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## 2011 ABSTRACT

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ADRENAL DISORDERS

Abstract #100

IMPROVEMENT OF SUBCLINICAL CUSHING’S SYNDROME AFTER TREATMENT WITH LEUPROLIDE IN A PATIENT WITH ACTH-INDEPENDENT MACRONODULAR HYPERPLASIA (AIMAH). ABERRANT LH RECEPTOR EXPRESSION IN A PATIENT WITH AIMAH?

Divya Yogi-morren, MD, Pascual De Santis, MD

Objective: To present a case of subclinical Cushing’s syndrome (CS) caused by Adrenocorticotropic hormone-independent macronodular adrenal hyperplasia (AIMAH).

Case Presentation: A 56 year old woman presented with weight gain of 45 pounds, fatigue, depression, anxiety and left flank pain. CT of the abdomen revealed nephrolithiasis which was treated. Coincidentally, bilateral adrenal masses were found. The right adrenal mass measured 4 cm x 2.3 cm and the left adrenal gland mass measured 4.8 x 2.7 cm with Hounsfield units less than ten. Biochemical workup revealed normal aldosterone-renin activity ratio, DHEA-S, plasma and urinary metanephrines. Evaluation for cortisol excess revealed a normal 24 hour urinary free cortisol but high salivary cortisol and there was lack of cortisol suppression with low dose and high dose dexamethasone suppression testing. Given the patient’s clinical history, macronodular adrenal glands and low normal ACTH, it was concluded that the patient had subclinical CS caused by AIMAH. In this post menopausal woman, we suspected that cortisol secretion may be Luteinizing Hormone (LH) mediated. She was started on leuprolide. After being treated with leuprolide 3.75 mg/day there was a 67.25% decrease in mean salivary cortisol levels. The difference between the baseline salivary cortisol levels and the levels after starting leuprolide were compared using an independent sample t-test which yielded a p value of 0.036. The leuprolide was then increased to 7.5 mg/day and further suppression of cortisol was demonstrated with repeat low and high dose dexamethasone suppression testing. Given that cortisol suppression occurred in a dose responsive manner to leuprolide, we postulate that this patient’s subclinical CS was due to AIMAH with aberrant expression of LH receptors.

Discussion: AIMAH is rare, and accounts for less than 1% of cases of CS. Bilateral adrenalectomy is the treatment of choice in patients with AIMAH and CS. This patient had subclinical CS which should cause concern as it has been shown to be associated with a high prevalence of obesity, hypertension and type II diabetes. The clinical judgment was made to pursue medical management after considering the inevitable sequelae of adrenalectomy

Conclusion: Long-term leuprolide treatment has been shown to normalize cortisol secretion in AIMAH and LH-dependent CS as well as in LH-dependent subclinical CS. In the future it will also be valuable to investigate whether treatment with these agents will alter the natural history of AIMAH when discovered in its subclinical stages.

Abstract #101

RARE CASE OF LIPOID CONGENITAL ADRENAL HYPERPLASIA DUE TO StAR GENE DEFECT

Avni Shah, MD, Michelle Rivera-Davila, MD

Objective: To describe a unique presentation of lipoid congenital adrenal hyperplasia (CLAH) due to steroid acute regulatory protein (StAR) gene defect.

Case Presentation: A term, phenotypic female newborn presented with hyperpigmentation, persistent tachypnea, and metabolic acidosis. Hyponatremia and hyperkalemia prompted a CAH workup. Random cortisol was 10.8ug/dl, ACTH >1250pg/dl. 250mcg cosyntropin stimulation yielded ACTH 810ug/dl, 60 minute cortisol 12.8ug/dl. 17-OHP and 17-OH pregnenolone of 56ng/dl and 17ng/dl, respectively, ruled out 3B hydroxysteroid deficiency. Pelvic ultrasound revealed testes-like structures bilaterally with no uterus; karyotype was XY. A homozygous sequence variant (c.64+1G>T) associated with CLAH in a recessive mode was found. Therapy with fludrocortisone and hydrocortisone was initiated at 3 weeks of age, then patient was transitioned to prednisolone, fludrocortisone, and sodium chloride. Gonadectomy was planned at 4 months of age to decrease malignancy risk.

