwent transphenoidal resection of the tumor. Pathology was consistent with a pituitary adenoma with focal immunoreactivity for growth hormones and prolactin. Post-operatively, she had normalization of the prolactin, but no significant change in testosterone level. She had no evidence of hypopituitarism. Nine years later, she had recurrent headaches and TIA symptoms, which prompted her to seek medical attention. Due to history of pituitary tumor, consultation was requested. On examination, mildly obese elderly Hispanic woman with mild facial hirsutism and significant male pattern balding. MRI brain showed a 12mm pituitary tumor. Hormonal work up showed normal TSH, Prolactin, IGF1, and cortisol, menopausal range LH/FSH, normal SHBG and DHEA-S, but persistently elevated testosterone level (212 ng/dL). Further work up with CT Abdomen and pelvis revealed normal adrenal glands and a right 5.4x4.2cm septated cystic adnexal mass. She underwent bilateral salpingo-oophorectomy with subsequent normalization of the testosterone level (25 ng/dL). Pathology revealed multiple bilateral ovarian serous cysts and a cystadenofibroma.

**Discussion:** Postmenopausal hyperandrogenism can be seen in both ovarian and adrenal pathologies. Testosterone levels greater than 100-140 ng/dL are of concern for tumoral etiology and warrant evaluation. Elevated DHEA-S levels are more suggestive of potential adrenal source, while elevated testosterone is seen in both adrenal and ovarian tumors. Our patient had a high testosterone level and normal DHEA-S, which was suggestive of ovarian origin. Imaging showed an adnexal mass which was removed with subsequent normalization of the testosterone level.

**Conclusion:** Most commonly excessive androgens are derived from ovarian tumor of stromal cell origin, less likely epithelial cell. Despite pathology showing multiple cysts, there was no histological evidence of hyperthecosis. Although uncommon, there has been at least one other case report of a virilizing serous cystadenoma with epithelial cell as the cause for the testosterone excess.

**Abstract #1010**

**RELIABILITY OF THE ANDROGEN DEFICIENCY IN AGING MALE QUESTIONNAIRE AS A SURROGATE TO BIOCHEMICAL DIAGNOSIS OF MALE HYPOGONADISM IN BLACK SUB-SAHARAN AFRICANS WITH DIABETES MELLITUS**

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**Objective:** To evaluate the diagnostic efficiency of the androgen deficiency in aging male (ADAM) questionnaire as a screening tool for male hypogonadism in a sub-Saharan African population with type 2 diabetes mellitus (DM).

**Methods:** In a cross-sectional survey of 200 type 2 DM males aged 30-69 years, total testosterone (TT) was measured in a morning blood sample. Testosterone < 8nmol/L was used as a gold standard for diagnosis of hypogonadism while TT > 12nmol/L was normal. Subjects with borderline TT of 8-12 nmol/L required a repeat testing and were excluded from the analysis to avoid ambiguity. Each participant completed the ADAM questionnaire, a 10-item screening instrument for male hypogonadism. A positive ADAM test is based on a “yes” response to any of the sexual questions including reduced libido and erectile dysfunction (ED) (questions 1 and 7 respectively) or any three other questions. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and overall accuracy of this screening tool were then determined.
**Results:** 47 subjects had borderline TT and were excluded. Of the remaining participants (n = 153), 59 subjects (38.6%) had a low TT. Subjects who had low TT were significantly older (59.7 ± 7.2 years vs. 56.1 ± 9.7; P = 0.014) and had higher waist circumference (97.0 ± 3.7 cm vs. 93.2 ± 4.2 cm; P = 0.009). Based on the ADAM questionnaire, 104 subjects (68.0%) had hypogonadism. ADAM questionnaire rendered a sensitivity of 88.1% and specificity of 44.7% with a PPV of 50%, NPV of 85.7% and an overall accuracy of 61.4%. Each of the questions in the sexual domain i.e., reduced libido (sensitivity 69.4%, specificity 75.5% and accuracy of 73.2%) and ED (sensitivity 79.7%, specificity 53.2% and accuracy of 63.4%) was a better predictor of hypogonadism than the complete questionnaire.

**Discussion:** Male hypogonadism is a common occurrence in persons with type 2 DM. Testosterone assays are not readily available in sub-Saharan Africa owing to poverty and lack of facilities. Several screening questionnaires have been developed for the clinical detection of male hypogonadism. The ADAM questionnaire appears to be more widely used, including in sub-Saharan Africa. This study has demonstrated that the ADAM questionnaire may not be a reliable tool in this population. However, presence of reduced libido or ED should arouse a high index of suspicion to the presence of hypogonadism.

**Conclusion:** Although highly sensitive, the ADAM questionnaire lacks specificity and has a low diagnostic efficiency for the clinical detection of male hypogonadism in black sub-Saharan Africans with type 2 DM. This underscores the need for testosterone assay in all suspected cases.

**Abstract #1011**

**GALACTORRHOEA IN A YOUNG MALE**

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**Objective:** To present a case of bilateral gynecomastia and galactorrhoea due to microprolactinoma in a young male

**Case Presentation:** A 15 year old male presented with progressive bilateral enlargement of breast for 5 months. The enlargement was painless, no H/O headache, visual disturbances, trauma to chest wall, change in overlying skin, bloody discharge, chronic liver, kidney, psychiatric or thyroid disease. No H/O medications (prescription or alternative medicine) or use of recreational drugs. Examination revealed bilateral non-tender breast enlargement 4X5 cm. There was expressive milky discharge of few drops on both sides. No axillary lymphadenopathy or thyromegaly. Testes were 8 ml, non-tender and no nodule felt. Rest of the general and physical examination was normal. Investigations: Hb 14.9 g/dl (14-18), TLC-6700/cumm (4000-11000), Platelet count- 320000/cumm (150000-400000), Total Bilirubin 0.9 mg/dl (0.6-1.2), AST 32 U/L (<50), ALT 28 U/L (<50), ALP 89.0 U/L (50-130), B. Urea 28 mg/dl (20-40), S Creatinine 0.8 mg/dl (0.6-1.2), TSH 2.08 mIU/ml (0.5-5.0), FT4- 0.80 ng/ml (0.6-2.2), FT3- 3.84 pg/ml (2.4-4.0), FSH 5.71 mIU/ml (1.2-5.8), LH 2.58 mIU/ml (0.2-5.0), Prolactin- 88.62 ng/ml, repeat value- 102 ng/ml (upto 20.), S. total testosterone- 418.16 ng/dl (15-827 ng/dl), E2- 26.2 pg/ml (<39.8), Serum beta HCG- <1.20 mIU/ml (<5.0). USG abdomen and testes were normal. CEMRI brain revealed an 8X9mm microadenoma on left side. Patient was put on 0.5 mg Cabergoline twice a week, 3 months later, there was no expressive galactorrhoea and slight decrease in gynaecomastia on both side.

**Discussion:** In this young male, microprolactinoma presented with bilateral gynaecomastia and expressive galactorrhoea. In workup of gynecomastia, prolactin levels are not estimated routinely If galactorrhoea was not detected patient would not have undergone prolactin estimation & the diagnosis of microadenoma could be delayed.

**Conclusion:** So it is to emphasise the need of complete and thorough examination.

**Abstract #1012**

**GESTATIONAL DIABETES MELLITUS (GDM) IN BANGLADESH**

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**Objective:** The prevalence of gestational diabetes mellitus (GDM), a disorder that has important health complications and impacts for both mother and child, is increasing all over the world rapidly. Although the high prevalence of GDM and its associated risk factors are not new in
developed and increasingly many developing countries, little is known about this disorder in some low-income countries, such as in Bangladesh. The aim of this study was to estimate the prevalence of GDM in Bangladesh and investigates its associated risk factors, including socio-demographic and anthropometric characteristics.

Methods: A cross-sectional institutional-based study was undertaken to know the prevalence of GDM among Bangladeshi pregnant women in three divisions of Bangladesh (Rajshahi, Dhaka, Chittagong). 35,225 pregnant women were screened for evidence of diabetes who were previously not known to be diabetic. Universal screening was performed and all pregnant women were screened for GDM with 50gm GCT (glucose challenge test) with subsequent validation by 75 g oral glucose tolerance test (OGTT). GDM was diagnosed as per the definition of WHO criteria as fasting PG (FPG) ≥7.0 or 2-h PG ≥7.8 mmol/l.

Results: Result: The prevalence of GDM of Bangladeshi women is 11.5% (urban) and 10.8% (rural) which is statistically non-significant. Prevalence of GDM increases with the increase number of parity. In our study population we found that prevalence of GDM increases with increase of maternal age. Mean blood pressure did not alter in pregnant women with or without GDM in Bangladesh. Percentage of metabolic profile parameters among GDM cases in Bangladesh: high LDL-C (25.8%); low HDL-C (65.5%); hypertriglyceridemia (55.5%); hypercholesterolemia (26.4%); and metabolic syndrome (35.4%). GDM positive cases have 11.62% positive family history of diabetes. More than 90% rural pregnant women in Bangladesh do not know about GDM. Still in Bangladesh, in rural context, around half of the pregnant women do not receive antenatal care. Still the acceptance of institutional delivery rate is very low in rural Bangladesh.

Top ranked risk factors for GDM: hypertension, metabolic syndrome, family history of hypertension, family history of diabetes, lack of regular exercise, lack of education, lack of health awareness and increased age in this population.

Conclusion: From the present study, we found a high prevalence of GDM in Bangladeshi rural women. The present study is the first report describing the prevalence of GDM among Bangladeshi rural women and calls for urgent action to stop and prevent the diabetes development in pregnancy and the associated complications both for mother and child.

Abstract #1013

INCIDENCE AND SEVERITY OF PROSTATE CANCER ARE LOWER IN HYPOGONADAL MEN TREATED WITH TESTOSTERONE COMPARED TO UNTREATED HYPOGONADAL AND EUGONADAL MEN: EXPERIENCE FROM A SINGLE UROLOGIST’S OFFICE

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Objective: Hypogonadal men seem to be at greater risk of high-grade prostate cancer (PCa). We analysed whether testosterone therapy (TTh) in hypogonadal men affected incidence and severity of PCa compared to untreated hypogonadal and eugonadal men.

Methods: Between 2004 and 2014, 1012 prostate biopsies were performed in a single urologist’s office. The decision for prostate biopsy was always made by the same urologist. 413 patients were diagnosed with PCa. Proportion of positive biopsies were calculated for the following groups: hypogonadal (T≤12.1 nmol/L) men receiving TTh, hypogonadal untreated, and eugonadal men. Pathological outcomes following radical prostatectomy (n=231) were also assessed for these three groups.

Results: Of 57 hypogonadal men receiving TTh, 9 (15.8%) had a positive biopsy. Of 290 untreated hypogonadal men, 120 (41.4%) had a positive biopsy. Of 665 eugonadal men, 284 (42.7%) had a positive biopsy. 231 men (55.9% of those diagnosed with PCa) underwent radical prostatectomy:

Of 9 hypogonadal men receiving TTh, all 9 (100%) had a Gleason score ≤6 and a predominant Gleason score of 3. Tumor grade was G2 in all 9 (100%), tumor stage T1 in 1 (11.1%) and T2 in 8 (88.9%) patients. Regional lymph nodes, distant metastases and surgical margin were negative (N0, M0, R0) in all 9 men.

Of 73 untreated hypogonadal men, 1 (1.4%) had a Gleason score ≤6 and 72 (98.6%) a Gleason score >6. Predominant Gleason score was 3 in 14 (19.2%), 4 in 54 (74%) and 5 in 5 (6.8%) men. Tumor grade was G2 in 14 (19.2%) and G3 in 59 (80.8%) men, tumor stage T2 in 25 (34.2%) and T3 in 48 (65.8%) men. 28 patients (38.4%) had positive lymph nodes (N1), 27 patients (37%) had metastases (M1), and 48 patients (65.8%) had a positive surgical margin (R1).

Of 149 eugonadal men, 74 (49.7%) had a Gleason score ≤6 and 75 (50.3%) a Gleason score >6. Predominant Gleason score was 3 in 14 (19.2%), 4 in 54 (74%) and 5 in 5 (6.8%) men. Tumor grade was G2 in 14 (19.2%) and G3 in 59 (80.8%) men, tumor stage T2 in 25 (34.2%) and T3 in 48 (65.8%) men. 28 patients (38.4%) had positive lymph nodes (N1), 27 patients (37%) had metastases (M1), and 48 patients (65.8%) had a positive surgical margin (R1).
nodes (N1), 7 patients (4.7%) had metastases (M1), and 18 patients (12.1%) had a positive surgical margin (R1).

**Conclusion:** Incidence of PCa was lowest in hypogonadal men receiving TTh and more than twice as high but similar between untreated hypogonadal and eugonadal men. Severity of PCa following radical prostatectomy was lowest in hypogonadal men receiving TTh, followed by eugonadal men and untreated hypogonadal. TTh may protect against incidence of PCa as well as high-grade PCa.

**Abstract #1014**

**TO ASSESS THE EFFICACY OF FENUGREEK SEEDS EXTRACT, AS A TESTOSTERONE BOOSTER SUPPLEMENT, IN HUMAN VOLUNTEERS: AN ADD-ON STUDY**

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**Objective:** To assess the efficacy and safety of Fenugreek (Trigonella foenum-graecum) seeds extract as testosterone booster, evaluate subjects responding and its effect on mood, mental alertness, reflex erection and overall performance.

**Methods:** Open label, single arm, monocentric, observational study in 50 males between 35 to 65 years of age, diagnosed with symptomatic hypogonadism and agreed to give informed consent, has been performed for 6 to 8 months, administering Fenugreek seeds extract branded as Furosap® for 12 weeks. Subjects with coronary artery disease, abnormal liver, kidney function tests, malignancy, hypersensitivity, coagulopathies, alcohol intake, psychiatric disorders, any medical condition where investigator felt participation in study could be detrimental to subject and those who were taking any other testosterone booster within last two months have been excluded. Data was analysed using appropriate parametric and non parametric tests.

**Results:** Free testosterone were improved up to 46% in approximately 90% of study population. Frequency of sexual intercourse increased in 98% participants, 85.4% shown improvement in sperm count while 14.6% shown improvement in sperm morphology. 95.2% had enhanced reflex erection. All enrolled patients in the study shown mood enhancement, improvement in mental alertness and overall performance. No significant change in serum liver & kidney function tests, lipid, hemogram was observed.

**Discussion:** It has been seen that the testosterone (Free testosterone and total testosterone) levels increase with the regular consumption of Fenugreek seed extract as Furosap®. Protodioscin present in Fenugreek increases the levels of testosterone. It boosts testosterone levels via stimulating pituitary gland. Protodioscin acts by stimulating 5-a-reductase enzyme, which plays a role in the conversion of testosterone into dihydrotestosterone. Dihydrotestosterone, enhances erythropoiesis and muscle development. Increase in free testosterone in the body has been helpful in increasing sperm count and sperm mobility. Sperm activity increased with the regular consumption of Fenugreek seed extract and the subjects shown improvement in the state of hypogonadism. Increased production of testosterone also contributes to the increase in sexual functions and it also increases the amount of unbound free testosterone improving muscle mass, fat loss, strength and endurance. Frequency of sexual intercourse increased as the testosterone deficient subjects consumed Furosap® regularly.

**Conclusion:** Fenugreek seeds extract in the form of herbal supplement is effective and safe for testosterone deficient or hypogonadism patients.

**Abstract #1015**

**SURGICAL TREATMENT FOR HIRSUTISM IN A POSTMENOPAUSAL WOMAN**

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Northern Ontario School of Medicine

**Objective:** We present case history of a 72-year-old woman with long standing hirsuitism and hyperandrogenemia for which no obvious cause was found initially.

**Case Presentation:** This patient was referred to us with regard to her hirsuitism. She had hypertension, fibromyalgia, rheumatoid arthritis and a multi-nodular goiter. She had undergone hysterectomy in the past. She had significant hair growth over her chest and abdomen and had to shave them once a week. There was no acne. She was treated with spironolactone initially with not much benefit and later with finasteride. On examination, she had hirsuitism and truncal obesity. She had a small goiter. There were no signs of virilization or Cushing’s syndrome. BP was 120/80 mmHg. Cardiorespiratory and abdominal examination was unremarkable.

Her testosterone level was elevated at 9 nmol per liter (<1.5). The free testosterone level was at 37 pmol/L (0.3–5.4), DHEA-S was normal 1.2 mcmol/L (<6.7)). Serum androstenedione level was high at 16.8 nmol/L (0.7–8.6). The FSH level was 26 IU/L (1-11), LH 26 IU/L (1-11) and estradiol was 95 pmol/L. Work up for Cushing’s syndrome was negative.

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CT scan and MRI of the abdomen showed normal adrenal glands. MRI pelvis did not show any lesions in the ovary in
2006 but in 2010, the MRI scan of the pelvis revealed cysts in the ovary and it was reported as physiologic cysts. The ultrasound scan of the ovaries in 2014 showed a hypoechoic area on the right adnexa measuring 2.3 cm. Leydig cell hyperplasia or ovarian hyperthecosis was considered. This woman underwent bilateral salpingo-oophorectomy and histopathology confirmed the diagnosis of bilateral Leydig cell hyperplasia. Postoperatively, her hirsutism improved, testosterone levels dropped to <1 nmol/L, androstenedione levels normalized to 1.2 nmol/L, estradiol level dropped to < 70 and FSH and LH levels increased to 54 and 51 IU/L respectively.

Discussion: Postmenopausal hirsuitism is a rare condition and most often undertreated or not recognized. Adrenal and ovarian neoplastic lesions needs to be ruled out in such a patient. In this patient’s case, DHEA-S was normal and androstenedione level was significantly high indicating that an ovarian lesion was more likely. It is important to keep a high index of suspicion and perform serial imaging whenever initial imaging studies are unhelpful. Imaging of the ovaries does not rule out ovarian disease if normal. Diffuse stromal Leydig cell hyperplasia and Leydig cell tumours (usually small) may escape imaging and in some cases diagnosis can only be made on pathology.

Conclusion: An androgen producing tumour should be excluded in every woman with evidence of hirsutism or frank virilization and markedly elevated testosterone levels.

Abstract #1016

APPROACH TO POSTMENOPAUSAL HYPERANDROGENISM

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1. Dumfries and Galloway Royal Infirmary, 2. Flushing memorial

Objective: Since post-menopausal hyperandrogenism is not commonly associated with menstrual disturbances and ageing process can be blamed for various hair changes, diagnosis of post-menopausal androgen excess can be challenging.

Methods: The following case report highlights the clinical work up and management of this commonly overlooked endocrine disorder.

A 64 year old post-menopausal Caucasian lady was referred with 15 year history of progressive development of hirsutism, male pattern balding. During pre-menopausal period she had regular periods and normal fertility. Her past medical history includes rheumatoid arthritis, MI, obstructive sleep apnoea and non-alcoholic fatty liver disease. She is an ex-smoker, a teetotal who lives with her husband and is a retired housewife. Ferriman-Gallwey score is 13/36.She had feminine voice, normal muscle mass and no stigmata of insulin resistance.

Case Presentation: She had detailed endocrinology work up which showed raised Testosterone (8.6 nmol/L), gonadotrophins (LH-48 U/L, FSH-57 U/L) and mildly raised Androstenedione (4.3 nmol/L). Plasma Metanephrines, short synacthen test, 17 OH, overnight 1 mg Dexamethasone suppression test, serum prolactin, SHBG, DHAS, blood glucose, HBA1c were normal. Pre and post Dexamethasone testing showed no meaningful changes in serum testosterone level. However, after four weeks of single dose of Leuprollein, serum testosterone level normalized (0.1 nmol/L). Trans-vaginal pelvic US and CT of abdomen, showed large right ovary (3x2x2cm), normal adrenals and no adnexal tumours.

Discussion: There is wide range of differential diagnosis for slowly progressive hyperandrogenism in postmenopausal women including PCOS, Cushing’s syndrome, Congenital adrenal hyperplasia, Ovarian hyperthecosis and androgen secreting adrenal/ovarian tumours. If serum total testosterone is >5.2 nmol/L, ovarian hyperthecosis and androgen secreting ovarian/adrenal tumours should be considered, though the latter are associated with much higher serum testosterones level. During GnRH agonist Suppression tests, suppression of both gonadotrophins and serum testosterone confirm LH driven non tumorous-ovarian hyper secretion of testosterone. In view of laboratory work up and normal adrenal CT, ovarian/adrenal venous sampling was not attempted.

Conclusion: Bilateral oophorectomy will provide definitive treatment for the hyperandrogenism. Long term GnRH- agonist treatment is an alternative to surgical intervention. She was reviewed by Gynaecology team and was keen for hyster-on-salphingo-oophorectomy but in view of obesity and multiple co-morbidities, she was classed as high risk surgical candidate. Currently she is receiving long term GnRH agonist treatment.

Abstract #1017

EFFECTS OF LONG-TERM TESTOSTERONE UNDECANOATE (TU) THERAPY IN HYPOGONADAL MEN WITH OSTEOPOROSIS: REAL-LIFE DATA FROM A REGISTRY STUDY

Farid Saad1, Ahmad Haider2, Karim Haider2, Gheorghe Doros3, Abdulmaged Traish4


Objective: To assess long-term effects and of testosterone therapy (TTh) with injectable TU in hypogonadal men with osteoporosis in a urological setting in comparison to an untreated hypogonadal control group.

Methods: Cumulative registry study in 656 men with
Objective: The intramuscular injection of the long-acting ester testosterone undecanoate (TU) offers a convenient modality for testosterone substitution. The effects of such a therapy on body composition have been well documented but long-term effects and inter-patient variability remain to be elucidated.

Methods: We report data from a total cohort of 453 patients who received treatment by testosterone undecanoate 1000 mg (intramuscular injections) for a treatment time of 4-7 years. Of these, 176 men (39%) were overweight (BMI 25-30 kg m-2) and 235 men (52%) were obese (BMI ≤30kg m-2). Increased waist circumference (WC) (94-102 cm) was seen in 99 men (22%) and a substantially increased waist circumference (>102 cm) in 312 men (69%). Age range of men with increased weight/WC was 21 to 68 years (mean 44±11 years).

Results: Individual dosing intervals ranged from 10 to 14 weeks Serum T concentrations increased from an average of 4.7 nmol/L to stable trough levels of 13.3 nmol/L within the first year of treatment and further on to levels between 15 and 16 nmol/l thereafter. Obese patients were not significantly different in this regard from overweight patients or normal weight patients. The proportion of men fulfilling the new Harmonized Criteria for definition of the Metabolic Syndrome decreased from initially 88% to 65% within the first year and further on to 45% within 7 years (Chi-square for trend; p<0.001). During the maximal duration of treatment, an overall favourable change from baseline was visible for a multitude of parameters related to androgen effects/metabolic risk, especially lipid parameters (total cholesterol, HDL-cholesterol, LDL-cholesterol, triglycerides), blood pressure and fasting glucose levels (all with p<0.001 in ANOVAs). Overall loss of weight, WC and also changes in metabolic parameters were log-linear interactions of initial obesity/WC, time and individual increment in testosterone levels. Advancing age was attenuating the effect of weight loss, but not completely. In summary a change of class was seen over time: 82 of 176 men changed from overweight to normal weight and 127 of 235 men from obese to overweight.

Conclusion: Intramuscular injections of testosterone undecanoate represent a feasible, safe and well tolerated modality of androgen substitution in hypogonadal men.
overweight and obese men of a wide age-range, substantiated by a long experience, facilitating a decrement of metabolic/cardiovascular risk factors and fundamental weight loss.

Abstract #1019

SERTOLI LEYDIG CELL TUMOR OF OVARY PRESENTING AS HIRSUITISM IN AN ADOLESCENT FEMALE

Sameer Aggarwal

PGIMS

Objective: Ovarian leydig cell tumor of ovary presenting as hirsuitism is rare.

Case Presentation: Ovarian Sertoli-Leydig cell tumors are extremely rare. 18-year old adolescent female referred for evaluation of hirsutism associated with hoarseness of voice, amenorrhea since three years. No history of abdominal striae, drug intake, proximal muscle weakness, acanthosis, galactorrhea, steroid intake. Coarse terminal hair was present over the upper lip, chin, chest, lower abdomen, inner thighs, upper and lower back. Her modified Ferriman-Gallwey score was seventeen. Endocrinologic work up revealed serum Testosterone of 1.2 ng per ml, Normal cortisol, thyroid functions and DHEAS. CT Abdomen showed right sided ovarian mass. A laparotomy with right salpingo-oophorectomy was performed and the pathological report confirmed the presence of Sertoli-Leydig cell tumor of intermediate differentiation. Immunohistochemistry showed positive for inhibin and vimentin.

Conclusion: Androgen-producing tumors rarely cause hirsutism but should be suspected in women with virilizing clinical symptoms and high testosterone levels. Sertoli-Leydig tumors are larger and usually found easily on imaging, whereas hilar Leydig cell tumors are smaller and often difficult to find on imaging.

Abstract #1020

HYPOGONADAL MEN WITH DIABETES BENEFIT FROM LPCN 1021 (ORAL TESTOSTERONE)

Christina Wang, MD1, Jed Kaminetsky, MD2, Martin Miner, MD3, Adrian Dobs, MD, MHS4, Anthony Delconte, MD5, Nachiappan Chidambaram, PhD6, Satish Nachaegari5, Mahesh Patel, PhD6, Mohit Khera, MD5


Objective: Hypogonadism is more prevalent in men with type 2 diabetes mellitus (DM). Testosterone (T) therapy is indicated for treating hypogonadism and related symptoms. LPCN 1021 is a novel oral T undecanoate formulation that may avoid some undesirable attributes of non-oral T formulations, such as transference or skin irritation. We sought to determine the effect of LPCN 1021 use in hypogonadal men with DM vs those without DM.

Methods: This was a randomized, active–controlled, 2-arm, 12-month, open-label, multicenter, dose-titration trial in hypogonadal (T<300ng/dL on 2 separate days) men between 18 and 80 years old. Subjects were randomized to either LPCN 1021 (n=210) or Androgel 1.62% (n=104). Of 314 hypogonadal men, 82 (26%) reported medical history of DM. The LPCN 1021 dose could be adjusted based on T Cmax and T Cavg levels at weeks 4 and 8, if required. Sexual function and mood changes were assessed by the Psychosexual Daily Questionnaire (PDQ) for 7 days preceding visits. Quality of life (QoL) was assessed by the SF-36 questionnaire at Weeks 1 and 52 (end of study, EOS).

Results: Hypogonadal (HG) men with DM were significantly (p<0.05) older (57 vs 52 years), with higher baseline HbA1c (7.5% vs 5.6%), lower QoL scores (physical functioning, role physical, general health and physical component summary) and lower PDQ scores (sexual desire, sexual pleasure with partner, and erectile function) than HG men without DM. Significant (p<0.05) reduction in sexual hormone binding globulin (22.8 vs 29.8 nmol/L) and HDL (1.1 vs 1.2 mmol/L) occurred post LPCN 1021 therapy (EOS) for HG men with DM vs baseline; significant (p<0.05) improvement in free T level (10.9 vs 5.8 ng/dL) and PDQ parameters (sexual desire and activity, sexual pleasure, erectile function, positive and negative mood) were observed for HG men with DM at EOS vs baseline. Mean T (430 vs 483 ng/dL), DHT (105 vs 117 ng/dL) and estradiol Cavg (26 vs 29 pg/mL) were comparable (p>0.05) between HG men with and
without DM at Week 13 (efficacy visit) post LPCN 1021 therapy, respectively. Parameters that showed significant improvements post LPCN 1021 in HG men with DM also showed significant improvements in men without DM.

**Discussion:** HG men with DM had significantly lower baseline scores for some QoL and sexual function scores vs HG men without DM. HG men with and without DM improved significantly in sexual domains post LPCN 1021, similar to men without DM. T, DHT and E2 levels were comparable post LPCN 1021 between HG men with and without DM.

**Conclusion:** LPCN 1021 is an effective treatment in HG men with or without DM for restoring serum T levels to the physiological range and relieving some HG symptoms.

**Abstract #1021**

**A COMPARISON OF PEAK FOLLICULAR PHASE SERA ESTRADIOL (E2) LEVELS IN NATURAL CYCLES IN WOMEN TREATED EXCLUSIVELY WITH LUTEAL PHASE PROGESTERONE (P) ACCORDING TO CONCEIVING OR NOT**

Jerome Check, MD, PhD1, Joanne Liss, MLT2, Jasmine Aly, MD1

1. Cooper Medical School of Rowan University, 2. Cooper Institute for Reproductive Hormonal Disorders, P.C.

**Objective:** A previous study of women with >1 year of infertility with out-of-phase endometrial biopsies had a far better success rate with luteal phase P treatment than follicle maturing drugs when the dominant follicle appeared mature (average diameter >18mm) with a peak serum E2 >200pg/mL. However, the opposite was found where the peak serum E2 never reached 200pg/mL. A recent study found that empirical use of P support in otherwise unexplained infertility in women >30 or <30 with pelvic pain found a 71.7% live delivered pregnancy rate (PR) within 6 months of therapy. The objective of the present study was to determine if the serum E2 is higher in those conceiving vs. not conceiving in women treated empirically for unexplained infertility with P (and where the minimum serum E2 was 200pg/mL). An additional objective was to determine if those conceiving vs. not conceiving and to determine if those women who miscarry have a lower peak E2 than those who successfully deliver.

**Methods:** Women aged 30 to <39 with at least 1 year of unexplained infertility were recruited. They were treated with Crinone vaginal gel® 8% twice daily if covered by their prescription plan. Otherwise they were prescribed compounded P vaginal suppositories 200mg twice daily. PRs and miscarriage rates were determined after 3 months of exclusive P therapy. Inclusion criteria included attaining a mature follicle, and confirming subsequent collapse of the mature follicle, indicating oocyte release. They had to attain a mature follicle of >18mm with a peak serum E2 >200pg/mL. Two days later collapse of the follicle (evidence of oocyte release) had to be documented.

**Results:** 42 couples were found eligible and who completed 3 cycles of therapy (or conceived prior to 3 months). There were 28 clinical pregnancies – 66.7% and 23 live deliveries – 54.7%. The average peak serum E2 for those conceiving was 282.6pg/mL vs. 294.2pg/mL in those not conceiving. The average peak serum E2 in the 23 with successful pregnancies was 246.8pg/mL whereas the serum E2 was 328.3pg/mL in those who miscarried.

**Discussion:** Because of finding similar serum E2 levels in those conceiving vs. not, there is no evidence that failure to conceive may be related to a subtle follicular maturation defect where serum E2 attains the 200pg/mL cut-off but the follicle was still not quite fully “mature”.

**Conclusion:** Thus there is no evidence to support empirical use of follicle maturing drugs plus P alone in women with unexplained infertility. However, these women likely need extra P for establishing immune tolerance to the fetal semi-allograft based on their age >30 or presence of pelvic pain at any age.

**Abstract #1022**

**PREMENSTRUAL SEVERE LABIAL SWELLING AND PAIN RELIEVED WITH SYMPATHOMIMETIC AMINES**

Jerome Check, MD, PhD1, Jasmine Aly, MD1, Rachael Cohen, DO2

1. Cooper Medical School of Rowan University, 2. Cooper Institute for Reproductive Hormonal Disorders, P.C.

**Objective:** Premenstrual dysmenorrhea and dyspareunia have shown dramatic improvement following treatment with dextroamphetamine sulfate. The purpose of this study was to determine if this therapy could also provide clinical improvement for a 44 year old woman who had an unusual presentation of severe labial swelling beginning years after developing moderate premenstrual dysmenorrhea.

**Methods:** Dextroamphetamine sulfate extended release capsules 15mg/day was initiated. The dosage could be titrated up to 60mg according to relief provided and side effects.

**Case Presentation:** The dosage of 15mg did not provide sufficient relief of the premenstrual labial swelling and pain. The dosage was increased to 30mg dextroamphetamine extended release capsules. She reported complete relief of the labial swelling, erythema and pain with remission of her symptoms for the 12 months she has remained on therapy. Even at the 15mg dosage, she noticed marked relief of her symptoms for the 12 months she has remained on therapy.
improvement of the dysmenorrhea as well as significant improvement of her symptoms of chronic fatigue.

**Discussion:** There have been several publications concluding that treatment with dextroamphetamine sulfate is probably the most efficacious and safest therapy (medical or surgical) for pelvic pain associated with the menstrual cycle. This medication is not only for premenstrual dysmenorrhea and dyspareunia, but also for mid-cycle events including mittelschmerz. The theory is that the dextroamphetamine sulfate causes dopamine release from sympathetic nerve fibers. The release of dopamine has been hypothesized to act by diminishing cellular permeability related to an intrinsic defect in the pelvic tissues (inherited, acquired, or both) allowing the penetration of unwanted chemicals and other toxins, causing inflammation and pain. Changes in estradiol and progesterone are hypothesized to cause a natural increase in cellular permeability at these times of cycles explaining the cyclical nature of the pain, and in this case, the addition of labial swelling. There has been a case report of completely correcting severe vulvovaginitis in the pediatric population with dextroamphetamine sulfate.

**Conclusion:** Based on frequency, the vulva appears to be more resistant to cellular permeability defects which cause pain. However, at times, this area of the pelvis may be associated with increased pain that some would attribute to “endometriosis”. The more likely explanation is that it is part of the sympathetic neural hyperalgesia edema syndrome, including, but not limited to, pelvic structures as evidenced by marked improvement in this patient’s chronic fatigue symptoms.

**Abstract #1023**

**DYSMENORRHEA AND SEVERE RAPIDLY RELAPSING AND REMITTING ANGIOEDEMA OF THE TONGUE RELIEVED FOLLOWING TREATMENT WITH LISDEXAMFETAMINE DIMESYLATE**

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**Objective:** To determine if sympathomimetic amine therapy, well known to ameliorate dysmenorrhea and other types of pelvic pain, could not only relieve the dysmenorrhea but also improve the strange syndrome of rapid relapsing and remitting angioedema of the tongue which had been present for >1 year.

**Methods:** The patient was initially started on extended release amphetamine salts containing dextroamphetamine sulfate. The dosage was titrated to relieve the main target of tongue angioedema. Episodes of tongue angioedema were extremely severe such that it manifested as a giant red ball that would protrude from the patient’s mouth and cause breathing difficulty. These episodes would occur 60-100 times per day. For convenience, if the dosage exceeded 60mg, the intention was to switch to lisdexamfetamine dimesylate which comes in higher dosages.

**Case Presentation:** With a 60mg and 70mg capsule of lisdexamfetamine dimesylate not only was there marked improvement of the dysmenorrhea, but the episodes of angioedema were reduced to only 1-3 episodes per month lasting only a few seconds.

**Discussion:** The mechanism by which certain sympathomimetic amines control dysmenorrhea is believed to be by releasing more dopamine from sympathetic nerve fibers. The dopamine, in turn, diminishes cellular permeability, and thus inhibits the absorption into pelvic tissues of toxic elements, which, in turn, leads to inflammation and pain. The effect is not limited to pelvic structures, and thus treatment can relieve pain in other tissues where a weakness in permeability may exist, e.g., brain tissues with resulting headaches. Dextroamphetamine sulfate has also been found to be very effective for chronic urticaria and angioedema probably by stabilizing the membrane of vesicles containing histamines. Sometimes a traumatic event can cause the permeability defect. In this case the problem of angioedema of the tongue occurred following a wisdom tooth extraction. The possibility exists that coupled with a specific permeability defect in a specific tissue or organ system, there may also be accompanying hypofunction of the sympathetic nervous system.

**Conclusion:** Pelvic pain is a common condition that can be treated effectively with amphetamines. The reproductive endocrinologist, who frequently treats pelvic pain, must also be aware of other pathologic entities that also respond to treatment with amphetamine. In the event that two disease states occur in conjunction, and both can be treated with amphetamine, this may influence the choice of this therapy over traditional medications. In this case, not only did amphetamine treat dysmenorrhea, but it also served to correct a more serious problem of rapid exacerbation and remission of angioedema of the tongue.
Abstract #1024

MARKED IMPROVEMENT OF DERMATITIS HERPETIFORMIS ASSOCIATED WITH PELVIC PAIN FOLLOWING TREATMENT WITH SYMPATHOMIMETIC AMINES

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Objective: Though pelvic pain associated with certain specific times of the menstrual cycle has been attributed to “endometriosis”, the newest theories suggest that the ectopic implants of endometriosis are not the cause of the pain, but a result of increased cellular permeability allowing menstrual tissue to filter in to other areas of the pelvis and establish a medium for endometrial growth. The increased permeability seems to be the etiologic factor causing pain related to absorption into the pelvic tissues of unwanted toxic elements that cause inflammation and subsequent pain. Thus, previously the mainstay of medical therapy for pelvic pain had been with either anti-estrogen medication, e.g., progestins, or various types of drugs that lower estrogen levels. A far more effective therapy, however, is the sympathomimetic amine dextroamphetamine sulfate. The permeability disorder is not restricted to pelvic tissues, and thus women with endometriosis frequently have other symptoms than can be attributed to increased cellular permeability, e.g., pain in other areas of the body, gastrointestinal illnesses, or chronic fatigue. The purpose of this study was to determine if treatment with dextroamphetamine sulfate, in the form of amphetamine salts, could improve very severe refractory dermatitis herpetiformis.

Methods: Amphetamine salts starting at 15mg extended release capsules were given to a 42 year old woman complaining of severe dermatitis herpetiformis, pelvic pain, memory impairment, unexplained weight gain, vomiting from eating, Reynaud’s phenomenon, constipation, and chronic fatigue. The dosage was to be increased to a dosage that was tolerated well and provided the best relief of her symptoms.

Case Presentation: Following taking 45mg of amphetamine salts, the dermatitis herpetiformis had improved by 99%. The abdominal discomfort and constipation markedly improved. The dysmenorrhea was 75% better. Memory impairment was corrected, energy improved, constipation resolved, and she lost 14 pounds (started at 133, 64 inches tall). Her dermatitis herpetiformis had not responded to previous glucocorticoid therapy.

Discussion: This is the first case report of successfully treating dermatitis herpetiformis with dextroamphetamine sulfate. All of her other symptoms that were also markedly improved have been previously reported to respond to sympathomimetic amine therapy.

Conclusion: The reproductive endocrinologist consulted to treat pelvic pain associated with menses, may consider dextroamphetamine sulfate as first line therapy especially if there is an associated extra pelvic problem which may also be likely to improve with therapy.

Abstract #1025

DIMINISHED OOCYTE RESERVE DESPITE A HIGH NORMAL LEVEL OF SERUM ANTIMÜLLERIAN HORMONE

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Objective: Diagnosis of diminished ovarian reserve can be determined by increased serum follicle stimulating hormone (FSH) level at a time of low serum estradiol(E2), or a decrease in serum anti-müllerian hormone (AMH) level. The purpose of this study is to report a case with the unusual paradoxical circumstance of oligomenorrhea, high serum FSH and high normal serum AMH and to determine the probable etiology.

Methods: A 20 year old woman with oligomenorrhea presented with a serum estradiol (E2) of 22pg/mL with a serum FSH of 121.3 mIU/mL. Her serum AMH however was 8.73 ng/mL. The following additional tests were ordered to try to help determine the etiology of this paradox: 1) magnetic resonance imaging (MRI) of the pituitary, 2) ultrasound of ovaries, 3) serum inhibit B levels, serum prolactin, serum cortisol and 4) response to gonadotropin stimulation, and 5) Also chromosome analysis was obtained.

Case Presentation: The prolactin was normal and the serum cortisol low normal at 4.9 mcg/dL. The pituitary MRI did not show a pituitary tumor. The ultrasound showed small ovaries (right – 14x19x14mm and left 11x12x11mm with 4 and 2 pre-antral follicles of <3mm respectively. Injection of 150 IU FSH and 150 IU of luteinizing hormone (LH) for 10 days failed to cause a rise in her serum E2 levels. Her endometrial thickness was only 3mm. The serum inhibit B level was not elevated (<10 pg/mL). Chromosome analysis showed 46xx.

Discussion: The negative MRI of the pituitary did not support the diagnosis of a pituitary gonadotropinoma. This was confirmed by the failure to respond to 10 days of 150 units of FSH and LH, thus making the likelihood of a gonadotropinoma too small to detect by MRI, and producing immunoreactive but biologically inert FSH, highly unlikely.
ABSTRACTS – Reproductive Endocrinology

**Conclusion:** The above findings strongly suggest that the woman had marked diminished oocyte reserve (DOR). However, DOR is usually accompanied by the finding of extremely low AMH, not high normal levels. Though the ultrasound did not reveal any tumors, this paradox is most consistent with a case of incipient ovarian failure accompanied by a probable granulosa theca cell tumor of the ovary making ectopic AMH. These tumors are frequently too small to be seen by pelvic sonography. Another source of ectopic AMH is still possible. This seems to be the first case reporting high AMH accompanying high FSH that is not related to a gonadotropinoma, but, in fact, related to premature ovarian failure with the possibility of a tumor secreting ectopic AMH.