Discussion: Loss-of-function mutations in the StAR gene, which are associated with CLAH and are autosomal recessive, account for a small percentage of CAH. StAR is a gatekeeper for steroid biosynthesis by facilitating transfer of cholesterol from the cytosol to the inner mitochondrial membrane, where steroidogenesis is initiated. This decrease in cholesterol transport is known as the “first-hit”. The “second-hit” is deposition of cholesterol esters in the cytosol which causes cell destruction. The result is impairment of
the glucocorticoid, mineralocorticoid and sex steroid pathways. In XY males, hCG stimulates sex steroid production in early gestation. Without StAR activity, cholesterol accumulation and cell destruction occurs in the testes, leading to impaired testosterone production and lack of development of male external genitalia. Thus, males tend to manifest gonadal failure earlier than the XX counterparts. In the adrenals, stimulation in utero affects primarily the fetal zone. The definitive zone, which develops into the zona glomerulosa and fasciculata, may remain partially functional for weeks after birth, demonstrated by the delay in adrenal insufficiency and salt wasting. XX females have lower StAR activity in the ovaries, thus delaying cholesterol accumulation and cell destruction. A late presentation may ensue and be less severe. Some have been reported to undergo spontaneous pubertal maturation, though many develop premature gonadal failure.

**Conclusion:** StAR gene defects result in CLAH which presents with severe adrenal insufficiency, salt wasting, and male sex reversal.

**Abstract #102**

**CLINICALLY SILENT CORTICOTROPH POSITIVE PITUITARY MACROADENOMA**

Devendra Wadwekar, MD, Marissa Grotzke, MD

**Objective:** To highlight the variety of presentations of giant pituitary macroadenomas.

**Case Presentation:** A previously healthy 33-year-old male was found slumped over in his kitchen and brought to the emergency room where initial computerized tomographic (CT) scan of the head was concerning for pituitary hemorrhage. He was empirically started on dexamethasone and his neurological symptoms resolved. Initial laboratory studies were notable for adrenocorticotrophic hormone (ACTH) of 160 pg/ml (normal <69) and an afternoon cortisol of 19.3 µg/dl after receiving two doses of dexamethasone. Upon further questioning, he reported chronic intermittent headaches for the last two years without any visual complaints, breast enlargement, muscle weakness, skin striae, hypertension, loss of libido, or changes in weight. His magnetic resonance imaging (MRI) scan of the brain revealed a large 4.2 cm heterogenous, hyperintense enhancing sellar mass having multiple areas of cystic foci and hemorrhage with extension into the surrounding structures. The next morning his ACTH was further elevated at 237 pg/ml with a cortisol of 9.4 µg/dl. The patient underwent partial trans-sphenoidal resection of the tumor which was found to be an ACTH staining pituitary adenoma. He was discharged home on desmopressin, levothyroxine and hydrocortisone. At a follow up visit 3 weeks later, he was asymptomatic and labs while still on high dose hydrocortisone revealed an ACTH of 74 pg/ml and an afternoon cortisol of 10.4 µg/dl. Two months after surgery, he underwent radiation therapy and received a total dose of 4500 cGy. He was initiated on testosterone replacement therapy for symptomatic hypogonadism and his steroids are gradually being tapered. A six month follow up MRI scan of the pituitary gland revealed post operative changes are gradually being tapered. A six month follow up MRI scan of the pituitary gland revealed post operative changes 

**Discussion:** This is an unusual presentation of a giant ACTH producing pituitary macroadenoma. The patient did not have any clinical or biochemical evidence of hypercortisolemia and presented with syncope from the mass effect of the tumor. This leads us to believe that he may have biologically inactive circulating ACTH as has been reported previously in several case reports. This case is consistent with the finding previously reported in literature that non functioning pituitary adenomas with positive immunoreactivity for ACTH behave more aggressively than ACTH immunonegative tumors.