**Abstract #1026**

**SERUM LEVELS OF THE PROGESTERONE INDUCED BLOCKING FACTOR (PIBF) IN WOMEN WITH A BREAST CANCER ANTIGEN (BRCA)-1 MUTATION AND A BRCA-2 WILD TYPE MUTATION NOT ASSOCIATED WITH MALIGNANCY**

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**Objective:** The BRCA-1 gene directs synthesis of ubiquitin which is one of the ways to degrade the progesterone (P) receptor. Mutation in BRCA-1 will lead to diminished ubiquitination and thus diminished degradation of the P receptor. Interaction of P with its receptor in circulating gamma delta T cells leads to the expression of a 34 kDa protein which suppresses natural killer (NK) cell activity by stabilizing perforin and granzyme molecules. PIBF also inhibits the conversion of the 90 kDa parent nucleoprotein to a 34-36 kDa intracytoplasmic splice variant. Thus failure to degrade the P receptor in rapidly growing cells could allow the production of a greater amount of the immunosuppressive intracytoplasmic splice variant of PIBF thus not only further protecting cancer cells from immune destruction by NK cells, but from other aspects of the cellular immune system. The objective of the present study was to determine if a woman with a history of having the BRCA-1 mutation and breast cancer at an early age might possibly demonstrate a high level of circulating PIBF. The study would also determine if serum PIBF is increased in a young woman with a BRCA-2 wild type mutation that heretofore has not been associated with a cancer risk.

**Methods:** Serum PIBF was measured by a non-commercial research ELISA assay in two women. One woman age 34 was known to be positive for the cancer associated BRCA-1 mutation and had breast cancer in her early 20’s. The second was a woman age 23 who was positive for a BRCA-2 wild type mutation not normally associated with malignancy.

**Case Presentation:** BRCA-1 patient – PIBF – 7.9 ng/mL. BRCA-2 wild type mutation showed serum PIBF over 800 ng/mL obtained 2 separate times but dropped to 8.6 one year later.

**Discussion:** The serum PIBF level in the woman with BRCA-1 mutation was similar to levels in women in their follicular phase or women with various gynecologic cancers or breast cancer (irrespective of P receptor status) or even women with BRCA-2 mutations. The P receptor modulator, mifepristone, has been shown to suppress the intracytoplasmic conversion to the 34-36 kDa splice variant in leukemia cell lines. However, this potent abortifacient did not suppress serum PIBF levels in females given exogenous progesterone. Intracytoplasmic PIBF is found in all rapidly growing cells. It was puzzling why serum PIBF levels were so high initially in the young woman with the BRCA-2 wild type mutation nor why it ceased to be elevated 1 year later.

**Conclusion:** Measurement of serum PIBF does not seem to be valuable as a tumor marker, but knowledge of its function seems to be leading to novel therapies for cancer with low toxicity.

**Abstract #1027**

**VASOMOTOR INSTABILITY, CHRONIC FATIGUE, AND RECURRENT APHTHOUS STOMATITIS (RAS) IN A BROTHER/SISTER PAIR EFFECTIVELY TREATED WITH DEXTROAMPHETAMINE SULFATE**

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**Objective:** To determine if dextroamphetamine sulfate can help severe vasomotor instability in a normal estrogenic female and also her brother. The study would also determine if other associated symptoms, e.g., recurrent aphthous stomatitis (RAS) and chronic fatigue syndrome, could also be ameliorated.

**Methods:** Dextroamphetamine sulfate, starting at 15mg extended release capsules was prescribed for these young adults. The dosage would be increased if needed based on response and/or side effects.

**Case Presentation:** The female sibling had severe RAS since early childhood with sometimes as many
as 100 mouth ulcers per day at least 2/3rds of each month and sometimes every day of the month. With 20mg dextroamphetamine sulfate the RAS disappeared completely. In addition her energy returned to normal allowing her to continue with competitive running, and her vasomotor instability disappeared. Prior to initial treatment, she also had unexplained weight gain of 20 pounds. Within a few months of initiating treatment, her weight returned to normal. Her brother who had less severe RAS and chronic fatigue but had even more severe vasomotor instability. All these symptoms disappeared within 1 month of starting dextroamphetamine sulfate. However, he had a side effect of joint pain. He was switched to lisdexamfetamine dimesylate and his joint pain disappeared and he remained asymptomatic for the RAS, vasomotor instability, and chronic fatigue. Both remained asymptomatic for 2 years while on therapy. The female sibling ran out of medication for a short time, and immediately her vasomotor symptoms returned and the aphthous ulcers severely returned. They immediately disappeared when she started on her medication again.

**Discussion:** Unwanted chemicals entering the mitochondria, due to increased cellular permeability, may be the cause of chronic fatigue. Dextroamphetamine sulfate may correct the problem. Dextroamphetamine sulfate is a sympathomimetic amine which has been hypothesized to release dopamine from sympathetic nerve fibers which, in turn, reduces cellular permeability. In addition, dextroamphetamine sulfate is able to ameliorate vasomotor symptoms as the sympathetic nervous system controls the temperature regulation center of the brain.

**Conclusion:** Amphetamines can suppress vasomotor instability even when not related to the perimenopausal or menopausal state. In addition, they may also help with other medical problems that are related to cellular permeability such as RAS and chronic fatigue syndrome.

Abstract #1028

**INTRACTABLE SEVERE PERI-OVULATORY SNEEZING ABROGATED BY INJECTION OF HUMAN CHORIONIC GONADOTROPIN**

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**Objective:** To present a cause of periovulatory severe sneezing and a unique effective therapy.

**Methods:** A 22 year old woman developed an enigmatic condition of intractable sneezing last one day that occurred at mid-cycle. The sneezing was so severe that her activities were limited to her home on this day. The sneezing occurred in 85% of her menstrual cycles always at the same time in cycle always lasting only 1 day for the next 10 years. In trying to achieve a pregnancy with intrauterine insemination (IUI) for a male factor problem she was given human chorionic gonadotropin (hCG) 10,000 IU for timing of the IUI.

**Case Presentation:** She failed to conceive in 8 IUI cycles in which she received hCG each time. However, she noticed absolutely no sneezing during these 8 IUI cycles. Unfortunately she failed to conceive during these 8 cycles. There was a 4 month gap before starting an in vitro fertilization-embryo transfer cycle. Her sneezing resumed full force during these 4 cycles in which she received no hCG injections. She did receive hCG for her IVF cycle and there was no sneezing. She conceived on her first IVF cycle and there has been no sneezing during her first 24 weeks of pregnancy.

**Discussion:** It is not clear exactly the mechanism of why hCG injection abrogated the 1 day of sneezing fits. The hCG was always given prior to the LH surge when the peak serum estradiol (E2) was reached. Since sneezing had not occurred yet it would seem likely that the triggering event would be the characteristic drop in serum E2 and/or the rise in serum progesterone (P). Since the hCG injection would generate a higher rise in P than the endogenous LH surge the day after the surge or the hCG injection, it would seem likely that it was the drop in E2 that somehow triggered the sneezing. If somehow the rise in LH was the triggering event it would be likely that the sneezing would last 2 days rather than 1 since the duration of the LH surge is 48 hours.

**Conclusion:** This case supports but does not provide definitive proof, that other periovulatory events, e.g., mittelschmertz, may be related to increased cellular permeability that may occur when serum estradiol levels drop. For mittelschmerz the hypothesis is that increased permeability allows toxic elements to permeate pelvic tissues causing inflammatory and thus subsequent pain. For intractable sneezing, vesicles containing histamines cannot prevent a leak at the mid-cycle because of increased permeability of these vesicles.
Abstract #1029

MALE AGING COULD POSSIBLY LEAD TO SPERM-ZONA PELLUCIDA BINDING DEFECTS AND FERTILIZATION BY INTRACYTOPLASMIC SPERM INJECTION (ICSI) MAY INCREASE THE RISK OF TRACHEAL AGENESIS

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Objective: Advanced male age is known to have a 5 fold increased frequency of a low hypo-osmotic swelling (HOS) test which leads to normal appearing embryos that do not implant. Tracheal agenesis is a rare congenital anomaly with less than 200 reported cases. Reported herein is a case of anenatal diagnosis of tracheal atresia that occurred in a fetus resulting from intracytoplasmic sperm injection of the oocytes of a young woman whose husband was in his late 50’s. Possible genetic linkages and other interesting considerations of sperm issues involved with male aging are discussed.

Methods: A level 2 ultrasound was performed on a woman with her second conception from her first in vitro fertilization-embryo transfer (IVF-ET) with ICSI following the transfer of 2 frozen embryos. The first resulted with a delivery of a normal female following the transfer of 2 fresh embryos. ICSI was performed because she had a previous IVF cycle with conventional oocyte insemination with failed fertilization related to failure of the sperm to bind to the zona pellucida.

Case Presentation: The level 2 ultrasound suggested the congenital high airway obstruction syndrome (CHAOS), which prompted magnetic resonance imaging of the fetus, revealing tracheal agenesis. The pregnancy was terminated.

Discussion: The occurrence of 2 rare events – failed fertilization related to a sperm zona pellucida binding defect and a fetus with a rare congenital anomaly could suggest a possible genetic link rather than shear coincidence. One could speculate that the penetrance of a mutated gene that produces an abnormal enzyme that is not only involved in sperm binding to the zona pellucida, but may be also involved in tracheal development. Perhaps this is nature’s way to prevent sperm from men of advanced age from producing offspring with lethal abnormalities.

Conclusion: Aside from speculation of the presence of 2 rare circumstances happening together possibly genetically linked, since this woman 1 year before her IVF cycle with failed fertilization conceived naturally, this case demonstrates that failed fertilization related to sperm zona pellucida binding defects can be an acquired defect. Since it occurred with advancing age, this could be another sperm defect that occurs with advancing age of the male. This case is one of only a few where tracheal agenesis has been detected antenatally in enough time to terminate the pregnancy.

Abstract #1030

DIAGNOSTIC CHALLENGES IN THE EVALUATION OF VIRILIZING TUMORS

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Objective: Diagnosis of hyperandrogenism is challenging. The source of endogenous androgen excess is the ovary or the adrenal gland. Neither Testosterone (T) nor DHEAS can reliably differentiate an ovarian from an adrenal source. Adrenal incidentalomas are common, and positive imaging must always be interpreted carefully. We present 3 cases of virilizing ovarian tumors, with varied presentations and diagnostic challenges.

Case Presentation: Case 1. 64y old woman presented for evaluation of polycythemia. She presented to the emergency room with chest pain and gave a 2y history of polycythemia, requiring phlebotomy, and progressively worsening hirsutism. On examination, she had masculine facies and clitoromegaly. Her Ferriman-Gallwey (FG) score was 28/36. A CT of the abdomen showed a possible left ovarian mass and a 1 cm adrenal nodule. Low dose dexamethasone did not suppress the elevated T level, confirming a tumorous cause of the hyperandrogenism. Baseline T level was 839 ng/dl(normal <75) and DHEAS level was 452 ng/ml (normal <1880). Venous sampling was considered high risk. At surgery, a 2 cm left ovarian mass, consistent with a steroid-cell tumor was found.

Case 2. 62y old woman presented for evaluation of worsening hirsutism and deepening of voice over 6y. She had a masculine physique and clitoromegaly. Her FG score was 20/36. T and DHEAS levels were 359 ng/dl and 1549 ng/ml respectively. A CT of the abdomen showed a 1.5 cm lipid poor adenoma in the adrenal gland. An adnexal mass was not seen. Because of equivocal imaging and laboratory data, we proceeded with adrenal and ovarian vein sampling, which localized to the right ovary. A 1.5 cm Leydig cell tumor was found at surgery.

Case 3. A 35y old woman presented with worsening hirsutism. She had been diagnosed with PCOS 10 years ago and was treated with oral contraceptives. In the last 6 months, she noted worsening of hisurtism and deepening of voice. On examination, her FG score was 20/36. She had a masculine physique without clitoromegaly. T level
was 251 ng/dl. CT of the abdomen showed a right ovarian mass. At surgery a 5 cm tumor was found, consistent with a steroid-cell tumor.

**Conclusion:** These varied clinical presentations exemplify the diagnostic challenges encountered in the evaluation of patients with hyperandrogenism. Imaging studies can be misleading, and venous sampling may be indicated. Androgen levels are not commensurate with the size or location of the tumor. Low dose dexamethasone testing has been recommended to differentiate a nontumorous cause of androgen excess, but about 12% of such patients fail to suppress. Multimodality testing is recommended to accurately find the source of androgen excess, as surgery can be curative.

**Abstract #1031**

**LIVE FETUS BY THE END OF THE FIRST TRIMESTER FOLLOWING THE TRANSFER OF A 3 CELL EMBRYO ON DAY 3 IN A WOMAN WITH DIMINISHED OOCYTE RESERVE**

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**Objective:** To describe the first reported case of a successful pregnancy resulting from the transfer of a 3 cell embryo on day 3 in a woman with diminished oocyte reserve.

**Methods:** A 36 year old woman with a baseline serum follicle stimulating hormone (FSH) of 53 mIU/mL and a serum estradiol (E2) of 40 pg/mL used mild FSH stimulation in preparation for in vitro fertilization-embryo transfer (IVF-ET) after lowering the elevated serum FSH with ethinyl estradiol.

**Case Presentation:** Four dominant follicles were developed and 4 metaphase II oocytes were retrieved. Two cleaved to day 3 and a 6-cell and a 3-cell embryo, both with no fragmentation, were transferred. A dichorionic diamniotic gestation resulted with completion of the first trimester.

**Discussion:** There were only 4 dominant follicles and oocytes were obtained from each one. Thus spontaneous ovulation is unlikely unless a follicle was consistently missed by sonography. Dichorionic diamniotic identical twins from one conceptus are very rare but possible. Nevertheless, the odds are that it was the 3-cell embryo developing into a live fetus. There would be many infertility specialists who would tell this couple that conceiving with their own oocyte was not possible based on the serum FSH of 153 mIU/mL. Indeed many IVF centers would be unsuccessful if they did not follow the principles of mild stimulation, i.e., restoring down-regulated FSH receptors by lowering the elevated serum FSH with ethinyl estradiol (followed by very mild FSH stimulation). The ethinyl estradiol is used because it does not cross-react in the serum E2 assay and allows the monitoring of follicular development by not only measuring follicle sizes, but serum E2, which is derived from the maturing follicles.

**Conclusion:** Though many (maybe even a majority) of infertility centers would steer this couple into a donor oocyte program, there are several anecdotal cases of successful pregnancies from women whose baseline serum FSH was >100 mIU/mL including one woman with an FSH of 185 mIU/mL and another with 164 mIU/mL. Thus this is not the reason for presenting this case since it is not unique (although it does not hurt to remind clinicians that pregnancies are possible if the proper techniques are followed). The typical high dose FSH stimulation leads to embryo aneuploidy by causing meiosis II errors. The uniqueness of this case is it is the first report of a successful pregnancy from transferring a slow growing embryo that only cleaved to 3-cells by day 3.

**Abstract #1032**

**THE ROLE OF TESTOSTERONE IN THE UTILIZATION OF IRON IN ERYTHROPOIESIS**

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**Objective:** Since the syndrome of hypogonadotrophic hypogonadism (HH) is associated with anemia and the administration of testosterone restores hematocrit to normal, we investigated the potential mechanisms which may contribute to it.

**Methods:** We measured basal serum concentrations of erythropoietin, iron, iron binding capacity, transferrin (saturated and unsaturated), ferritin and hepcidin and the expression of ferroportin in peripheral blood mononuclear cells (MNC) of 94 men with type 2 diabetes. 44 men had HH (defined as free testosterone <5ng/dl along with low or normal LH concentrations) while 50 were eugonadal. Men with HH were randomized to testosterone treatment (200 mg i.m., every two weeks) or placebo (saline 1 ml every 2 weeks) for 14 weeks. Twenty men in testosterone group and 14 men in placebo group completed the study.

**Results:** Hematocrit concentrations were lower in hypogonadal men (41.2±3.8% vs. 43.8±3.2%, p=0.001). There were no differences in plasma concentrations of hepcidin, ferritin, erythropoietin, transferrin, iron or transferrin saturation or in ferroportin expression in MNC among hypogonadal and eugonadal men. Free testosterone
concentrations increased from 4.5±1.3 to 13.7±3.9ng/dl (p<0.001) after testosterone therapy but did not change in placebo group. The hematocrit increased from 42.0±2.7% to 45.4±4.6% (p<0.001) but did not change after placebo (40.7±2.9% to 41.6±3.1%, p=0.22). There was a 28±7% decrease in plasma hepcidin (p<0.01) and 21±7% increase in erythropoietin concentrations (p<0.05) after testosterone therapy. There was no significant change in iron or ferritin concentrations but transferrin concentration increased by 22±5% and transferrin saturation decreased by 21±6% (p<0.01). Ferroportin and transferrin receptor mRNA expression in MNC increased by 70±13% and 43±10%, respectively, (p<0.01) after testosterone therapy. There was no change in any of these parameters after placebo.

Discussion: The administration of testosterone to restore normal testosterone concentration led to a significant increase in plasma erythropoietin concentrations, reduction in plasma hepcidin concentration, marked increase in ferroportin expression, a smaller but significant increase in transferrin and a small reduction in plasma iron concentrations.

Conclusion: Clearly, therefore, the increase in hematocrit is supported by an increase in erythropoietin and an increase in iron transport through an increase in ferroportin. This increase is probably through the known suppression of hepcidin which inhibits ferroportin activity.

Abstract #1033

FAMILY WITH AROMATASE EXCESS SYNDROME (AXES)

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Objective: To report a case of a mother and son with AXES and Hypothyroidism.

Methods: Literature Review, Case Reports of prior and post treatment of thyroid dysfunction, abnormal androgen and estrogen levels.

Case Presentation: 41 year old female with history of post-surgical Total hysterectomy with bilateral salpingoophorectomy and Hypothyroidism due to Papillary Thyroid Cancer, presents with symptoms of weight gain, hirsuitism and fatigue. Lab evaluation of hormone levels were drawn after physical examination yielded visible hirsuitism, waist circumference 40cm, Ht: 65 inches, Wt: 198 lbs, BMI: 31.8m, and new onset hypertension 145/89. Lab values obtained: TSH 22ng/dl, HgbA1c 5.6%, 50mcg/mg/creatinine microalbuminuria, Total Testosterone 22ng/dl, Total Estrogen 96pg/ml, Estrone 85pg/ml↑, Estradiol 31.2pg/ml, negative Thyroid scan, abnormal ECG.

Social history of A student in junior high school, with a decrease in performance and grades after onset of puberty, only completed 2 years of college, has not ever been in serious relationship, denies use of ETOH/Drugs/Tobacco. Physical Exam revealed HT: 70 inches, Wt: 120 lbs., BMI: 17.3m, BP 100/50, other vitals WNL, sparse facial hair, multi-nodular goiter, bilateral gynecomastia, muscle strength symmetrically reduced 4+/5. Lab evaluation revealed: Total Testosterone 759ng/dl, Free Testosterone 20.9pg/dl↑, Total Estrogen 157pg/ml↑, Estradiol 43pg/ml↑, Estril 0.3ng/ml↑, Estrone 47.3pg/ml, Calcitonin and TSH/T4 WNL, Vitamin D 24.2pg/ml.

Discussion: The son began treatment with Ergocalciferol 50,000 units/week. His repeat Vitamin D level 47.4pg/ml and his energy level improved. Anastrazole, aromatase inhibitor, was started slowly and after 3 weeks of therapy his Total Testosterone 708ng/dl, Free Testosterone 19pg/dl↓, Total Estrogen 18pg/ml. After 2.5 months of therapy he made summer plans to go solo hiking from Missouri to California and plans to return to college.

41 year old mother was started on Metformin which resulted in 9 lb. weight loss. Benazepril which reduced the hypertension, BP 124/90 and proteinuria reduced to 26.7mcg/mg/creatinine.

Conclusion: Vague Symptoms like fatigue and decreased school performance are not unusual. This case of hyper-sexuality after puberty shows the wisdom of a thorough investigation of all endocrine systems. Since such a diagnostic investigation is complex, it should best be done by an experienced endocrinologist.
THYROID DISEASE

Abstract #1100

PAPILLARY THYROID CANCER ASSOCIATED WITH DICER-1 MUTATION LINKED SERTOLI LEYDING CELL TUMOR: A CASE REPORT

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Case Presentation: A 29-year-old female patient was referred to endocrinology clinic for evaluation of a thyroid nodule. She had been complaining of dysphagia for the past few months for which she underwent a thyroid ultrasound that showed a 1.6 cm right sided solid hypoechoic nodule. She was clinically and biochemically euthyroid.

A year prior to this, she had been diagnosed with poorly differentiated Sertoli Leydig Cell Tumor (SLCT) of the right ovary for which she had undergone right salpingo-oophorectomy and total hysterectomy followed by adjuvant chemotherapy. Testing for DICER1 mutation had revealed truncating mutation c.947G>A; pTrp376* in exon 8 of the DICER1 gene in the peripheral blood as well as in the ovarian tumor specimen. Family history of cancer could not be retrieved as she had been adopted.

A Fine needle aspiration (FNA) of the thyroid nodule was performed and showed follicular lesion of undetermined significance (FLUS-Bethesda classification). Because she harbors DICER1 mutation and the concern of increase risk of thyroid hyperplasia and malignancy it was recommended that she proceed with total thyroidectomy. The final histopathology showed a 1 cm papillary thyroid cancer-follicular variant, with no lymphovascular invasion or extrathyroidal extension but positive inked margins. She was started on levothyroxine after her surgery and a radioactive iodine ablation is planned.

Discussion: In 2009, germline DICER1 mutations were identified in familial pleuropulmonary blastoma (PPB), adding to the list of rare familial cancer syndromes that have yielded evidence linking essential biological processes with cancer causation. DICER1 syndrome is a characterized phenotypic association of distinctive hyperplastic or malignant tumors. The most frequent is the rare childhood lung malignancy PPB. Other, primarily endocrine manifestations include ovarian Sertoli-Leydig cell tumors, nodular thyroid hyperplasia, pituitary blastoma, pineoblastoma, papillary and follicular thyroid carcinoma, cervical rhabdomyosarcoma, cystic nephroma, and Wilms tumor.

MNG is frequently present in families with germline DICER1 mutation. However differentiated thyroid carcinoma is infrequently seen in DICER1 pedigrees.

Conclusion: DICER-1 mutation associated thyroid cancer is not common. Moreover, it is unclear if there are common pathways in the tumorigenesis of ovarian and thyroid malignancies. Based on the findings in the case report, further studies on the epidemiology of DICER1 mutation associated thyroid cancer should reveal more about the incidence and prevalence of this condition.

Abstract #1101

THE IMPORTANCE OF PATIENT EDUCATION WITH RARE MEDICATION SIDE EFFECTS: CLASSIC EXAMPLE OF AGRANULOCYTOSIS WITH METHIMAZOLE

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Objective: Describe a case of MMI-induced agranulocytosis (AG) and importance of patient education for prompt diagnosis and intervention.

Case Presentation: A 44-year old woman was found to have low TSH with sn and sx of thyrotoxicosis during work up for giant cell arteritis. Thyroid scan/uptake was consistent w/ Graves’ disease. MMI 20mg daily was added to propranolol. ~ 1 month after MMI, TSH was still low, but symptoms resolving and FT4 normalizing. Later, developed headaches, sore throat and fevers to 103.2F. As instructed, she contacted her PCP and Endocrinologist with onset of fevers. CBC with differential checked, was found to be neutropenic (ANC 20) and admitted. MMI was d/c and ANC improved. Day 4 she was no longer neutropenic and sent home with propranolol only. Later scheduled for total thyroidectomy and given SSKI for 10 days prior to surgery.

First visit, she was having episodes of anxiety, palpitations, blurry vision, diaphoresis, hyperdefecation, headaches and low-grade fevers. She had an enlarged thyroid, tachycardia with murmur and brisk reflexes. After 1 month of MMI and propranolol, patient was symptomatically improved with resolution of all but anxiety. Still had thyroid enlargement, tachycardia, but no murmur and normal reflexes. Later developed headaches, sore throat and fevers to 103.2F. TFTs before MMI, 1 month after treatment and 1 week after discontinuation were TSH 0.01, 0.01, 0.06 mIU/L; FT4 2.73, not measured, 0.97ng/dL; TT4 16.7, 9.5, 9.5 ng/dL; FTI 6.3, 3.1,3.0; T3 Uptake 38, 33, 32%. TT3 175 ng/dL, TPOab >900, TGab 2, and TSI 437 were measured before treatment. WBC before MMI, 1 month after treatment and 1 week after discontinuation were 9.8, 2,3,11.0 x 109/L; neutrophil 79.6, 2, 63% and ANC 7800, 20, 8300. Thyroid scan and uptake was 51% at 6 hours, with fairly uniform bilobar uptake.

Discussion: In 2009, germline DICER1 mutations were identified in familial pleuropulmonary blastoma (PPB), adding to the list of rare familial cancer syndromes that have yielded evidence linking essential biological processes with cancer causation. DICER1 syndrome is a characterized phenotypic association of distinctive hyperplastic or malignant tumors. The most frequent is the rare childhood lung malignancy PPB. Other, primarily endocrine manifestations include ovarian Sertoli-Leydig cell tumors, nodular thyroid hyperplasia, pituitary blastoma, pineoblastoma, papillary and follicular thyroid carcinoma, cervical rhabdomyosarcoma, cystic nephroma, and Wilms tumor.

MNG is frequently present in families with germline DICER1 mutation. However differentiated thyroid carcinoma is infrequently seen in DICER1 pedigrees.

Conclusion: DICER-1 mutation associated thyroid cancer is not common. Moreover, it is unclear if there are common pathways in the tumorigenesis of ovarian and thyroid malignancies. Based on the findings in the case report, further studies on the epidemiology of DICER1 mutation associated thyroid cancer should reveal more about the incidence and prevalence of this condition.
inhibit the synthesis of thyroid hormones. MMI is the drug of choice over PTU because it brings patients to a euthyroid state faster with fewer side effects. AG, a rare (prevalence 0.1-0.5%) but serious complication, can occur with MMI. The time of occurrence can be from 11-233 days, but usually occurs within the 1st 2 months. Since monitoring of WBC count is not recommended, it is important that patients be aware of side effects of MMI. This patient recognized possible complications of MMI and quickly contacted her physicians, allowing for quick intervention. 

**Conclusion:** It is important that detailed discussions be had with patients about the side effects of MMI, common and rare, as well as the importance of physician notification. This allows for early intervention, especially for serious life-threatening complications such as AG.

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**Abstract #1102**

**ANGIOSARCOMA OF THE THYROID ASSOCIATED WITH TOXIC MULTINODULAR GOITER, GRAVES’ DISEASE AND PAPILLARY THYROID CARCINOMA**

Megan Crawford, DO, Eren Berber, MD, Valeria Arrossi, MD, Georgiana Dobri, MD

Cleveland Clinic

**Objective:** To describe a case of angiosarcoma of the thyroid associated with toxic multinodular goiter, Graves’ disease and papillary thyroid carcinoma.

**Case Presentation:** A 61 year old female of Hungarian, Russian and Polish descent with 20 year history of nontoxic goiter presented with rapidly enlarging neck girth and symptoms of thyrotoxicosis. TSH was <0.005 uIU/mL (N: 0.400-5.500), free T4 3.0 ng/dL (N: 0.7-1.8) and free T3 5.9 pg/mL (N: 1.8-4.6). I-123 uptake and scan demonstrated elevated 4 hour uptake of 37% (N: 5-25%) and 24 hour uptake of 41.9% (N: 5-40%) with heterogeneous bilateral distribution suggestive of multinodular goiter. CT imaging revealed a right thyroid lobe mass measuring 9.7 x 8.3 x 12.9 cm (AP x transverse x craniocaudal) with tracheal displacement. She required high dose beta blockade and methimazole 20mg three times daily with subsequent normalization of free T4 and T3. She underwent total thyroideectomy and surgical pathology revealed bilateral multinodular thyroid follicular hyperplasia, an 8 cm focus of epithelioid angiosarcoma in the right lobe, a single focus of angiosarcoma in a lymphovascular space in the left lobe, and a 1 mm focus of papillary thyroid carcinoma in the left lobe. The patient underwent 33 cycles of radiation therapy followed by adjuvant Paclitaxel chemotherapy for 12 weeks. The patient also has a history of breast cancer at age 46 and probable ovarian malignant neoplasm at age 44, and she was referred for genetic analysis. Analysis was negative for BRCA mutation, however revealed mutations of unknown significance in the MUTYH, ATM, and RAD51D genes.

**Discussion:** Angiosarcoma of the thyroid is a rare finding, comprising < 1% of thyroid cancers with about 50 cases described in the literature.1 Furthermore, association with hyperthyroidism has been described in only four reported cases.2 Epithelioid angiosarcoma of the thyroid is a rare thyroid neoplasm, especially when diagnosed outside the Alpine region of Europe where it is seen with disproportionately high incidence. Of note, fine needle aspiration can yield a false negative result with many cases reported to show hypocellularity, hemorrhagic material or inadequate specimen on cytology.3 Hyperthyroidism in the presence of angiosarcoma of the thyroid may be due to increased vascularity of the gland as a result of the neoplasm, in a susceptible individual, though this association is not well understood.4

**Conclusion:** Ours is the first case in the literature to describe the presence of four concomitant thyroid diagnoses, one being a rare thyroid angiosarcoma. High clinical suspicion and the knowledge that FNA can yield a false negative result are needed to make an appropriate diagnosis of thyroid angiosarcoma.

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**Abstract #1103**

**THYROTOXIC PERIODIC PARALYSIS IN A CAUCASIAN MALE**

Romona Satchi, MD, Richard Haber, MD

Mount Sinai Hospital

**Objective:** To present a case of a Caucasian man with thyrotoxic periodic paralysis (TPP).

**Case Presentation:** A 28 year-old Caucasian man presented with acute muscle paralysis. Five months earlier, he began to have frequent bowel movements, palpitations, heat intolerance, and insomnia. He was found to be hyperthyroid and propranolol was prescribed, but he was noncompliant. On the day of admission, he developed sudden weakness, fell and was unable to move his extremities. On arrival at a hospital, laboratory results showed serum potassium=1.5mEq/L, TSH <.005 uIU/mL, and elevated free T4 =5.43 ng/dL. He was treated with intravenous potassium, methimazole, and propranolol. He was referred for genetic analysis. Analysis showed serum potassium=1.5mEq/L, TSH <.005 uIU/mL, and elevated free T4 =5.43 ng/dL. He was treated with intravenous potassium, methimazole, and propranolol. After several hours, his muscle strength returned, and he was transferred to our institution. On exam, his heart rate was 115 bpm and he had bilateral hand tremor. There was no proptosis, and no thyroid tenderness or enlargement. He had normal deep tendon reflexes and normal motor strength in all extremities. Laboratory results...
showed serum potassium=5.4 mEq/L, TSH=0.06 uIU/ml, Free T4=3.53 ng/dL (normal range .6-1.10 ng/dL), total T3=126 ng/dL, and TSH receptor antibody=11.52 IU/L (normal range <1.75 IU/L), confirming Graves’ disease. Methimazole and propranolol were continued. The following day, while walking to the bathroom, he again had acute muscle weakness and fell. His weakness resolved spontaneously. Serum potassium the following day was 4.9 mEq/L. He was discharged on methimazole 10mg BID and nadalol 40mg BID. One week later, he reported improvement in his tremor and palpitations and free T4 was 1.43 ng/dL. Ten days later, he was asked to perform a treadmill test at work, which provoked a recurrent episode of diffuse weakness. Subsequent thyroid function tests were normal with no further episodes of acute paralysis.

Discussion: TPP is a rare complication of thyrotoxicosis that is characterized by acute episodes of hypokalemia and flaccid paralysis. It occurs most frequently in Asian males with hyperthyroidism. The incidence has been reported as 1.8% of Chinese and 1.9% of Japanese, whereas it occurs in 0.1-0.2% of North Americans. TPP is due to a rapid intracellular shift of potassium while total body potassium stores remain normal. Treatment should include cautious potassium supplementation to avoid rebound hyperkalemia, antithyroid medications, and non-selective beta blockers. Patients should be advised to avoid precipitating factors such as exercise, carbohydrate rich meals, high salt diet, and alcohol intake.

Conclusion: TPP should be recognized and treated promptly to prevent dangerous acute hypokalemia and paralysis.

Abstract #1104

SUBMANDIBULAR MASS: TO BE OR NOT TO BE ECTOPIC THYROID TISSUE

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Objective: Ectopic thyroid tissue is a rare entity occurring as a result of faulty embryogenesis and migration of the thyroid gland. Usually located in the midline along the course of the thyroglossal duct and rarely located in the lateral neck. Until recently, cases of ectopic thyroid detected in the lateral cervical region were regarded as malignant (metastatic) lesions and were termed lateral aberrant thyroid(1). We present a case of a lateral ectopic thyroid nodule initially considered to be a malignant lymph node, ended up being a benign thyroid nodule.

Case Presentation: A 83 y/o F with history of coronary artery disease, hypertension, type 2 diabetes and COPD presented with a progressively increasing, palpable thyroid nodule over a period of 4 months. She denied dysphagia, palpitations or tremors. She had no family history of thyroid malignancy or prior radiation exposure. TSH was 1.24mIU/ml(0.2-5.1). CT neck with contrast revealed a peripherally enhancing soft tissue mass measuring 2.3x2.7cm abutting the right thyrohyoid muscle. US reported a 2.7x2.3x2.6cm mass which was heterogeneous with peripheral vascularity consistent with thyroid tissue likely a pedunculated thyroid nodule. The rest of the thyroid gland contained multiple mixed solid and cystic nodules consistent with multinodular goiter. The submandibular nodule features were comparable to the nodules in the thyroid. Nodule was benign on FNA, consistent with a dominant nodule in multinodular goiter. She is awaiting I131 scintigraphy for confirmation of uptake in the region of the nodule and will be followed closely with US, thus avoiding surgery in this high risk patient.

Conclusion: In rare cases, a lateral ectopic thyroid gland is formed when the cells of the lateral anlage do not join those of the median. When this occurs, its location is usually submandibular(1,2). Such ectopic tissue becomes evident earlier in life and presents as a lateral, palpable, mobile, painless mass or noticed during adolescence or pregnancy. Our case is unusual due to the age of the patient and in its rapid growth. Thyroid cancer metastases should always be excluded, as they can manifest as ectopic thyroid tissue(3).There is no consensus about the optimal therapeutic strategy, due to the rarity of this clinical entity. Most authors agree that surgical treatment of ectopic thyroid in the neck depends on size and local symptoms(2,4,5). Some recommend complete surgical resection, considering the potential of malignant transformation(6,7). For most, regular follow-up is recommended. This case also highlights the importance of thyroid US and USGFNA in avoidance of surgery in otherwise surgical thyroid cases.

Abstract #1105

APPROACH TO A HEMODIALYSIS PATIENT REQUIRING I 131 THERAPY FOR PAPILLARY THYROID CANCER

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Objective: We describe our approach to treating a woman with locally metastatic papillary thyroid cancer (PTC) who was receiving hemodialysis (HD) for End Stage Renal Disease (ESRD), as there is no definitive protocol for ablative doses of iodine for patients on HD.
**Case Presentation:** 62 year old woman with ESRD on HD presented to our clinic 4 months after total thyroidectomy for PTC at another facility. She had bilateral 1 cm mobile lymph nodes. The rest of the exam was unremarkable. Total thyroidectomy showed a right sided unifocal 1.8 cm, well differentiated papillary carcinoma follicular variant with small foci showing tall cell and insular morphology, as well as capsular, perineural, lympho-vascular invasion, and extrathyroidal extension. Notably, patient was not on suppressive therapy with levothyroxine when transferred to our care. To evaluate the extent of the disease and to collect data for radiation dosimetry, Whole Body Scans (WBS) were obtained using 1.59mCi of I131. She was dialyzed 24hrs after tracer dose. WBS were taken at 24, 48, and 72 hours after the administration of tracer dose. The count rates were measured at 12 feet just prior to and immediately after HD using our picker thyroid probe. The absorbed dose was calculated according to Benua and Martinelli. The results showed that one cycle of HD eliminated 80% of the administered I131. A 125.8mCi I131capsule was administered orally. 24 hrs after the treatment dose, she was dialyzed for 4 hours. She was again dialyzed 1 day later for 3 hours, approximately 48hours after treatment dose. Post-ablation WBS showed a focus of moderately increased activity in center of the neck, contiguous with the right lateral side of the trachea.

**Discussion:** The management of thyroid cancer in patients on HD has not been standardized. A review of the literature yielded data on 37 patients with PTC who had ESRD on HD and received ablation with I131. After reviewing the literature in order to maximize effectiveness while minimizing total body dose of radiation the following protocol was used. The patient continued her usual HD schedule. She received the tracer dose of I131 48hrs post HD. She had WBS at 24, 48, and 72 hours. The next week, at 24 hrs post-HD, the treatment dose of I131 was given, followed by HD at 24 and 48 hrs. The results showed that one cycle of HD eliminated 80% of the administered I131.

**Conclusion:** Given the concerns of extra-thyroidal toxicity, the best therapeutic approach should ideally be to use dosimetry calculations to estimate the most safe and effective dose, perform HD at 24, 48hrs post ablation. We also recommend radiation monitoring and precautions use for the first 3 HD sessions after treatment, in order to ensure safety overall.

**Abstract #1106**

**TWO CASES OF ANTI-THYROIDAL MEDICATION INDUCED AGRANULOCYTOSIS**

**Lauren LaBryer, MD, Mitali Talsania, MD, Madona Azar, MD**

University of Oklahoma

**Case Presentation:** Case #1: 48 year old Native American man with history of Graves’ disease presented to the Emergency Department with a 3 day history of progressive fatigue, fever, sore throat, and difficulty swallowing. Patient had been started on methimazole 3 months prior to presentation. Physical exam was remarkable for tachycardia, fever, and enlarged pustular tonsils. Laboratory studies revealed hyperthyroidism (FT3 15.3 pg/dl) and severe neutropenia (WBC 0.32 k/mm3) with ANC of 0. Methimazole was discontinued. Patient was hospitalized and started on propranolol and broad spectrum antibiotics. Patient was ultimately treated with thyroidectomy.

Case #2: 36 year old Native American woman with Graves’ disease presented to the Emergency Department with severe thyrotoxicosis (FT3 15.3 pg/dl) and atrial fibrillation. She was initially started on methimazole, but changed to PTU due to lack of response. Two months after hospitalization, patient was seen at primary care clinic. Labwork revealed neutropenia (WBC 2.55 k/mm3) with ANC of 432. Patient was asymptomatic. She was diagnosed with PTU induced agranulocytosis. PTU was discontinued. radioactive iodine uptake scan revealed 95% homogenous uptake and she received 22 mCi of radioactive iodine for treatment of Graves’ disease. Her ANC improved to 1888 on day #10 after discontinuing PTU.

**Discussion:** Anti-thyroidal medication-induced agranulocytosis is rare, occurring in ~ 0.35% of patients on methimazole or PTU. It usually occurs within the first 2-3 months of therapy initiation. Despite the rarity of this adverse reaction, we report 2 cases occurring within the same month at our institution. Both patients developed neutropenia within the first 3 months of re-initiation of the medication at a higher dose. In case #1, patient had not received counseling about the risks of agranulocytosis, and, thus, did not stop taking his medication or seek help for several days. In case #2, routine monitoring detected neutropenia and allowed for outpatient management and treatment before clinical deterioration developed. Interestingly, both patients at our institution were of Native American heritage. While it is known that among Japanese patients with Graves’ disease the HLA DRB1*08032 allele appears to be strongly associated with susceptibility to methimazole-induced agranulocytosis, no other data currently exists for risk among other ethnicities.

**Conclusion:** These cases highlight the importance of
counseling patients about the potential risk of agranulocytosis. Additionally, physicians should consider the risk/benefit of initiating treatment with higher doses of the medication.

Abstract #1107

UNDER-MONITORED AND OVER-TREATED: A CASE OF PROPYLTHIOURICIL INDUCED MYXEDEMA COMA

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**Objective:**
1. Review clinical manifestations of myxedema coma.
2. Understand side effects of propylthiouricil (PTU).