**Conclusion:** ACTH producing giant pituitary macroadenomas can present without clinical or biochemical hypercortisolemia.

**Abstract #103**

**HYDROCODONE INDUCED ADRENAL INSUFFICIENCY**

Maria Luisa Ramirez, MD, Kathie Hermayer MD, MS

**Objective:** To recognize opiates as a potential cause of adrenal insufficiency (AI).

**Case Presentation:** A 66 year old white female was referred to Endocrinology for management of Osteopenia. She had a history of hypertension, chronic kidney disease, syncope, and ovarian cancer, status post total hysterectomy, bilateral salpingo-oophorectomy, in remission. On her initial visit, she was orthostatic and had fatigue and dizziness. Her medications included Boniva, Benicar 40/25mg daily, and Hydrocodone-Acetaminophen 7.5/500mg twice a day, which she had been taking for 2 years. On further evaluation for secondary causes of osteopenia, she was found to have a low 24 hour free urine cortisol of less than 1ug/d (nl<45ug/d). Morning cortisol level was 0.8mcg/dl (4.3-22.5mcg/dl), with an ACTH of 10.7pg/ml (nl<45pg/ml). A high dose Cosyntropin stimulation test (250mcg) had a suboptimal response: baseline ACTH less than 5.9pg/ml, cortisol less than 0.7mcg/dl, 30min 7.2mcg/dl, 60min 9.6mcg/dl, and 90 min 10.5mcg/dl. MRI of the brain and CT of the abdomen were normal. She was diagnosed with secondary or tertiary AI due to chronic opiate therapy. Prednisone
5mg was started and weaning prednisone and opiates were unsuccessful due to recurrence of symptoms.

**Discussion:** Chronic use of opiates for malignant and non-malignant pain has increased significantly in the past decade and their use may be associated with undesirable side effects (e.g. sweating, sexual dysfunction, lethargy) which may be secondary to changes in the endocrine system. Several animals and human studies in heroin addicts, patients on methadone therapy, chronic fentanyl and hydromorphone use, demonstrate that long term opiates may cause inhibition of hypothalamic-pituitary function, including effects on the hypothalamic-pituitary-gonadal axis, pituitary, adrenal, growth hormone axis, and effects on prolactin. Different theories exist about how opiates may affect the adrenal axis; some studies in methadone addicts conclude that secondary hypoadrenalism is due to depletion of the ACTH/beta-endorphin system, while others suggest that the defect may lie in the adrenal cortex. These patients have symptoms suggestive of AI that may remain unrecognized for years. Treatment may improve the symptoms and the endocrine dysfunction may reverse with withdrawal or decrease in the dose of opiates.

**Conclusion:** This case underscores the importance for clinicians to consider opiates as a possible cause for adrenal insufficiency and assess endocrine function in chronic opiate users if they have symptoms suggestive of AI or hypogonadism.

**Abstract #104**

**ADRENAL INSUFFICIENCY AFTER INTRAARTICULAR CORTICOSTEROID INJECTION IN AN HIV-INFECTED PATIENT TREATED WITH RITONAVIR**

Nicoleta Ionica, MD, Elizabeth Streeten, MD

**Objective:** Recent reports suggest that adrenal insufficiency, a rare complication of intra-articular (IA) corticosteroid injection, is significantly higher in HIV-infected patients receiving ritonavir-boosted protease inhibitor (PI) regimens. Unlike prior reports, we present a case of an HIV-infected patient who developed central adrenal insufficiency after receiving a single dose of IA triamcinolone without intervening Cushing syndrome.