**Case Presentation:**
A 61 year old Caucasian female with history of hepatitis C (HCV) cirrhosis and thyroid disease admitted from an outside hospital with elevated liver function tests, confusion, bradycardia and worsening edema. Due to her history of cirrhosis, she was admitted for acute on chronic liver failure. It was believed her HCV medication was the cause. She was reportedly on PTU however it was not known what dose. At the outside hospital her temperature was 36.1 C and her heart rate was 18. PTU was started at 100 mg three times a day. Free T4 was 0.02, TSH was 0.05 sodium was 126 and glucose was 130 on admission. She was transferred to a liver transplant service with a heart rate of 49, temperature of 34.7 and an Oxygen saturation of 88%. Her free T4 0.51, TSH 0.03, Na 125 and glucose 77. PTU was stopped and Intravenous levothyroxine, triiodothyronine and hydrocortisone were starte. Within 48 hours her temperature, heart rate, sodium and free T4 level normalized. Her confusion improved and she revealed she was diagnosed with hyperthyroidism about 10 years prior. She did not have insurance and so she took PTU intermittently and only had her labs checked once every two years. Her only other records were from 2013 when she was taking PTU and had normal TSH per a discharge summary. She revealed that she recently started taking PTU because her TSH was low but she did not return for subsequent labs. Although she initially clinically improved she died from acute liver failure during the admission.

**Conclusion:**
This patient either had over-treated hyperthyroidism or central hypothyroidism that was treated incorrectly. The PTU caused hypothyroidism and possibly myxedema coma. Myxedema coma has a 25 – 60% mortality rate. It is rare and often masked by other serious illnesses such as sepsis. It can occur in any patient that has hypothyroidism. Although there is no concensus for diagnosis, patients often have neuro symptoms, bradycardia, hypothermia, hypotension, edema, renal failure, hyponatremia, hypoglycemia, hypercapnia and decreased thyroid hormone levels. Our patient had an unclear thyroid history with a very low TSH. She was started on PTU empirically despite low free T4 and hypothyroid symptoms. PTU may also have been responsible for her worsening liver function tests. Hepatotoxicity is a well-recognized adverse reaction to PTU. Other side effects include lupus like syndrome, bone marrow suppression and vasculitis. It is important to monitor for side effects of the medication and confirm the diagnosis prior to starting medication.

Abstract #1108

A RARE CASE OF PAPILLARY THYROID CANCER PRESENTING AS LUNG CANCER

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Larkin Community Hospital

**Case Presentation:**
58 year old female with past medical history of hyperthyroidism status post radioactive iodine therapy, hypertension, dyslipidemia and non-insulin dependent diabetes mellitus presented to the hospital because for the past two weeks she was experiencing numbness in the left side of her mouth. She had a CT angiogram done as part of her hospital workup and incidentally a nodule was identified in the left lower lung. A PET-CT scan done showed intense focal region of increased uptake corresponding to the left lobe noncalcified pulmonary nodule, consistent with an FDG avid malignant process. There was no evidence of regional lymphadenopathy or distant metastasis. The patient then underwent left thoracoscopic biopsy followed by a left thoracotomy. The pathology of the left pulmonary nodule showed a 1cm metastatic carcinoma consistent with papillary thyroid carcinoma that was resected with negative margins. There was no evidence of malignancy in the hilar lymph nodes. The carcinoma was strongly positive for thyroglobulin, HBME-1 and TTF-1. A thyroglobulin level that was checked was 18.3 and thyroglobulin antibodies were 1. Patient had an ultrasound of her thyroid done which showed a right thyroid lobe 1.1x3x0.8cm and the left lobe 0.7x3.2x0.6cm. The isthmus was 3mm. However, what was of concern was a 0.4x0.5x0.4cm hypechoic calcified nodule within the right superior thyroid lobe and two other hypechoic nodules within the bilateral thyroid lobe measuring up to 3mm with internal vascularity. Patient subsequently underwent a total thyroidectomy. Pathology showed a 0.8cm papillary carcinoma of the thyroid without angioinvasion, lymphatic invasion, or
extrathyroidal extension. A sample lymph node that was tested was also free of malignancy. Patient then underwent a whole body iodine scan which showed focal radiotracer uptake in distribution of thyroid bed more so toward the right but no evidence of metastatic disease. She was then treated with radioactive iodine without complications. **Discussion:** Papillary thyroid cancer is the most common thyroid cancer and is more common in woman. Despite the fact it had metastasized to the lung and was at stage IV, it was able to be resected since it was a solitary pulmonary nodule thus improving the patient’s survival. **Conclusion:** This case is unique because it describes the presentation of papillary thyroid cancer presenting as metastasis to the lung as a solitary lung nodule first then leading to the discovery of papillary thyroid cancer within the thyroid. It is important to recognize that patients with papillary thyroid cancer can present with vague symptoms of facial numbness.

**Abstract #1109**

**RECURRENTNE OF THYROTOXICOSIS (GRAVES) AFTER A PROTRACTED PERIOD OF HYPOTHYROIDISM FOLLOWING RAI THERAPY**

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**Objective:** RAI is the most cost effective therapy in treating graves disease when compared with surgery and thionamides. Patient with graves disease who have become hypothyroid after therapeutic RAI, rarely have recurrence of disease. Herein we describe a case of recurrence of thyrotoxicosis after 2-3 year period of hypothyroidism. **Case Presentation:** 48 year old male presented to ER with 2 days of palpitations and chest discomfort. He also lost weight of 30 lbs. Exam was remarkable for rapid and irregular pulse, diffuse thyromegaly and brisk reflexes but no exophthalamos, edema and tremors. Labs showed TSH of <0.004 (0.3-5.6 mIU/ml), FT4 4.96 (0.9-1.8 ng/dl), FT3 12 (1.8-4.7 pg/ml). EKG showed atrial fibrillation with RVR. Radioactive iodine uptake and scan showed a homogenous gland with 54% uptake in 6 hrs and 45% in 24 hrs. He was started on high doses of propanalol and PTU with some clinical improvement. PTU was held a week prior to radioactive iodine ablation. Eight weeks after ablation, he had clinical and laboratory evidence of hypothyroidism and was started on levothyroxine. 2 years after ablation, he had symptoms of hyperthyroidism along with suppressed TSH. The levothyroxine dose was titrated down and eventually stopped. 3 weeks after stopping levothyroxine, he was clearly hyperthyroid with TSH of 0.008 and FT4 of 1.62 and FT3 of 4.8. Uptake showed 17% absorption in 24 hrs. **Discussion:** RAI therapy is highly effective and safe for the permanent control of graves disease and multinodular goiter. RAI will cure 75% to 90% of individuals with GD after a single treatment, a number much greater than the 30% to 50% of remissions induced by ATDs. The cell necrosis induced by radioiodine occurs gradually, and an interval of 6 to 18 wks or longer must elapse before a hypothyroid or euthyroid state is achieved. During that interval, hyperthyroidism may transiently worsen before it resolves. There is 1-6% of transient hypothyroidism followed by recurrent hyperthyroidism. The possible mechanism behind that event is transient radiation thyroiditis superimposed on thyroid gland depleted of thyroid hormone by PTU. Patient with elevated TSH should not to be assumed to be permanently hypothyroid until at least 4 months have been passed without recurrence. But in this case pt was hypothyroid for 2 years before he developed recurrent graves. **Conclusion:** Hyperthyroidism rarely occurs in Graves disease after treatment with relatively large dose RAI and 2 year+ delay in which pt has been hypothyroid both clinically and laboratory wise. Patient with elevated TSH should not to be assumed to be permanently hypothyroid and continuation of outpt followup is clearly indicated.

**Abstract #1110**

**ANATOMIC MIMICRY: TUBERCLE OF ZUCKERKANDL**

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Temple University Hospital

**Objective:** Zuckerkanrdl’s tubercle (ZT) is a distinct anatomical feature of the thyroid gland emerging from the posterolateral margin in the vicinity of the inferior recurrent laryngeal nerve. It has been a standard landmark in surgeons due to its relevance in locating the recurrent laryngeal nerve and parathyroids. Majority of ZT are found by Computed Tomography (CT), however confirmation is generally made through sonography. Accurate recognition as a normal structure rather than a worrisome mass or metastatic lymph node may avoid unnecessary fine needle aspiration biopsy (FNAB). **Case Presentation:** A 40 year old female with no previous medical history presented for evaluation of abnormal thyroid function tests. She noticed weight loss of 35 pounds, heart palpitations, muscle aches, shortness of breath and anxiety. Labs were diagnostic of hyperthyroidism due to Graves’ disease with TSH: 0.001 (0.46-4.7 MIU/L), Free T4: >5.0...
(0.58-1.64), Free T3: 1959 (250-390), TSI: 268 (<140%). Methimazole 20 mg daily and atenolol 25 mg daily were initiated. Thyroid ultrasound (US) showed an enlarged heterogeneous, hypervascular gland with a heterogeneous isoechoic solid mass measuring 2.6 x 1.8 x 1.7 cm arising exophytically from the inferior pole of the right thyroid lobe and a complex spongiform nodule in the lower pole of the right thyroid lobe measuring 1.4 x 1.7 x 1.1 cm. No discrete lesion was seen in the left lobe of the thyroid gland. A CT scan was obtained for further evaluation since there was a suspicion for a possible tubercle of zuckerkandl. The CT confirmed the presence of the right tubercle of zuckerkandl with no other discrete thyroid nodules. The patient did not require an FNAB since this is a benign finding. She will have a repeat ultrasound in a year and continues to be managed for hyperthyroidism with methimazole and atenolol.

**Conclusion:** ZT is an important structure composed of normal thyroid tissue that is not widely recognized as a frequent normal finding on US and CT imaging. Although surgeons have long recognized ZT as a helpful landmark, review of the literature reveals a paucity of imaging examples to guide the interpreter, especially in thyroid sonography. ZT may be mistaken for a thyroid nodule or lymph node leading to unnecessary FNAB in a posterior location close to the recurrent laryngeal nerve. The majority of ZT are incidentally found on CT with several radiologic variations, the nodular subtype as the most common. In this case, our patient was not submitted to FNAB since there was early recognition of this landmark by the use of ultrasound and confirmation by CT. Diagnosis would be improved by greater awareness of the US appearance of ZT among radiologists and endocrinologist.

**Abstract #1111**

**SYNCHRONOUS PAPILLARY THYROID CANCERS ARISING IN STRUMA OVARII AND THE CERVICAL THYROID**

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Yale School of Medicine

**Objective:** We discuss a rare case of synchronous tumors found in struma ovarii and the cervical thyroid.

**Case Presentation:** A 57-year-old woman presented to her gynecologist complaining of right lower quadrant pain. A transvaginal ultrasound showed a 2.8 cm echogenic focus in the right pelvis, felt to be an ovarian dermoid cyst. Given her symptoms, she elected to undergo right oophorectomy and bilateral salpingectomy. Pathology demonstrated a 4 cm struma ovarii containing a 2 cm focus of papillary thyroid cancer. In anticipation of possible adjuvant therapy, an ultrasound of the thyroid was performed, revealing a 1.1 cm hypoechoic nodule that was suspicious for papillary thyroid cancer based on fine needle aspiration. The patient underwent total thyroidectomy and right-sided central neck dissection with final pathology confirming a 1.2 cm papillary thyroid cancer with minimal extrathyroidal extension and no involved lymph nodes. She was started on a suppressive dose of levothyroxine and is scheduled to undergo radioactive iodine therapy.

**Discussion:** Accounting for less than 1% of all ovarian tumors, struma ovarii is defined as an ovarian teratoma comprised of at least 50% mature thyroid tissue. 5-10% of struma ovarii are malignant, most commonly containing papillary thyroid cancer. We conducted a brief literature review of malignant struma ovarii and found no clear consensus on its metastatic potential, recurrence rates, or overall prognosis, resulting in considerable uncertainty as to the best management strategy for this rare disease. Some authors favor surveillance of what they believe to be a rather indolent process, while others advocate for a more aggressive approach involving total thyroidectomy and adjuvant radioactive iodine therapy. Interestingly, an additional focus of papillary thyroid cancer was discovered in our patient’s thyroid. In this case, the absence of metastatic disease in more typical locations such as regional lymph nodes and the presence of normal thyroid tissue in the struma argue against the idea that the ovarian lesion is metastatic from the thyroid or vice versa, and thus more likely represents synchronous disease. When there are multiple foci of malignancy, further clinical management becomes less controversial, as most would agree that radioactive iodine therapy is indicated.

**Conclusion:** Papillary thyroid cancer in struma ovarii is an uncommon disease, and there is no true consensus on appropriate management. Synchronous papillary thyroid cancers presenting in the cervical thyroid and in struma ovarii are exceedingly rare, with only about 10 other cases previously reported, but the appropriateness of adjuvant radioactive iodine therapy may be clearer in this setting.
Abstract #1112

SUGGESTIVE ULTRASOUND FEATURES SHOULD PROMPT CORE BIOPSY IN A CASE WITH RAPIDLY ENLARGING NECK MASS

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Objective: We present a case of Primary Thyroid Lymphoma (PTL), where timely diagnosis and initiation of therapy has achieved a favorable outcome. PTL is a rare type (1-5%) of all thyroid malignancies. Historically noted more with female gender, older age, a rapidly growing painless neck mass and has increased morbidity and mortality if left untreated. It is a heterogenous disease involving a wide spectrum of histological subtypes of malignant lymphoma. Typical history and suggestive ultrasound features should prompt core biopsy and flow cytometry to establish diagnosis.

Case Presentation: A 64 year-old male, with primary hypothyroidism diagnosed 2 years prior and on stable dose of levothyroxine 125 mcg/d with TSH: 1.7-1.9, presented with enlarging neck mass over 2 months and associated with minimal compressive symptoms. Bedside neck ultrasound showed diffusely enlarged thyroid with asymmetric hypoechoic pseudocystic pattern, normal blood flow and a benign looking lymph node in the left side. Fine needle biopsy of the thyroid mass was suspicious for malignancy, and a core biopsy with flow cytometry performed was consistent with Diffuse Large B-Cell Lymphoma (DLBCL).

He was admitted and PET-CT done showed markedly FDG-avid thyroid along with mildly metabolically active cervical lymph nodes. Bone marrow biopsy done for completing staging showed positive involvement. CT chest, abdomen and pelvis were negative for metastatic disease. For stage IV-E DLBCL, he was started on RCHOP and completed 6 cycles of chemotherapy. Post therapy bone marrow biopsy was negative for lymphoma. Thyroid gland size decreased significantly and compressive symptoms resolved. He has been followed periodically and remains in remission.

Conclusion: Primary thyroid lymphoma (PTL) patients present with rapidly enlarging mass in the neck with compressive symptoms on the background of hypothyroidism (most likely Hashimoto’s thyroiditis). An early diagnosis is crucial for initiation of treatment and good prognosis. Ultrasound patterns of the thyroid lymphoma have been documented in some reports as diffuse hypoechoic mass without definitive nodules but description may vary. More recently it was classified as diffuse and nodular or segmental types, based on the distribution of the hypoechoic and echogenic structures within the lesions. It is important to recognize these features in a patient with suggestive history to facilitate the diagnostic process with a core biopsy and flow cytometry instead of regular fine needle biopsy as the treatment is different than other thyroid malignancies. This case underscores the importance of ultrasound and identifying typical characteristics for timely diagnosis and success of the treatment.

Abstract #1113

SUCCESSFUL TREATMENT OF A RARE CASE OF THYROID ACROPACHY OF GRAVES’ DISEASE

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Objective: Graves’ orbitopathy (GO), thyroid dermopathy (also called pretibial myxedema) and acropachy are the extrathyroidal manifestations of Graves’ disease. They occur in 25, 1.5, and 0.3 % of Graves’ patients, respectively. Acropachy occurs only in patients who also have thyroid dermopathy and is almost always associated with thyroid ophthalmopathy as well. Here, we present a very rare case of a 33 y/. old woman with a history of Graves’, dx diagnosed in 2003, with orbitopathy status-post Radioactive Iodine ablation (11/2003) with post-ablative hypothyroidism (01/2004) with previous treatment with IVIG who was managed for thyroid acropachy.

Methods: Patient was managed with high dose Intravenous Methylprednisone and intralesional steroids

Case Presentation: Patient had marked improvement of symptoms.

Discussion: Despite these results, further investigation is needed to better understand the long-term effects of this therapy. Other novel therapies currently being looked into with this patient is Rituximab, which we are currently considering in this patient, in conjunction with our Dermatology service.

Conclusion: Thyroid acropachy is a very rare condition that manifests from thyroid pathology. While steroids still appear to be the mainstay of therapy, novel therapies are emerging for the management of acropachy that may be front-runners for the future.
THYROTOXIC PERIODIC PARALYSIS: ETHNIC DIVERSITY

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Case Presentation: Case 1: 49 Y Hispanic man, with known hyperthyroidism, presented with acute onset of weakness in bilateral upper and lower extremities following an episode of binge drinking. He reported a history of similar episodes for the past 9 months. Hyperthyroidism was diagnosed 7 months ago, though patient had not been adherent to treatment with methimazole (MMI). Physical exam showed an alert, anxious looking patient, and was remarkable for a diffusely enlarged thyroid gland, and flaccid paralysis with hyporeflexia, in all four extremities. Thyroid function tests revealed hyperthyroidism (TSH 0.004 mIU/mL, free T4 7.2 ng/dL and free T3 > 20 pg/mL) and hypokalemia was present with serum potassium level of 1.5 meQ/L. Patient was admitted to the intensive care unit, hypokalemia was corrected judiciously and MMI was started. Motor weakness resolved gradually and patient had full recovery of muscle strength in 16 hours. He was discharged on MMI and propranolol, with instructions to follow up in endocrinology clinic.

Case 2: 43 year old Korean man, was referred to our clinic for recurrent episodes of transient weakness in his legs for the past year. Severity and frequency of episodes was progressive, and eventually patient presented to the emergency department where labs revealed hypokalemia and hyperthyroidism. After potassium supplementation and resolution of weakness, patient was referred to endocrinology clinic. Physical examination in clinic showed a thin man, with a diffusely enlarged thyroid gland, and normal strength in all muscle groups. Thyroid function tests revealed TSH of < 0.01 mIU/mL, Free T4 of 4.2 ng/dL and Free T3 of 13.5 pg/mL. Patient was started on MMI, with subsequent normalization of his thyroid function. Propranolol was added to treatment regimen in the beginning to control symptoms of hyperthyroidism.

Conclusion: TPP, characterized by acute onset of severe hypokalemia and profound proximal muscle weakness in patients with thyrotoxicosis, has highest incidence in Asian countries. However, it is being reported increasingly in the United States and in non-Asian populations, like our patient in case 1. Nearly half of all patients with TPP do not have obvious symptoms of hyperthyroidism. Therefore, it is important to suspect the diagnosis and check thyroid function tests to differentiate it from familial periodic paralysis, since further episodes of paralysis can be prevented by achieving a euthyroid state.

PATIENTS’ KNOWLEDGE REGARDING THE OUT-COMES OF ULTRASOUND GUIDED FINE NEEDLE ASPIRATION BIOPSY FOR THYROID NODULES

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Objective: Ultrasound guided fine needle aspiration biopsy (USFNA) of the thyroid is a pivotal diagnostic procedure during the evaluation of thyroid nodules. Physicians are encouraged to discuss indications, risks and outcomes with patients when recommending diagnostic procedures. To explore this process, we evaluated the patients’ knowledge regarding the outcomes of USFNA.

Methods: A cross sectional survey of patients evaluated in the Thyroid fine needle aspiration clinic between November 2014 and December 2015 was performed. Eligible patients were adults undergoing their first single nodule USFNA and without a previous diagnosis of thyroid cancer. The survey consisted of 8 questions and was completed just after the USFNA.

Results: 297 patients were approached and 199 (67%) completed the survey. The majority of the patients were women (75%), with a mean age of 58 years (SD=13) and with adequate health literacy (78%). Most patients (86%) were able to identify evaluation for thyroid cancer as the main indication for their USFNA. Although most of the patients (79%), reported they were informed that the potential USFNA outcomes included benign and malignant results, only 52% recalled information about the possibility of indeterminate and non-diagnostic results. This correlated with the fact that only a minority of the patients (33%) were aware of the possibility of further diagnostic testing, while 42% was unaware of the need of further follow up in case of benign results.

Most patients (55%) were not aware of their risk for thyroid cancer. The majority (71%) were very concerned about the possibility of a new diagnosis of thyroid cancer as compared to 87% being very concerned if given a new diagnosis of stroke causing disability, 83% for colorectal cancer, 81% for dementia and 52% in the case of diabetes.

Discussion: Although multiple studies have addressed the diagnostic limitations and the perception of physicians regarding our current diagnostic approach for thyroid nodules, the knowledge of patients undergoing this diagnostic pathway has not been explored. Future research should identify interventions to improve patients understanding of outcomes of USFNA.
Conclusion: The majority of patients with thyroid nodules are able to identify the main indication for USFNA. However, they seem to be unaware about the possibility of indeterminate results and need for further testing, their overall risk for cancer and the prognosis of thyroid cancer. The extent to which further engagement of patients in the diagnostic decision process will impact our current approach is unknown.

Abstract #1116

THYROTOXIC HYPOKALEMIC PERIODIC PARALYSIS

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Objective: Thyrotoxic hypokalemic periodic paralysis (THPP) is a rare, though potentially lethal manifestation of hyperthyroidism characterized by severe muscle paralysis and hypokalemia. We report the case of a 47-year-old Asian man who was seen in clinic for thyrotoxicosis and refused treatment due to cultural beliefs. He presented a few weeks later to the Emergency Department (ED) with THPP.

Case Presentation: A 47-year-old Hmong male presented for evaluation of 20 lbs of unintentional weight loss. Initial labs revealed suppressed TSH < 0.03 mIU/mL and elevated Free T4 and Free T3 of 2.04 ng/dL and 5.0 pg/mL, respectively. Further workup showed diffusely elevated uptake of 33% on Nuclear Medicine uptake and scan, evident of Graves’ disease. He was offered treatment but he refused due to his cultural and spiritual beliefs. Four weeks from the initial visit, he presented to the ED with progressive muscle weakness. Physical exam was significant for tachycardia, systolic hypertension, hypotonia of lower extremities and absent deep tendon reflexes. Initial labs showed severe hypokalemia with potassium of 1.8 mEq/L (3.5 to 5.1) causing periodic paralysis. He was also found to have an HbA1c of 12%, diagnosing new onset diabetes. He was given IV and PO potassium supplementation with slow improvement of serum potassium to normal at 4.1 on discharge, as well as resolution of muscle weakness. He also received IV beta-blockers for hyper-adrenergic state. He was offered treatment for hyperthyroidism and diabetes but he refused again for similar reasons.

Discussion: THPP has been mostly reported and studied in Asians, in whom the incidence amongst patients with hyperthyroidism is approximately 2%, of which 95% of the cases occur in men. The pathophysiology is proposed to be due to excess of thyroid hormones predisposing to paralytic episodes, by increasing the susceptibility to the hypokalemic action of epinephrine and insulin. The treatment must be performed with immediate potassium supplementation which prevents severe cardiopulmonary complications and can accelerate recovery from muscle weakness. Additionally, non-selective beta-blockers can relieve and prevent the recurrence of episodes of paralysis. In addition to these measures, it is necessary to control hyperthyroidism using anti-thyroid drugs, radioactive iodine or surgery.

Conclusion: THPP is a rare endocrine emergency. The events that lead to paralysis in patients with THPP are complex and include hyperthyroidism, a genetic/racial predisposition, a hyper-adrenergic state and an exaggerated insulin response. Adequate and timely treatment of hyperthyroidism is mandatory and its definitive treatment should be recommended to prevent further crises.

Abstract #1117

NIVOLUMAB INDUCED THYROIDITIS, A CASE SERIES

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Objective: Nivolumab is a human immunoglobulin G4 (IgG4) anti-PD-1 monoclonal antibody, approved for the treatment of advanced non-small cell lung cancer, renal cell carcinoma and melanoma. Nivolumab has only recently been found to be associated with case reports of thyroiditis in combination with ipilimumab, interferon-alpha, bevacizumab or fotemustine. An exact mechanism of nivolumab-induced thyroiditis is unclear but has been speculated to be autoimmune activation. We present two cases of thyroiditis occurring in patients recently started on nivolumab without concomitant immunomodulator therapy.

Case Presentation: Case #1 is a 47-year old female with a history of metastatic triple-negative breast cancer treated with RRX-001 (a novel anticancer agent) and nivolumab, who developed clinically significant hyperthyroidism two weeks after the start of chemotherapy. Patient had a suppressed TSH and elevated free T4 for nearly 2 months. Patient has positive thyroid peroxidase (TPO), thyroglobulin (TG) but negative TSH receptor (TSR) antibodies. Patient remains on nivolumab therapy with normalization of TSH and free T4 one month from thyroiditis. Case #2 is a 91-year-old female with a history of metastatic melanoma treated with nivolumab, who developed subclinical hyperthyroidism 3 months after the start of chemotherapy. Patient had a suppressed TSH for nearly 3 months with diffusely decreased uptake to 2% at four hours on thyroid uptake and scan. Patient has negative TSR, TPO, TG antibodies. Patient remains on nivolumab...
therapy with most recent free T4 of 0.86 ng/dL and a TSH of 0.573 mIU/mL two weeks from thyroiditis.

Discussion: To the best of our knowledge, this is the first report that shows nivolumab monotherapy may induce hyperthyroidism with no evidence of pre-existing autoimmunity. We suspect case two experienced a case of destructive thyroiditis, similar to the effect seen with type 2 amiodarone-induced thyroiditis. This also may be the first report of nivolumab and RRX-001 induced autoimmune thyroiditis. Case reports, while limited, noted variable progression in disease course with most cases resolving within 1-3 months without toxic therapies.

Conclusion: Antithyroglobulin and antithyroid peroxidase antibodies, a thyroid uptake and scan and close monitoring of thyroid function are recommended during the evaluation of nivolumab-induced hyperthyroidism.

Abstract #1118

GRAVES DISEASE PRESENTING AS IMPENDING THYROID STORM FOLLOWING NON THYROIDAL SURGERY: A LATE MANIFESTATION OF IMMUNE RESTORATION IN HIV

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Objective: Immune Restoration Disease (IRD) is an established phenomenon in patients infected by Human Immunodeficiency Virus (HIV) and presents within weeks to months after anti-retroviral therapy (ART) initiation. IRD manifests in cases of Acquired Immunodeficiency Syndrome as an overwhelming inflammatory response to opportunistic infections. Preexisting autoimmune disorders, such as Graves’ disease (GD) or autoimmune hypothyroidism, may be exacerbated. We present a case of Graves’ thyrotoxicosis with impending thyroid storm, a rare but known complication of IRD.

Case Presentation: 50 year old man with HIV presented 12 months after ART initiation. His CD4 count had improved from 172 cells/μL to 275 cells/μL and viral load was undetectable. The patient underwent sinus surgery complicated by pneumoceles, treated by a second surgery. Post-operatively he developed high grade fever, tachycardia and leukocytosis. Broad-spectrum antibiotics minimally abated fevers and leukocytosis. Tachycardia persisted despite beta-blockade, and neurological status declined to delirium. Thyroid function testing revealed low thyroid stimulating hormone level (0.1MIU/mL) and elevated free thyroxine level (5.17ng/dl). Increased thyroid stimulating immunoglobulins (234%) and thyroid peroxidase antibodies (164 IU/ml) supported the diagnosis of autoimmune thyroid disease. The patient was diagnosed with Graves’ disease, with impending thyroid storm. Prompt initiation of methimazole, high dose steroids, propranolol followed by potassium iodide resulted in effective clinical response. Liver toxicity precluded ongoing methimazole therapy. The patient then underwent total thyroidectomy. Thyroid hormone replacement was thereafter initiated. This is the first known case of GD presenting as impending thyroid storm, a manifestation of IRD.

Discussion: IRD after initiation of ART has the potential to induce an altered T-cell repertoire resulting in aberrant and exaggerated response to subclinical infection and/or autoimmune predisposition. The preexisting disturbance in T-cell profile and preponderance for proinflammatory state associated with cytokine dysregulation, may be the primary pathogenesis for IRD. In patients on ART, unmasking autoimmune disorders, such as Graves’ disease, can have potentially life-threatening implications, if untreated.

Conclusion: Graves’ disease presenting as impending thyroid storm is a rare but potentially life-threatening manifestation of IRD in patients on ART. In this patient population, frequent monitoring of thyroid hormone levels may permit early identification and prompt treatment of thyroid dysfunction.

Abstract #1119

NIVOLUMAB-INDUCED THYROID DYSFUNCTION

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Objective: Immune checkpoint inhibitors have been developed to treat malignancies such as melanoma and non-small cell lung cancer (NSCLC). Nivolumab is a monoclonal antibody against programmed cell death-1 (PD-1) receptor. We report 3 cases of nivolumab-induced thyroid dysfunction.

Case Presentation: Case 1 is a 63 year old female with stage 4 NSCLC metastatic to the brain, who, after receiving two cycles of nivolumab, developed subclinical hyperthyroidism, which then progressed to overt hyperthyroidism. She complained of hot flashes. Treatment with prednisone 0.5 mg/kg was initiated, which was tapered over two weeks and stopped. Labs reverted to overt hypothyroidism and levothyroxine replacement was initiated. Case 2 is a 62 year old male with stage 4 NSCLC metastatic to the bone, who developed overt hyperthyroidism after receiving two cycles of nivolumab. Thyroid peroxidase (TPO) antibody was elevated. His symptoms were anxiety and insomnia. Thyroid uptake and scan could not be performed due to intermittent iodinated contrast exposure for monitoring the cancer.
Labs reverted to overt hypothyroidism and levothyroxine replacement was initiated. Case 3 is a 53 year old female with stage 4 NSCLC metastatic to the brain who developed subclinical hyperthyroidism after receiving two cycles of nivolumab. TPO and thyroid stimulating immunoglobulin (TSI) antibodies were negative. Patient was managed conservatively. Repeat labs revealed euthyroidism. In all the three patients, baseline thyroid function was normal and nivolumab was discontinued upon detection of thyroid dysfunction. In patient 3, nivolumab was resumed after patient attained euthyroidism.

Discussion: Immune checkpoint proteins such as PD-1 help to maintain immune homeostasis by down-regulating T-cell signaling. Blockade of this immune checkpoint can lead to breaking of immune self-tolerance, thereby resulting in autoimmune side effects, which may affect endocrine glands such as the thyroid, pituitary or adrenals. The reported incidence of nivolumab-induced thyroid dysfunction is 1-3%. Treatment involves corticosteroids for hyperthyroidism and hormone supplementation for hypothyroidism.

Conclusion: Immune checkpoint inhibitors may cause clinically significant endocrine dysfunction. The reason why some individuals are predisposed to nivolumab-induced thyroid dysfunction is currently unknown. Thyroid uptake and scan may help guide management in those with hyperthyroidism.

Abstract #1120

COEXISTING PAPILLARY THYROID CANCER AND SARCOIDOSIS - A COINCIDENTAL OR CAUSAL CORRELATION?

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Objective: Sarcoidosis (SA) is a systemic inflammatory disease of unknown etiology characterized by non-necrotizing epithelioid granulomata causing pulmonary, ocular and skin symptoms in >90% of patients. Direct involvement of thyroid gland with SA is rare and is seen in 4% of cases. SA has been associated with increased risk of malignancy and there are a few case reports of papillary thyroid cancer (PTC) in association with SA. We report herein a case of coexisting PTC and SA involving the thyroid gland presenting as cervical lymphadenopathy, unveiling the diagnosis of systemic SA.

Case Presentation: 59 year old female with history of hypothyroidism and pulmonary nodules was referred for evaluation of left thyroid density and cervical lymphadenopathy. Patient had computerized tomogram (CT) scan of the chest for pulmonary nodules surveillance, which showed interval increase in nodules, hepatomegaly and multiple splenic lesions. Positron emission tomography CT scan showed cervical, mediastinal, retroperitoneal lymphadenopathy and patchy skeletal uptake suggestive of metastatic involvement. Upper GI endoscopy followed by flexible laryngoscopy was normal. Neck ultrasound showed 8 x 7 mm partially calcified lesion in the left thyroid lobe and a calcified cervical adenopathy. Fine needle aspiration of right cervical lymph node showed malignant cells and elevated thyroglobulin of 111 in needle washing suggestive of PTC. Patient underwent total thyroidectomy with selective neck dissection. Pathology revealed multiple foci of PTC with background lymphocytic thyroiditis and incidental finding of non-necrotizing granulomata within the thyroid, and nodal involvement with metastatic PTC and non-necrotizing granulomatous lymphadenitis. She was diagnosed with concomitant systemic SA.

Conclusion: The association between SA and thyroid disease remains unknown despite various hypotheses. SA has been reported in association with hypothyroidism in 5.3% and Graves’ disease in 4% of female patients. PTC has been described in association with SA in less than a dozen case reports. This association poses a diagnostic challenge during workup of cervical lymphadenopathy due to comparable prevalence and clinical presentations. It is important to recognize this, as the presence of one disease may lead to premature closure and preclude the diagnosis of the other. Thyroid autoimmunity has been recognized in 17% of SA cases. Histopathological evidence of SA is seen in 4-14% of all patients with malignancy. Whether the association between PTC and SA is due to increased autoimmunity, inherent risk of malignancy with SA, or is incidental remains unclear and requires additional studies.

Abstract #1121

EVALUATION OF VARIOUS PRACTICE GUIDELINES FOR MANAGEMENT OF THYROID NODES AND CLINICAL OUTCOMES

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Objective: Fine-needle aspiration (FNA) biopsy is the standard of care for work-up of thyroid nodules. Various practice guidelines for management of thyroid nodules are published, two being those by the American Thyroid Association (ATA) and those by the American Association of Clinical Endocrinologists (AACE). Few studies have reported how patients with thyroid nodules are managed in accordance with the clinical guidelines and their outcomes. We evaluated the difference between the AACE
and ATA 2009 guidelines in determining necessity for FNA-guided biopsy of thyroid nodules and to evaluate the adherence to those guidelines.

**Methods:** A retrospective chart review was conducted at a Midwest academic medical center between January 2010 and December 2011. Results of 273 biopsies were randomly selected for evaluation. We assessed clinical measures for each nodule, including family history, TSH value, I-scan result, and US results. We identified which nodules underwent UGFNA, biopsy results, and the surgical pathology. Using both AACE and ATA guidelines, we then determined which nodules met each of those criteria for UGFNA biopsy.

**Results:** Of the 273 nodules that underwent UGFNA, 221 were benign, 36 were follicular neoplasm, 3 were suspicious, and 4 were malignant. Based on the ATA criteria, 59% of the nodules met the recommended guidelines for FNA, and 41% of nodules biopsied met AACE guidelines for FNA. A greater discrepancy was noted with follicular nodules and those suspicious for malignancy. In follicular nodules, biopsy criteria was met 61% of the time by ATA and 50% of the time by AACE guidelines. Of the 3 nodules suspicious for malignancy, 2 met ATA criteria, while 0 met AACE criteria. Both ATA and AACE criteria were met 100% of the time in malignant nodules.

**Discussion:** The ATA guidelines for thyroid biopsy include clinical history and nodule size and features on US. There are recommendations for solid and mixed nodules and criteria for hypoechoic, isoechoic, and hyperechoic nodules. In comparison, the AACE criteria include solid hypoechoic nodules >1cm, and nodules with microcalcifications, irregular margins, abnormal lymph nodes, and high risk history. Even with these criteria, some malignant lesions can be missed, and a greater discrepancy occurs with suspicious or follicular nodules.

**Conclusion:** There are multiple divergences between ATA and AACE guidelines for evaluation of thyroid nodules. ATA has specific guidelines in terms of sonographic findings. AACE focuses on specific sonographic features, making other data points more susceptible to interpretation. Both guidelines seem to identify benign and malignant nodules, but clinical judgment must be used on those nodules that may be suspicious.

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**Abstract #1122**

**USE OF PLASMAPHERESIS AS A BRIDGE TO THYROIDECTOMY IN SEVERE AMIODARONE-INDUCED THYROTOXICOSIS**

Marcos Lamas, Dawn Davis, Rahul Sharma

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**Objective:** Increase awareness of the use of plasmapheresis as a bridge to thyroidectomy in Amiodarone-Induced Thyrotoxicosis (AIT) refractory to medical therapy.

**Case Presentation:** We present the case of a 67 year-old man with primary cardiomyopathy, paroxysmal atrial fibrillation/atrial flutter/ventricular tachycardia status post automatic implantable cardioverter-defibrillator, and hypertension. He had been on amiodarone for the last 2 years. Over a 3 month period, he noted worsening palpitations, fatigue, dysphagia, hoarse voice, 40 pound weight loss, anxiety, and insomnia. Laboratory results revealed a suppressed TSH (<0.005 mIU/mL) and elevated free T4 (5.36 ng/dL). A diagnosis of AIT was made. Interleukin-6 was normal (2.89 pg/mL) and no hypervascularity was noted on thyroid ultrasound. Methimazole 20mg twice daily and prednisone 40mg/day were started. Amiodarone was continued given his severe arrhythmias. Thyroid hormone levels continued to rise (Free T3: 12.57 pg/mL and Free T4: > 8.0 ng/dL), prompting an increase in the methimazole to 40mg twice daily and prednisone to 60 mg/day. Lithium (300 mg three times daily) was also started. His clinical status continued to worsen, so he was hospitalized with persistent thyrotoxicosis. Amiodarone was continued given his severe arrhythmias. Thyroid hormone levels continued to rise (Free T3: 12.57 pg/mL and Free T4: > 8.0 ng/dL), prompting an increase in the methimazole to 40mg twice daily and prednisone to 60 mg/day. Lithium (300 mg three times daily) was also started. His clinical status continued to worsen, so he was hospitalized with persistent elevation in thyroid hormone levels (Free T3 was 8.41 pg/mL and Free T4 remained >8.0 ng/dL). Liver function tests were elevated on admission (AST: 314 U/L, ALT: 711 U/L, Bilirubin: 5.4 mg/dl, Alkaline Phosphatase: 370 U/L, and GGT: 937 IU/L). This was likely secondary to methimazole-induced cholestasis and hepatitis. Despite this, it allows rapid clearing of both amiodarone and thyroid hormones from the circulation, and should be considered in patients refractory to medical therapy or in whom thionamides are contraindicated. The effects are usually transient but
create a window of opportunity to perform surgery safely for definitive treatment.

**Conclusion:** Plasmapheresis should be considered in the treatment of severe, refractory Hashimoto’s thyroiditis as a bridge to thyroidectomy.

**Abstract #1123**

**UNINTENDED CONSEQUENCES: ENDOCRINE COMPLICATIONS OF PROGRAM DEATH-1 RECEPTOR INHIBITORS**

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**Objective:** To describe 2 patients presenting with endocrine adverse effects after cancer treatment with a program death-1 (PD-1) receptor inhibitor.

**Case Presentation:** Case 1. A 77-year-old African-American male was admitted to the hospital for shortness of breath, fatigue, and fever with history of recent hospitalization for pleural effusion, which was drained without incident. TSH was suppressed at 0.007 UIU/ml. Further questioning did not elucidate a reason for abnormal thyroid function. He had been undergoing treatment for recurrent non-small cell lung carcinoma with nivolumab (Opdivo). Follow-up testing showed free T4 1.77 ng/dl and total T3 2.93 ng/dl. Bedside ultrasound revealed a normal thyroid with decreased blood flow. TSH two years prior was 1.200 UIU/ml. Extensive investigation found no cause for thyroiditis except for nivolumab.

Case 2. A 73-year-old Caucasian female was referred for abnormal thyroid function after she was started on nivolumab. Thyroid function after starting nivolumab was TSH 1.60 IUU/ml, total T4 16.2 ng/dl, and total T3 169 ng/dl. The patient presented with fatigue, thin hair, and enlarged thyroid with a palpable nodule in the right lobe. Thyroid uptake and scan demonstrated a multinodular goiter with a hypofunctioning nodule. Two days later tests showed TSH 1.230 IUU/ml, free T4 2.02 ng/dl, and total T3 15.5 ng/dl. Anti-thyroid peroxidase antibodies were 43 IU/ml. Nodule biopsy findings were consistent with Hashimoto’s thyroiditis.

**Discussion:** PD-1 is a key immune checkpoint pathway that regulates the immune response to microbes while maintaining self-tolerance. PD-1 ligands 1 and 2 (PD-L1 and PD-L2) are expressed broadly in the thymus. When an immature T cell is activated, the PD-1 receptor is upregulated. The interaction between antigen presenting cells, which express PD-1 ligands, and immature T cells with high levels of surface PD-1 expression, will determine if the cell will be stimulated to reproduce or inhibited to die. PD-1 inhibitor medications are used in cancer treatment because some cancer cells have an upregulated expression of PD-1 ligands. However, PD-1 pathway inhibition decreases tolerance both to cellular antigens from the host’s tissue and to those from cancer cells. Prior studies have reported development of autoimmune thyroid disease in as many as 10% of patients treated with these drugs.

**Conclusion:** Unmasking or causing of autoimmunity is a potential side-effect of use of PD-1 receptor inhibitors in cancer. These medications are likely to be used more frequently in treating other types of cancer. These case reports suggest that clinicians should be aware of possible endocrine side-effects of these medications, including silent thyroiditis.

**Abstract #1124**

**A CASE REPORT OF THYROID CARCINOMA SHOWING THYMUS LIKE DIFFERENTIATION (CASTLE)**

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**Case Presentation:** 45 yo woman scheduled for parathyroid exploration due to primary hyperparathyroidism. Pre-operative thyroid u/s reported a 27 mm hypoechoic solid nodule in the inferior pole of the left thyroid lobe. She had a right upper parathyroid adenoma removed. The remaining parathyroid glands were normal. During the surgery it was noted that she had an exophytic left lower thyroid mass, which excised and sent to pathology. A left thyroid mass, 9.1g, 35x25x15mm, oval pink tissue encapsulated with a thin fibrous membrane. Immunohistochemical studies demonstrated immunoreactivity for CK 903, CK 5/6, p63, pankeratin, p16, synaptophysin, CK7, CD5, CD 117, BCL-2, monoclonal CEA. Being non-reactive for calcitonin, chromogranin, TTF-1, thyroglobulin, CKD 20 and MOC31. Studies for Epstein Barr virus were negative. Congo red stain negative for amyloid deposition. The slides were sent for review with final diagnosis of Carcinoma showing thymus-like differentiation (CASTLE) with lymph/vascular invasion and extrathyroidal extension. Based on current recommendations this patient underwent total thyroidectomy and neck exploration. Surgical pathology was negative for residual thymic like carcinoma. This case is being reviewed for possible external radiation.

**Discussion:** Thyroid carcinoma showing thymus-like differentiation (CASTLE) is a rare tumor of the thyroid gland or adjacent soft tissues of the neck. During embryological development, thymic tissue derived from the 3rd and 4th brachial pouches migrates through the neck into the mediastinum. Persistence of thymic remnants along the pathway can manifest as ectopic thymic tissue. CASTLE arises either from this ectopic
Abstract #1125

IT IS THE WORK OF A HIGHER POWER – AN UNUSUAL PRESENTATION OF ISOLATED CENTRAL HYPOTHYROIDISM

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Objective: Central hypothyroidism (CH) is a rare cause of hypothyroidism generally related to a hypothalamic-pituitary disorder or an iatrogenic complication. It affects both men and women equally but its incidence is probably underestimated (1). It frequently presents as an acquired CH in adults (1, 2). We present here an unusual case of isolated CH without obvious underlying hypothalamic-pituitary insult.

Case Presentation: A 43 y/o F with history of bipolar disorder presented with palpitations, insomnia and anxiety of a few years’ duration. Her medications were trazodone, quetiapine and alprazolam. She had a prior thyroid ultrasound indicative of multinodular goiter. She was initially diagnosed with subclinical hyperthyroidism with TSH-0.23mIU/l (0.4-4.5), free T4(FT4)-0.8ng/dl(0.8-1.8),free T3-2.9pg/ml(2.3-4.2). She was intermittently placed on methimazole before being referred to us. She continued to be symptomatic with TSH-0.14, FT4-0.7, total T3–53 ng/dl(76-181) off methimazole. TSI and TPO were negative. On repeat measurements TSH was 0.14-0.33, FT4 0.7-0.8 and totalT3 47-70 for next 6 months. TSH did not rise above normal when this patient was made iatrogenically hypothyroid on methimazole; TSH-0.31, FT4-0.7, T3-49. This seemed to represent secondary hypothyroidism with superimposed hyperfunctioning nodular goiter. Other pituitary hormones were checked and found to be normal; ACTH-10pg/ml(6-50),Cortisol stimulation test 12,27,32 mcg/dl at baseline,30 and 60 minutes respectively, Estradiol–129pg/ml,Prolactin–3.3ng/ml. She denied prior head trauma, surgery, radiation or steroids. Pituitary MRI was normal. NM thyroid uptake scan showed 2-hour uptake = 6% and 24-hour uptake = 19% (overall normal); heterogenous uptake with functioning nodules. Antipituitary antibodies to rule out autoimmune insult to the pituitary gland are currently pending. She will be treated with a trial of levothyroxine to keep FT4 in midnormal range.

Conclusion: Central hypothyroidism is a difficult disorder to diagnose clinically as it has nonspecific symptoms and is less intense due to possible constitutive activity of TSH receptors or other mechanisms of thyroid hormone synthesis independent of TSH (1, 2, 3). Furthermore isolated CH is rare in adults. Hormonal diagnosis is based on a low free T4 concentration with low, inappropriately normal or even high TSH (1,2,4,5). TRH stimulation test confirms the diagnosis (not available in US). This case highlights the necessity to consider CH as a possible diagnosis in cases with borderline low TSH and low to normal FT4 levels, even in the absence of clear hypothalamic-pituitary insult as there might be a contiguous hyperfunctioning MNG.

Abstract #1126

EFFECTS OF INCREASING LEVOTHYROXINE ON PREGNANCY OUTCOMES IN WOMEN WITH UNCONTROLLED HYPOTHYROIDISM

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Objective: Uncontrolled hypothyroidism has been associated with an increased risk of adverse pregnancy outcomes. Our aim was to assess the effectiveness of increasing levothyroxine (LT4) therapy on reducing the risk of adverse outcomes for pregnant women with TSH level greater than the recommended 1st trimester limit.

Methods: We retrospectively reviewed the electronic medical records of pregnant women evaluated from January 2011 to December 2013, who had history of LT4-treated hypothyroidism and were found to have TSH > 2.5 mU/L in 1st trimester. Women were divided into two groups; group A-LT4 dose was increased within 2 weeks from the TSH test, group B-LT4 dose remained stable. Women were followed until pregnancy loss or post-partum visit. We excluded subjects with twin pregnancy or use of medications affecting thyroid function. We compared the
rate of pregnancy loss (primary outcome) and other pre-specified adverse outcomes between groups.

**Results:** There were 85 women in group A (median TSH: 5, interquartile range 3.8-6.8 mU/L) and 11 in group B (median TSH: 4.5, interquartile range 3.2-4.9 mU/L). The groups were not different regarding age, BMI, history of pregnancy loss, smoking status, or TPO-antibody positivity. The mean interval between TSH test and LT4 dose increase was 4.2 days. There was a significant decrease in pregnancy loss in group A (2/85, 2.3%, mean gestational age: 13.7 weeks) vs. group B (4/11, 36.4%, mean gestational age: 7.4 weeks) (p<0.01). There was no significant difference between the two groups in the rates of: preterm delivery, gestational diabetes, gestational hypertension, pre-eclampsia, premature rupture of membranes, intrauterine growth restriction, placenta previa, placenta abruption, neonatal death, low birth weight, Apgar score ≤ 7 at 5 min, or congenital malformations.

**Discussion:** Recent data suggest that the majority of LT4-treated women have early gestational TSH levels above the recommended goals with a high risk of miscarriage especially if TSH is >4.5 mU/L. Our study found an association of increasing LT4 dose in 1st trimester of pregnancy with decreased risk of pregnancy loss, however no difference was found in other maternal and neonatal outcomes. Given the limitations of our study, this association awaits further confirmation in larger studies that will also establish the optimal TSH target during pregnancy.

**Conclusion:** Increasing LT4 dose to improve the adequacy of thyroid hormone replacement for uncontrolled hypothyroidism during pregnancy is associated with a potential decreased risk of pregnancy loss.

**Abstract #1127**

**HYPERCOAGULABILITY IN A PATIENT WITH OVERT HYPERTHYROIDISM**

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**Objective:** Hyperthyroidism has been associated with hypercoagulability by various mechanisms. However, whether hyperthyroidism is a true contributing factor for hypercoagulable state is not yet well known.

**Case Presentation:** A 30 year old female with untreated Hyperthyroidism presented with dyspnea. She had noted goiter, heat intolerance, palpitations, anxiety & increased appetite x 3 years. She had not sought medical attention until recognizing pregnancy at 6 weeks gestation. She had spontaneous abortion at 9 weeks gestation, presenting 1 week thereafter with cough, diarrhea, & acute onset of dyspnea. On presentation she was in respiratory distress, HR 106, O2 sat 86 % on RA & afebrile. She was found to have goiter, proximal myopathy, tremor & bilateral diffuse crackles on chest exam. Chest CT showed pulmonary edema. TSH was suppressed <0.01mU/ml (0.45-4.50) and 1.57 (nl. 0.60-1.30), respectively. Propylthiouracil was changed to methimazole 20 mg daily. Pregnancy work-ups including a variety of tumor markers and computed tomography of chest, abdomen, pelvis as well as head were negative without evidence for internal malignancy or adenopathy. Extensive hypercoagulable investigations including protein C, S deficiency, fibrinogen level, factor V mutation, anti-thrombin III activity, prothrombin gene mutation, paroxysmal nocturnal hemoglobinuria, JAK2 gene mutation, serum homocystein level, cardiolipin antibody, antinuclear antibody, antiphospholipid antibody, and beta 2 glycoprotein were all unremarkable except that factor VIII activity was elevated at 397% (nl. 69 – 212). Approximately 2 months later, factor VIII activity decreased down to 212% as he became biochemically euthyroid with TSH and free T4 of 2.72 and 0.72, respectively.

**Conclusion:** This case demonstrated sustained but transient elevation of factor VIII activity with overt hyperthyroidism. The elevation in factor VIII resolved with hyperthyroidism treatment suggesting a causative association between hyperthyroidism and the elevation in factor VIII activity. Though hyperthyroidism is not well recognized as a risk factor for DVT and PE, screening for hyperthyroidism may be considered in thrombophilia cases.

**Abstract #1128**

**PULMONARY HYPERTENSION: AN UNDER-RECOGNISED SEQUELA OF GRAVES’ THYROTOXICOSIS WITH ACUTE PULMONARY EDEMA.**

Shailesh Baral, MD, Michael Jakoby, IV, MD/MA, Rama Poola, MD, Carmel Fratianni, MD, FACE

Southern Illinois University School of Medicine

**Case Presentation:** 30 year old female with untreated Hypertension presented with dyspnea. She had noted goiter, heat intolerance, palpitations, anxiety & increased appetite x 3 years. She had not sought medical attention until recognizing pregnancy at 6 weeks gestation. She had spontaneous abortion at 9 weeks gestation, presenting 1 week thereafter with cough, diarrhea, & acute onset of dyspnea. On presentation she was in respiratory distress, HR 106, O2 sat 86 % on RA & afebrile. She was found to have goiter, proximal myopathy, tremor & bilateral diffuse crackles on chest exam. Chest CT showed pulmonary edema. TSH was suppressed <0.01mU/ml (0.45-4.50), Free T4 was elevated 3.1* ng/ml (0.9 – 1.5). TSH Receptor
ABSTRACTS – Thyroid Disease

Antibody 12* (0.0 – 1.75). Echocardiogram showed mildly depressed left ventricular systolic function with EF 41% with severe Pulmonary Hypertension (PHT) with Peak pulmonary artery systolic pressure of 66* mmHg (Normal: 15-25 mmHg). USG Thyroid showed hypervascularity with diffusely heterogeneous echogenicity & no discrete nodularity. Transvaginal USG and falling HCG levels excluded molar pregnancy. Patient had acute pulmonary edema & Severe PHT with impending Thyroid storm from untreated Graves’ disease likely precipitated by spontaneous abortion. She responded well to Methimazole, SSKI, Beta blocker & Diuretics.

Discussion: Our case highlights that Hyperthyroidism itself is an under-recognized cause of PHT. Moreover, PHT is usually reversible with anti-thyroid treatment. Prevalence of PHT in hyperthyroidism has been reportedly as high as 35 – 47% although patients are often largely asymptomatic from the PHT. (Marvisi, et al.; Siu et al.) The prevalence of PHT is higher than generally recognized in hyperthyroid patients. While the mechanisms of this are unclear, proposed etiologies includes: a) Autoimmune damage b) Increased cardiac output mediated pulmonary endothelial damage. c) Sympathetic outflow induced decreased pulmonary vasculature compliance and d) Accelerated metabolism of intrinsic pulmonary vasodilators (Nitric oxide & Prostacyclin) or decreased metabolism of vasoconstrictors (ET1, serotonin, thromboxane).

Conclusion: All patients with PHT should be screened for hyperthyroidism as a treatable cause of PHT. In a hyperthyroid patient, clinicians should forestall further diagnostic interventions for PHT (such as Right heart catheterization) until thyrotoxicosis has been definitively treated as PHT may improve with this, avoiding unnecessary interventions and side effects from PHT treatment.

Abstract #1129

THE GOOD AND BAD OF “THE GOOD CANCER”

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University of Wisconsin

Objective: Papillary thyroid cancer is often described as the “Good Cancer” because of its treatability and relatively favorable survival rates, but this terminology minimizes the difficulties patients face in dealing with this diagnosis. We sought to characterize the thoughts of patients with papillary thyroid cancer as they relate to having the “Good Cancer.”

Methods: This qualitative study included 31 papillary thyroid cancer patients enrolled in an ongoing randomized clinical trial. We conducted semi-structured interviews with each patient at initial consultation and again at 2 weeks, 6 weeks, and 6 months after surgery. We used modified grounded theory, thematically coding the first 84 transcripts with Nvivo.

Results: The concept of thyroid cancer being “the good cancer” emerged unprompted from 84% of patients (n=26) and was most heavily concentrated around the time of diagnosis. Patients hear this perception from healthcare providers, internet research, and the general public, through words like lucky, easy, and ‘the cancer to have.’ While patients with thyroid cancer generally appreciate the optimistic outlook, this idea often creates both psychological and social conflicts. It eases the diagnosis but invalidates the fears and concerns associated with having a cancer diagnosis. Others feel simultaneously lucky and guilty as they see loved ones fighting more aggressive cancers. Patients’ discussions with treating physicians at diagnosis are reassuring. In contrast, anecdotes from family and friends based on their peripheral knowledge of thyroid cancer are dismissive. Although intended to be encouraging, these comments downplay the effect of thyroid cancer on patients’ lives and actually leave them feeling a lack of support. Thyroid cancer patients do not want to hear that it’s “only thyroid cancer” and that it’s “no big deal,” because “cancer is cancer” and it is a big deal.

Discussion: Patients with papillary thyroid cancer are commonly confronted with the perception that their malignancy is “the good one,” but a favorable prognosis and the treatability of the disease do not comprehensively represent their fight against cancer. Furthermore, the “good cancer” perception is at the root of many psychological and social conflicts that arise while coping with the diagnosis. Clinicians emphasize excellent survival rates hoping to comfort patients, but may inadvertently invalidate the impact thyroid cancer has on patients’ lives.

Conclusion: Clinicians portraying thyroid cancer as the “good” cancer can be reassuring to patients at diagnosis, but this point should not be overemphasized as it seems to minimize the life-changing impact of a cancer diagnosis.
Abstract #1130

AN UNUSUAL NEUROENDOCRINE TUMOR OF THE THYROID

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Texas Tech University Health Sciences Center Paul L. Foster School of Medicine

Objective: Important alternative diagnoses exist for medullary thyroid carcinoma although they are extremely rare. We report a case of calcitonin negative neuroendocrine thyroid tumor of follicular origin that was initially thought to be medullary thyroid carcinoma.

Case Presentation: A 74 year old female presented due to voice hoarseness and difficulty swallowing liquids. Bilateral thyroid nodules were discovered on ultrasound and FNA was suspicious for malignancy, in particular medullary thyroid carcinoma. After total thyroidectomy, pathology revealed positive staining for neuroendocrine markers chromogranin A and synaptophysin and for follicular marker thyroid transcription factor-1. There was negative staining for calcitonin, a diagnostic requirement for medullary thyroid carcinoma. For this reason, the tumor was diagnosed as a calcitonin negative neuroendocrine thyroid tumor of follicular origin.

Discussion: Only 3 cases of calcitonin negative neuroendocrine thyroid tumors of follicular origin have previously been reported. Two of these case reports separately described incidentally identified thyroid nodules that were consistent with calcitonin negative neuroendocrine tumors of follicular origin. Additionally, a case of a small cell neuroendocrine carcinoma of the thyroid which demonstrated positive neuroendocrine and follicular markers and negative calcitonin has been reported. Two other cases identified as calcitonin negative neuroendocrine thyroid tumors have been described in the literature, however both stained negative for thyroglobulin implying they were not of follicular origin. One of these reported cases described a calcitonin negative neuroendocrine tumor of the thyroid that had initially been diagnosed as anaplastic carcinoma due to its aggressive nature; however upon immunohistochemical staining it was found to be a calcitonin-negative neuroendocrine tumor of the thyroid.

Conclusion: Few other cases of calcitonin negative thyroid tumors have been reported. We discuss the importance of this pathologic entity in the differential diagnosis for medullary thyroid carcinoma due to different prognostic and recurrence factors. The discrepancy between the few cases of calcitonin negative neuroendocrine thyroid tumors reported indicates a need for further study in order to classify this unique pathological entity.

Abstract #1131

CRIBRIFORM-MORULAR VARIANT OF PAPILLARY THYROID CANCER: A REVIEW OF THE LITERATURE WITH RECOMMENDATIONS FOR DIAGNOSIS AND MANAGEMENT

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University of Chicago

Objective: Cribriform-morular variant (CMV) is a rare subtype of papillary thyroid cancer (PTC) that has primarily been reported in association with familial adenomatous polyposis (FAP). A sporadic form of the disease not associated with FAP has additionally been reported. The goal of this study was to further elucidate the diagnostic and management principles for CMV-PTC.

Methods: A retrospective review of our institutional pathology database was performed between 1990 and 2014. PubMed and Google Scholar queries were conducted using the keyword “cribriform morular” for an extensive literature review comparing disease presentation, pathology, and outcomes of sporadic and FAP-associated CMVPTC.

Case Presentation: Three patients at our institution were diagnosed with CMV-PTC. Two patients (66.7%) had multi-centric, FAP-associated CMV-PTC, while one patient (33.3%) had a sporadic presentation. In our literature review, of the 260 identified cases of CMV-PTC, the majority occurred among women (91.4%) and those with FAP (70.7%). Sporadic CMV-PTC accounted for the remaining 29.3% of cases from the literature. Multi-centric disease was diagnosed more often in FAP-associated cases than in sporadic cases (38.5% vs. 11.1%, p<0.001). Six cases of PTC recurrence were identified in our literature review; all were associated with FAP. Of 53 FAP-associated cases in the literature with available APC genetic analysis, 37 patients had germline APC mutations in a region not typically associated with tumorigenesis. Analysis of other genes was limited, but somatic mutations in CTNNB1 were reported in 5 cases of FAP-associated and sporadic CMV-PTC.

Discussion: Our institutional experience and a thorough literature review revealed that sporadic CMV-PTC accounts for close to one-third of cases. However, FAP-associated cases have a more aggressive course, with greater likelihood of multi-centric disease and increased rate of recurrence. Review of genetic analysis suggests a distinct molecular pathogenesis for CMV-PTC compared to other thyroid cancers.

Conclusion: We propose the following recommendations for diagnosis and management of CMV-PTC patients: 1) APC mutational analysis for all patients diagnosed with CMV-PTC; 2) close follow-up for patients with multi-centric disease; 3) consideration for genetic testing for patients with sporadic CMV-PTC; 4) consideration for treatment with anti-angiogenic agents due to their potential impact on multi-centric disease.
CMV-PTC, 2) Thyroid ultrasound for FAP patients identified by APC genetic analysis to be at higher risk of thyroid malignancy, and 3) Consideration of total thyroidectomy in patients with FAP-associated CMV-PTC given the increased risk of multi-centric and recurrent disease.

Abstract #1132

APLASTIC ANEMIA SECONDARY TO METHIMAZOLE: A CASE REPORT

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Makati Medical Center

Objective: To describe a case of Aplastic anemia secondary to anti-thyroid medication use.

Case Presentation: This is a case of a 28 year old female who consulted due to easy bruising. 2 weeks prior the patient noted heavy flow of menstruation. 2 days prior, petechiae was noted on her upper extremities. She denied fever and abdominal pain. She consulted a haematologist with a CBC showing: anemia (Hb 10.5 gm/dL) and Thrombocytopenia (9,000). WBC count was normal. She was admitted for work up. She has hyperthyroidism, on 40 mg per day of Methimazole. It was titrated down to 20mg/day once a day, 5x a week. Subsequent blood counts showed pancytopenia: haemoglobin- 9.9 gm/dl, haematocrit- 27.9, wbc- 2,480, segmenters 25%, lymphocyte 74% and platelet of 12,000. TSH - 0.037 mIU/L, FT4 - 21.047 ng/dL (normal). While admitted she had episodes of gum bleeding, palpitations, tremors and fever. Propranolol 40mg and Cefepime 1 gm every 8 hours were started. Microbiology investigations was negative. Bone marrow biopsy revealed: Markedly hypocellular bone marrow (<5%) with marked panhypoplasia, indicative of aplastic anemia. The marrow aspirate was negative for acute leukemic blast cell population. The patient was given ATG 40 mg/day for 4 days and Cyclosporine 100 mg 1 tab daily. Hydrocortisone was continued at 100 mg every 6 hours. Post therapy, CBC was monitored daily. Platelet and PRBC transfusions, G-CSF were given accordingly. Hydrocortisone was shifted to Methyprednisolone, 16 mg.

Discussion: Antithyroid drugs (ATD) have been used for decades for the management of hyperthyroidism. Among these, agranulocytosis is deemed to be one of the life-threatening effect usually occurring within the first 3 months and in the older patients who may be receiving high doses of ATD. Aplastic anemia is a rare but severe complication of Methimazole. The current concept is linked to either a direct cytotoxic effect or an autoimmune mechanism. Most drug-induced idiosyncratic reaction to hematopoietic cells should be managed as idiopathic aplastic anemia either by replacement of deficient stem cells or suppression of a destructive immunologic process with the use of immunosuppressive agents such as Anti thymocyte immunoglobulin, cyclosporine and corticosteroids. The course of MMI-induced aplastic anemia is highly variable.

Conclusion: This is a case of severe aplastic anemia induced by Methimazole. Immunosuppressive therapy, high dose steroids with G CSF administration and supportive blood and platelet transfusion therapy were given to the patient.

Abstract #1133

A SYSTEMATIC REVIEW OF D2 THR92ALA POLYMORPHISM ON RESPONSE TO COMBINATION T3/T4 THERAPY IN THE ADULT HYPOTHYROID POPULATION

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Objective: The D2 deiodinase enzyme is an enzyme that converts thyroxine (T4) to triiodothyronine (T3) in important metabolically active tissues such as the brain, thyroid and brown adipose tissue. D2 polymorphisms are associated with clinical syndromes such as diabetes and hypertension. Thr92Ala is the most common and most studied D2 polymorphism. The purpose of the systematic review is to review available evidence surrounding the effect of Thr92ala polymorphism on clinical response to combination T3/T4 therapy in hypothyroid adults.

Methods: A literature search of the Pubmed and EMBASE databases from September 1, 1980 to September 1, 2015 was conducted using MeSH terms deiodinase, Triiodothyronine and genetic polymorphism. Retrieved studies were examined for clinical use of T3 in the context of D2 polymorphism. Review articles and non-english articles were excluded.

Results: Out of 15 initially identified primary research articles, 6/15 involved the Thr92Ala polymorphism and 2/6 studies involved Triiodothyronine therapy. Study 1 (N=141) was performed by Appelhof et al, J Clin Endocrinol Metab. 2005 Nov;90(11):6296-9 and Study 2 (N=552) was performed by Panicker et al, J Clin Endocrinol Metab. 2009 May;94(5):1623-9. Both studies are post hoc genotyping of previous randomized, double blind trials of combination T3/T4 therapy in hypothyroid patients. The pooled baseline fT4 was 20.2±3.7pmol/L for wild type, 19.6±3.5pmol/L for heterozygous and 19.5±3.6pmol/L for homozygous Thr92Ala. There was no statistically significant differences based on genotype via one way ANOVA (P=0.083). Baseline TSH was not amenable to pooling due to being expressed
as a median and interquartile range. Study 1 found no effect of Thr92Ala polymorphism via the Profile of Mood States Dutch shortened version (POMS). Study 2 found a dose dependent effect of the Thr92Ala allele on improving response to T3/T4 combination therapy based on the General Health Questionnaire, 12-question version (GHQ-12).

Discussion: Both studies suggest that homozygous Thr92Ala is associated with increased baseline symptoms and agree that genotype did not affect measurable thyroid markers. The two studies disagree about the effect of Thr92Ala polymorphism on clinical response to T3/T4 therapy but comparison of the two studies is limited by substantial methodological differences in the original studies which include mid study alterations of T3 dosing.

Conclusion: Based on limited data, the Thr92ala allelle appears to be associated with increased symptoms at baseline. However the responsiveness of these symptoms to combination T4/T3 therapy requires further study, ideally with a priori clinical trials that involves randomization by genotype.

Abstract #1134

A SYSTEMATIC REVIEW ON PATHOPHYSIOLOGY AND CLINICAL DATA OF MONOCARBOXYLATE TRANSPORTER 8 (MCT8) POLYMORPHISMS ON THYROID HORMONE IN THE ADULT POPULATION

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Objective: MCT8 plays an important role in the transport of thyroid hormone; however a single nucleotide polymorphism has been associated with X-linked psychomotor retardation, known as Allan-Herndon-Dudley syndrome (AHDS) in the pediatric population. There is emerging data in euthyroid patients to explore clinical and pathophysiology implications of MCT8 polymorphisms. The objective of this study was to systematically explore the available data on the impact of MCT8 polymorphisms on thyroid hormone metabolism in the euthyroid adult population from a clinical perspective.

Methods: A systematic literature search was performed using EMBASE and PubMed databases from 1947 to September 2015, with a variety of MeSH term combinations. Bibliography mining was also completed on relevant journals for full inclusion. Articles in non-English languages were excluded.

Case Presentation: Twelve articles evaluating MCT8 deficiency in animal studies consisting of 10 mice and 2 zebrafish models were identified. The studies conducted on mice revealed abnormal thyroid hormone serology consisting of high T3, low T4 and normal to slightly elevated TSH levels, with a normal neurological phenotype, whereas the zebrafish models revealed an abnormal neurological phenotype. In addition, a total of 3 articles found had pooled clinical data on 3785 euthyroid adults with MCT8 genetic polymorphisms, without AHDS. The TSH from the studies were similar and within normal limits with a weighted mean of 1.51 +/- 0.57. One study revealed lower T3, FT3 and FT4 in males with a normal TSH, however, the other two studies found no association between the MCT8 genetic polymorphisms and T3, T4 or TSH levels.

Conclusion: Even though animal models showed a positive correlation between MCT8 deficiency and abnormal thyroid serology, no positive correlation was seen in human studies. The pooled clinical human data revealed no statistically significant differences between having the MCT8 genetic polymorphisms and thyroid hormones, as well as TSH levels. There is limited clinical data currently available on the impact of MCT8 polymorphisms, so it is unclear whether the polymorphisms have an impact on the euthyroid population in a clinical setting. More data collection and analysis is required to determine if there is a need to study the function and clinical significance of MCT8 genetic polymorphisms. Polymorphisms in thyroid hormone transporters may provide insight into clinical practice, however its importance still requires more published data.

Abstract #1135

IDENTIFYING THYROTOXICOSIS FACTITIA

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Objective: Thyrotoxicosis is a life-threatening hypermetabolic condition caused by excess release of thyroid hormone. Because this condition is fatal, rapid diagnosis and treatment are essential for survival. There are multiple etiologies of thyrotoxicosis with the most prevalent being uncontrolled Graves’ disease. Exogenous thyroid hormone ingestion is another rare cause. It is important to suspect exogenous ingestion in patients who present in thyroid storm with an undetectable serum thyroglobulin (TG). However, in other etiologies of thyroid storm, serum TG is elevated.

Case Presentation: A 38-year-old man with a history of alcohol abuse presented with tachycardia to the 160s, tachypnea to the 40s, and epigastric abdominal pain with intractable vomiting. He was intubated in the emergency room after abdominal imaging confirmed necrotizing pancreatitis. He then became hypotensive.
and unresponsive to intravenous fluid boluses so he was placed on pressor support. His abdominal distension continued to worsen and he developed oliguria which was concerning for abdominal compartment syndrome. The suspicion was confirmed by elevated bladder pressures, and he was emergently taken to the Operating Room for an exploratory laparotomy. Post-operatively, his thyroid function was checked and thyroid-stimulating hormone was undetectable while free thyroxine (fT4) and total triiodothyronine (TT3) were markedly elevated. Further workup revealed an undetectable serum TG and negative thyroid peroxidase antibody and thyroid stimulating immunoglobulin. His mother found evidence of exogenous triiodothyronine (T3) intake and gave the history of a recent 30 pound weight loss and new onset resting tremor. He was treated with stress-dose intravenous hydrocortisone, oral iodine drops, and oral propylthiouracil. He was unable to tolerate low doses of propranolol due to his hypotension. Although fT4 and TT3 levels downtrended significantly with aggressive treatment, his blood pressure continued to be tenuous and he developed shock liver and renal failure. His mother then made the decision to withdraw support to allow natural death.

**Conclusion:** This is a case of thyrotoxicosis caused by exogenous T3 ingestion which was treated promptly and aggressively with an appropriate response in thyroid function tests. Although thyrotoxicosis factitia is a rare cause of thyroid storm, a low serum TG will aid in making a definitive diagnosis. Thyrotoxicosis can be treated either medically or with plasmapheresis, but medical management is preferred in patients with hypotension.

**Abstract #1136**

**NO GOITER WHEN YOU MOST EXPECT IT**

*Nisha Suda, MD, MHA, Frank Wang, MD, Chris Estiverne, MD*

Rutgers-NJMS

**Objective:** (1) Present an evaluation of thyromegaly after iodine administration during a workup of a pheochromocytoma. (2) Discuss the utility of serum metanephrines.

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

**Case Presentation:** 51 year old Black man with a history of bilateral nephrectomy for renal cell carcinoma (now on hemodialysis), parathyroidectomy, refractory hypertension and a shellfish allergy, initially presented for management of hypertensive emergency. During hospitalization his blood pressure was intermittently controllable, however this was never sustainable. Due to the inability to consistently maintain appropriate blood pressure control despite aggressive fluid removal during hemodialysis and numerous medications, the decision was made to evaluate for a possible pheochromocytoma. Since the patient did not make urine, measuring urine metanephrines was not possible, therefore the patient was given a saturated solution of potassium iodide (SSKI) in preparation for a Metaiodobenzylguanidine (MIBG) scan. However, 24 hours after receiving his first dose of SSKI he experienced neck swelling. He did not endorse dysphasia, and exam revealed significant anterior neck and submandibular swelling, making the thyroid indiscernible to palpation. TSH was 3.46 mU/L. Of note, patient had had a prior thyroid ultrasound that revealed small nodules throughout (4-7mm) and one 1.2 x 1.1 cm hypoechoic nodule. Iodine administration was halted and the neck swelling resolved. Patient did not have any symptoms of tremor, diarrhea, heat intolerance or excessive anxiety during this time. Patient is still undergoing his workup.

**Discussion:** Typically drug induced thyrotoxicosis presents with functional abnormalities in the gland and infrequently with a goiter. Numerous medications can lead to thyrotoxicosis, including iodine. Though the patient received iodine, his glandular function remained stable both clinically and biochemically. This should indicate that perhaps an allergy is more likely than thyrotoxicosis; nevertheless, it is important to follow-up for possible iodine induced thyroid toxicities as they are a well-recognized complication.

The second issue at hand is obtaining a biochemical confirmation of a pheochromocytoma prior to pursuing imaging studies in a patient that does not make urine. It is important for a clinician to recognize there can be considerable discordance between serum and urine metanephrines, as the latter has a higher specificity and is therefore preferred.

**Conclusion:** Perhaps this patient got “lucky” to have experienced an allergy rather than an insult to his thyroid gland, though both workups should be followed through equally as iodine induced neck swelling could very well be thyrotoxicosis.
Abstract #1137

HYPOTHYROIDISM: A REVERSIBLE CAUSE OF HEART FAILURE

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Allegheny General Hospital

Objective: Hypothyroidism is characterized by a decrease in oxygen and substrate utilization by major organ systems of the body. Hence patients with angina pectoris have fewer symptoms if they become hypothyroid. Hypothyroidism also results in bradycardia and weakening of myocardial contraction and relaxation. Cardiac preload is decreased due to impaired diastolic function, cardiac afterload is increased, and chronotropic and inotropic functions are reduced. The impairment of the measures of left ventricular performance leads to a reduction in cardiac output.

Case Presentation: A 69-year-old male presents after a syncope. After receiving CPR, his ECG showed incomplete right bundle branch block and left anterior fascicular block. He was started on a heparin drip for elevated cardiac enzymes. The patient reported no history of angina, syncope or seizure disorder except recent onset fatigue and dyspnea on exertion. He also complained of recent hair loss, hoarse voice and scrotal swelling.

The patient had no thyromegaly but had bilateral non-pitting pedal edema. Initial results showed, TSH of 122.1 mcL/mL (0.4 – 4.0 mcL/mL), free T4 of <0.02 ng/dL (0.7 – 1.9 ng/dL), total T3 of 22 ng/dL (80–200 ng/dL). Thyroglobulin and thyroid microsomal antibodies were detectable in his serum. His mental status was intact and showed no features of myxedema coma. He was started on a lower dose of levothyroxine (LT4) for his weight to prevent an exacerbation of an acute coronary syndrome or an arrhythmia. Hydrocortisone was started prior to administrating LT4, till co-existing adrenal insufficiency was ruled out.

Patient had a transthoracic ECHO that showed severe left ventricular systolic dysfunction with an ejection fraction (EF) of 25% and global hypokinesis with regional variation. Left heart catheterization showed triple vessel disease without complete vessel occlusion. However from the left ventriculogram, the EF improved to 60% after 3 days of LT4. The free T4 also increased to 0.2 mg/dL. Eventultely the patient had a coronary artery bypass grafting (CABG) where intraoperatively, the EF remained stable at 50%.

Conclusion: Our case is distinct in describing a patient who was profoundly hypothyroid, yet had no features of myxedema coma and showed dramatic improvement with initiation of LT4. The improvement in cardiac contractility prior to the CABG demonstrates the relationship between hypothyroidism and left ventricular dysfunction, and its reversible nature with restoration of thyroid function. This is due to the improvement in chronotropic and inotropic function along with decrease in afterload and increase in preload. At the same time appropriate LT4 dose initiation is important to prevent arrhythmias.

Abstract #1138

HOFFMAN’S SYNDROME: A RARE CASE OF HYPOTHYROID MYOPATHY

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Mount Sinai Beth Israel

Objective: Hoffman’s Syndrome (HS) is a rare neurological manifestation of hypothyroidism with muscle stiffness and pseudohypertrophy.

Case Presentation: 53-year-old female with history of Post-ablative Hypothyroidism was sent to emergency room for abnormal labs: TSH 72 (0.55-4.78 uIU/mL), undetectable T3, T4, Creatine Kinase [CK]1864 (30-135 U/L), Cr 1.4 (0.52-1.04 mg/dL). Patient had 10-year history of hypothyroidism since Radioactive Iodine therapy for Grave’s Disease and was noncompliant to levothyroxine treatment. Two years ago her TSH was 66. Patient denied any acute symptoms. However, review of symptoms revealed constipation, fatigue, cold intolerance, hoarse voice, brittle hair, weight gain, swelling of lower extremities, and myalgia.

On exam, vitals within normal limits; she was alert, oriented, obese female (BMI 30) with dry skin, periorbital edema, symmetrically and diffusely enlarged non tender thyroid, bilateral calf hypertrophy with non-pitting edema and normal muscle strength. Admission labs confirmed severe hypothyroidism. CK 2000’s-3000’s U/L. UA, ACTH, prolactin, random cortisol, lipid, hepatic panel were within normal limits. Patient received IV hydration and was started on triiodothyronine and levothyroxine. Her CK level remained elevated in the mid-2000s and she was discharged in three days with outpatient follow up.

Discussion: HS defines a severe form of myopathy due to hypothyroidism causing proximal muscle weakness, cramping, stiffness, and pseudohypertrophy. Associated with the syndrome is an elevation of CK. While asymptomatic hypothyroid patients often have mildly elevated CK <1000 IU/L, a persistently elevated CK leads to suspicion for hypothyroid myopathy. The pathophysiology behind the elevated CK is thought to be related to myofiber degeneration, impairment in glycogenolysis and mitochondrial oxidation and change
in muscle fiber type. The most heavily involved muscle groups include the gastrocnemius, deltoid, and trapezius muscle. Diagnosis of HS is made clinically, but is supported with EMG to distinguish from other myopathies. Although not required, muscle biopsy can show hypertrophy of slow type I muscle fibers with atrophy of fast type II muscle fibers. Treatment involves thyroid replacement therapy, which results in improvement in CK and usually resolution of myopathy symptoms within six months. Normalization of muscle size is also seen with treatment.

**Conclusion:** Our case highlights a rare form of hypothyroid myopathy known as HS. It is important to consider HS as a differential for calf hypertrophy as correct diagnosis and treatment are successful in reducing symptoms.

**Abstract #1139**

**METASTATIC ANAPLASTIC THYROID CANCER FOLLOWING TREATMENT OF TOXIC MULTINODULAR GOITER**

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University of Central Florida

**Objective:** Anaplastic thyroid cancers (ATC) are undifferentiated tumors with almost 100 percent mortality. Antecedent thyroid disease, specifically differentiated thyroid cancers, have been reported in patients with anaplastic carcinomas. However, the exact relationship between thyrotoxicosis and ATCs is still obscure. This case sheds light on our understanding of thyrotoxicosis and thyroid cancer risk.

**Case Presentation:** A 75 year old man presented with weight loss, tachycardia, tremor, and lab findings suggestive of primary hyperthyroidism. Ultrasound and thyroid scan were consistent with toxic multinodular goiter. He received methimazole for 2 months with no significant improvement of the hyperthyroid state, leading to radioactive iodine (RAI) ablation therapy. Shortly afterwards, he was started on levothyroxine due to RAI-induced hypothyroidism. One year after the RAI treatment, he presented with complaints of rapidly enlarging neck mass, dysphagia, and hoarseness over 3 weeks. Further workup and imaging were consistent with metastatic anaplastic thyroid carcinoma. He experienced rapid progression of disease over the following weeks causing poor nutritional status and dehydration. Given his poor prognosis, he opted for hospice and palliative care.

**Discussion:** This is a very rare case of anaplastic thyroid cancer that occurred very shortly after thyrotoxicosis and radioactive iodine treatment. There are conflicting studies about the occurrence of thyroid cancers in thyrotoxic states like toxic multinodular goiter. Some studies suggest that there is no protective role for thyrotoxicosis in the incidence of thyroid cancer. An alternative culprit for carcinogenesis in this patient is RAI treatment. Although relatively safe, RAI has been associated with a small increased risk of thyroid cancer. Increased TSH receptor antibodies, nuclear atypia, cellular metaplasia, and inactivation of tumor suppressor genes are all proposed mechanisms of how RAI treatment may lead to increased risk of thyroid carcinoma. Few cases are reported describing thyroid carcinomas in thyrotoxic disease patients despite medical and RAI treatment. Analysis of these cases is noteworthy, because it promotes awareness regarding the importance of vigilance and long-term follow up of patients with thyrotoxic conditions.

**Conclusion:** It is unclear whether differentiated or anaplastic thyroid cancer occurs as an infrequent complication of hyperthyroidism or as a consequence of radioactive iodine treatment. And while the incidence of thyroid cancer in a single hot nodule is low, a toxic gland is at increased risk. This case documents the need for close follow-up for all patients with a history of hyperthyroidism.

**Abstract #1140**

**THE IMPORTANCE OF LEVOTHYROXINE BIOAVAILABILITY FOR A TSH AT GOAL**

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Saint Vincent Charity Medical Center

**Objective:** Multiple factors can hamper the ability to maintain a desired TSH level. Variables like patient adherence, medical conditions, medications, food and beverages that affect the LT4 absorption and metabolism are among the most common ones.

**Case Presentation:** A 35 year old Caucasian woman with a PMH of Hypothyroidism, Depression, Insomnia, Alcohol use and Tobacco dependency presented with the chief complaint of swelling which extended from periorbital to the face, abdomen, upper and lower extremities. The symptoms progressed within 48 hours and were associated with a brief episode of shortness of breath. She denied any food/drug allergies, or exposure to any possible allergen. On the review of systems she reported weight gain of 9 lbs in 1 month. She was compliant with all of the medications, including solid tablet LT4, which she was taking it every morning 30 minutes before breakfast with a cup of coffee. Other medications used were Duloxetine and Trazodone. On exam vitals were stable with the exception of HR of 100. The pertinent findings were periorbital and face edema, tachycardia, diffuse abdominal swelling, bilateral distal upper extremities and lower extremities nonpitting...
edema and DTR of upper extremities 3+, lower extremities 4+. Her WBC was 15.8, MCV of 99.2, CK of 256, TSH of 145.400, fT3 of 1.26 and fT4 of 0.51

Discussion: Treatment failure in hypothyroidism is easily unrecognized. It happened in our patient due to the concurrent intake of LT4 and drinking coffee. One study comparing intake of LT4 fasting, at bedtime and with breakfast showed optimal absorption under fasting conditions, with reduction from 80% to 40-64% with concurrent food. The TSH results were highest on the regimen where the LT4 was given with breakfast, lower at bedtime and lowest in fasting state. LT4 should be taken on an empty stomach, ideally an hour before breakfast. In patients who are not able to wait a full hour, LT4 administration with breakfast could be an alternative, but these patients should be followed more closely due to the TSH variability. Oral liquid LT4 formulations could diminish the problem of malabsorption caused by coffee when using the traditional tablet formulations.