**Case Presentation:** A 59 year old Caucasian male with a history of HIV infection was referred to endocrine clinic for evaluation of generalized weakness, lightheadedness and undetectable morning cortisol level, two weeks after receiving a single IA injection of triamcinolone (80 mg). In addition to HIV, his past medical history was significant for hypertension and dyslipidemia. His antiretroviral regimen included emtricitabine, tenofovir and lopinavir boosted with low doses of ritonavir. Review of system was positive for profound fatigue, lightheadedness and postural changes. He denied weight loss, nausea, vomiting and abdominal pain. On examination, he had normal blood pressure and heart rate, without orthostatic change, no central obesity or abdominal striae. Biochemical work-up revealed normal comprehensive metabolic panel, complete blood count, plasma renin activity (4.01; 0.25-5.82 ng/ml/hr) and aldosterone (4; 2-45 ng/dL). Morning cortisol level was 1.8 mcg/dL, and ACTH level was 6 pg/mL (7-50 pg/mL), consistent with suppression of his hypothalamic-pituitary-adrenal (HPA) axis. Cosyntropin stimulation test (250 µg) confirmed the diagnosis of adrenal insufficiency (peak cortisol: 11.2 mcg/dL). Central adrenal insufficiency induced by triamcinolone was suspected and he was started on hydrocortisone replacement therapy. This treatment allowed a rapid recovery of his general health status. We plan to repeat cosyntropin stimulation testing every two months until his HPA axis recovers.

**Discussion:** Ritonavir, a PI used in the treatment of HIV infection, is an extremely potent inhibitor of cytochrome P450 3A4 (CYP 3A4), involved in the catabolism of corticosteroids. Prolonged exposure to high level of corticosteroids leads to direct suppression of the HPA axis as illustrated in our case without going through an obvious Cushing syndrome phase. Our planned serial repeat cosyntropin stimulation testing will help to determine how long the HPA axis suppression lasts.

**Conclusion:** HIV-positive patients receiving ritonavir who receive IA corticosteroids should be closely monitored for signs of adrenal insufficiency.

**Abstract #105**

**A RARE CASE OF EXTRA-ADRENAL PHEOCHROMOCYTOMA IN A PREGNANT PATIENT WITH VON HIPPEL - LINDAU DISEASE**

Seenia Varghese Peechkara, MBBS, Yogesh Shah, MD, Laurence Kennedy, MD, Charles Faiman, MD, Amir Hamrahan, MD

**Objective:** To report the presentation and management of extra- adrenal pheochromocytoma in a pregnant woman with Von Hippel-Lindau (VHL) disease.

**Case Presentation:** A 33-year old woman, a known carrier for a VHL gene mutation was referred at 24 weeks’ gestation for evaluation of pheochromocytoma after she was found to have elevated urinary and plasma metanephrines. She denied a history of hypertension, palpitations, diaphoresis or headaches. Physical exam: pulse 111 bpm and regular, blood pressure 124/75 mm Hg; otherwise unremarkable. Labs: 24-hr urinary metanephrine 86 µg (52-341), normetanephrine 1568 µg (88-444), epinephrine 7 µg (2-24), norepinephrine 175 µg.
We have described a rare case of bilateral Objective Dwain Woode, MD, Maryam Rivaz, MD Omid Rad Pour, MD, Beverly Williams-Cleaves, MD, HYPERPLASIA A YOUNG MALE WITH CONGENITAL ADRENAL ASSOCIATED WITH TESTICULAR TUMORS IN BILATERAL GIANT ADRENAL MYELOLIPOMA

Abstract #106

Close monitoring is recommended for most patients. Pregnancy with adequate alpha-adrenergic blockade and catastrophic events. Conservative management during timely diagnosis of pheochromocytoma during PG to avoid intervention.