Conclusion: Physicians should discuss with their patients the importance of the timing of LT4 administration, its relationship to food, and its impact on disease manifestations.

Abstract #1141

AV NODAL REENTRANT TACHYCARDIA: A CASE OF IATROGENIC HYPERTHYROIDISM

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GRMEP/ Michigan State University

Objective: Hypothyroidism is a common problem affecting the American population. Treatment with supplementation requires monitoring to prevent side effects from improper dosing. We present a case of iatrogenic Hyperthyroidism causing as AV Nodal Reentrant Tachycardia (AVNRT) as a result of failed monitoring as an outpatient.

Case Presentation: A 51 year old woman with a history of hypothyroidism presented with palpitations, shortness of breath and lightheadedness. She was found to be in AVNRT with a pulse in the 270s, blood pressure of 126/74, respiratory rate of 16, temperature of 36.8 Celsius. She was given IV adenosine with conversion to sinus rhythm. Labs showed an undetectable TSH and normal T4. She had been on the same dose of levothyroxine for 4 years and had not had her labs monitored. Her levothyroxine was held during her hospital stay. She was discharged in stable condition with weekly monitoring of TSH and T4 and will wait for her TSH to normalize before restarting levothyroxine at a lower dose.

Discussion: Chronic over supplementation of thyroid hormone can cause overt or subclinical hyperthyroidism. Thyroid hormone in excess amounts causes cardiac symptoms through adrenergic, chronotropic and inotropic stimulation of cardiac myocytes, leading to cardiac dysrhythmias. Thyroid hormone enhances atrial excitability, increases the frequency of atrial beats and shortens the refractory period of conductive tissues. This can lead to atrial fibrillation and also supraventricular tachycardia (SVT), AVNRT is the most common cause of paroxysmal SVT. It is typically a narrow QRS complex tachycardia and its physiologic mechanism involves dual pathways of the AV node. There is a fast pathway with fast conduction and a slow refractory period. There is a slow pathway with slow conduction and a fast refractory period. A premature atrial beat arrives at the AV node during the refractory period of the fast pathway while the slow pathway is excitable. The beat goes retrograde through the node and a conductive loop is triggered leading to reentrant tachycardia

Conclusion: This case presents an expected side effect of thyroid replacement therapy. Thyroid hormones can enhance AV node excitability leading to reentry though the AV node. She had subclinical hyperthyroidism from not monitoring her thyroid function as an outpatient which brought on her episode of AVNRT. This case highlights the importance of monitoring patients on thyroid supplementation at a minimum of once a year to ensure correct dosing and avoid chronic over supplementation, with attendant risk of cardiac dysrhythmias. Through proper monitoring one can avoid such issues that our patient had.

Abstract #1142

INTRATHYROIDAL LYMPHOEPITHELIAL CYST: A RARE FINDING AND ASSOCIATION

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1. Wright State University, 2. Department of Veteran Affairs

Objective: We present a case of a lymphoepithelial cyst in the thyroid with coexisting papillary thyroid carcinoma.

Case Presentation: A 48-year-old male was referred to endocrinology for evaluation of multinodular goiter. Thyroid function tests were normal. He denied changes in the neck, dysphonia, dysphagia or weight loss. On physical exam, thyroid was symmetric and normal in size without palpable nodules. There was no significant cervical lymphadenopathy. Ultrasonography revealed multiple thyroid nodules and enlarged lymph nodes bilaterally. Fine needle aspiration (FNA) biopsy of a 1.1 cm right mid-thyroid nodule (hypoechoic with irregular border and macrocalcifications), a 3.3 cm left lower lobe nodule (hypoechoic), and a 2.1 cm cervical lymph node (ovar without fatty hilum) in left neck was performed.
A lymph node sample was sent for flow cytometry. The specimen from right thyroid nodule showed increased cellularity with atypical cells concerning for thyroid neoplasm. Straw colored fluid was aspirated from left thyroid nodule indicating a cyst. This specimen revealed squamous cells, histiocytes and calcific bodies suggestive of branchial cleft cyst. Lymph node FNA biopsy and flow cytometry was positive for small lymphocytic/chronic lymphocytic leukemia (SLL/CLL). The patient underwent total thyroidectomy and excision of the lymph node. On surgical pathology, he was noted to have follicular variant of papillary thyroid carcinoma in the right thyroid gland and a lymphoepithelial cyst in the left. Excisional biopsy confirmed SLL/CLL in the lymph node.

**Discussion:** Lymphoepithelial cysts of the thyroid gland are rare and only 30 such cases have been reported. They are histologically similar to branchial cleft cysts. The pathogenesis and embryologic basis of thyroid lymphoepithelial cysts is uncertain. It has been postulated that these cysts originate from solid cell nests of the thyroid, thought to be remnants of the ultimobranchial body. The average age of onset is 42 years and it is more common in females. These cysts are benign and asymptomatic. However, in one case report, the patient developed right vocal cord palsy due to compression from a cyst. Four of the cases were noted to have separate papillary thyroid cancer. Chronic thyroiditis has been reported in many of these cases.

**Conclusion:** Intrathyroidal lymphoepithelial cysts are a rare finding that can be associated with other thyroid conditions including malignancy. This is the fifth reported case of an intrathyroidal lymphoepithelial cyst coexisting with papillary thyroid cancer in medical literature. We hope to see more of these rare thyroid lesions in the future to better understand them, as well as their association with other thyroid disease.

Abstract #1143

**AGRAINOCYTOSIS SECONDARY TO METHIMAZOLE COMPLICATED BY PERFORATED SIGMOID COLON**

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Heart of Lancaster Regional Medical Center

**Objective:** Describe a case of agranulocytosis secondary to methimazole that was complicated by acute perforated sigmoid colon.

**Case Presentation:** 51-year-old female with history of graves induced hyperthyroidism was started on methimazole 10 mg/tablet daily for three weeks. She presented with fever, sore throat, and abdominal pain. Vital Signs: Temperature 39.1, Heart rate: 145 bpm, Blood pressure: 119/58 mmHg, exophthalmos, thyromegaly, left lower quadrant tenderness. Initial laboratory studies showed WBC 0.3 with ANC 0, TSH 0.01 uIU/ml, FT4 0.43 ng/ml. Abdominal CT revealed uncomplicated sigmoid diverticulitis. She was started on metoprolol 2.5mg IV every 6 hours, cefepime 2g IV daily, and flagyl 500mg IV every 8 hours. Hematology was consulted, and filgrastim 480mcg subcutaneously daily was started. Blood cultures were positive for cefepime sensitive Pseudomonas and antibiotics were adjusted. Otolaryngology was consulted for consideration for thyroidectomy. Hospital day eight, WBC improved to 0.9 and she remained afebrile. Filgrastim was discontinued and antibiotic therapy continued. Hospital day ten, WBC 20.1, the patient was noted to be febrile, with increased abdominal tenderness and guarding. Abdominal CT showed free intra-abdominal air. Repeat blood cultures were drawn. Surgery was consulted and the patient underwent a Hartmann’s procedure for perforated sigmoid colon. Post operatively she was kept in the ICU, and extubated one day later. Her repeat blood cultures showed no growth. She remained afebrile and was transitioned to metoprolol 12.5mg PO BID. Repeat TSH 0.84 uIU/ml, FT4 0.36 ng/ml. The patient was later discharged to a skilled nursing facility on levothyroxine 50mcg daily, and awaiting thyroidectomy.

**Discussion:** Agranulocytosis is a feared side effect of methimazole treatment with most cases presenting within 90 days, though it may occur at a later point in treatment or with subsequent treatments. A greater risk is seen with elderly patients. Patients who develop fever, chills, and sore throats are instructed to discontinue therapy and contact a physician. The diagnosis is made by CBC and differential. Treatment consists of discontinuing methimazole, blood cultures with broad spectrum antibiotics and initiation of granulocyte stimulating factor which may decrease recovery time and hospital stay.

**Conclusion:** Agranulocytosis is a rare complication of methimazole treatment, which must be considered in a patient who presents with fever, sore throat, and agranulocytosis. This case emphasizes the need for early recognition and aggressive management.
Abstract #1144

**DOSING OF LEVOthyroxine IN A HYPO-Thyroid PATIENT FOLLOWING GASTRIC BY-PASS SURGERY**

*Emad Ali, Katherine Butler, Alan Peiris*

Texas Tech University Health Science Center

**Objective:** Drugs absorption occurs mainly in small intestine, which is by-passed in several bariatric surgeries. Functional absence of this part leads to decreased mucosal surface area and alters intestinal pH, which in turn has the potential to alter drug absorption.

**Methods:** Case Report

**Case Presentation:** 48-year-old male referred to our clinic in June of 2015 for chronic fatigue. He has hypothyroidism treated successfully with Levothyroxine. He underwent gastric bypass surgery for morbid obesity in 2009 and he lost 140 lbs over six years. He takes Synthroid 350 µg and Fluoxetine and clinically euthyroid. Labs showed mild hypothyroidism in January of 2015 but repeat testing indicated normal free T4 and TSH in April of 2015. Levothyroxine dose had been increased several times throughout this interval. Based on his current weight, the calculated dose should be 200-225 µg daily (1.7 µg /kg). However, he is euthyroid at the 350 µg dosage which is higher than anticipated and no changes were made. Hypothyroidism was explained to be unlikely given his normal thyroid function.

We searched literature to look for correlation between bariatric surgery and thyroxine absorption.

**Discussion:** Bariatric surgery has been more prevalent lately but medication malabsorption is a potential concern following surgery. Gastric acidity plays a significant rule in thyroxine absorption and alteration in gastric pH is known to influence its absorption [1]. Since bariatric surgery bypasses almost the entire stomach thus significantly, minimizing acid secretion and this could impair Levothyroxine absorption. It was more of an issue with diversionary procedures like jejunoileal bypass but to less extent with gastric bypass [2]. Padwal, et al., studied the effects of bariatric surgery on the absorption of different drugs and results showed reduced absorption of thyroxine post bariatric surgery [2]. In contrast, one study compared Levothyroxine absorption before and after Roux-en-Y gastric bypass and results did not show reduced absorption but significant delay of absorption was noted [3].

**Conclusion:** Clearly, we still do not have full understanding of Levothyroxine absorption and dosing following bariatric surgery, only few studies have been done and are contradictory. Since weight loss is the main goal of surgery, theoretically clinicians should continue to dose thyroxine based on body weight. Moreover, due to altered motility following bypass in some instances crushing the tablets or trying cautious dosing incensement can be considered. Our patient illustrated that in selected cases higher than anticipated doses may be needed to maintain euthyroidism.

Abstract #1145

**ATYPICAL CARDIAC PRESENTATION OF THYROID STORM**

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Beaumont Hospital

**Case Presentation:** Our patient was a 51 year old female with no past medical history who was diagnosed with Grave’s disease because of symptoms of anxiety, heat intolerance and weight loss. This was confirmed by thyroid function and radioactive iodine uptake studies. She was started on Methimazole and scheduled for radioactive iodine treatment. She failed to follow up and stopped taking her medication shortly after. Two years after her diagnosis she was found by her family with lethargy and severe dyspnea. She was brought to the emergency room and upon arrival she was found to be tachycardia, hypotensive and hypoxic. Physical exam showed tachycardia and firm goiter but no exophthalmos. Further testing showed she was in SVT rhythm with a heart rate of 166 and chest X-ray was consistent with pulmonary edema. Echocardiogram showed ejection fraction of 15% with global hypokinesis. She had no previous cardiac ultrasounds available for comparison. She had negative troponins and ECG did not suggest any ischemic event. Thyroid function testing was done and revealed an undetectable TSH and an elevated T3 and T4. The patient was intubated after failure to improve and she was admitted to the intensive care unit. Methimazole followed by Iodine and hydrocortisone was administered. Over the following days, Her heart rate went down and pulmonary edema resolved. She was extubated. Her mental status gradually went back to her baseline. Intravenous steroids were weaned down and she was continued on Methimazole upon discharge with plan for radioactive iodine treatment as an outpatient.

**Discussion:** Thyroid storm is a rare complication of thyrotoxicosis. It is estimated to occur in only 1 to 2 percent of patients with hyperthyroidism, with an incidence rate of 0.5 per 100,000 persons per year. It carries however a high mortality rate reaching up to 20 to 30 percent. It is important to recognize the symptoms of thyroid storm and treat it accordingly without waiting for laboratory confirmation as these will usually be delayed.
Cardiac manifestations are common in thyroid storm and can be present in up to 60% of cases. These usually include tachycardia and arrhythmias. High output congestive heart failure can be seen in up to 6% of the patients. On the other hand, low output congestive heart failure has not been described as frequently.

**Conclusion:** Thyroid storm is a rare but fatal presentation of thyrotoxicosis. It is vital to recognize this syndrome and treat it rapidly and aggressively. Cardiac manifestations of thyroid storm can vary, ranging from sinus tachycardia to cardiac failure and hemodynamic collapse. These complications usually improve with supportive care and treatment of the thyroid disease.

**Abstract #1146**

**TIMELINE OF DEVELOPING AGRANULOCYTOSIS AND HEPATOTOXICITY AFTER STARTING ON METHIMAZOLE**

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**Objective:** To report a case of “impending agranulocytosis” (AG) and hepatotoxicity (HT) after Methimazole (MZ) administration for thyrotoxicosis (TT).

**Case Presentation:** 29 year old Chinese male with no significant past medical history presented to our hospital with 1 day of nausea and vomiting. He denied abdominal pain, diarrhea, fever and antecedent history of upper respiratory tract infection. He was not on any medications. Initial vital signs were pulse rate of 143 bpm, blood pressure 144/82 mm Hg. Physical examination was significant for generalized sweating, anxiety, hand tremors and a diffusely enlarged non-tender goiter. No orbitopathy or pre-tibial myxedema. EKG showed normal sinus rhythm. Initially his tachycardia was attributed to hypovolemia and 3 liters of crystalloids were given. Tachycardia did not improve after fluids and bedside echocardiogram suggested a low likelihood of hypovolemia. A CT angiogram of the chest was negative for pulmonary embolism (PE). Laboratory tests on day of admission revealed a normal complete blood count (CBC) and isolated elevation of serum alkaline phosphatase (AP). Remainder of liver function tests (LFT’s) was normal. Basic metabolic panel revealed ↓ serum bicarbonate levels and ↓ anion gap. Thyroid function tests revealed TSH of 0.110 mIU/L (0.34-5.60), T4 of 4.96 ng/dl (0.58-1.64) and FT3 of 12.97 pg/ml (2.5-3.9). On day 1, he was diagnosed with TT and was started on MZ 20mg orally q6hrs. On day 3, absolute neutrophil count (ANC) ↓ from 5100/mm3 to 1600/mm3. Serum Aspartate aminotransferase (AST) (0-40 U/L), and Alanine aminotransferase (ALT) (5-35U/L) ↑ 1.5 time’s from their baseline values of 39 and 40. Viral hepatitis screen was negative. MZ was decreased to 30mg orally BID. Despite a reduction in the dose, AST & ALT continued to ↑ and by day 5 AST and ALT were up to 105 and 131. ANC reached a nadir of 1300/mm3. MZ was stopped and patient was started on Lithium 300 mg TID. Radioactive Iodine was not considered as he received prior iodine load to facilitate imaging. Outpatient follow up was facilitated in 1 week after stopping MZ. ANC improved to 2200/mm3, AST normalized to 32 U/L and ALT ↓ to 88 U/L.

**Conclusion:** AG and HT are rare complications of anti-thyroid drugs but are well known complications. Reported timelines for developing these complications are usually in the ranges of 8-90 days after starting MZ (Cooper, 2005). We report a case of granulocytopenia with a concern to develop AG and HT very early (~48 hours) after starting MZ. A high index of suspicion is necessary and methimazole toxicity should be considered in patients presenting with symptoms of infection and hepatotoxicity as early as 48 hours after starting methimazole.

**Abstract #1147**

**INDIRECT METHOD OF CONFIRMING A EU-THYROID STATE**

Nisha Suda, MD, MHA

Rutgers-NJMS

**Objective:** To highlight how Propylthiouracil (PTU) can assist in establishing a diagnosis.

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

**Case Presentation:** A 60 year old Caucasian female with past medical history of hypertension was sent by her PMD with complaints of nervousness, anxiety, palpitations and fine tremor. Initial labs revealed an elevation in Total Thyroxine (T4) and Free Thyroxine Index (FTI), but a TSH, Free T4 (FT4), T3 and FT3 were within normal range. Repeat labs confirmed these results. Since her T4 was elevated Thyroid Binding Globulin was measured, which was found to be within normal limits. Patient was advised that she was euthyroid, but she was not satisfied with the conclusion that her lab abnormalities were due to measurement error. Furthermore, at this juncture (5 years since initial presentation) her FT4 had now become elevated to 2.48 ng/dL, and she was insistent about seeking treatment in order to resolve her symptoms. Measuring Free Thyroxine by a direct dialysis method was suggested, however her insurance did not cover this method. Repeat labs yielded similar results and after careful discussion Propylthiouracil (PTU) was initiated with close
monitoring. Her TSH became elevated to the hypothyroid range, and there was only a slight decrease in her FT4, which remained elevated well above normal range. Her T3 remained normal. Despite treatment with PTU, her symptoms persisted and she was finally convinced that her results were false.

Eventually, a lab was found that was able to measure her FT4 by dialysis, and results yielded a normal value of 1.5 ng/dL. **Discussion:** Patients with elevated FT4 values, but no elevation in T3 or FT3 and with a normal TSH should lead clinicians to suspect an error in FT4 measurement. It has been shown that Heterophile antibodies, such as Rheumatoid Factor, can interfere with the assay and give spuriously high values that can be seen in the competitive FT4 assay. Fortunately, these autoantibodies can be blocked by specific blocking reagents, nevertheless it is possible that a patient could have such high titers that there could still be interference with the assay. **Conclusion:** It is crucial to recognize assay interference when assessing a patient with questionable lab values. Furthermore, when there is no access to a direct dialysis lab, careful initiation of PTU may be a secondary option for confirming a euthyroid state when assay interference is suggested and may also prove that the autoantibodies may not have any thyroid stimulating effect or an inhibitory affect on the TSH.

**Abstract #1148**

**METHIMAZOLE INDUCED HEPATOTOXICITY IN A PATIENT WITH AMIODARONE-INDUCED THYROTOXICOSIS: A CASE REPORT**

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**Objective:** Methimazole is the thioamide of choice for hyperthyroidism. Although generally well-tolerated, it may cause a cholestatic pattern of hepatotoxicity in 0.02% of patients. We report a case of a patient treated with methimazole for amiodarone-induced thyrotoxicosis who developed a non-cholestatic picture of acute liver injury. **Case Presentation:** A 75 year old male with a past medical history of cardiovascular disease, hypertension, diabetes mellitus, and liver disease was admitted to the hospital three weeks after initiation of methimazole with the complaint of new onset dark urine. Methimazole dose was increased from 20 mg to 40 mg daily, ten days prior to the patient’s current presentation. Amiodarone was discontinued four weeks before the initiation of methimazole. At the time of initiation of methimazole, liver enzymes were within normal limits. However on current presentation, his hepatic function tests were markedly deranged with ALT= 569 U/L (12-78 U/L), AST= 328 U/L (9-37 U/L), alkaline phosphatase= 180 U/L (46-116 U/L), total bilirubin 1.2 mg/dL (0.2-1 mg/dL) and direct bilirubin= 0.72 mg/dL (0.00-0.20 mg/dL). All causes of hepatotoxicity including drugs, infections and gallstones were ruled out by history and diagnostics. Identified as the possible cause of the new onset hepatitis, the patient was taken off of methimazole with notable decrease in the liver enzymes after discontinuation of the drug and clinical improvement (normal color of urine). **Discussion:** Due to reports of severe propylthiouracil-related hepatotoxicity and liver failure, methimazole is considered the initial thioamide of choice for hyperthyroidism. Although less common, methimazole may also cause hepatotoxicity but the pattern is usually cholestatic and occurs more often in the elderly and at higher doses. A few case reports and at least one cohort study have also reported non-cholestatic hepatotoxicity by methimazole. The mechanism of methimazole-induced hepatotoxicity is thought to be partially related to formation of reactive metabolites via the CYP 450 system. Given its long half-life, effects on the CYP 450 system and hepatotoxicity, it is also possible that amiodarone may have contributed to the non-cholestatic pattern of methimazole-induced hepatotoxicity in this patient. **Conclusion:** A high index of suspicion for drug induced hepatitis should be maintained in the setting of acute liver injury after initiation of high dose (more than 30 mg) methimazole, especially after all other etiologies of hepatitis are ruled out. Further studies should also be done to ascertain significant drug interaction between amiodarone and methimazole in further contributing to the hepatotoxic effects of methimazole.

**Abstract #1149**

**ALTERNATE ROUTE TO ADMINISTER THIONAMIDES IN A PATIENT WITH THYROID STORM**

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**Case Presentation:** A 57 year old African American male with a past medical history of non-ischemic cardiomyopathy status post defibrillator placement, hepatitis C, polysubstance abuse and severe emphysema secondary to chronic tobacco use, presents with several months of progressive neck mass swelling with worsening dysphagia, hoarseness of voice, weight loss, and hemoptysis. CT of the neck showed an irregular left neck mass extending from the left thyroid gland to the level of the hypopharynx. On day two the patient underwent...
ABSTRACTS – Thyroid Disease

a tracheostomy and biopsy with the pathology returning positive for an invasive squamous cell carcinoma of the left piriform sinus. LABS : TSH 0.01, Free T4 3.61, T3 4.3. EKG showed sinus tachycardia at 106 bpm. The patient developed signs of thyroid storm, including tachycardia and change in mental status, requiring immediate treatment with oral anti-thyroid medication. Unfortunately an NG tube could not be advanced secondary to the obstructing neck mass. The patient was started on Decadron and propranolol and transferred to the ICU. Since oral anti-thyroid medication was not an option, a propylthiouracil (PTU) retention enema was administered. After receiving an open G-tube the next day, he was started on oral PTU.

Conclusion: Thyroid storm is a rare, life-threatening condition characterized by severe clinical manifestations of thyrotoxicosis including tachycardia, hyperpyrexia, and CNS and GI abnormalities. Laboratory results show a suppressed TSH and elevated free thyroxine (T4) and triiodothyronine (T3) levels. Therapy with thionamide medications (propylthiouracil and methimazole) is aimed at targeting the thyroid and blocking de novo hormone synthesis. Thyroid storm is a medical emergency with a mortality rate is 10 to 30%; and as high as 90% if left untreated. PTU is recommend as initial therapy in patients with life-threatening thyroid storm as PTU blocks T4 to T3 conversion and more rapidly reduces serum T3 concentrations than methimazole. It is important to recognize that both PTU and methimazole are also available in suppository and retention enema form for rectal administration. One study showed comparable therapeutic effects as measured by a significant decrease in serum free T3 levels however; the enema form appeared to provide better bioavailability than the suppository. IV forms of both medications are available as well. Treatment for adults has reduced mortality to less than 20% with resolution of crisis typically within one week. It is important to recognize the various forms of thionamide medications available to control thyrotoxicosis, especially in patients in whom an oral route is not possible, as in the patient described above.

Abstract #1150

AN UNUSUAL CASE OF DIFFUSE LARGE B-CELL LYMPHOMA OF THE THYROID.

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Objective: Primary thyroid lymphomas are rare, representing around two percent of all malignant thyroid tumors and two percent of extranodal lymphomas. Histopathology is almost always that of B-cell lineage, of these, the majority are diffuse large B-cell lymphomas. A history of Hashimoto’s thyroiditis is the only known risk factor. Presentation is usually in the sixth or seventh decade of life, with a female prevalence.

Case Presentation: A 59 year old male with a two year history of diffuse goiter presented with neck pain, dysphagia and an acute worsening of his goiter size after been started on thyroid replacement therapy with levothyroxine 125 mcg daily about a month before. Review of systems was pertinent for an unintentional ten to fifteen pound weight loss over a two week course. Physical examination revealed a significantly enlarged thyroid gland, hard and non-tender to palpation, without bruits, nodules or cervical lymphadenopathy. Thyroid function tests were as follows, TSH 0.09 uIO/ml (0.30-4.35), free T3 4.03 pg/ml (2.30-3.40), free T4 1.83 ng/dl (0.82-1.77), Thyroid Peroxidase antibodies and Thyroglobulin antibodies were negative. CT of the neck revealed a large thyroid goiter with mass effect and tracheal deviation to the left, the right lobe measured 10.5 x 5.3 x 6.1 cm while the left lobe measured 10.1 x 4.8 x 5.3 cm. The patient was started on high dose steroids and underwent an ultrasound guided core needle biopsy of the thyroid gland. Immunohistochemistry of the sample analyzed was consistent with diffuse large B-cell lymphoma. Cells stained positive for CD20, CD79a, PAX-5 and BCL-6, with a proliferative index (Ki – 67) of 50%. Concurrent flow cytometric analysis was cancelled due to low cell count and viability. His disease was classified Stage IIA bulky disease by the Lunago Classification. Following steroid therapy there was a rapid improvement of the goiter size. The patient completed six cycles of chemotherapy with Rituximab, Cyclophosphamide, Doxorubicin, Vincristine and Prednisone (R-CHOP). Follow up CT/PET scan of the neck and chest showed interval disease progression of the right nodal mass. He then received adjuvant radiation therapy and is currently being evaluated for autologous stem cell transplantation.

Conclusion: Primary thyroid lymphomas although rare should always be part of the differential when evaluating...
a patient with a rapidly growing goiter, mainly because its management defers from other thyroid neoplasms. Although a history of Hashimoto’s thyroiditis may be present, that is not always the case as it was with our patient. Prognosis is poor, especially with diffuse large B-cell lymphoma subtype in which the overall 5-year survival is less than 50%.

Abstract #1151

NOCICEPTIVE SIGNALLING IN MEDULLARY THYROID CARCINOMA

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Objective: This study was conducted to identify the types of nociceptive purinergic receptors expressed by the human parafollicular (CA77) cancer cell line. Pain associated with head and neck cancer has recently been shown to directly correlate with survivability and prognosis. In this study we explore the mechanisms of nociception in a medullary thyroid cancer cell line (CA77).

Methods: CA77 cells were grown in culture and the expression of purinergic receptors was studied using Fura-2 am during live cell imaging to measure changes in intracellular calcium levels in response to stimulation with Adenosine Triphosphate (ATP) alone and in combination with suramin (10 µm) and α,β-methylene ATP (10 µm) P2X3, P2X2/3, P2X4 receptor antagonists. To investigate transcriptional expression, primers for P2X3, P2X2/3, P2X4 receptors were used in reverse transcriptase polymerase chain reaction (RT-PCR). Finally, primary antibodies against P2X3 and P2X2/3 receptors were used in immunohistochemistry to qualitatively assess receptor localization.

Results: Significant increases in intracellular calcium levels were measured in response to ATP (P < .001, n = 45), which was not repressed by suramin, and antagonist for P2X4 receptors (10 µm) (P = .893, n = 34). However, ATP-mediated intracellular calcium increase was repressed by α,β-methylene ATP, an antagonist for P2X3 receptors (10 µm) (P < .001, n = 42). Using RT-PCR, mRNA for P2X3 and P2X2/3 was detectable but not the mRNA for the P2X4 receptors. Finally, immunohistochemical data suggests that P2X3 receptors are expressed on the cell membrane in CA77 cells.

Discussion: Several recent studies have suggested that pain associated with the presentation of thyroid cancer is positively correlated with a more severe prognosis. These endpoints include more aggressive cancers, advanced stage at diagnosis and lymph node involvement. Our data is the first to attempt to characterize these nociceptive signaling pathways. Our data suggest that purinergic nociceptive signaling may be involved in this process. Specifically, the P2X3 receptor which has been shown to promote nociceptive signaling in the CNS and also promote peripheral inflammation in chronic pain states.

Conclusion: Taken together, our results provide evidence that CA77 cells express P2X3 and P2X2/3 purinergic receptors, which are known to promote increased neuronal excitability, inflammation, and nociception. Thus, significant pain states experienced by patients with medullary thyroid carcinoma may be attributable, in part, to purinergic signaling in malignant parafollicular C-cells.

Abstract #1152

PULMONARY CONTAMINATION OF IODINE-131: AN INTERESTING CASE OF FALSE-POSITIVE UPTAKE

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Objective: We present a rare case of abnormal radioactive iodine accumulation following ablation therapy for thyroid carcinoma. Recognition for potential false-positive contamination as an alternative to a metastatic process avoids unnecessary medical and surgical treatments.

Case Presentation: 58 year-old female with past medical history of gastroesophageal reflux underwent total thyroidectomy for a symptomatic 4.4 cm follicular neoplasm. Fine needle aspiration showed a follicular lesion of undetermined significance and gene expression classifier labeled the lesion as suspicious. Surgical pathology revealed a 2.5 cm follicular carcinoma of the right lobe and an incidental 2.5 mm papillary microcarcinoma of the contralateral lobe. The tumor was a minimally invasive oncocytic variant of follicular carcinoma without other worrisome features. She underwent radioactive iodine ablation and her post-operative visits proved the patient to be doing well, denying dysphagia or dysphonia, negative Chvostek’s sign, and no obvious lymphadenopathy. The patient’s thyroglobulin value was low. The post-ablation scan revealed a suspected small thyroglossal duct cyst remnant, which was ablated, and an area of activity in the left lower lung. The left lung focus was felt to be an area of pneumonitis without underlying malignancy. Clinically, no respiratory complications developed and she currently has follow-up with her endocrinologist and surgeon at 6 month intervals.

Discussion: Radioactive iodine ablation with whole body scans are used following resection of thyroid carcinoma to detect normal thyroid remnant, recurrent...
and metastatic disease. In order to avoid misreading iodine-131 body imaging, physicians must be aware of unusual but possible false-positive results. As described by Siema et al., four main categories exist for mechanisms of radioactive I-131 uptake: physiologic tissue uptake such as seen in the breast and thyroid, pathologic reaction to another disease or inflammatory response, residual secretions due to esophageal or tracheal pathology, and external contamination (skin, clothing, etc.). The most frequent explanation for a lung false-positive is a tumor. Our patient’s history is not significant for any chronic respiratory infections or lung pathology. Likely, her false-positive result was due to her moderate degree of reflux and/or contamination from secretions.

**Conclusion:** Our case of pulmonary aspiration of I-131 demonstrates an opportunity to avoid a costly and unnecessary misstep in the management of thyroid carcinoma. Acknowledging the potential locations and patterns for false-positive results of the whole body scans avoids inappropriate imaging and treatment.

**Abstract #1153**

**COMBINATION OF T3 AND T4 THERAPY FOR IMPROVING HYPOTHYROIDISM AND OVERALL QUALITY OF LIFE**

Anam Tariq, MD

Pinnacle Health

**Objective:** To study the benefits and side effects of combination T4 and T3 treatment for hypothyroidism in suboptimal patients on LT4 monotherapy.

**Methods:** A retrospective chart review over 5 years at Pinnacle Health Endocrinology to measure vitamin D, free T3, free T4, and TSH levels pre and post therapy along with comparison of Armor vs. Cytomel. Secondly, a cross sectional interview subjectively assessed the patients through SF-20 questionnaire and clinical follow up encounters. Side effects of hyperthyroidism were assessed by symptoms, abnormal labs and hospitalizations.

**Results:** Hypothyroidism results in decreased mood and cognition, weight gain, dyslipidemia, cardiac dysfunction, anemia, and multiple other effects. Although normal physiology involves T4 and T3 as an 11-1 ratio, the American Association of Clinical Endocrinologists and The Endocrine Society recommend LT4 monotherapy as the treatment for hypothyroidism. After years of therapy, some patients feel sub-optimal with decreased quality of life, mood, and cognition. Research indicates suboptimal T3 levels even on full doses of T4 monotherapy. Multiple clinical trials including meta-analysis for combination T3 and T4 therapy have not shown positive results. Some of them did not exclude patients who had normal T3 levels or other causes of fatigue. Finally, the ratios of T3 and T4 varied significantly and in many studies were of short duration < 6 months.

**Discussion:** In our study we used Armour and Cytomel for combination therapy. Since there was no consensus in previous studies on what T3/T4 ratios should be used, and these are the most readily available products, we felt this was an appropriate starting point. Patients who did not improve on Armour were switched to a custom preparation of Cytomel and vice versa in the event they did not develop arrhythmia from becoming hyperthyroid. In our study 69 of the 82 patients (84.1%) were on Armour. Of these 69 patients, 65 (94.2%) reported significant improvement in their symptoms. The remaining 13 were switched to Cytomel and Levothyroxine. All 13 patients, (100%) experienced an improvement in symptoms.

**Conclusion:** Over an average follow-up of 25 months, (range 18-31), TSH remained normal in 88% with Armor compared to 59% of Cytomel, and the p-value was significant. 65% of patients on Armor compared to 53% on Cytomel had normalized their T3 levels. Only 8% had TSH in hyperthyroid ranges and p-value was not significant. On the survey, almost 93% of patients stated their health was better with combination therapy. In our study, patient satisfaction and quality of life were enhanced with combination therapy without causing any significant hyperthyroidism.

**Abstract #1154**

**OCULAR MYASTHENIA GRAVIS IN THE SETTING OF GRAVES’ DISEASE**

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**Objective:** A milder form of myasthenia gravis (MG) is noted in conjunction with autoimmune thyroid disease. We present a patient with diplopia and ptosis related to ocular myasthenia gravis (OMG) in the setting of Graves’ disease (GD).

**Case Presentation:** A 44 year old African-American woman presented with a 5-day history of ptosis and diplopia with normal visual acuity. Prior to ocular symptoms, she had a 7 pound weight loss, anxiety, heat intolerance and diarrhea. She denied dysphagia, dysnea, dysarthria or palpitations. Vital signs were normal and bilateral ptosis with significant fatigability was noted. There was no exophthalmos, thryomegaly or palpable thyroid nodules on exam. Bilateral proximal muscle weakness with fatigability was present; sensation and reflexes were normal. Laboratory testing
revealed suppressed TSH <0.003 (0.35-5 mU/mL), high free T4 1.6 (0.8-1.5 ng/dL), normal free T3 3.5 (2.2-4 pg/ mL), elevated thyroid stimulating IgG 2090 (<130%), elevated anti-microsomal antibody 145 (<60 unit/mL) and normal anti-thyroglobulin antibody 2.1 (0-4 unit/mL). Anti-acetylcholine receptor antibodies were elevated, with positive anti-striational antibody, which is highly associated with thymoma. However, CT chest failed to demonstrate a thymoma. She was discharged on methimazole 5mg twice daily for GD, pyridostigmine and prednisone for coexisting OMG. The patient developed transaminitis due to methimazole and underwent total thyroidectomy, but declined concurrent thymectomy. Supplemental levothyroxine 100mcg was initiated; however she experienced progressive fatigable weakness and worsening diplopia. An orbital MRI excluded Graves’ ophthalmopathy. Repeat TSH remained suppressed at 0.096 mU/mL with normal free T4 of 1.0 ng/dL. Steroids and azathioprine provided drastic improvement of visual symptoms.

Discussion: Although rare, concurrent presentation of MG and GD has been reported. A milder OMG is seen in association with GD in young females and thymoma is often absent. Hypotheses for the coexistence of MG and GD involve shared pathogenetic mechanisms including association with HLA-DQ3, T helper 17 cells mediating the immune response, or immunological cross-reactivity against autoantigens shared by thyroid and ocular muscles. A “see-saw relationship” is described between MG and GD, where worsening of one disease and simultaneous improvement in the other is noted, as in our patient after her thyroidectomy.

Conclusion: Myasthenia gravis, in the setting of Graves’ disease, presents as a milder ocular variant. Ptosis is not a symptom related to Graves’ ophthalmopathy and it is imperative that clinicians distinguish and differentiate between two similarly presenting autoimmune illnesses.

Abstract #1155

ACUTE NECK SWELLING: A RARE CASE OF SPONTANEOUS HEMORRHAGE IN THYROID NODULE

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UIC/Advocate Christ Medical Center

Case Presentation: Spontaneous hemorrhage into a thyroid nodule is very rare and presents with painful or painless sudden neck swelling. This may result in acute airway obstruction and can also manifest as thyrotoxicosis. Etiologies include trauma from fine needle biopsy, blunt or deceleration injury. Other causes can be straining during heavy lifting and hemorrhage in a rare anaplastic thyroid carcinoma. Here we present a case of spontaneous hemorrhage in a thyroid nodule with acute development of compressive symptoms with no obvious predisposing factors.

A 68 year old female with history of thyroid nodules presented to the emergency department (ED) with acute onset of neck swelling and tenderness of one day duration. She had dyspnea on lying down and dysphagia and felt her thyroid was more firm than before. She had a biopsy of her thyroid nodule two years ago with benign findings. No trauma, fever or upper respiratory symptoms. No symptoms of hyperthyroidism. She was not on anticoagulation therapy. In the ED, her BP was 149/81 mmHg, HR 106 beats per minute, RR 20 breaths per minute, temperature 36.6 degree Celsius and oxygen saturation of 97% in room air. Physical examination was negative for stridor and showed a firm thyroid with tenderness and enlarged left lobe. No ptosis, no bruit over the thyroid and no neck lymphadenopathy. Laboratory studies showed normal hemoglobin, WBC, platelets and coagulation panel. Calcium normal at 9.4 mg/dL, TSH normal at 0.477 mcunit/mL, total T4 normal at 10.7 mcg/dL. CT scan of the neck showed enlarged left thyroid lobe (7.8 x 5.0 cm) with heterogeneous attenuation. Trachea was deviated to the right but patent. Right lobe was 6.8 x 2.2 cm with low density nodules. Patient underwent total thyroidectomy with no complications and cytology showed benign multinodular goiter with extensive hemorrhage into the left lobe.

Conclusion: Sudden neck swelling is usually caused by acute inflammation and spontaneous bleeding into the thyroid gland is rare. Two possible underlying mechanisms are: (1) abnormal vessel anatomy with resultant weakened veins; (2) arteriovenous shunting within the nodule hence simple exertion like coughing and straining can cause extravasation of blood into the nodule with increased risk for patients under anticoagulation therapy. Conservative management can be initiated if there are no signs of stridor or dyspnea. Increasing size and airway compromise should prompt emergency intubation and surgery. This patient had total thyroidectomy because of lack of improvement in symptoms. Diagnosis of spontaneous hemorrhage into the thyroid nodule can be challenging, however early diagnosis is important as this can be life threatening.
Abstract #1156

IMPACT OF THYROID HORMONES ON CLINICAL OUTCOMES IN NON-SMALL CELL LUNG CANCER PATIENTS, EXPERIENCE OF A UNIVERSITY HOSPITAL

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Objective: There has been evidence that thyroid hormones contribute to cancer progression by promoting tumor angiogenesis. It has also been suggested that decreasing thyroid hormones within the body may have a protective effect. The aim of this study was to investigate the role of thyroid hormones in non-small cell lung cancer (NSCLC).

Methods: We conducted a retrospective review of all patients diagnosed with non-small cell lung cancer at our Institution from 2011 to 2013. Demographics, clinical characteristics, comorbidities, thyroid stimulating hormone (TSH), free T4 and total T4 levels were studied. Kaplan-Meier was use for survival analysis and Cox regression for multivariate analysis.

Results: A total of 730 patients with NSCLC were analyzed. Median age at diagnosis was 70 years. Patients were staged as I (26.3%), II (13.4%), III (18.5%) or IV (41.7%). 240 (32.8%) patients had TSH levels measured. We found overall prevalence of 9.2% (22) of hypothyroidism and <1% of hyperthyroidism. The median serum TSH was 1.41 (range: 0.01-37.8), median free T4 1.14 (range: 0.77-2.76) and median total T4 was 7 (31.-11.1). There was no substantial difference in median TSH and total T4 levels between lower and higher stages of disease. Patients with TSH levels lower than 3.5 were associated with a better histologic grade (OR: 0.68, p<0.03). TSH and T4 levels were not predictors of survival by univariate or multivariate analysis.

Discussion: The patients in our study had similar prevalence of hypothyroidism and hyperthyroidism compared to the general population. Thyroid hormone levels were similar across all stages of NSCLC. However, a significant relationship was seen between TSH level and histologic grade. This finding supports the theory that thyroid hormones play a role in progression of cancer cells.

Conclusion: There may be an association between elevated thyroid hormones and poor cell differentiation. In order to further evaluate if thyroid hormones play a direct role in the pathophysiology of NSCLC an increased sample is required.

Abstract #1157

TRENDS IN THE US FOR INPATIENT HOSPITALIZATION AND COSTS FOR HYPERTHYROID EMERGENCIES (1993-2013)

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Objective: Thyrotoxic crisis (TC) is a life threatening condition approaching 10-20% mortality. Hyperthyroid emergencies mainly includes Thyrotoxic Crisis (TC) or Thyroid Storm. Descriptive epidemiological narratives for hyperthyroid emergencies in the United States are not available. High quality descriptive data are needed to facilitate outcomes research and cost-effective care in hyperthyroid emergencies.

Methods: Data was obtained from an all-payer, 20% random sample of US hospitals (Nationwide Inpatient Sample-NIS) for the years 1993-2013. SUDAAN software was employed for data collection and analysis. International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) was used.

ICD-9-CM codes used for analyses are as follows and describe various etiologies for underlying hyperthyroidism (242.01, 242.11, 242.21, 242.31, 242.41, 242.81, and 242.91). For example, 242.01 denotes TC due to underlying Grave’s disease. An all cause outcomes analysis was done with subsequent individual analyses where data were available.

Results: Hospital discharges for all cause TCs during 1993-2013 were as follows - 1,715 pts in 1993 & 1,895 patients in 2013, Length of stay (LOS in days) was 6.8 in 1993 & 5.3 in 2013, Mean charges were 11,962 United States Dollars (USD) in 1993 & 46,845 USD in 2013. When adjusted to inflation, 2013 costs (i.e. 46,845 USD) were equivalent to 19,688.71 USD. Due to grouping of TC etiologies under disparate ICD-9-CM codes, standard deviations were not available for all cause TC’s. Where possible, outcomes analyses for individual etiologies were performed.

Discussion: Costs for TC inpatient care in the US have increased from 1993-2013 and this persists after being controlled for inflation. Overall, there has been no change in the prevalence of TC in the US measured via hospital discharges. There has been no improvement in LOS noted for inpatient admissions in the US for TC.
**Conclusion:** Despite advances made in decreasing LOS for other acute morbid conditions, no such improvement in LOS for TC was seen. Further research is needed to devise cost effective care of hyperthyroid emergencies in the era of accountable care.

**Abstract #1158**

**THE USE OF MOLECULAR MARKER PANELS FOR TREATMENT OF PAPILLARY THYROID CANCER: KNOWING WHAT WE DO NOT KNOW**

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**Objective:** To determine if the addition of BRAF gene mutation analysis among patients with papillary thyroid cancer along with routine pathologic evaluation would change postoperative course including prognosis, follow-up, and administration of radioactive iodine ablation.

**Methods:** Retrospective review from 2004 through 2014 to include all patients who carried a final pathologic diagnosis of papillary thyroid cancer. Demographic data collection along with tumor characteristics, BRAF detection, and post-operative course were evaluated.

Descriptive multivariate statistics were calculated for BRAF (+) tumors, BRAF (-) tumors, and the combination of both diagnosis groups incorporating clinical variables such as size, capsular invasion, extra-thyroidal extension, multiple tumors, and lymphatic or vascular invasion.

**Results:** From 2004 through 2014, 575 patients underwent surgical treatment for papillary thyroid cancer. Women consisted of 82% of the population and mean age of patients was 51 years. Overall recurrence, mortality, and postoperative treatment systems were scrutinized between BRAF (+) and BRAF (-) tumors along with the well-known routine pathologic variables of capsular invasion, margin involvement, extra-thyroidal extension, metastasis, and multiple tumors. During the BRAF testing period from 2010-2014, a total of 178 patients underwent postoperative radioactive iodine ablation with 69% of BRAF (+) patients treated with ablation and 65% of BRAF (-) patients treated with ablation.

**Discussion:** Understanding that BRAF mutation may carry a poor prognosis did not seem to change overall management and outcomes in our patient population. The decision to provide the patient with radioactive iodine ablation could be determined from poor tumor characteristics found on routine pathology reports. No clinical benefit was observed by the addition of molecular analysis on patient outcomes. Given the excellent overall prognosis of papillary thyroid cancer and the widespread availability to established prognostic indicators with routine pathologic review, we found insufficient evidence to support initial testing for BRAF mutations among our patient population. BRAF testing may prove cost-effective with more impact if limited to the setting of recurrent and advanced metastatic disease.

**Conclusion:** Among our patient population, additional send-off evaluation with BRAF gene mutational analysis did not change post-operative management of patients diagnosed with papillary thyroid cancer compared to those patients only undergoing routine pathologic analysis.

**Abstract #1159**

**DIFFUSE SCLEROSING PAPILLARY CARCINOMA IN A PEDIATRIC PATIENT WITH INTRAUTERINE DIAGNOSTIC XRAY EXPOSURE**

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**Objective:** The relationship between occurrence of childhood cancer and intrauterine exposure to radiation is well known. We describe a case of diffuse sclerosing papillary carcinoma (PTC) in a pediatric patient exposed to diagnostic radiation in utero.

**Methods:** Clinical presentation, including radiation history and outcome, was reported.

**Case Presentation:** A 14 year old male was referred for a thyroid cancer consultation in 2008. His history was notable for a rapidly growing thyroid mass during the preceding 3 months and in utero exposure to radiation, in the form of multiple xrays and CT scans, at 12 weeks gestation as a result of maternal multiple traumas due to a car accident. A total thyroidectomy with bilateral central, level 7 and right modified neck dissection for a rapidly growing thyroid mass was performed. Pathology revealed multifocal, bilateral, moderately differentiated, diffuse sclerosing PTC 8.6 cm in greatest dimension. The tumor was not encapsulated, with vascular invasion and extensive extrathyroidal extension. Metastases were positive in 32 of 36 lymph nodes sampled. Post-operative unstimulated thyroglobulin (Tg) by RIA and Tg antibody (TgAb) were 137 (0-39 ng/mL) and 4183 (0-100 IU/mL), respectively. Ultrasound (US), PET/CT and post I-131 treatment scan revealed abnormal nodes but no distant metastases. To date, he has had an additional right neck dissection for poorly differentiated PTC lymph node metastases, a total of 340 mCi of I-131, and has persistently positive unstimulated Tg and TgAb at 9.2 (<40 ng/mL) and 36 (<1.0 IU/mL) respectively, without evidence of structural disease.
Discussion: Diffuse sclerosing PTC occurred in this pediatric patient exposed to diagnostic radiation in utero. His clinical course was notable for locally aggressive behavior of the PTC and biochemically persistent disease. A causal relationship between the timing and quantity of the radiation exposure and the development of a rare variant of PTC in this patient was suspected.

Conclusion: The relationship between radiation exposure and PTC is well known. Case control studies have documented an increased risk of childhood cancer in those exposed to radiation over 10 mSv in utero. Although radiation exposure to the developing fetus rarely occurs, consideration should be given for close monitoring of in utero radiation exposed patients for the development of PTC.

Abstract #1160

PERFORMANCE OF 4-D CT SCAN IN LOCALIZATION OF PARATHYROID ADENOMAS IN ULTRASOUND NEGATIVE POPULATION

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Objective: Ultrasound remains the most cost effective imaging modality in use for this purpose, it is non-invasive with no radiation exposure and anatomically precise, and its sensitivity varies and overall is around 75-80% in centers that are experienced. (1-3)

For ultrasound negative patients the use of 4D-CT scans has been proposed, this study looks at the performance of this modality in the group of patients who were u/s negative for pre-op localization

Methods: Retrospective chart review of patients who were diagnosed with primary hyperparathyroidism with subsequent Parathyroidectomy and confirmed surgical cure by normalization of post-op calcium's

Inclusion criteria.

20 patients were selected. All were hypercalcemic with inappropriate IPTH levels and absence of Familial Hypocalciuric Hypercalcemia.

They all underwent high resolution ultrasound evaluation for parathyroid adenoma at a high volume center with one experienced ultra-sonographer, sensitivity of this center at localization is around 70-75%.

All 20 were also evaluated by 4D CT scan, 18 done at a community based hospital and 2 scans at a tertiary university hospital.

All 20 patients then underwent surgical resection with intra-operative IPTH monitoring by a group of 4 experienced parathyroid Surgeons.

Results: In u/s negative patients the 4D CT localized adenomas in 8 out of 15 patients, out of which 4 were false positives. Hence its sensitivity was 36.36% with a positive predictive value of 50%.

Meaning the 4 DCT was able to localize the parathyroid adenoma in patient with negative thyroid u/s (53% of this group) with an accuracy equivalent to flipping a coin.

5 patients were deemed suspicious for a parathyroid adenoma on u/s and 4D-CT agreed with the ultrasound in 3 of those cases and was negative in 2.

The 4DCT did localize 3 cases of five, but looking at the results retrospectively a low suspicion US did localize the 5 parathyroid adenomas in all 5 cases.

Overall the sensitivity of 4 DCT to localize a PHPT was 43.75%, and its PPV was 63.64%.

Discussion: Study is limited by the small sample size it has and slowly building expertise on part of the radiologists at reading these scans whereas u/s also being operator dependent has a longer experience. Adding to the patient sample to maximize statistical significance will help get more information in the future.

Conclusion: In patients who are ultrasound negative for parathyroid adenoma localization , adding a 4D CT scan routinely is not recommended as a imaging modality for the majority of patients due to poor sensitivity and poor positive predictive value, 14* times higher cost and 50 times higher radiation exposure.(5)

Abstract #1161

IDIOPATHIC HYPOKALEMIC PARALYSIS SUCCESSFULLY TREATED WITH SYMPATHOMIMETIC AMINES

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Objective: Hypokalemic periodic paralysis (HPP) is most known to the endocrinologist when associated with thyrotoxicosis. When thyroid abnormalities are not present, it is generally is related to familial HPP. If there is no known family history it is considered idiopathic. In both cases it is considered to be related to missense mutations of voltage sensor domains within the alpha, subunit of L-type calcium channels or the skeletal Na+ channel.

These mutations generate an abnormal gating pore current activated by hyperpolarization. Sympathomimetics, e.g., pseudoephedrine and ephedrine are known to occasionally cause HPP, and therefore precipitate associated symptoms of hypokalemia such as numbness. Nevertheless, the purpose of this study was to determine if the use of the sympathomimetic amine could improve HPP in view of other conditions that were present that typically show
favorable response to dextroamphetamine sulfate.  

Methods: A 29 year old woman with a 10 year history of HPP which had required several hospitalizations was started on dextroamphetamine sulfate extended release capsules 15mg/day to treat severe premenstrual nausea and pelvic pain not related to hypokalemia.  

Case Presentation: The patient had been able to keep herself from hospitalization by taking oral potassium supplementation whenever the classic symptoms begin of lip quivering, numb tongue, and cold and numb hands. In the past these episodes were associated with a drop in potassium to subnormal levels even though most of the time the serum potassium is normal. With a dosage of 25mg extended release dextroamphetamine capsules, not only did her premenstrual nausea disappear, her pelvic pain was reduced, and surprisingly episodes associated with hypokalemia were abolished (which before averaged 2 episodes per month). Because of an accident with a fractured hip she went 4 months without dextroamphetamine. She redeveloped episodes associated with her hypokalemia at the same rate as before. These symptoms disappeared again when the drug was restarted.  

Discussion: It is not clear why in some instances hypokalemia seems to be precipitated by pseudoephedrine in cough medicine or diet pills with other amphetamines, but in this case dextroamphetamine corrected HPP episodes.  

Conclusion: Dextroamphetamine sulfate seems to work by inhibiting cellular permeability. Perhaps chemicals leaking into CA++ or Na+ channels causes the drop in potassium. It is not clear what factors may precipitate the increased cellular permeability.

Abstract #1162  

EVALUATION OF THYROID FNA GENOMIC SIGNATURES: (ENHANCE) A UNIQUE BIO-REPOSITORY FOR ADVANCING SCIENCE  

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Objective: The Bethesda criteria and advances in cytopathology have facilitated the appropriate management of the majority of thyroid nodules. Nonetheless, 15-30% remain cytologically indeterminate (Cyto-I), predominantly in Bethesda classes III and IV. Genomics has provided additional clarity in these two classes for guiding the use and extent of diagnostic surgery. The 142-gene mRNA Afirma Gene Expression Classifier (GEC) is identified in the 2015 ATA and NCCN Guidelines with high NPV as a cancer ‘rule-out test’ to assist informing diagnostic surgery decisions in cyto-I nodules. Extensive independent clinical utility publications have shown a marked reduction in the use of surgery among patients with benign 142-gene GEC results. Recently, certain DNA mutations have been suggested as a ‘rule-in test’. Clinical utility for this latter approach in Cyto-I is unclear. Despite advances in genomic technology, opportunities remain for additional precision. The ENHANCE trial is intended as a unique comprehensively annotated biorepository of paired genomic and histopathological samples, essential to further the understanding of mutations and transcriptional expression in Cyto-I patients.  

Methods: This is an IRB-approved study to accrue thyroid FNA samples and associated nucleic acid as well as associated clinical, radiological and histopathological data, if applicable, from patients who have already undergone either the Afirma Thyroid FNA Analysis or GEC only analysis. The study is comprised of 2 arms, Arm 1: patients who have been recommended surgery or have undergone surgery, Arm 2: patients with either a benign GEC or benign cytopathology with a minimum of 2 years follow up. Histopathology for Arm 1 patients are centrally reviewed and assigned a guidelines-compliant pathology label by a panel of blinded expert pathologists.  

Results: As of December 2015, 39 sites have been opened across the US of which 20% are academic centers, and 80% represent community practices. More than 350 of 700 planned patients have enrolled in the study. 80% of these patients fall under Arm 1 of the protocol and 20% under Arm 2. Centrally adjudicated pathology labels have been obtained for >150 patients. Full genomic mutational and transcriptional data is being collected. Data will be presented.  

Discussion: As disease management and technology advance, expert guidelines help to inform physician decisions. Genomics rooted in the right clinical questions augments the understanding of pathophysiology which in turn benefits patients.  

Conclusion: This extensively annotated bio-repository will serve as an invaluable resource to address critical future scientific and clinical questions.
Abstract #1163

THYROTOXIC PERIODIC PARALYSIS: CHALLENGING DIAGNOSIS IN A CASE WITH MIXED ETHNICITY

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Objective: Thyrotoxic periodic paralysis (TPP), commonly seen in East Asians, may be missed in western individuals of mixed ethnicity.

Case Presentation: 27 yo African American (AA) Female with no significant past medical history presented with acute onset of profound lower extremity (LE) weakness with inability to walk. She had previously been seen for intermittent LE weakness and was diagnosed with hypokalemia and sent home on oral potassium (K). She reported recent 30 lb weight loss, fatigue, and heat intolerance. Examination revealed tachycardia, tremor, mild thyromegaly with a bruit, significant bilateral LE weakness, diminished LE reflexes and LE edema. Laboratory data included K 2.3 mg/dL, TSH < 0.01 uIU/mL, free T4 7.4 ng/mL, free T3 16.3 pg/mL. EKG showed sinus tachycardia. She was treated with potassium IV and PO for 48 hours and was started on propranolol and methimazole. Thyroid stimulating immunoglobulin was 219% baseline (normal<140). On outpatient follow up 3 weeks later, LE strength was 4+/5 and free T4 was 1.79 and K 3.7 on propranolol and methimazole. At that time additional history revealed some Native American ancestry.

Discussion: TPP is characterized by severe hypokalemia with muscle weakness associated with thyrotoxicosis and is due to intracellular influx of potassium in response to beta adrenergic activity. Nonselective β-adrenergic blockers can prevent recurrence of the paralytic attacks. The episodic paralysis remits with control of hyperthyroidism. A strong genetic predisposition has been assumed due to Asian racial preference (1.8-1.9% of thyrotoxic Asians compared to 0.1-0.2% of thyrotoxic North Americans). Association has been found between TPP and the KCNJ2 gene which encodes a K channel. Unlike thyrotoxicosis, which is 9 fold more common in females, TPP occurs 6-20 fold more commonly in males. Only two cases have been reported in AAFs. TPP has been reported to be more common in Native Americans (NA) than in Caucasians or AAs. There is evidence that NAs and Asians have common ancestry due to migration of humans from Asia to North America 11000-23000 years ago. Our patient’s expected low risk for TPP as an AAF was likely influenced by her NA ancestry, giving credence to a genetic susceptibility of the patient for the condition.

Conclusion: Early diagnosis and prompt treatment prevent life-threatening complications associated with TPP. Even patients with apparent low epidemiological risk who present with hypokalemic paralysis should undergo assessment of thyroid function to distinguish TPP from other forms of hypokalemic periodic paralysis, as the management approach differs.

Abstract #1164

PROFOUND HYPOTHYROIDISM IN SEVERE RHEUMATOID ARTHRITIS (RA) WITH GRAVES ORBITOPATHY AND AMIODARONE EXPOSURE

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Objective: Autoimmune Thyroiditis is the most common cause of hypothyroidism, with high prevalence in patients with RA and Systemic Lupus Erythematosus (SLE), which can amplify its cardiovascular risk. Additionally certain medications such as amiodarone, can cause thyroid dysfunction.

Case Presentation: A 45-year-old African American man with SLE, RA, Pericarditis, seizure disorder, and atrial flutter, with no previous known thyroid disorder presented with dyspnea and fatigue. Consultation was placed for evaluation of adrenal insufficiency and new onset profound hypothyroidism. Within several hours of evaluation hospital course was complicated by PEA arrest requiring mechanical intubation. TSH measured 107 uIU/mL, (n=0.35-5.50), with undetectable free T4 level (FT4), CT head interestingly demonstrated Graves’ orbitopathy and chest CT confirmed large goiter. Medical history was significant for atrial flutter treated with Amiodarone. He received intensive care, stress dose glucocorticoids and IV levothyroxine. Several weeks after clinical improvement he has required supraphysiologic doses of levothyroxine likely in setting of concurrent treatment with phenobarbital and phenytoin, which can interfere with levothyroxine therapy by increasing thyroxine metabolism. The patient remains treated with alleviated thyroid symptoms.

Discussion: Concern for Type 1 Amiodarone induced Thyroiditis (T1AIT) with transition to Type II Amiodarone induced Thyroiditis (TIIAIT) was gathered through history. Amiodarone is a class III anti-arrhythmic known to cause both hypo- and hyperthyroidism, partly due to high iodine content and direct toxicity on the thyroid. Patient had been treated with Amiodarone for two years possibly increasing synthesis of T4 via excess iodine substrate, in setting of latent Graves’ disease (GD). Clinically patient exhibits overt manifestations, including profound exophthalmos, peri orbital edema, goiter and myxomatous...
dermopathy. The underlying mechanism of TSH >100 with undetectable FT4 coincides with a “burned out state” in which substrates for hormone production are depleted. The question of possible burned out GD was considered given clinical findings, however TSI and TPO antibodies were within reference.

**Conclusion:** In conclusion, this is an exemplary case of increasing awareness of thyroid dysfunction in severe Rheumatologic disease complicated by medication effects of p450 inducers.

**Abstract #1165**

A SHRAPNEL FRAGMENT DEPOSITED 45 YEARS AGO CAUSED A FALSE POSITIVE RAI UPTAKE IN THE SPINE IN A PATIENT WITH PAPILLARY THYROID CARCINOMA: A REVIEW OF MECHANISM AND LITERATURE.

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**Objective:** Radioiodine total body scan is used to detect recurrent differentiated thyroid cancer in neck and metastatic lesions. We recently encounter a case of false positive in a veteran who suffered from shrapnel wound 45 years ago in the back.

**Case Presentation:** A 69 yo Vietnam war veteran with paraplegia and a history of PTC, s/p total thyroidectomy 5/13 (T3, N1) multifocal with lymphovascular and capsular invasion. 8/8 lymph nodes were positive and s/p I-131 remnant ablation 7/13 with 143 mCi. Suppressed Tg in 1/14 was 5.9 ng/mL. A dose of 254 mCi of I-131was given in 8/14 for metastatic PTC after L sided neck dissection and found 5/8 LN positive in 4/14. A post-RAI treatment scan revealed a focal uptake in the posterior component of T10//T11 vertebra which, in retrospect, was present in the prior post-ablation scan in 7/13 without any interval change. A chest CT in 9/14 revealed a subcentimeter metallic density in the same site, likely shrapnel deposited 45 years ago. Thus, focal radioiodine uptake likely relates to inflammatory/benign etiology. Suppressed Tg was 3.9 ng/mL in 8/15, decreased from 5.3 ng/mL in 2/15.

**Discussion:** Focal radioiodine uptake is a sensitive marker for detection of recurrence of differentiated thyroid cancer, s/p total thyroidectomy and RAI ablation. However, radioiodine uptake is not specific for thyroid tissue. It can also be seen in healthy tissue, including thymus, breast, liver, and gastrointestinal tract, or in benign diseases, such as cysts and inflammation, or in a variety of benign and malignant non-thyroidal tumors, which could be mistaken for thyroid cancer. In order to accurately interpret radioiodine scintigraphy results, one must be familiar with the normal physiologic distribution of the tracer and frequently encountered physiologic and pathologic variants of radioiodine uptake. This case study provides another example of potential false-positive uptake of radioiodine in the whole body scan and illustrate how such unexpected findings can be appropriately evaluated. Chronic trauma may recruit leukocytes that known to induce iodide organification by means of a myeloperoxidase. Therefore, retention of radioiodine in leukocytes of posttraumatic tissues may also explain various reports of false-positive uptake in sites of inflammation. Secretion of mucin containing iodide salts has also been suggested as another possible mechanism of iodine accumulation associated with chronic inflammatory conditions.

**Conclusion:** Wounds caused by shrapnel fragments could be a common problem for veterans returning from overseas. Recognizing that false positive results could occur in RAI total body scan is clinically important.

**Abstract #1166**

MEDULLARY THYROID CARCINOMA: DIAGNOSTIC CHALLENGES OF FINE NEEDLE ASPIRATION CYTOLOGY – CASE PRESENTATION OF A WOMAN WITH A THYROID NODULE AND EVENTUAL DIAGNOSIS OF MULTIPLE ENDOCRINE NEOPLASIA TYPE 2

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**Objective:** To highlight some diagnostic challenges of fine needle aspiration (FNA) in detecting medullary thyroid carcinoma (MTC) in thyroid nodules, and the role of IHC (immunohistochemistry) and calcitonin (Ctn) measurement in cases of seemingly inconclusive cytology.

**Methods:** Case report of a middle-aged woman with a thyroid nodule discovered on a routine examination, and apparently benign or inconclusive initial FNA, but subsequently diagnosed with MTC, and she was positive for a RET proto-oncogene mutation.

**Case Presentation:** A 50-year old woman had FNA for a 1.3 cm complex nodule in the left thyroid lobe on ultrasound (US), initially found on a routine examination. The cytological diagnosis was a cellular adenomatoid nodule, or possibly a follicular neoplasm. However, there were mildly crowded nuclei and scattered vaguely spindle-shaped cells; the chromatin was fine and homogenous.
without nucleoli. An interval size increase to 1.6 cm was noted on a follow-up thyroid US 6 months later; a repeat FNA was performed. The smears were less cellular but with morphology similar to the previous FNA. The tumor cells were positive for AE1/AE3, chromogranin, synaptophysin, TTF-1 and calcitonin, consistent with MTC. She had genetic testing, and was heterozygous positive for a RET mutation p.C609Y, associated with multiple endocrine neoplasia type 2 (MEN2) or familial medullary thyroid cancer. Her older brother also tested positive for this mutation. Her serum Ctn was 1138 pg/ml; neck US was negative for metastasis. Screening for PHEO and primary hyperparathyroidism was negative. She underwent total thyroidectomy with left neck dissection. A 1.4 cm MTC was identified in the left lobe, and there were 2 foci of C-cell hyperplasia in the right lobe. The tumor cells were positive for Ctn, CEA, synaptophysin, chromogranin, and negative for thyroglobulin; 0/39 lymph nodes identified was positive for a metastatic carcinoma.

Discussion: It is not surprising that MTC was not diagnosed in the initial aspiration cytology in this patient. MTC has a variable appearance on FNA cytology. The tumor cells are usually discohesive and may be epitheloid, spindle-shaped or plasmacytoid; these may mimic thyroid follicular lesions, sarcomas, and plasmacytomas respectively. Diagnostic accuracy can be improved significantly with IHC and Ctn assay of the aspirate. Of note, in spite of the very high serum Ctn in this patient, there was no extrathyroidal involvement.

Conclusion: There is marked variability in cytological appearance of FNA from MTC nodules, thus posing diagnostic challenges. Although MTC is rare, whenever aspiration cytology is inconclusive or if there is subtle suggestion of MTC, IHC of the specimen and Ctn measurement are vital.

Abstract #1167

PROGNOSTIC VALUE OF SERUM THYROGLOBULIN MEASURED IN 48 HOURS AFTER SECOND DOSE OF RECOMBINANT HUMAN THYROTROPIN IN SURVEILLANCE OF WELL-DIFFERENTIATED THYROID CANCER

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Objective: Thyroglobulin (Tg) plays an important role in surveillance of differentiated thyroid cancer (DTC). In the past 2 decades, recombinant human Thyrotropin (rhTSH) has been used to increase sensitivity of Tg. Based on phase 3 studies by Genzyme, the optimum window to measure Tg was suggested to be 72 hours (h) after the second (2nd) dose of rhTSH. Due to a lower sensitivity of Tg assays at the time (1990s), radioactive iodine (RAI) whole body scan (WBS) was obtained often. The sensitivity of WBS increases with serum TSH level and use of lower energy I-123 WBS obtained at 48 h after the 2nd rhTSH injection. At our institution, many Tg measurements were performed on the same day as the I-123 WBS. 20 years later, revisiting this initial protocol is important as Tg (without WBS) is done increasingly. We conducted a retrospective study, comparing the prognostic value of Tg obtained in 48 h after 2nd dose of rhTSH to 72 h.

Methods: 608 DTC patients (already consented to be part of Thyroid Cancer Registry at Boston Medical Center) were evaluated in this study. Patients with rhTSH stimulated Tg in one year after initial RAI were included and divided to 2 groups based on the time of Tg measurement in regard to 2nd rhTSH dose (48 vs. 72 h). Information about American Thyroid Association (ATA) risk category and AJCC staging at baseline and level of response to treatment at final visit was obtained. The ability of rhTSH stimulated Tg predict patient’s response category was compared between the two groups.

Results: The average age of subjects was 47; more than half belonged to low ATA risk category at baseline. Average duration of follow up was 6 years. Tg was considered detectable if more than 1 ng/mL. Cases with Tg antibody were excluded. 1 year after RAI therapy, no patient with excellent response at final visit, had a detectable rhTSH stimulated Tg in any of ATA risk categories (regardless of the time of Tg testing). In low ATA risk group at baseline, patients with excellent response to treatment at final visit, had undetectable and all subjects with biochemical and
structural response, had detectable Tg in 48 h and 72 h after 2nd dose of rhTSH.

Discussion: Traditionally serum Tg has been checked in 72 h after the 2nd dose of rhTSH. Recently Genzyme has published the data showing the Tg elevation was similar at 48 h and 72 h and has encouraged more studies to identify other possible protocols with expanding the window to check serum Tg.

Conclusion: Serum Tg obtained 48 h after 2nd dose of rhTSH may provide a comparable prognostic value in DTC patients with low ATA risk as a Tg obtained at 72 h. Larger prospective studies would be beneficial to confirm our data and expand it to the other ATA risk categories.

Abstract #1168

SYSTEMATIC REVIEW OF THE POSITIVE PREDICTIVE VALUE OF RAS MUTATIONS IN CYTOLOGICALLY INDETERMINATE THYROID NODULES

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Objective: The positive predictive value (PPV) of RAS mutations in cyto-I nodules is uncertain, and factors accounting for differences between publications are unknown.

Methods: We conducted a systematic literature review in PubMed through 12/1/2015. Studies were included that reported RAS mutations in cyto-I nodules with confirmed histology. We abstracted the true positive (TP), false positive (FP), true negative (TN), and false negative (FN) rates of RAS mutations in cyto-I categories. Meta analyses were constructed calculating the sensitivity, specificity, and PPV of RAS mutations in cyto-I nodules.

Results: Seventeen studies reported clinical or surgical follow-up for all cyto-I nodules positive and negative for RAS mutations. Among these 2,035 cyto-I nodules, RAS mutations had a sensitivity for detecting malignancy of 30.4% and a specificity of 94.0%. In total, 264 (13.0%) RAS mutations were identified in histology benign and malignant nodules. A meta-analysis was performed of 19 studies reporting the TP and FP rates for RAS mutations with surgical follow-up in 2,099 nodules. The overall RAS PPV was 67.7% (range 13.3%-100%). In only 4 studies the histopathologist was blinded to the RAS mutation status. There was a discordance in the overall PPV between studies with unblinded histopathology compared to blinded studies (68.8% vs 60.0%, respectively). Furthermore, when comparing the 6 UPMC based studies (all unblinded) vs the 13 nonUPMC studies there was a significant difference in the overall PPVs (84.0% vs 51.5% respectively, p<0.01).

Discussion: Multiple studies report the PPV of RAS mutations among cyto-I nodules. With few exceptions, these studies are single-center retrospective clinical experience studies with unblinded histology leading to significant variation in the reported PPV. The significant probability of nodule benignity despite a RAS mutation limits its role in surgical decision making. In addition, RAS mutation analysis misses 70% of cancers in cyto-I nodules. Together, these findings raise questions about the validity of this biomarker to rule-in or rule-out thyroid carcinoma.

Conclusion: The reported PPV of a RAS mutation is highly variable. Unblinded pathologists diagnose RAS mutated thyroid nodules as malignant more frequently than those blinded to the molecular test result. These findings raise significant questions about the value and accuracy of RAS mutations to identify or predict malignancy in cyto-I thyroid nodules. Physicians should be cautious that pathologists are more likely to label a nodule as malignant when they know a RAS mutation is present. This bias may result in cancer over-diagnosis and over-treatment.

Abstract #1169

80 YEAR OLD WOMAN WITH THYROID CANCER THAT ORIGINATES IN AN AUTONOMOUS TOXIC NODULE PRETREATED RADIOIODINE

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Objective: Present an interesting and rare case of thyroid cancer in a toxic autonomous nodule

Methods: We present the characteristics and evolution of the patient

Case Presentation: Women 80 years old, comes to evaluating left thyroid nodule and dysphonia. Three years previously treated with radiiodine (10 mCi) for toxic autonomous nodule another institution: TSH: 0.029uIU/ml on ultrasound and hot nodule 13mm in LTI in I-131 scintigraphy and 99mTc; FNA was not performed. She was presented with a nodule of 2 cm in LTI increased consistency,no lymph. TSH: 7.6uIU/ml;FT4: 0.77;AbTPO/AbTg (-). Ultrasound: hypoechoic and heterogeneous nodule of 20x16mm with central microcalcifications and mixed vascularity. In the scintigraphy with 99mTc: decreased volume of LTL vs cold nodule. FNA: Bethesda VI. She underwent total thyroidectomy, stony tumor was found in LTI with extracapsular extension to pre-thyroid muscles and commitment of the left recurrent laryngeal nerve. The pathology reported: papillary thyroid cancer of 30mm, follicular variety (80%), classic (20%) non-
encapsulated with lymphatic tumor microemboli that infiltrates the thyroid capsule to muscle planes. Four weeks after surgery: TSH: 66.4uUI/ml; Tg: 12.9ng/ml; received radioiodine (120 mCi), the post-therapy WBS (+) on the neck. When no structural or biochemical evidence of disease at present.

Discussion: Most autonomous nodules are benign follicular neoplasms; however, there are presentations of hot malignant nodules, in which the presence of activating TSH receptor is usually detected. Chronic activation of the TSH receptor could cause mutations in other oncogenes thyroid.

Conclusion: We should consider this association in cases of elderly or large nodules.

Abstract #1170

HYPERTHYROIDISM PRESENTING AS PERIODIC PARALYSIS

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Objective: We present case history of a 24-year-old Caucasian man who presented with muscle cramps, muscle weakness and hypokalemia.

Case Presentation: This patient presented to the emergency department initially with muscle cramps and transient lower limb weakness following a carbohydrate binge the night before. He was not on any prescription medications and had no other medical or surgical problems. He was noted to be hypokalemic with serum potassium level of 2.7 mmol/L (3.5-5.5) and was given potassium supplements parenterally. His lower limb weakness improved with this. He had similar presentation a few weeks later and this time he was noted to have potassium level of 2.3 mmol/L. He gave history of significant weight loss, tremors and palpitations during this visit. His father had Graves’ disease and sister had hypothyroidism. He was a smoker for the past 5 years but denied any substance abuse. He had a moderate sized goiter and mild proptosis with no lid lag or lid retraction. There was no pretibial myxedema. Lower limb muscle weakness and difficulty in walking was noted at presentation. Cranial nerves were normal and there were no sensory defects. Cardiorespiratory and abdominal examination was unremarkable.

During the second presentation, apart from a low potassium level of 2.7 mmol, thyroid function tests done confirmed hyperthyroidism. Free T4 was 61 pmol per liter (11.5–22.7) with free T3 of 30.8 pmol per liter (3.5–6.5) and TSH level of < 0.01 mu per liter. TSH receptor antibody was high at 248 units/L ( < 10) confirming the diagnosis of Grave’s disease. He was initiated on methimazole treatment. On Methimazole treatment, thyroid function tests improved and potassium level has been consistently normal. He hasn’t had any muscle cramps or lower limb weakness since then.

Discussion: The association between hypokalemic periodic paralysis and thyrotoxicosis is mostly reported in Asians and Hispanics. Our report documents the existence of such an entity in Caucasians. The incidence of Thyrotoxic Periodic Paralysis (TPP) in North America is between 0.1% to 0.2%. TPP is a rare but potentially fatal complication of thyrotoxicosis. The paralysis is mediated by channelopathies, abnormalities of Na-K-ATPase pump, hyperinsulinemia and hyperadrenergic state. TPP should be considered as a differential diagnosis in patients presenting with sudden muscle weakness.

Conclusion: Our report highlights the association between Thyrotoxic periodic paralysis and Grave’s disease in Caucasians. TPP is a rare but reversible complication of thyrotoxicosis.

Abstract #1171

ANTITHYROID DRUG INDUCED AGRANULOCYTOSIS: A RARE BUT SERIOUS COMPLICATION CAN HAVE A VERY LATE PRESENTATION

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Objective: To report agranulocytosis associated with thionamide therapy in a lady who was using Propythiouracil (PTU) for last 6 years for Graves’ Disease.

Methods: Using the case format to present clinical course, laboratory testing data to support clinical decision making.

Case Presentation: In August 2009, a 20 years old lady was referred to the Endocrine Clinic for evaluation of her hyperthyroidism. She was 12 weeks pregnant and was clinically hyperthyroid, had a grade 2 goiter with bruit and exophthalmos. Her TSH: 0.01uU/mL (0.4–4.2 uU/mL), FT4: >6.0 ng/dl (0.93–1.7 ng/dl). A diagnosis of Graves’ disease was made and she was started on Propylthiouracil (PTU). After delivery, she was switched over to Neomercazole which she could not tolerate and thus was kept on PTU. She could not be weaned off her thionamide therapy. Radioactive Iodine treatment as a definite treatment could not be opted since within last 6 years, she had three pregnancies and was either pregnant or breast feeding her young babies. She followed-up at the clinic very infrequently. On 2nd December 2015, she presented with history of high grade fever with rigors and oral ulcers. Her Complete Blood Count (CBC) showed Agranulocytosis with White cell count (WBC) of 1.5x10E9/L (4.0-10.0x10E9/L) with Absolute Neutrophil
Count (ANC) of 0.27x10E9/L, her Platelet Count was 133x10E9/L, along with that she had Iron Deficiency Anemia. She was admitted, her PTU was stopped, she was given Amoxicillin/Calvulanate intravenously, her cultures and Chest X-rays all were negative. She was given a stat dose of Granulocyte Colony Stimulating Factor (Filgrastim 300 mcg). Next day her WBC rose to 3.1x10E9/L with ANC of 1.2x10E9/L and her condition got better and within a week the WBC normalized to 5.1x10E9/L with ANC of 2.9x10E9/L. Now she has made arrangements and is being referred for Radioactive Iodine Treatment.

**Discussion:** Agranulocytosis is a rare but serious complication of thionamide therapy with a prevalence of 0.1 to 0.5 percent. Most cases of agranulocytosis occur within the first 90 days of treatment, but this can occur even a year or more after starting therapy. It is advised that patients on thionamide therapy should have an immediate WBC with differential at the earliest sign of a fever, sore throat or other infection, and to stop the drug until the result is available.

Recovery from agranulocytosis usually takes a few days, but can be prolonged, and morbidity and death from serious infections can occur. Granulocyte colony-stimulating factor (G-CSF) has been used as adjunctive therapy in severe cases.

**Conclusion:** Physicians should be aware of late presentation of agranulocytosis with thionamide treatment and should counsel their patients accordingly.

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**Abstract #1172**

**FAMILIAL VERSUS SPORADIC ENCAPSULATED FOLLICULAR VARIANT OF PAPILLARY THYROID CARCINOMA: NEED FOR MORE AGGRESSIVE THERAPY?**


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**Objective:** Current management dilemmas in rarer familial encapsulated follicular variant of papillary thyroid carcinoma.

**Methods:** A kindred with 6 women with malignancies eFVPTC [3] and non thyroidal [3].

**Case Presentation:**

Sister A: 30 y female, swelling neck; US Right thyroid lobe nodule hyperechoic 24x14x15 mm increased vascularity; FNAC Nodular goiter with cystic changes; Surgery Right hemithyroidectomy; HPE: Follicular variant of encapsulated papillary carcinoma, diffuse CK 19 staining positive; Hypothyroidism L Thyroxine 50 ug/d; TPOAb/TGAb negative; Family history: Squamous cell carcinoma esophagus maternal grandmother, Adenocarcinoma pancreas maternal aunt, Carcinoma Uterus maternal grandaunt.

Sister B: 27 y, swelling neck noticed by Sister A; US Right thyroid lobe irregular heterogeneously hypoechoic nodule 11x8x9 mm with calcifications and increased peripheral and internal vascularity TIRADS 3/4A category; TPOAb and TGAb positive; euthyroid; FNAC Possible differentiated thyroid neoplasm; Surgery Right hemithyroidectomy; HPE Follicular variant of papillary thyroid carcinoma, no capsular or vascular invasion; Completion thyroidectomy; HPE Chronic lymphocytic thyroiditis.

Mother C: 48 y, swelling neck noticed by Daughter A; US Left thyroid lobe hypoechoic nodule 7x5 mm, irregular inferior margins, no increased vascularity or calcifications; FNAC Differentiated thyroid neoplasm favoring papillary carcinoma; TPOAb positive; euthyroid. Surgery: Total thyroidectomy. HPE Follicular variant of papillary carcinoma of thyroid, no capsular invasion,
chronic lymphocytic thyroiditis.

**Discussion:** Sporadic eFVPTC is a low-risk cancer with disease-free long-term outcomes even when treated with lobectomy and without radioiodine therapy. Since the clinical behavior of familial eFVPTC is currently unclear, the management guidelines for sporadic eFVPTC, may not be applicable for familial eFVPTC, which may demand more aggressive approach [ie total/completion thyroidectomy and radioactive iodine ablation].

**Conclusion:** Although the majority of papillary (PTC) and follicular thyroid carcinomas (FTC) are sporadic, familial tumors account for over 5% of cases [Familial non-medullary thyroid carcinoma FNMT]. Two groups of FNMT are: a. as a Minor Component of a Familial Tumor Syndrome; and b. as the Predominant Tumor of a Familial Tumor Syndrome. Since the recurrence rates may be greater in FNMT than in sporadic NMTC, careful monitoring is indicated for affected individuals. Screening strategies for asymptomatic members of FNMT kindreds with thyroid ultrasound need clarification. Future molecular genetic studies [susceptibility genes] can be expected to have therapeutic and prognostic implications.

**Abstract #1173**

**TYPE 1 DIABETES MELLITUS AND GRAVES’ DISEASE IN DOWN’S SYNDROME- A RARE COMBINATION**

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**Objective:** Autoimmune diseases including thyroid disorders, type 1 diabetes and celiac disease are commoner in persons with Down’s syndrome compared with the general population. Coexistent type 1 diabetes and hyperthyroidism in Down’s syndrome is not commonly reported in literature. We report a case of a lady with Down’s syndrome who presented with features of hyperthyroidism as well as diabetes mellitus.