Discussion: Paraganglioma or pheochromocytoma in PG associated with familial syndromes like MEN, VHL, and SDH gene mutations are rare. The presence of hypertension may be wrongly ascribed to preeclampsia in PG. Maternal mortality in undiagnosed patients is reported 17-56% and fetal mortality 26-58%. For tumor localization during PG, MRI is known to be safe. For the mode of delivery, cesarean section is preferred as it allows for greater control. With close monitoring and adequate alpha-adrenergic blockade, it is safe to advance through PG without complications or the need for surgical intervention.

Conclusion: High clinical suspicion is warranted for timely diagnosis of pheochromocytoma during PG to avoid catastrophic events. Conservative management during pregnancy with adequate alpha-adrenergic blockade and close monitoring is recommended for most patients.

Abstract #106

BILATERAL GIANT ADRENAL MYELOLIPOMA ASSOCIATED WITH TESTICULAR TUMORS IN A YOUNG MALE WITH CONGENITAL ADRENAL HYPERPLASIA

Omid Rad Pour, MD, Beverly Williams-Cleaves, MD, Dwain Woode, MD, Maryam Rivaz, MD

Objective: We have described a rare case of bilateral giant Adrenal Myelolipoma associated with Testicular Tumors of the Adrenogenital Syndrome (TTAGS) in a patient with Congenital Adrenal Hyperplasia (CAH) who required bilateral adrenalectomy due to the size of adrenal tumors and severe abdominal pain.

Case Presentation: 35 y/o white male presented with bilateral flank pain of one-year duration and aggravation of the symptom for one month. The pain on the left side was more severe. He was diagnosed with CAH in infancy and was on hydrocortisone and fludrocortisones at the time of presentation. He underwent bilateral orchiectomy two years prior due to large and painful testicular masses. Pathology report was confirmatory for TTAGS. He was started on testosterone replacement after the orchiectomy. In physical exam he had diffuse abdominal tenderness with no rebound. Deep palpation was not performed due to the patient’s discomfort. He had bilateral flank tenderness more prominent on the left side. CT abdomen with contrast showed 20x15 cm adrenal mass on the left and 10x4 cm adrenal mass on the right. The appearances of these masses were suggestive for adrenal myelolipoma. Surgical intervention was planned due to the size of adrenal masses and patient’s symptoms. Bilateral adrenalectomy was performed and pathology report confirmed the diagnosis of bilateral adrenal myelolipoma. Patient tolerated the surgery with no sever complication and was discharged with outpatient follow up few days after the surgery.

Discussion: Myelolipomas are rare, benign tumors, usually found in the adrenal gland. They are composed of mature adipocytes and normal hematopoietic tissue. Although the pathogenesis of myelolipomas remains speculative, the most widely accepted theory is the existence of metaplasia of reticuloendothelial cells of blood capillaries in the adrenal glands, in response to stimuli, such as necrosis, infection, stress or long-term ACTH stimulation. Adrenal myelolipoma in association with Cushing’s syndrome, Conn’s syndrome, and congenital adrenal hyperplasia have been reported.

Abstract #107

PHEOCHROMOCYTOMA MASQUERADING AS AN ADRENAL INCIDENTALOMA

Jason Glenn Daily, MD, Vinh Mai, DO, Patrick Clyde, MD, FACP, FACE, Mohamed Shakir, MD, MACP, MACE, FRCP, FACN

Objective: To describe a case of a patient with an apparent adrenal incidentaloma with normal initial biochemical evaluation, who was confirmed to have pheochromocytoma 7 years later.