**Case Presentation:** A 22-year-old lady with Down’s syndrome who presented with weight loss, polyuria, polydipsia and an anterior neck swelling. Examination revealed a young female with dysmorphic facies (upslanting palpebral fissures, flat nasal bridge and low set ears). BMI was 19 kg/m2. There was a goitre which was firm and smooth with no bruit. Other systems were normal. RPG was 331mg/dl at presentation while HbA1c was 12.3%. Thyroid function test revealed: FT4 >100.0 (Ref range 12-22) pmol/L, FT3 35.3 (Ref range 3.9-6.7) pmol/L, TSH 0.170 (Ref. range 0.270-4.20) miU/L. Thyroid peroxidase antibodies >1087.0 (Ref range 0-9) IU/ml. Liver function tests, abdomino-pelvic ultrasound scan and urine m/c/s were normal while ECG showed sinus tachycardia. Assessment was type 1 diabetes mellitus and Grave’s disease with background Down’s syndrome. Insulin, Carbimazole and propanolol were given.

**Discussion:** Thyroid disorders and other autoimmune disorders are commoner in persons with Down’s syndrome and these have been reported in literature. What makes our case interesting is that our patient presented with two endocrine disorders (Grave’s disease and type 1 diabetes) at the same time. Most reports have been of one or the other disease in persons with Down’s syndrome. Many differences have been found between the immune system of persons with Down’s syndrome and those without Down’s syndrome. These immunologic impairments are thought to be responsible for the increased susceptibility to infections and autoimmune disorders seen in Down’s syndrome. Hypothyroidism is reported to be much more common in persons with Down’s syndrome compared to hyperthyroidism which our patient had. Overall, type 1 diabetes is also reported to be more prevalent in persons with Down’s compared to the general population. However, type 2 diabetes may also occur in persons with Down’s syndrome due to the association between obesity and insulin resistance in persons with Down’s syndrome. Indeed there have been reports of Type 2 diabetes in persons with Down’s syndrome.

**Conclusion:** Physicians need to have a high index of suspicion for the detection of autoimmune diseases in persons with Down’s syndrome. This is crucial so as to aid prompt detection and reduce the attendant morbidity and mortality.
Abstract #1174

A COMPARISON OF AMERICAN THYROID ASSOCIATION AND CONVENTIONAL CRITERIA: IN EVALUATION OF THYROID HORMONE PROFILE OF CLINICALLY EUTHYROID PREGNANT WOMEN ATTENDING IN A TERTIARY HOSPITAL OF BANGLADESH

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Objective: To observe the thyroid hormone profile in apparently euthyroid pregnant women of any trimester.

Methods: This cross-sectional study investigated 350 pregnant women irrespective of gestational age ([age 24±4, m±SDyr; 1st trimester = 101, 2nd trimester=111, 3rd trimester=138] for thyroid stimulating hormone (TSH) and for free thyroxine (FT4)) to assess their thyroid function during pregnancy following the criteria of American Thyroid Association (ATA) and conventional criteria.

Results: About 58% (204/350) subjects were euthyroid, 41% (142/350) subclinical hypothyroid and only 1% was subclinical hyperthyroid as defined by ATA criteria, which were 84%, 13%, 3% respectively under conventional criteria for thyroid function. While there were none to be found as overt hypothyroidism, isolated hypothyroxinemia, nor frank hyperthyroid. Frequency of goiter (63% vs. 62%, euthyroid vs. dysfunction) was not significantly different between dysfunction and normal groups.

Discussion: Among 294 euthyroid women as detected by conventional reference value, 97 subjects were detected as subclinical hypothyroidism by ATA reference value. And 11 subclinical hyperthyroid by conventional criteria considered as euthyroid by ATA criteria. So, about one third of patient with subclinical hypothyroidism could be missed if we would use non pregnant reference value.

Conclusion: It is concluded that many of the apparently euthyroid pregnant mother have dysfunction as defined by ATA reference ranges for TSH. Simple screening for thyroid function may have greater implication for better pregnancy outcome.

Abstract #1175

ADEQUATE RESTITUTION IN PRIMARY HYPOTHYROIDISM DEPENDING ON LEVOTHYROXINE PRESENTATIONS

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Objective: The prevalence of primary hypothyroidism (PH) is around 3.8% - 4.6% in the general population. Within the patients under treatment with levothyroxine, approximately 40% are over or under-treated, having altered levels of TSH. The objective is to determine the prevalence of euthyroidism in patients under treatment for PH in two local clinics, considering that the number of presentations of levothyroxine could be a contributing factor to the inadequate restitution.

Methods: This is a descriptive, comparative cohort, non-probability sampling study, conducted during 2014 with PH patients who were treated with a stable dose of levothyroxine for at least six months. Patients that were treated with mixtures of liothyronine/levothyroxine, with postsurgical hypothyroidism, pregnant or nursing, and with mental illnesses were discarded. Medical clinic 1 was a public center that had only access to levothyroxine 100 µg, and medical clinic 2 was a private clinic with access to 25, 50, 75 and 100 µg levothyroxine presentations. The most recent measurements of free T4 and TSH by electrochemiluminescence using standardized procedures were searched in the medical records, the doses were correlated and determined for whether they were an appropriate restitution (free T4 and TSH among normal limits) or not.

Results: A total of 350 patients were evaluated. 190 patients were obtained at clinic 1, and 160 patients at clinic 2. The average age was 47 ± 19 and 54 ± 12 (P value = No Significant [NS]), respectively. Likewise, levothyroxine dose in mg/kg was 1.13 ± 0.56 at clinic 1 and 1.63 ± 0.66 at clinic 2 (P value= NS). At clinic 1, only 120 of the 190 (63%) received the appropriate dose, while at clinic 2, 120 of 160 patients (75%) were medicated with the correct dose (P value= 0.02).

Conclusion: Approximately 40% of patients treated of PH in a public entity do not receive the appropriate dose of levothyroxine; however, in private centers, with access to more presentations of the drug, this number drops to 25%. Therefore, the number of presentations could be a factor for the risk of inadequate restitution.
Abstract #1176

VARIED PRESENTATIONS OF THYROID STORM

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Objective: To analyse the various presenting features of patients with Thyroid Storm.

Methods: Case records of 18 patients admitted to a tertiary care hospital in Northern India with Thyroid Storm were reviewed. The ages ranged from 24-78 years and 11 were male and 7 female. Their clinical history, drug history, radioactive iodine therapy, iodinated contrast use, amiodarone therapy and duration & treatment of thyroid disease and comorbidities, need for mechanical ventilatory support, detailed evaluation of laboratory results, thyroid function test, adrenocortical reserve, sepsis panel, ECG, echocardiography, radiological brain imaging and other investigations were analysed in detail.

Case Presentation: Fever, altered sensorium and diarrhea was present in all patients. Cardiac manifestations included atrial fibrillation(n=14 ; 77.8%) and myocardial infarction(n=3; 16.7%). Neurological manifestations included seizures(n=3; 16.7%) and cortical vein thrombosis(n=1; 5.6%). The patient with cortical vein thrombosis had sagittal, transverse, sigmoid sinuses thrombosis(n=1; 5.6%). The patient with cortical vein thrombosis had hypomagnesemia and their admission was associated with agranulocytosis(n=1; 5.6%), fungal sepsis(n=1; 5.6%) and radiiodine therapy(n=1; 5.6%). All patients in mortality group, seizure group and cortical vein thrombosis had hypomagnesemia and their admission serum free T3 level was more than 13.0 pg/mL.

Discussion: Thyroid storm is a rare and severe form of thyrotoxicosis. Fever and atrial fibrillation with fast ventricular rate are common and well known manifestations. However, in our study cortical vein thrombosis which is rarely reported was present in 1 patient along with seizures in 3. These neurological manifestations should also be looked out for. Reason for cortical vein thrombosis is not known. Our patients who had cortical vein thrombosis did not have oral contraceptive use.

Conclusion: 1. During last 13 years mortality was 16.6% in patients with thyroid storm.
2. Both cardiac and neurological manifestation are important at early diagnosis and management.
3. Patients with seizures and a extensive cortical vein thrombosis are among the rarer presentations we encountered.
4. A high index of suspicion should be kept for Cortical Vein Thrombosis in patients with thyroid storm and seizures.

Abstract #1177

CEREBRAL VENOUS SINUS THROMBOSIS PRECIPITATED BY GRAVES’ DISEASE

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Objective: Cerebral venous sinus thrombosis has been rarely reported as an associated condition with Graves’ disease. Previously reported cases in the literature do not confirm an association between cerebral venous sinus thrombosis and Graves’ disease. We present the case of a young man who was initially diagnosed with Graves’ disease and later developed cerebral venous sinus thrombosis with no other obvious precipitating cause.

Case Presentation: A 31-year-old man presented to the emergency department with a 4-day history of severe headache and projectile vomiting. He was diagnosed with Graves’ disease 2 weeks prior to his presentation, but no treatment was started. On examination, he was afebrile with a regular pulse of 82 beats per minute and blood pressure of 125/80 mmHg. He was lethargic and in distress due to pain, but without confusion. He had no focal neurologic deficits or signs of meningeal irritation. Fundoscopic examination showed no evidence of papilledema. Computed tomography of the head with contrast demonstrated extensive thrombosis in the superior sagittal, straight and bilateral transverse sinuses. His thyroid function tests revealed a thyroid stimulating hormone (TSH) level of < 0.01 mIU/L (reference range: 0.45–4.5 mIU/L), free triiodothyronine (FT3) level of 23.8 pmol/L (reference range: 2.6–5.7 pmol/L) and free thyroxine (FT4) level of 30.5 pmol/L (reference range: 9–20 pmol/L). An extensive work-up for coagulation disorders excluded the presence of protein C and protein S deficiency, hyperhomocysteinemia, factor V Leiden mutation, anti-thrombin III deficiency, anti-phospholipid antibody syndrome, or anti-glycoprotein antibodies. Based on these findings, it was concluded that Graves’ disease was the likely precipitating factor for cerebral venous sinus thrombosis in this patient.

Discussion: A total of 35 cases reported in the literature have suggested a possible association between hyperthyroidism and cerebral venous sinus thrombosis. Although coagulation abnormalities are common in hyperthyroidism, an association between hyperthyroidism and cerebral venous sinus thrombosis has not been well established. In the present case, an extensive evaluation for other causes of thrombosis was not yielding; Graves’ disease was the likely factor that has precipitated cerebral venous sinus thrombosis. It has been proposed that
hyperthyroidism leads to abnormalities in coagulation parameters particularly increased factor VIII activity, causing increased risk of venous thrombosis. The increased adrenergic activity has been also implicated in elevating the levels of factor VIII.  

**Conclusion:** Cerebral venous sinus thrombosis should be considered a possible complication of Graves’ disease.

**Abstract #1178**

**THYROID MICROFILARIASIS**

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**Objective:** To present a case of incidental detection of microfilariae in thyroid FNAC.

**Case Presentation:** 36yr old female presented with a swelling in front of her neck moving with swallowing and slowly growing to present size over last 3 months. No H/O pain in swelling, weight gain/loss, fever, heat/cold intolerance, palpitations, fatigue, malaise, swelling in feet or anywhere else over the body, hair fall or change in voice. She has been a resident of endemic area for filariasis in her childhood

Examination: Normal vitals with normal general and systemic examination. Neck examination solitary right sided 2cm X 2cm, non tender, firm swelling in anterior part of neck moving with deglutition, overlying skin was normal, rest of the thyroid gland was normal. Both the carotid arteries were equally palpable without any bruit. No lymphadenopathy or retrosternal extension of thyroid gland. Pemberton sign negative. No eye signs.

Investigations: Hb12.4gm/dl (12-15.8), TLC-9800/cumm (4000-11000), DLC-N (40-1000). Absolute Eosinophil Count 830cumm (<500), ESR-9mm1st hour (<20), FT3- 4.1 pg/ml (2.0-4.4), FT4-1.4 ng/dl (0.8-2.2), TSH- 2.0 mIU/L (0.5-5.0). Rest of biochemical profile was normal. USG neck suggestive of well defined hyperechoic nodule of size 14 x 11 x 15 mm with hypoechoic rim showing peripheral vascularity in right lobe of thyroid with evidence of multiple centimeter lymph nodes in level II, III, IV on left side and in level II on right side. FNAC from nodule was suggestive of a colloid nodule with microfilaria of W. Bancrofti. Repeat peripheral smear taken at night showed microfilaria of W.bancrofti (70/ml blood). BMA showed eosinophilia and increase in mature plasma cells. Diagnosis of solitary thyroid nodule with microfilarial infestation was made. Patient was advised Diethylcarbamazine 100 mg PO tid X 14 days along with antihistaminic. The swelling improved with gradual resolution. Hence an unnecessary surgery was avoided due to finding of a treatable cause for the thyroid nodule.

**Conclusion:** Filariasis is an endemic disease in most of tropical countries including India. The case shows an unusual presentation of filariasis with thyroid nodule. This case is being presented because of absolutely unexpected finding of microfilaria in a thyroid aspirate and appropriate treatment avoided the surgery. There are very few case reports of similar finding in literature.

**Abstract #1179**

**THYROID ABNORMALITIES IN ADULT PATIENTS UNDERGOING CHRONIC HEMODIALYSIS**

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**Objective:** To determine the frequency of thyroid abnormalities in adult patients with end-stage renal disease treated with chronic hemodialysis.

**Methods:** Fifty adult patients with end-stage renal disease (ESRD) receiving chronic and regular hemodialysis at the Hemodialysis Center of the Universidad Peruana Cayetano Heredia and 24 age- and sex- matched controls were included. Patients with history of thyroid disease, goiter, use of levotiroxine or thionamides, and liver disease were excluded. Statistical analysis included Student t test for numerical variables, chi-square test for categorical variables and Fisher’s exact test. We determined TSH, free T4, total T3 and reverse T3 (T3r). All samples were collected fasting, before starting the dialysis session and after the long interdialytic period. The Ethics Committee approved the study protocol, and all patients signed an informed consent.

**Results:** The median age was 57.3 years-old (SD 17.1) and 59.5% of patients were female. Of patients treated with hemodialysis, 90% had a diagnosis of hypertension and the most common cause of chronic kidney disease was type 2 diabetes (38%). The median time on hemodialysis was 19 months (IQR 41-70). The frequency of hypothyroidism, subclinical hypothyroidism, and low T3 were 6%, 28% and 16%, respectively. In patients with ESRD, TSH levels were higher (4.4 mIU/dl vs. 2.2 mIU/dl, p= 0.009) and T3 levels were lower (95.68 ng/dl vs. 133.95 ng/dl, p<0.000). There were no differences in FT4 or T3r levels.

**Conclusion:** Patients with chronic kidney disease (CKD) undergoing hemodialysis, have an increased frequency of thyroid dysfunction. On the other hand, it has reported an increase in the prevalence of hypothyroidism as it descends the rate of glomerular filtration, and alterations in thyroid function are associated with increased mortality;
especially low levels of T3. In conclusion, changes in thyroid function are common in adult patients receiving chronic hemodialysis. The most common change is subclinical hypothyroidism and low T3.

Abstract #1180

TRIMESTER SPECIFIC REFERENCE INTERVAL FOR THYROID HORMONES DURING PREGNANCY AT A TERTIARY CARE HOSPITAL IN HARYANA, INDIA.

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Objective: To establish trimester specific reference range for thyroid hormone during pregnancy in a tertiary care center in Haryana.

Methods: 1430 pregnant women were recruited for the study and out of which these 461,469,500 pregnant women were in first, second and third trimester respectively. Participants having any history of chronic illness, goiter on physical examination, thyroid illness in the past or present, consuming thyroid medications (current and past), family history of thyroid illness, presence of anti-thyroid peroxidase antibody (TPO antibodies), poor obstetrics history included 3 or more abortions were excluded from the study and reference population was identified to calculate serum FT3, FT4 and TSH for each trimester of pregnancy.

Results: Mean age of study population was 23.89±3.24 years (range 17-38 years). The 2.5th - 97.5th percentiles for FT3, FT4, and TSH obtained in this study were 2.53-4.54 pg/ml, 0.88-1.78 ng/ml and 0.37-3.69 mIU/ml in the first trimester, 2.0-4.73 pg/ml, 0.91-1.78 ng/ml and 0.54-4.47 mIU/ml in the second trimester, 2.01-4.01 pg/ml, 0.83-1.73 ng/ml and 0.70-4.64 mIU/ml in the third trimester of pregnancy. Mean TSH increased and mean FT3 decreased significantly with the progression of gestational period. FT4 decreased from trimester 1st to 3rd but the decrease was non-significant from 2nd to 3rd trimester.

Discussion: The recent Endocrine Society guidelines for thyroid dysfunction in pregnancy published in 2012 have lowered the upper limit of reference range for normal TSH and suggested 0.1-2.5 mIU/L, 0.2-3.0 mIU/L and 0.3-3.0 mIU/L, respectively, in first, second and third trimester of pregnancy. When the trimester-wise 2.5th & 97.5th percentile of TSH derived from the reference population in the present study was applied to the total population, the number of women with subclinical hypothyroidism were decreased from 99 (21.5%), 74 (15.8%) and 129 (25.8%) to 31 (6.7%), 50 (10.7%), 40 (8%) in 1st, 2nd and 3rd trimester respectively. It means 68 (14.8), 24 (5.1%) and 89(17.8%) pregnant females would have been misclassified as having SCH or we can say that over treated if we would have applied endocrine society guidelines on our study population.

Conclusion: To conclude with, in the present study we established the trimester specific FT3,FT4 and TSH hormones range in pregnant women from a tertiary care center in Haryana India. Existing results for trimester-specific reference intervals for thyroid hormones are inconsistent and cannot be extrapolated due to differences in ethnicity, maternal iodine status, laboratory assay method, and rigor for selection of reference population. Thus, establishment of reference intervals in each region is of great importance.

Abstract #1181

IODINE STATUS IN PATIENTS WITH THYROID DISEASES

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Objective: To examine the iodine status among patients with thyroid diseases attending the Endocrine clinic at a single centre in Sharjah, United Arab Emirates (UAE).

Methods: Urinary iodine levels were obtained in patients with thyroid disorders attending the Endocrine centre of Al Zahra Hospital, Sharjah, over an 18-month period from July 2014 to December 2015. A random urine sample was obtained for iodine test and was analyzed at a single referral laboratory. Patients who had recent iodine exposure, those with elevated creatinine and pregnant women were excluded. Thyroid diseases were classified into 3 groups - Euthyroid goiter, Hypothyroid and Hyperthyroid. Demographic variables like age, gender and ethnicity and investigations like thyroid function test and thyroid antibody levels were collected. Urine iodine results were classified as per WHO ICCIDD cutoffs. Data was analyzed using SPSS software.

Results: 496 patients with thyroid disease had urinary iodine levels measured in the study period. 84% were women and 16% men. The mean (± SD) age of the sample was 37.6 (± 9.7) years. There were almost 40 different nationalities represented and were grouped into UAE nationals, other Arabs/ White, South Asians, East Asians and others. Majority of the patients had hypothyroidism (64.1%) followed by euthyroid goiter (27%) and hyperthyroidism (8.9%). The mean (± SD) urine iodine concentration (UIC) of the entire sample was 217.1 (± 310) mcg/L and the mean urine iodine/creatinine ratio (UICR) was 234.4 (± 240.4) mcg/g. There was no significant difference in the mean iodine levels in men and women. Between different diagnostic groups, the mean UIC was 444.2 ±876.3 mcg/L in the hyperthyroid
group vs 194.6 ± 156 mcg/L in the hypothyroid group and 196.7 ± 189.6 mcg/L in the goiter group. Based on WHO cut-offs, 1.7% of patients had severe iodine deficiency, 11.2% had moderate deficiency and 20.4% had mild iodine deficiency. UIC was optimal in 29.5%, above adequate in 15.7% and excessive in 21.6% of patients. There was no significant difference in the prevalence of deficiency in the three diagnostic groups or by gender. While using the UICR criteria, iodine deficiency was found to be present in 18.3% of the entire sample. There was a significant correlation between random UIC and UICR (r= 0.69, p 0.00).

**Conclusion:** We present the urinary iodine levels in patients with thyroid diseases from an Endocrine center in UAE. One-third of our patients have some degree of iodine deficiency. Since the majority of patients are women and of child-bearing age in our sample, this finding has potential public health importance. Further studies may be warranted to assess the public health importance of our finding.

**Abstract #1182**

**WEEKLY DOSES OF L-THYROXINE AS A FIRST LINE TREATMENT FOR HYPOTHYROIDISM IN YOUNG AND MIDDLE AGED WORKING WOMEN**

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Park Hospital

**Objective:** To demonstrate the effectiveness and compliance to L-thyroxine in the treatment of Hypothyroidism in a weekly dose of 7 times of normal dose as an alternative to daily dosing in young and middle aged working women in North India.

**Methods:** Randomised trial on 40 female subjects aged between 25 to 55 years with long standing hypothyroidism of 5 years or more currently on daily dose of L-thyroxine assigned to weekly dose. The patients were randomised in 2 groups.

Group 1: 20 females with an established diagnosis of primary hypothyroidism of 5 years or more with TSH of 4.12 mIU/L or less. The dose of L-thyroxine was changed to 7 fold of there normal daily dose.

Group 2: 20 females with an established diagnosis of primary hypothyroidism of 5 years or more with TSH of 4.12 mIU/L or more. The dose in this group was individualized as per the body weight and TSH value. The minimum to maximum dose of L-thyroxine used in the study was 175 mcg to 1050 mcg. All subjects in both the groups were screened for malabsorption and were not receiving any drugs which interferes with the absorption of L-thyroxine.

**Case Presentation:** We achieved complete restoration of euthyroidism in all 20 subjects in Group 1 at 12 weeks and it continued to 24 weeks. In Group 2 we achieved complete euthyroidism in 16 subjects at 12 weeks and it increased to 18 subjects with some dose adjustments at 24 weeks. We could not achieve euthyroidism in 2 subjects because of other underlying metabolic disorders like diabetes and obesity.

**Discussion:** Once weekly L-thyroxine replacement was well tolerated and there was no indication of acute toxicity or hypothyroidism symptoms compared with daily therapy. Our results suggest that once weekly L-thyroxine replacement therapy for hypothyroidism is efficacious and safe, making it a possible alternative to customary daily therapy.

**Conclusion:** Once weekly dose of L-thyroxine as an alternative to daily dosing regimen was shown to be efficacious and safe for the treatment of hypothyroidism in young and middle aged females. Once a week L-thyroxine an be considered as first line therapy in working young and middle aged women facing impaired absorption due to early breakfast (no need to wait for 30 min for breakfast).

**Abstract #1183**

**PARANEOPLASTIC HYPEREOSINOPHILIA AND NEUTROPHILIA DUE TO ANAPLASTIC THYROID CARCINOMA**

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**Objective:** Anaplastic thyroid carcinoma is an aggressive malignancy, usually metastatic at diagnosis and comprising <2% of all thyroid cancers. We present a rare case of anaplastic thyroid carcinoma causing paraneoplastic hypereosinophilia and neutrophilia. 

**Case Presentation:** A 63-year-old man with history of metastatic anaplastic thyroid carcinoma presented with fever, night sweats and tender distended abdomen for three weeks. His thyroid cancer was initially treated with total thyroidectomy and lymph node removal. Four years prior to admission, he received radioactive iodine therapy for lung and adrenal metastases. Admission physical exam was notable for fever 102°F, healed surgical scar without palpable thyroid tissue or lymphadenopathy and right upper quadrant pain without guarding. TSH was 0.16 μIu/mL (0.27-4.2) with free T4 1.16 ng/dL (0.9-1.8). Morning cortisol was 25 μg/dL
(8-19). CT scan showed pulmonary, left adrenal and hepatic nodules, enlarged pancreas and splenic vein thrombosis with collaterals. Endoscopic ultrasound pancreatic biopsies revealed anaplastic thyroid carcinoma.

The patient exhibited persistent leukocytosis ranging from 41.8x10⁹/L to 116.6x10⁹/L WBC with 16-47% eosinophils, 28-55% neutrophils and 2-5% lymphocytes (normal: 3.8-10.5x10⁹/L WBC, 0-6% eosinophils, 43-77% neutrophils, 13-44% lymphocytes). Highest absolute eosinophil count (AEC) was 51.3x10⁹/L with highest absolute neutrophil count 64.1x10⁹/L. Medication review was unremarkable. Parasitic infection such as Strongyloides and adrenal insufficiency were ruled out. Differential diagnosis included leukemoid reaction, hematologic malignancy including myeloproliferative disorder or paraneoplastic condition. Leukocyte alkaline phosphatase was normal. Bone marrow biopsy showed leukocytosis with eosinophilia, neutrophilia, and no increase in immature cells. JAK-2 and BCR/Abl mutations were absent. Granulocyte-macrophage colony-stimulating factor (GM-CSF) was 23.6 pg/mL (<3).

Discussion: Hypereosinophilia - defined as AEC >1.5X10⁹/L - has been associated with hematologic malignancies and bladder cancer. It is also identified as a paraneoplastic manifestation of thyroid carcinomas in several case reports: one papillary, one medullary, one undifferentiated and four anaplastic. Similarly, paraneoplastic neutrophilia has been linked to lung cancer and undifferentiated thyroid carcinoma. The pathophysiology is ectopic overproduction of CSF.

Conclusion: Our patient’s prior diagnosis of anaplastic thyroid carcinoma provided an etiology of exclusion for concomitant hypereosinophilia and neutrophilia as supported by elevated GM-CSF. This relationship is important to recognize because hematologic changes could herald thyroid carcinoma.

Abstract #1185

PULMONARY EMBOLISM IN A PATIENT WITH BOTH GRAVES’ DISEASE AND ANTIPHOSPHOLIPID SYNDROME

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Objective: Several case reports have suggested the association of Graves’ disease (GD) and a hypercoagulable state. A prospective study also showed that the risk of pulmonary embolism (PE) was 2.3 times greater for patients with hyperthyroidism. Cases of PE in patients with both GD and Anti phospholipid syndrome (APS) have also been reported, further suggesting an association between hyperthyroidism and hypercoagulable state.

Case Presentation: A 55 year old African American Male was diagnosed with bilateral PE in May 2008, after he presented to the emergency department with chest pain. He was tested positive for Lupus anticoagulant and was advised to take lifelong anticoagulation with warfarin. He was subsequently diagnosed with Graves’ disease (FT4 2.72ng/dl, TSH 0.005ng/dl, TSI 138%) in August 2011 and was started on daily methimazole. The patient was closely followed by Hematology and Endocrinology clinics for management of his INR and Graves’ disease respectively. Methimazole was stopped in March 2013 after circulating thyroid levels normalized and he was determined to be in remission from GD (FT4 1.00ng/dl, TSH 1.420ng/dl, TT3 94ng/dl). Patient then began to miss his Coumadin clinic appointments frequently, did not follow up with Hematology and completely stopped taking warfarin in 2013. He developed a second PE in September 2015 and was started on rivaroxaban. Interestingly, he also developed recurrent symptoms of hyperthyroidism around the same time and presented to his Endocrinologist with complaints of bilateral hand tremors and profuse sweating. Labs revealed that he was in sub clinical hyperthyroidism (TSH 0.005ng/dl, FT4 1.70ng/dl, TT3 179ng/dl), thus he was restarted on methimazole with quick improvement in his symptoms.

Conclusion: Hyperthyroidism is associated with an increased risk for venous thromboembolism (VTE) including PE. The pathophysiology is thought to be from endothelial dysfunction, decreased fibrinolytic activity and increased coagulation factor levels, especially Factor VIII. Similarly, APS is well known to be associated with increased risk of thrombotic events. The occurrence of these conditions together may potentiate the risk of thrombotic events, as seen in this patient who initially presented with bilateral PE and new onset GD. This case is interesting because the patient developed recurrent PE more than two years after he stopped anticoagulation therapy and concurrently with recurrence of his GD, suggesting simultaneous remission and relapse from both autoimmune disorders. This case further suggests an association between autoimmunity of GD and APS, as well as an increased risk of VTE when both disorders are active concurrently.
Abstract #1186

DOSE INDIVIDUALIZATION OF LEVOTHYROXINE IN PATIENTS WITH POST THYROIDECTOMY 131I ABLATION THERAPY BY USING POPULATION PHARMACOKINETIC APPROACH

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Objective: To individualize the dose of Levothyroxine based on the pharmacokinetic model using population pharmacokinetic parameters.

Specific objectives:
1. To collect drug level data of patients with differentiated thyroid cancer undergone complete thyroidectomy followed by radio iodine [131I] ablation treatment and in patients with Thyrotoxicosis in treatment with Radio Iodine [131I].
2. To collect demographic data of patients and study the effect of covariates (age, sex, bodyweight, circadian rhythm etc.) on the population pharmacokinetic parameters like clearance and volume of distribution.

Methods: Methods for estimation of POPPK

The Nonlinear Mixed-Effects Modeling Approach

Sparse data situations, where the traditional two-stage approach is not applicable. Considers the population study sample - estimation of the distribution of parameters and their relationships with covariates within the population. Individual PK data which may be sparse, unbalanced, and fragmentary.

Results: Levothyroxine sodium has a narrow therapeutic range.

Sub-optimal doses could result in perpetuation of hypothyroid state induced by the radio-iodine ablation in thyroid cancer patients and thyrotoxicosis patients and higher doses result in toxic manifestations of hyperthyroidism such as, sweating, tremors, palpitations, cardiac arrhythmias, nervousness, increased appetite and weight loss.

Guidelines for the prediction of the final replacement dose are scarce and current practice of dose determination is by titration according to serum TSH levels, which requires regular follow-up visits and repeated laboratory testing.

Discussion: Population pharmacokinetics is the study of the sources and correlates of variability in drug concentrations among individuals who are the target patient population receiving clinically relevant doses of a drug of interest.

Population modeling seeks to evaluate the interindividual and intraindividuality based on raw subject data and the assay error, and to describe findings in terms that useful both for research and for optimal patient care.

Conclusion: Much of the previous literature on T4 requirements has focused on primary hypothyroidism and these studies may not accurately predict T4 requirements after total thyroidectomy. A dose prediction model for Levothyroxine sodium based upon a population pharmacokinetic approach would be a welcome solution both to patients and their treating physicians.

Abstract #1187

SARCOIDOSIS IN THE THYROID GLAND WITH HASHIMOTO’S THYROIDITIS

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Objective: We describe a case of thyroidal sarcoidosis presenting as a thyroid nodule and describe the epidemiology, clinical presentation, and pathologic findings of this rare entity.

Case Presentation: A 45 year old male with history of ocular and pulmonary sarcoidosis presented with dysphagia, hoarseness, and neck tenderness for one year. He also noted fatigue, depression, and decreased libido. He was not on any medications. Family history was negative for malignancy or thyroid disease. Vitals and BMI were normal. Exam disclosed an enlarged firm thyroid with a nodule on the right without lymphadenopathy. Labs showed elevated TPO Ab, high serum thyroglobulin, normal TSH, normal total T3 and T4, and negative thyroglobulin Ab. Ultrasound showed a top-normal sized hypervascular thyroid with two lesions in the right lobe. Ultrasound-guided fine-needle aspiration of the 1.1 cm dominant solid mass revealed granulomatous inflammation consistent with sarcoidosis. Annual ultrasound was planned for surveillance of these nodules. The patient was also started on levothyroxine for symptomatic Hashimoto’s thyroiditis.

Discussion: Sarcoidosis is a multisystem granulomatous disorder that affects the thyroid gland in 4% of patients. When it involves the thyroid, sarcoidosis usually causes diffuse goiter but can rarely cause a solitary nodule resembling malignancy. Most patients are euthyroid, though in rare cases the extent of thyroidal disease can cause destruction leading to hypothyroidism or inflammation leading to transient hyperthyroidism. Women with sarcoidosis had significantly higher prevalence of TPO antibody positivity, ultrasound features of autoimmune, and clinical and subclinical hypothyroidism compared to age-matched controls in one study. The histology of sarcoidosis of the thyroid is similar to sarcoidosis elsewhere, with noncaseating granulomas with epithelioid cells, multinucleated giant
cells, and lymphocytic infiltration. These lesions must be differentiated from fungal or mycobacterial infections and Hashimoto’s thyroiditis. There is no specific treatment for thyroidal sarcoidosis. As with other etiologies, thyroidectomy is indicated for obstructive symptoms, thyrotoxicosis, or cancer, and hormone replacement is given for hypothyroidism. The effects of steroids or radiation on sarcoid goiter are not known.

**Conclusion:** This case demonstrates that sarcoidosis can rarely involve the thyroid gland, presenting as nodules or a goiter. These patients may concomitantly have autoimmune thyroid diseases such as Hashimoto’s thyroiditis, and may in fact be at increased risk of such disorders.

Abstract #1188

**A CASE REPORT OF HYPOKALEMIC PARALYSIS AS INITIAL MANIFESTATION OF THYROTOXICOSIS**

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**Case Presentation:** Thyrotoxic hypokalemic paralysis (TPP) is characterized by a triad composed of acute hypokalemia due to a massive transient of potassium into cells, thyrotoxicosis and various degrees of muscle paralysis. This medical condition is a very rare complication of thyrotoxicosis in Caucasians, but very frequently encountered in Asian populations.

We present a Romanian male patient, Caucasian, aged 36 years, who presented to the emergency room for flaccid acute tetraparesis in the New Year’s Eve. The symptoms started suddenly after a high-carbohydrate dinner, with muscle weakness and cramps first in the lower limbs, and then in the upper limbs. The patient also complained of palpitation, and diaphoresis. Vision and mental status were in normal limits, with no breathing difficulty. Neurological examination demonstrated flaccid symmetrical weakness of the legs and arms (power: legs 2/5, arms 3/5) with an intact sensation. Knee deep tendon reflexes were diminished bilaterally (grade 2/4). On clinical examination the patient had a body mass index of 23.93 kg/m². Body temperature was normal and there was a resting tachycardia of 100 beats/min. The skin was observed to be perspired and warm. Clinical history was negative for any trauma, alcohol, diarrhoea, vomiting, diuretics, laxative or liquorice abuse. Personal and family history was negative for endocrinological or neuromuscular disease. Laboratory analysis revealed mild hypokalemia K⁺ 2.9 mmol/L (normal range: 3.6–5.1) with no other abnormality. In the emergency department, the patient was started on intravenous potassium supplementation with hydration and the plasmatic potassium returned to normal values of 3.7 mmol/L (normal range 3.6–5.1). The patient was referred to the endocrinological department for further investigation in order to elucidate the etiology of hypokalemia. Thyroid function tests showed hyperthyroidism with thyroid-stimulating hormone (TSH) less than 0.004 mIU/L (normal range 0.5–4.5 mIU/L), serum free thyroxine FT₄= 46.3 pmol/L (normal range 10.3–24.4 pmol/L), serum triiodothyronine T₃= 350 ng/dL IU/mL (normal range 80–200 ng/dL). Serum TSH receptor antibodies were high values of 5 IU/L (normal range 0–1.75 IU/L). Thus, the patient was diagnosed as having thyrotoxic hypokalemic paralysis due to Graves’ thyrotoxicosis. The treatment with an antithyroid drug (methimazole 20 mg twice daily) was started, together with a non selective β-adrenergic blocker (propranolol 50 mg once daily).

**Conclusion:** We present a case of TPP in a Caucasian male due to Graves’ disease with good response to potassium supplements, propranolol, and therapy with methymazol.

Abstract #1189

**INTRATHYROID HEMORRHAGE FOLLOWING THROMBOLYTIC THERAPY AND ANTICOAGULATION**

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**Objective:** To present a case of intrathyroid hemorrhage following systemic tissue plasminogen activator (tPA) and unfractionated heparin administration for pulmonary embolism (PE).

**Case Presentation:** A 68-year old woman with a past medical history of Hashimoto’s thyroiditis and non-toxic multinodular goiter (MNG) presented with a massive saddle PE in the setting of immobility after surgery. There is a history of thyroid nodules since 1979 with multiple fine needle aspirations (FNA) of dominant nodules negative for malignancy. She had been followed with serial thyroid ultrasounds and thyroid function tests (TFTs). Surgery was declined in the past due to lack of compressive symptoms. Admission Computed Tomography Angiography (CTA) confirmed PE and demonstrated an enlarged right thyroid lobe 5.5 x 3.3 cm with left tracheal deviation. She subsequently became hemodynamically unstable and required bolused systemic tPA, unfractionated heparin infusion, and intubation. She was extubated the next day. 72 hours after tPA use, the patient became acutely short of breath with scant hemoptysis. Repeat CTA revealed a
heterogenous, diffusely enlarged right thyroid now 5.1 x 5.5 cm with mass effect on the trachea. It was consistent with intrathyroid hemorrhage. An urgent right thyroid lobectomy was performed to remove airway obstruction. Pathology confirmed loculated hemorrhage in the resected lobe. TFTs after exposure to radiographic contrast were: TSH 0.04 mIU/L (n: 0.35-5.50 mIU/L) and FT4 1.72 (n: 0.90 -1.80 ng/dL). Post-operatively, patient’s clinical status improved and she was discharged home one week later. TFTs normalized on subsequent follow-ups.

**Discussion:** Intrathyroid hemorrhages are rare events that are associated with a high mortality rate. Precipitating causes include trauma, iatrogenic injury, malignancy, or in rare cases, anticoagulation. However, anticoagulation and thrombolytic therapy remain the mainstays in the treatment of PEs. Both therapies have an associated risk of major bleeding. While much of the focus is on life threatening complications of thrombolytics (intracranial hemorrhage, critical hemoglobin drop, etc), there are also other infrequent complications such as an acute intrathyroid hemorrhage. There have been several cases of thyroid hemorrhage in both MNG and non-pathological thyroids following systemic tPA use in the medical literature.

**Conclusion:** Our case presentation illustrates a rare case of intrathyroid hemorrhage likely secondary to the combined therapy of bolused systemic tPA and unfractionated heparin. Despite the rarity of the condition, it is an important complication to recognize because it can lead to acute airway compromise.

**Abstract #1190**

**THYROID ABSCESS: THE GREAT MIMICKER**

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**Objective:** Thyroid abscess is a rare pathology of the thyroid gland. The thyroid is highly resistant to infection due its high iodine content, capsular encapsement and rich vascular and lymphatic drainage. Acute suppurative thyroiditis only represents <1% of all thyroid diseases resulting from a bacterial infection that could potentially become a life-threatening endocrine emergency.

**Case Presentation:** 48 year old female with AIDS (CD4 count 7, viral load 873000 a month prior to admission), Hepatitis C and Diabetes mellitus type 2 presents to the emergency department with 3 days of nausea, vomiting, diarrhea, subjective fever and sudden onset of sore throat and odynophagia. Upon admission, she was afebrile, tachycardic and hypotensive with evident neck swelling, hoarseness and tenderness to palpation. Labs revealed leukocytosis with left shift and acute kidney injury. Thyroid function test revealed TSH 3.74 mIU/ml (0.35-3.74), Free T4 2.3ng/dl (0.76-1.46), Free T3 5.16pg/ml (2.18-3.98), urine analysis revealed pyuria and bacteruria. Abnormal renal function precluded contrast base study and patient underwent plain Computerized-Tomography (CT) of the neck revealing fat stranding around the thyroid with marked narrowing of the subglottic airway and retropharyngeal swelling. Patient was admitted to intensive care unit, and was started on broad-spectrum antibiotic. Clinic presentation was concerning for possible subacute thyroiditis versus acute suppurative thyroiditis (AST). Thyroid ultrasound, failed to show any obvious fluid collection or features of AST. Two days after admission blood cultures revealed methicillin resistant Staphylococcus Aureus (MRSA), and antibiotic therapy was narrowed to vancomycin only. Trans-esophageal echocardiogram did not show evidence of endocarditis. On day 4 of hospital course she had worsening neck pain and stridor, CT of the neck with contrast showed multiloculated abscesses involving the whole thyroid and retropharyngeal region extending to the thoracic inlet. Patient underwent trans-oral and trans-cervical drainage of the thyroid abscesses. Wound cultures were positive for MRSA.

**Conclusion:** AST is a rare presentation of thyroid disease, generally occurs in patients with preexisting disorders of the thyroid gland or immune compromised such as AIDS. The most common pathogen is Staphylococcus Aureus. In the early inflammatory stage of AST, imaging can be inconclusive and lead to an erroneous diagnosis of subacute thyroiditis. CT neck with contrast played an important role in the final diagnosis of thyroid abscess. Our case highlights the importance to recognize AST as a cause of new onset thyroid pain and swelling in immune compromised patients.

**Abstract #1191**

**SCHWANNOMA-PERINEURIOMA OF THE THYROID**

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**Objective:** Schwannomas are benign nerve sheath tumors composed of Schwann cells. One third of all schwannomas occur in the head and neck, however laryngeal involvement is uncommon (0.1% to 1.5% of case). When they occur in the head and neck, the majority (80%) originate from the aryepiglottic fold, and the remaining (20%) are tumors of the vocal cord or vestibular fold. In addition, tumors showing hybrid features of schwannoma and perineurioma
are rare. The largest series of these mixed tumors describes 42 tumors, of which 6 were from head and neck origin, and only one was from the neck more precisely at the submental location. Here we describe the first and unusual case of a mixed schwannoma-perineuroma associated with the nerves of the thyroid gland.

**Case Presentation:** A 17 yo man was referred to our endocrine surgery clinic for workup of a neck mass found during a high school football screening physical examination. The nodule bothered the patient because it was visible but it was otherwise asymptomatic. Further medical history was unremarkable, and there was no family history of thyroid disease. On physical exam a visible and palpable large, firm, non-tender left thyroid mass was noted. His TSH was normal (1.595 mIU/L), and thyroid peroxidase antibody was elevated (25.41 IU/mL). Thyroid ultrasound showed a normal right lobe measuring 4.7 x1.1 x1.6 cm. The left lobe was 5.2x 3.3x 4.1 cm with a large heterogeneous mass of 4.2 x 3.3x 3.7 cm with increased vascularity. Fine needle aspiration was nondiagnostic, showing fibrous tissue fragments in a background of blood, without thyroid follicular cells or colloid identified. The patient did not experience any unusual pain during the FNA. Since the patient was a young male with a 4 cm left thyroid nodule that was visible and with high vascularity, he was brought to the operating room for a diagnostic left thyroid lobectomy. The left lobectomy was done without complication. It was noted during the surgery that the thyroid gland was more adherent to the trachea than usual, which made this part of the dissection challenging. The left recurrent laryngeal was identified and maintained a positive nerve signal throughout the case. Final histology showed a benign nerve sheath tumor consistent with a hybrid schwannoma-perineurioma of 3.6 cm, and an otherwise normal left thyroid lobe with patchy thyroiditis.

**Conclusion:** This is, to our knowledge, the first reported schwannoma-perineurioma associated with the thyroid. The origin of the tumor remains unclear, however we hypothesize that it arose from either the recurrent or external branch of the superior laryngeal nerve.

**Abstract #1192**

**DETECTION OF MALIGNANCY IN THYROID CARCINOMA SAMPLES THROUGH TARGETED DNA SEQUENCING**

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**Objective:** Thyroid carcinomas frequently contain genetic variants associated with transformation. Recent studies from a number of groups, including The Cancer Genome Atlas (TCGA) have elucidated several of these mutations. However, it is unclear how well a comprehensive panel of mutations performs in the detection of malignancy across a broad range of thyroid malignancy subtypes. We sought to measure this performance in the context of both fine needle aspirate (FNA) and tissue samples.

**Methods:** DNA and RNA was isolated from FNA samples, collected pre-operatively and diagnosed post-surgically by a panel of experts as malignant or benign (n=82), as well as from thyroid tissue samples with histopathology truth (n=38). Three different targeted DNA sequencing strategies were applied to identify variants within these samples and RNA sequencing was used to identify fusions. The first approach assessed 229 nucleotide variants in 14 genes using the AmpliSeq Cancer Hotspot Panel v2. Secondly we analyzed a custom panel targeting 854 variants in 357 genes derived from the literature, including TCGA. Lastly, we analyzed tissue samples with The Jackson Laboratory Cancer Treatment Profile (CTP), which targets 358 genes associated with cancer diagnosis and therapeutic treatment selection.

**Results:** The sensitivity for detection of malignancy in the 82 FNA samples with the Cancer Hotspot assay was 55% (95% CI 38-71%) and the specificity was 90% (77-97%). The sensitivity for detection of malignancy in 38 thyroid tissue samples using variants detected with the 854 variant panel was 56% (31-78%), similar to that observed in FNA samples with the smaller Cancer Hotspot panel, while the specificity was 70% (46-88%). The CTP assay was analyzed in 19 tissue samples that contained sufficient DNA. The sensitivity obtained with a smaller set of commonly studied thyroid cancer specific genes (12 genes, as the CTP assay does not include EIF1AX or the TERT promoter variants) was 50% (19-81%) and the specificity was 67% (30-93%). Using
the entire set of genes in the CTP assay, the sensitivity increased to 90% (55-100%), but was accompanied by a drastic decrease in specificity to 11% (0-48%).

**Conclusion:** Three methods detecting DNA variants and fusions lacked sensitivity when assessing common thyroid cancer associated variants. This finding is consistent with previous analyses using an RNA-based sequencing assay. Increasing variants from 14 genes to 357 did not improve performance. These results demonstrate that these variant panels applied to thyroid FNA samples have limited sensitivity for detection of malignancy. With a 24% prevalence of malignancy in indeterminate FNAs, the resulting NPV of 86% is too low to rule out surgery.

**Abstract #1193**

**TRANSAMINITIS IN THE SETTING OF THYROIDOTOXICOSIS**

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**Case Presentation:** Graves’ disease is characterized by thyroid stimulating hormone (TSH) receptor antibodies. These activate the TSH receptor and result in clinical manifestations of hyperthyroidism. One complication of undiagnosed hyperthyroidism is liver damage, which can be seen objectively in elevated liver function tests (LFTs). We present a case of Graves’ disease with elevated LFT’s that responded to anti-thyroid treatment. We also review mechanisms of abnormal liver enzymes in the setting of hyperthyroidism.

A 30-year-old female presented to the emergency department with one week of nausea and vomiting. In addition, she reported palpitations and significant weight loss. On physical exam the patient was noted to be in sinus tachycardia. Thyroid exam revealed an enlarged thyroid gland. Lab results are as follows: TSH < 0.003 mU/mL, free T4 4.0 ng/dL, total T3 > 8.0 ng/mL, thyroid stimulating IG 227, aspartate aminotransferase (AST) 141 u/L, alanine aminotransferase (ALT) 131 u/L, alkaline phosphatase 153 u/L, and total bilirubin 2.3 mg/dL. Thyroid ultrasound reported an enlarged thyroid. Management included propranolol and methimazole. Methimazole was initiated at a lower dose due to transaminitis. Workup for autoimmune hepatitis was negative. LFTs were closely monitored. On follow up, thyroid and liver function tests had normalized after several weeks of therapy.

**Conclusion:** There are several reasons for liver injury in a hyperthyroid state. First, the liver metabolizes thyroid hormone. Relative hepatic ischemia secondary to a hypermetabolic state has been shown to increase LFTs. There have been rare case reports of autoimmune hepatitis and cholestasis with Graves’ disease. In addition, excess thyroid hormone can be damaging to the liver. With these etiologies in mind, a workup of transaminitis in the setting of hyperthyroidism should include a toxin screen, autoimmune panel, and imaging. In our patient, the autoimmune workup was negative. She responded to methimazole and her transaminitis improved. Steroids or thyroidectomy are considered if the LFTs do not improve after initiation of medical therapy. Anti-thyroid medications require careful monitoring as they can also contribute to hepatic dysfunction. This case underscores the need to include a liver profile in the workup of a patient with hyperthyroidism. Liver transaminase levels more than fivefold the upper limit of normal are a contraindication to initiating antithyroid medications. Furthermore, this case illustrates that antithyroid medications should not be held in the setting of mild transaminitis. The treatment of hyperthyroidism in most cases will result in normalization of LFTs.

**Abstract #1194**

**PROGNOSTIC SIGNIFICANCE OF SUBCLINICAL HYPOTHYROIDISM IN PATIENTS WITH HEART FAILURE WITH PRESERVED EJECTION FRACTION**

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**Objective:** Subclinical hypothyroidism (SCH) is under-diagnosed in patients with heart disease, however, there has been controversy surrounding whether it is a cardiovascular risk factor or not. To determine the prognostic significance of SCH in Heart Failure (HF) with Preserved Ejection Fraction (HFpEF) we followed a cohort of patients for 9 years.

**Methods:** In this retrospective cohort, we queried our HF data base to identify HFpEF patients diagnosed in 2006 (registry initiation date) based on symptoms, BNP, and Echocardiogram with no history of hypothyroidism. Primary outcome was cardiovascular disease (CVD) mortality. Subjects divided into 2 groups based on presence or absence of SCH. SCH was defined as TSH of 5-10 mIU/L and normal free T4 in the absence of symptoms or hypothyroidism history.

**Results:** We identified 249 eligible patients, of who 71 had SCH (28.5%). Mean age was 72.1 ± 13.4 years. Women constituted 56.6%. Follow up was for 8.75 ± 0.17 years. The CVD mortality rate for SCH patients was 29.6 % versus 14.9 % for the others (P=0.008). The median survival time for SCH patients was significantly lower than patients with normal thyroid function, 99.9 ± 2.9 and 107.7 ± 1.5
months, respectively (P=0.008 after adjustment for age, sex, hypertension, diabetes, coronary artery disease, BMI, atrial fibrillation, and other risk factors).

Discussion: The associations of SCH with all-cause or CVD mortality were controversial in previous studies. Several studies reported no association of SCH with death from CVD or all-cause mortality. All the reported studies focused on the presence of coronary artery disease and systolic heart failure, but none were conducted on patients with HFpEF and TSH <10 mIU/L. The pathophysiology of SCH-induced diastolic dysfunction is not completely understood, but mostly related to loss of T3-induced genomic and non-genomic effects on the cardiac myocyte (through transcription factors and membrane iron-channels) leading to higher resistance, stiffness, and impaired diastolic filling.

Conclusion: Mild SCH is a significant predictor of mortality in HFpEF patients, despite controlling for all major risk factors. Therefore a mild asymptomatic elevation in TSH has a significant impact on outcome, perhaps as a consequence on left ventricular stiffness.

Abstract #1195

IODINE THYROTOXICOSIS- INDUCED ATRIAL FIBRILLATION

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Case Presentation: Iodinated contrast is often used in various radiologic examinations and interventional procedures and can result in massive iodide exposure to the thyroid gland and subsequent development of incident hyperthyroidism and thyrotoxicosis, which could lead to potentially life-threatening consequences, including arrhythmias. We present the case of a 79 year old male with past history of laryngeal squamous cell carcinoma who underwent total laryngectomy with cricopharyngeal myotomy, tracheal esophageal puncture and prosthesis insertion. History was significant for COPD, hypertension, stable coronary artery disease. Her hospitalization was complicated with development of atrial fibrillation with rapid ventricular response. Thyroid function tests were significant for TSH of 1.060 uIU/ML (0.350-4.940 uIU/ML) and FT4 of 0.8 ng/dl (0.7-1.5 ng/dl) total T3 0.8 ng/ml (0.6 -1.6 ng/ml ). His methimazole was stopped but betablocker and digoxin were continued.

Discussion: The administration of iodine to patients with underlying thyroid disease could potentially result in hypersecretion of thyroid hormones which can develop over 2 to 12 weeks as the iodine is used as a substrate for new hormone formation. People with nodular thyroid disease, Graves disease with thyroid autonomy, the elderly and people living in areas of iodine deficiency are vulnerable to the condition. However, exposure to a large iodide load such as occurs with iodinated contrast studies can also cause acute destructive thyrotoxicosis in people without thyroid disease such as seen in our patient after undergoing two consecutive contrast CT scans. He developed atrial fibrillation with rapid ventricular response needing control with betablocker and digoxin. Clinically, iodine-induced hyperthyroidism cannot be differentiated from other forms of thyrotoxicosis and it is of utmost importance to monitor its cardiovascular manifestations.

Conclusion: As providers, we must always be mindful of the amount of testing we subject our patients to, especially the elderly population, as they can lead to excessive , and sometimes unnecessary, iodine and radiation exposure.

Abstract #1196

REFRACTORY HYPOTHYROIDISM DUE TO L-THYROXINE MALABSORPTION

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Objective: Inter-individual variability in the dose requirement of levothyroxine (LT4) is often manageable after adjustment for body weight. Malabsorption further increases LT4 requirements. We report a case of refractory primary hypothyroidism due to malabsorption status-post (s/p) total pancreatectomy. The patient responded poorly to oral LT4, but did well with intravenous (IV) and intramuscular (IM) doses. After assessment with an LT4 absorption test, she was transitioned successfully to a higher LT4 oral dose.

Case Presentation: The patient was a 48-year-old Caucasian, cachectic woman with pancreoprivic diabetes mellitus, severe malabsorption, and failure to thrive s/p a total pancreatectomy revision of a Whipple procedure for a neuroendocrine tumor in 2006. In 2012, Hashimoto’s thyroiditis with hypothyroidism was treated with oral LT4. Despite increased LT4 doses up to 250 mcg daily,
she remained hypothyroid. In January 2014, she was hospitalized with intractable vomiting, diarrhea, and hypothyroidism; TSH-102 uIU/mL (ref: 0.4-5.0) and FT4<0.2 ng/dL (ref: 0.6-1.5). With IV LT4 100mcg daily, TSH decreased to 25 uIU/mL and FT4 to 1.0 ng/dL. On discharge she resumed oral LT4 250 mcg daily, but never attained euthyroidism. In January 2015, she was admitted for altered mental status. Her TSH and FT4 normalized on IV LT4 100 mcg daily. She became severely hypothyroid on oral LT4 250 mcg daily after 8 weeks and did not respond to escalating oral doses. Extensive evaluation for other causes of malabsorption was negative. LT4 was changed to IV and TSH normalized in 3 weeks. Our challenge was to develop a treatment regimen for a skilled nursing facility. IM LT4, up to 800 mcg weekly controlled her hypothyroidism. She did not tolerate IM injections, and long-term weekly dosing was not feasible due to expense. An LT4 absorption test was done with an oral dose of 1000 mcg and FT4 levels at baseline and at 30, 60, 90, 240, and 360 min. FT4 increased 62.5% from 0.8 to 1.3ng/dL. Titration of a daily oral LT4 dose to 450 mcg normalized her TSH and FT4.

**Conclusion:** Our patient suffered from refractory hypothyroidism with oral LT4 in both outpatient and inpatient settings; supervised medicine intake made pseudomalabsorption unlikely. LT4 malabsorption was related to pancreatic deficiency, altered gut transit and multiple medicines. The LT4 absorption test indicated she did absorb some of the dose, and highlighted the value of this test in selected patients for developing a treatment plan. Her daily dose required to achieve a normal TSH was 10.2mcg/kg. The large oral LT4 dose of has remained well-tolerated long-term, and more financially feasible than IV or IM injections.

**Abstract #1197**

**TOTALTHYROIDECTOMYVERSUSNEARTOTALTHYROIDECTOMYWITHRADIOABLATIONOFRESIDUALTHYROIDFORDIFFERENTIATEDTHYROIDCANCERCONFINEDTOONELOBEOFTHYROIDGLAND:ARANDOMIZEDCONTROLLEDTRIAL**

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**Objective:** Is Near total Thyroidectomy better than Total thyroidectomy in reducing hypocalcaemia and voice change without compromising on oncological safety in patients with low risk differentiated thyroid carcinoma?

**Methods:** A non-inferiority randomised controlled trial was conducted on 30 patients (with differentiated thyroid carcinoma < 4 cm confined to one lobe) being randomised to Near total thyroidectomy or Total thyroidectomy. In Near total thyroidectomy, 1 cm (anteroposterior) strip of contralateral normal lobe (extended Hartley-Dunhill procedure) was left behind. Patients were monitored for post operative hypocalcemia. Two weeks after radioactive ablation, a speech analysis was performed. Radioactive ablation was done when the postoperative radioiodine scan showed uptake of more than 0.2%.

**Results:** Compared to Total thyroidectomy, Near total thyroidectomy had less immediate postoperative complications in terms of duration of intravenous calcium therapy (1 vs 10: p = 0.019). There was an associated increased postoperative stay. Despite an increased postoperative iodine uptake after Near total thyroidectomy (7.6 vs 0.7%, p = 0.004), there was no correlation between uptake and thyroid residuum (R = 0.2141, p = 0.527). Certain amount of tissue is always left behind after most Total thyroidectomy (83%) requiring ablation. Neither re-ablation nor high doses were needed after Near total thyroidectomy.

**Discussion:** Despite the increased uptake in diagnostic whole body scanning after Near total thyroidectomy, similar amounts of radioiodine could achieve complete ablation in all patients. No correlation could be drawn between the thyroid residuum and the uptake in diagnostic whole body scanning or the amount of radioiodine needed for ablation, thus disproving the common notion that more tissue means more uptake and higher doses. The advantage
of Near total thyroidectomy over Total thyroidectomy should be correlated with the fact that most low risk thyroid carcinoma are operated by general surgeons at low volume centres with less surgical skills. It is prudent for these surgeons to perform less aggressive surgeries for disease with such a good prognosis. However, the study has a small sample size with a short follow up to assess for oncological safety in terms of local recurrence.

**Conclusion:** This study is the first randomised controlled study in the world attempting to find the ideal extent of surgery for low risk thyroid carcinoma. We conclude that near total thyroidectomy when compared to total thyroidectomy has less immediate postoperative complications in terms of manifest hypocalcaemia, number of days intravenous calcium required and days of total hospital stay.

**Abstract #1198**

**THE WHOLE PICTURE: ADEQUACY OF LYMPH NODE EVALUATION IN PRE-REFERRAL CERVICAL ULTRASOUND ASSESSMENT**

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**Objective:** Cervical ultrasonography is an essential part of the evaluation of thyroid disease, and ultrasound assessment of the cervical lymph nodes (LNs) is an important component of preoperative staging for thyroid cancer that often determines the operative plan. Patients with known or suspected thyroid malignancy referred to tertiary care centers have frequently undergone diagnostic ultrasound evaluation prior to referral. The current study sought to evaluate the difference of initial cervical ultrasound evaluation performed for diagnostic purposes with comprehensive, standardized ultrasound assessment performed for surgical purposes at a specialized cancer center.

**Methods:** Following IRB approval, a retrospective review was performed of 100 consecutive patients who underwent documented cervical ultrasound examination prior to referral for surgical evaluation of thyroid disease at a single high-volume center. Ultrasound reports used for referral purposes were reviewed for documentation of the presence or absence of suspicious sonographic features, performance of fine-needle aspiration biopsy (FNA) and cervical LN evaluation. Per institutional standard, all patients underwent comprehensive pre-surgical cervical ultrasound at our referral center.

**Results:** Fourteen of 100 (14%) patients had cervical LN evaluation documented on diagnostic ultrasound. Patients with documented pre-referral cervical LN assessment included only 10 of 38 (26%) with a sonographically suspicious thyroid nodule, and only 10 of 73 (14%) in whom pre-referral FNA was performed [including 4 of 30 (13%) with a cytologic diagnosis of Bethesda category 5/6]. No significant difference in cervical LN assessment was noted based on provider (p = 0.306) or facility (p = 0.478) performing the pre-referral ultrasound (hospital, imaging center, endocrinology clinic). In contrast, cervical LN evaluation was consistently performed at the tertiary referral center (97 of 100, 97%) (p<0.001), resulting in additional biopsies or changes in treatment plan in 40 patients (40%, C.I. 30.4-49.6%).

**Conclusion:** Complete ultrasound evaluation of central and lateral neck LNs is imperative for accurately staging and preoperative treatment planning for thyroid disease. Initial diagnostic ultrasounds rarely evaluate lymph node basins, which often omits details pertinent to adequate surgical treatment of confirmed or suspected malignancy. A standardized comprehensive thyroid ultrasound evaluation and documentation of cervical LNs is needed for preoperative planning.

**Abstract #1199**

**THYROID CANCER IN ITS RARE AND MORTIFEROUS FORM**

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Medstar Washington Hospital Center

**Objective:** Lack of squamous epithelium in the thyroid gland makes Primary squamous cell carcinoma of the thyroid gland a rare entity, with an incidence of less than 1% out of all thyroid malignancies.

**Case Presentation:** A 77 year old female presented to her primary care physician complaining of left sided headaches since 2 months and was noted to have a left sided lump in her neck which had been increasing in size since one month. Physical exam revealed a rock hard, left sided neck mass, fixed to the left clavicle, tender to palpation with rightward tracheal deviation and a 2 cm nodule in mid pole. No lymphadenopathies were noted and she had a normal respiratory effort without a stridor. Patient underwent a CT of neck with contrast which showed a large mass on the left side, posterior to the sternocleidomastoid, displacing the trachea and esophagus and an additional 1.5 cm left sided anterior cervical lymph node. Whole body FDG PET-CT showed a large metabolic mass on left side of thyroid gland with no additional uptake to indicate metastatic disease. Flexible laryngoscopy was normal and FNA of the left thyroid mass showed sheets and clusters of carcinoma cells that were positive for AE1/AE3, Cam5.2, CK5/6 and P63 and
negative for TTF1, thyroglobin, CD56, chromogranin, synaptophysin and CD45. A diagnosis of Primary squamous cell carcinoma of the thyroid gland was made. Patient was not considered to be a surgical candidate, underwent XRT and chemotherapy, but had tumor growth during that period. She was started on lenvatinib, with a fifty percent decrease in mass size. However, it had to be discontinued due to pulmonary metastasis and is now planning to seek hospice services.

Conclusion: Primary squamous cell carcinoma of thyroid gland is not only a rare and deadly disease but also a challenging diagnosis because squamous metaplasia can be seen in upto 43 per cent of papillary thyroid carcinomas and also in some anaplastic thyroid carcinomas. It could also represent a direct extension of a primary SCC from adjacent structures or metastases from a distant SCC. Three theories have been postulated regarding its etiology among which, the metaplasia theory explains that in the setting of inflammation or lymphocytic thyroiditis, continuous stimuli of follicular cells can lead to squamous metaplasia, which could be the case in our patient. The median age of presentation is between the fifth and sixth decades of life and it carries a poor prognosis with low median survival rates, despite the use of multimodal treatment approaches.

Abstract #1200

AMBULATORY THYROIDECTOMY: IS IT SAFE?

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Objective: With the increased diagnosis of thyroid nodules and cancer, ambulatory thyroidectomy has significantly increased in frequency. Establishing the safety of this practice is imperative to preserving non-maleficence. Therefore, our objective was to examine outcomes, including complications and readmissions, in a large cohort of ambulatory thyroidectomy patients.

Methods: The 2011 California State Inpatient and Ambulatory Surgery Databases were linked to California Hospitals Utilization data to identify a cohort of 9,885 thyroidectomy patients. CPT and ICD-9 codes were used to define the outcome variables. Statistical analysis was performed with univariate and multivariate logistic regression methods.

Results: Of the 9,885 thyroidectomies identified, 33.6% were ambulatory surgeries, and 47.6% were total thyroidectomies (TT). The proportion of ambulatory patients who had a TT was 23.6%. Ambulatory patients were younger and more likely to be female, Caucasian, and privately insured ($p<0.002$ for all). They also had fewer comorbidities and were less likely to have thyroid cancer ($p<0.002$ for all). Both ambulatory partial thyroidectomy (PT) and TT were associated with fewer complications, hematomas, hypocalcemia, voice problems, and 30-day readmission ($p<0.001$ for all). In PT patients, having a multinodular goiter was associated with higher odds of complications (OR 4.9) and 30-day readmissions (OR 4.1) when controlling for all differences in baseline characteristics. In this group, patients with increased comorbidities also had increased odds of complications (OR 1.2).

In TT patients, complications were more likely to occur with younger age (OR 1.7), hypothyroidism (OR 1.6), thyroid cancer (OR 1.5), and increased comorbidities (OR 1.2). The risk of 30-day readmission was greater in African Americans (OR 3.9), Hispanics (OR 2.4), patients insured with Medicaid (OR 2.2), those with more comorbidities (OR 1.7), females (OR 1.5), and at low-volume centers (OR 1.6).

Discussion: In this large cohort of thyroidectomy patients, a significant proportion underwent ambulatory procedures with acceptable complication and 30-day readmission rates. In addition, the percentage of patients who underwent an ambulatory TT was high compared to much of the published literature. Identification of factors associated with increased odds of complications or readmission, such as age, race, or insurance status, is important in aiding the decision as to where to safely perform thyroidectomy.

Conclusion: In this large cohort of patients, ambulatory thyroidectomy appears to be safe. Careful patient selection of ambulatory patients, particularly those needing TT, may allow further safe utilization of these procedures.
Abstract #1201

CLINICAL AND ANALYTICAL VALIDATION OF ROSETTAGX REVEALTM – A MICRORNA-BASED DIAGNOSTIC TEST FOR CLASSIFICATION OF THYROID NODULES

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1. Rosetta Genomics Ltd, 2. H. Lee Moffitt Cancer Center and Research, 3. Pathology Institute, Tel-Aviv Sourasky Medical Center, 4. The Sackler School of Medicine, Tel-Aviv University, 5. National BioService LLC, 6. National Centre of Clinical and Morphological Diagnostics, 7. Institute of Molecular and Translational Medicine, Faculty of Medicine and Dentistry, 8. The Johns Hopkins University School of Medicine, 9. Rosetta Genomics Inc

Objective: The distinction between benign and malignant thyroid nodules has important therapeutic implications. Many thyroid nodules are cytologically classified as indeterminate, a classification which often results in unnecessary surgical procedures. MicroRNAs constitute a class of short, non-coding RNAs and their expression profile has been shown to be reliable biomarkers for cancer subtype classification. We present here the clinical and analytical validation of a microRNA-based test that can stratify thyroid lesions as “benign” or “suspicious for malignancy” in stained pre-operative FNA smears.

Methods: Clinical validation- Over 200 stained FNA smears were collected medical centers in the US, EU and Israel for blinded validation. Matching H&E from thyroid resections were reviewed by three expert thyroid pathologists to determine final diagnosis. Using proprietary technologies, high-quality RNA was extracted and the expression levels of the test’s microRNA biomarkers were measured by qRT-PCR. Analytical validation- Over 150 FNA smears and Formalin-Fixed Paraffin Embedded (FFPE) samples from thyroid resections were profiled by two independent laboratories.

Results: The developed assay accurately differentiates benign from malignant thyroid nodules in indeterminate FNA smears. The assay’s performance on cases where all reviewing pathologists were in agreement regarding final diagnosis is: Sensitivity: 97%; Specificity: 78%; Negative Predictive Value: 98.9%; Positive Predictive Value: 62%. Performance for the overall sample set: Sensitivity: 85%; Specificity: 72%; Negative Predictive Value: 91%; Positive Predictive Value: 59%. Analytical validation correlation was higher than 0.9 for all samples tested in the two laboratories.

Conclusion: A first-of-its-kind assay utilizing microRNA expression in FNA smears for distinguishing benign from malignant thyroid nodules was developed and validated. This assay offers a valuable tool for classification of pre-operative thyroid samples, including those that cytological evaluation currently deems indeterminate.

Abstract #1202

A CASE OF GRAVES’ DISEASE WITH FLUCTUATING THYROID FUNCTION

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Advocate Christ Medical Center

Objective: Graves’ disease (GD) is the most common etiology of hyperthyroidism. It is generally diagnosed in women. GD is characterized by the presence of thyroid stimulating hormone (TSH) receptor antibodies which usually cause hyperthyroidism. We report a rare case of a patient with Graves’ disease with fluctuating thyroid function.

Case Presentation: A 72 year old female presented with shortness of breath, palpitations and tremors. She had a history of hypothyroidism and was on thyroid hormone replacement for 25 years. Levothyroxine was stopped 6 months earlier because of persistent hyperthyroidism. Patient also endorsed a 75lbs weight loss and family history of thyroid disease. On exam, patient was afebrile and tachycardic in the 140’s. Thyroid exam revealed a diffuse goiter with no palpable nodules. She had mild periorbital edema, brisk reflexes and trace pedal edema. Labs demonstrated a positive troponin, elevated b-type natriuretic peptide, suppressed TSH of <0.006 mcunit/mL (0.350-5.000), elevated free T4 2.0 ng/dL (0.8-1.5), elevated free T3 7.9 pg/dL (2.2-4.0), elevated TSH binding inhibition of 21 units/L (<1.0), elevated thyroid stimulating Ig 4,344 % (<150%). Chest x-ray showed vascular congestion. 2D ECHO revealed an ejection fraction of 45-50% with grade 2 diastolic dysfunction. In view of acute thyrotoxicosis, decision was made to hold off on uptake scan and treatment was initiated with methimazole 10mg TID, hydrocortisone and beta-blocker. Patient was readmitted within one month. Repeat biochemical testing suggested hypothyroid status. Labs revealed a TSH 0.037mcunit/mL, low free T4 0.3 ng/dL, and low free T3 1.6 pg/dL. Methimazole was held for a week and then resumed at a lower dosage.
**Abstract #1203**

**GRAVES’ DISEASES ASSOCIATED WITH PRIMARY HYPERPARATHYROIDISM**

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**Case Presentation:** We have presented the case of a 53 years old woman who was admitted in National Institute of Endocrinology C.I.Parhon Bucharest for the evaluation of Graves’ disease. Two month ago the patient was hospitalised in an emergency hospital for a heart attack that was complicated with respiratory failure, hypoxic encephalopathy, congestive heart failure and bilateral pleuresia that have required ventilatory support. At that time TSH was suppressed, T4 was high and the patient had hypopotasemia. Ultrasound of the thyroid has showed unomogenous and hypoechoic structure with intense vascularity of thyroid tissue. They have started therapy with Tyrozol 10 mg*2/zi, Metoprolol 100 mg/zi , Aspacardin 3 cp/zi, Spironalactone 100 mg/zi. Cardiopulmonary resuscitative measures including intubation were successful and the patient was fully stabilised after a time in intensive care unit. Pulmonary and mediastinal CT scan have showed bilateral pleuresia and mediastinal lymphadenopathy with normal cerebral, abdominal and pelvic CT scan. Neoplastic cells were present in the pleural fluid but the pleural biopsy was negative for the neoplastic cells. Antibiotherapy and corticostreoid treatment was started. Evolution was good with slow withdrawal of pleural effusion and the recovery of cardiopulmonary function. In our department she has TSH: 0,5 with free T4: 8,36 (N: 12-22 pmol/L), normal potasemia but we have discovered increased value of calcium (10,9 mg/dl) with low fosfatemia, increased PTH and low 25(OH)VitD. Parathyroid imaging with Tc-99m sestamibi showed left inferior parathyroid adenoma. DXA at the lumbar spine, left hip and 1/3 distal radius is normal and she has no active Graves ‘disease ophtalmopathy. We have started vitamine D replacement therapy and we consider patient for radioiod therapy because at this moment our patient does not meet the criteria for parathyroidectomy with close monitoring of serum calcium and kidney function.

**Conclusion:** We have presented the case of a Graves’ disease that was incidental discovered in the context of a heart attack but that definitely contributed to congestive heart failure and bilateral pleuresia. Hypopotasemia is unusual but not impossible in severe Graves’ disease (we could not appreciated the severity of Graves’ diseases, TSH, fT4 were not disponible at the onset of the disease). Hypercalcemia is not due to hyperthyroidism, as originally thought, but is mainly caused by primary hyperparathyroidism. Primary hyperparathyroidism remains under close observation with the opportunity of thyroidectomy and parathyroidectomy at the same time as surgery.

**Abstract #1204**

**TUBERCULOSIS THYROIDITIS: A RARE MANIFESTATION OF EXTRAPULMONARY TUBERCULOSIS**

Nadeem Tajuddin, MD1, Amir Hassan, MD2

1. Baylor College of Medicine, 2. Clinic of Endocrinology & Rheumatology

**Objective:** 1. Recognize tuberculosis as a form of thyroiditis that can present with thyroid nodules. 2. Discuss management of tuberculosis thyroiditis.

**Case Presentation:** A 16-year-old Vietnamese female who was born in the United States presented with weight loss, neck swelling and supraclavicular lymphadenopathy, which had progressed over three months. She had difficulty swallowing as the swelling worsened but denied any fevers, chills, night sweats, cough, hemoptysis, pain in the neck, upper respiratory symptoms or sick contacts. She lived with her parents, who were born in Vietnam, but no one from her household had recently travelled outside the United States. There was no family history of TB infection or thyroid disease. Exam was significant for a left-sided palpable thyroid mass and multiple left supraclavicular lymph nodes. Laboratory studies showed a WBC count of 13.3 x 10E3/uL and an erythrocyte sedimentation rate of 45 mm/hr. Thyroid studies were within normal limits. Excisional biopsy of supraclavicular lymph nodes and ultrasound-guided fine needle aspiration cytology of the thyroid mass revealed caseating granulomatous inflammation, and cultures were positive for Mycobacterium tuberculosis. She was subsequently treated with Isoniazid, Rifampin, Pyrazinamide and Ethambutol for 8 weeks followed by Isoniazid and Rifampin for 7 months. Her symptoms...
completely resolved by her 3-month follow-up visit, and the previously visualized left thyroid nodule and supraclavicular lymphadenopathy had resolved on repeat ultrasound after 9 months of treatment.

**Discussion:** Although extrapulmonary TB can manifest in any organ, involvement of the thyroid gland is rare, partly due to the bactericidal properties of colloid material and high thyroid blood flow. TB of the thyroid gland can be primary, present in conjunction with TB of other organs, or be due to disseminated disease. Symptoms can overlap with other thyroid diseases such as Hashimoto’s thyroiditis, subacute thyroiditis, malignancy, and sarcoidosis, and thus, diagnosis can be a challenge. The mainstay of treatment is the same as for pulmonary TB, and generally, TB of the thyroid gland responds well to antitubercular medications with complete resolution of symptoms and granulomatous nodules.

**Conclusion:** Although a rare occurrence, the differential for thyroid nodules should include extrapulmonary TB as a cause, especially in patients who are high risk for TB infection. Treatment generally results in complete resolution of symptoms and granulomatous nodules.

**Abstract #1205**

**THE “SOLE” OF RADIATION SAFETY IN THYROID CANCER**

Nidhi Agrawal, MD, Roy Raad, MD, Yana Garger, MD, Kent Friedman, MD, Munir Ghesani, MD, Alina Gouller, MD, Manfred Blum, MD

NYU Langone Medical Center

**Objective:** Radiation safety is an essential component in the treatment of thyroid cancer patients with I-131. Multiple societies have contributed to methods and ideas which are used to guide physicians, patients and caregivers to the attainment of radiation safety in the care of these patients. Contamination hazard from I-131 excretion via sweat, urine, saliva are well described in the literature.

**Case Presentation:** A 75 year old male with diabetes, chronic kidney disease, benign prostatic hypertrophy and recurrent papillary thyroid cancer was referred to the nuclear medicine service for I-131 treatment following total thyroidectomy and modified neck dissection. After meticulous radiation dosimetry, he received 206 mCi of I-131 and was hospitalized under strict isolation precautions. When the body burden of I-131 had decreased to regulatory acceptable levels, he was discharged but isolation precautions were maintained. A 7-day post-treatment Whole Body Scan (WBS) showed abnormal intense I-131 uptake at the base of the neck and the right axilla (Figure A). In addition, there was uptake in the groin (diaper) and soles of the feet which were compatible with urinary contamination. Additional planar and sequential single photon emission computed tomography/x-ray computed tomography (SPECT/CT) imaging on day 13 demonstrated right axillary and mediastinal uptake compatible with metastases, as well as uptake in the abdomen localizing to colonic diverticulae (Figure B-D). Contamination of the soles of the feet had reduced but was still evident.

**Discussion:** Patient-specific iodine biokinetics are important in understanding safe potential doses of I-131 to nearby individuals and caregivers. I-131 is largely excreted from the kidneys. In patients with renal insufficiency the biological half-life of this agent is increased, leading to possibility of extended environmental contamination. The burden of radioactive iodine and level of contamination are largely related to the behavior of the individual and associated medical problems. Thus, when considering therapy, to minimize the risk of urine contamination and hypothetical harm to exposed individuals, the effects of chronic kidney disease, urinary incontinence and diaper dependence are important considerations.

**Conclusion:** Radiation protection is an integral part of radionuclide therapy. Understanding and complying with strict radiation precautions can help physicians and patients maintain radiation safety after therapy to protect the environment and the patient’s care-givers and contacts.

**Abstract #1206**

**IDENTIFICATION OF INTRATHYROIDAL GRANULAR CELL TUMOR IN A 60 YEAR OLD WOMAN WITH MULTINODULAR GOITER**

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1. Creighton University, 2. Dignity Health

**Case Presentation:** A 60 year old female presented with multinodular goiter associated with voice change and dysphagia. No known family history of thyroid disease, nor any prior irradiation to the head or neck. Past medical history includes depression, anxiety, and dyslipidemia. An ultrasound evaluation of the thyroid revealed three hyperechoic nodules and one hypoechoic nodule. The hypoechoic nodule measured 17 x 12 x 11mm and was located in the lower left pole with moderate peripheral vascularity. Hormonal analysis revealed normal fT4, fT3, and calcitonin levels. TSH level was low at 0.33. Radioactive iodine uptake showed a cold defect in the left lobe which correlated with the hypoechoic nodule noted on ultrasound evaluation. Fine needle aspiration (FNA) of the mass revealed a mildly cellular sample with predominantly Hurthle Cell metaplasia. The sample was...
ABSTRACTS – Thyroid Disease

identified as AUS (Atypia of Undermined Significance). An intraoperative frozen section of the left lobe provided the provisional diagnosis of Hurthle Cell adenoma-follicular lesion, with cytologically bland follicular cells and granular cells. Immunohistochemical staining revealed positivity for periodic acid Schiff (PAS), synaptophysin, CD163, and S-100. Congo red was negative for amyloid. The tumor was negative for calcitonin, CEA, thyroglobulin and TTF-1. Diagnosis was then confirmed as Granular Cell Tumor (GCT).

Conclusion: Thyroid nodules represent a diverse spectrum of lesions, ranging from benign to malignant which must be explored in order to determine treatment plan and prognosis. GCT are masses that occur primarily in the head and neck, but can be found virtually anywhere in the body, including muscle and internal organs. At present, only 14 cases of intrathyroidal GCT tumors have been identified. GCT are believed to be of Schwann cell descent due to positive immunohistochemical staining for S-100, neuron specific enolase, and melanocytic markers. These tumors are generally regarded as benign and have a recurrence rate of 5%, attributed largely to incomplete removal. Characteristics of malignancy in GCT include increased nuclear-cytoplasmic ratio, nuclear pleomorphism, necrosis, spindling of tumor cells, vesicular nuclei with prominent nucleoli, and a mitotic count of more than two in 10 high power fields. In our case, a left lobectomy was preferred over total thyroidectomy following reassuring cytological features seen on intraoperative frozen section. The patient has suffered no local recurrence at six months postoperatively and is recommended to return for reevaluation in one year.

Abstract #1207

EVOLUTION OF LIVER FUNCTION TESTS IN NEWLY DIAGNOSED, OVERT HYPERTHYROIDISM TREATED WITH METHIMAZOLE

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1. Carol Davila University, 2. C. I. Parhon Institute of Endocrinology

Objective: Overt hyperthyroidism is frequently associated with abnormal liver function tests (LFT). Our objective was to describe the evolution of LFT in patients newly diagnosed with overt hyperthyroidism of different etiologies treated with methimazole (MMI).

Methods: We retrospectively analyzed all patients (62 women, 15 men) presenting with newly diagnosed overt hyperthyroidism (59 Graves diseases, 11 toxic nodular goiters, 4 toxic adenomas, 3 amiodarone-induced thyrotoxicosis) between 2012 and 2014. All patients started MMI between 10 and 60 mg/day that was gradually tapered based on clinical judgment. All patients had their TSH, freeT4, AST and ALT measured at baseline and at 6 weeks, 4.5 months and 10 months after starting the MMI treatment. The concomitant medication did not change over the period of MMI treatment.

Results: At baseline there were 25 patients (32.5%) with abnormal LFT. There were no significant clinical differences between patients with normal and abnormal LFT. The highest level of ALT and AST was 3.6 the upper limit of normal (ULN) and 2.5 the ULN respectively. In patients with abnormal LFT, MMI treatment resulted in a rapid (6 weeks) significant decrease of median serum levels. At the 1.5, 4.5 and 10 months evaluations there were no significant differences in ALT and AST levels between patients with initially normal or abnormal LFT. In a last observation carried forward analysis on treated patients, at the end of study, AST and/or ALT serum levels over the ULN were found in 17.9% of patients with initially normal levels and 11.1% of patients with initially increased levels. In a Cox proportional hazard regression model, abnormal LFT at baseline, abnormal thyroid function at the last evaluation and MMI dose were not predictors of abnormal LFT at the final evaluation.

Discussion: To our knowledge this is the first study evaluating the sequential changes of liver function test in MMI-treated hyperthyroidism. Abnormal baseline LFT are frequent in newly diagnosed overt hyperthyroidism but the vast majority of patients had AST/ALT serum levels below 2 x ULN with only 5.2% having AST of ALT levels over 2 x ULN. MMI treatment resulted in a rapid decrease of AST and ALT serum levels in patients with abnormal LFT suggesting that hyperthyroidism was the cause of liver dysfunction. However, as MMI treatment induced mild elevations of LFT in patients with baseline normal hepatic function, the global percentage of abnormal LFT decreased more slowly.

Conclusion: Our data show that MMI treatment can be safely administered in hyperthyroid patients with abnormal LFT and normalization of increased AST and ALT levels should be anticipated.
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