Case Presentation: A 60 year-old man with Hashimoto’s thyroiditis was referred to our endocrine clinic for evaluation of a 3-cm left adrenal mass which was discovered on a CT of the abdomen 7 years ago. Previous evaluation of this mass was consistent with an adrenal incidentaloma including normal urinary metanephrines and catecholamines. He denied a history
of hypertension, fluctuation in body weight or paroxysms of palpitation, headache, pallor or sweating. Exam was notable for normal blood pressure and heart rate without clinical evidence of hypercortisolism. A CT of the adrenal glands was repeated revealing a stable 3-cm left adrenal mass with 36 Hounsfield units on precontrast images. The MRI showed the mass to be isointense on T2-weighted images with central region of T2 hyperintensity consistent with necrosis. His total plasma and urinary metanephrines were elevated, 698 (<205 pg/mL) and 1366 (224-832 mcg/24h) respectively. Repeated levels were persistently elevated. Other biochemical evaluation was normal including chromogranin A. An MIBG scan localized a focal abnormal radiotracer accumulation in the left adrenal gland correlating with findings on CT and MRI. The patient underwent laparoscopic left adrenalectomy without complications, and pathology confirmed a pheochromocytoma. His plasma and urine metanephrines completely normalized after surgery.

Discussion: The incidence of incidentally found adrenal masses has been reported to be 4% which increases with increasing age. All adrenal incidentalomas should undergo biochemical evaluation. The incidence of pheochromocytoma is about 4-7% of all adrenal incidentalomas with up to 40% of patients having no signs and symptoms to suggest such a diagnosis. These patients are often referred as subclinical pheochromocytoma. The development of hormonal oversecretion in adrenal incidentaloma in long term follow-up is rare. In a prospective study, only one patient out of 151 was noted to have a pheochromocytoma on repeat biochemical testing. Complete resection of the mass is the standard treatment after proper preoperative management. This case illustrates the importance of increased vigilance in monitoring patients with adrenal incidentalomas.

Conclusion: It is strongly recommended that yearly biochemical evaluation be performed in these patients with appropriate imaging studies to follow for localization purposes.

Abstract #108

SPONTANEOUS ADRENAL HEMORRHAGE WITH ASSOCIATED MASSES: ETIOLOGY & MANAGEMENT

Jennifer Lynn Marti, MD, John Millet, BA,
Julie Ann Sosa, MD, Tobias Carling, MD, PhD,
Robert Udelsman, MD

Objective: Spontaneous adrenal hemorrhage with an associated mass is a rare occurrence. Treatment strategies are not standardized, and data on the etiology and optimal management of these patients has been limited to several case reports. Current treatment modalities range from blood transfusion and supportive management alone, to embolization or immediate operative extirpation. Our objective was to use a case series of 6 patients from a single institution and a review of the literature to make recommendations on the management of patients with hemorrhagic adrenal neoplasms.

Case Presentation: Six patients (ages 31-70 years, 3 men and 3 women) presented between 2002-2010 with spontaneous adrenal hemorrhage that appeared to be associated with a neoplasm. Four presented with acute flank pain, one presented with septic shock from a hand abscess, and one mass was incidentally noted on imaging. In all patients, imaging revealed hemorrhagic adrenal masses with tumor sizes ranging from 4-10 cm. Biochemical testing (cortisol, ACTH, catecholamines, aldosterone, and DHEA) was indicative of hormonally active tumors in two cases, which proved to be pheochromocytomas. A third patient underwent surgery, for what proved to be an adrenocortical carcinoma. One patient was found to have an adrenal metastasis from a primary lung adenocarcinoma with additional distant metastases and did not undergo adrenalectomy. One patient with active bleeding requiring extensive blood transfusions underwent urgent endovascular embolization and awaits definitive surgery pending interval imaging. One patient had resolution of the adrenal mass on follow-up imaging; in retrospect, this pseudoneoplasm was an adrenal hematoma.

Discussion: Patients with adrenal neoplasms uncommonly present with hemorrhage. A high level of suspicion for malignant disease or pheochromocytoma should be maintained, as well as for the possibility of hematoma masquerading as a neoplasm. In select cases of acute hemorrhage, endovascular embolization may be a lifesaving temporizing measure. In this current series, only 3 of 6 patients have undergone adrenalectomy.

Conclusion: Because surgery may not be indicated in all patients with hemorrhagic adrenal neoplasms, a cautious approach with complete biochemical and imaging workup is advised prior to operation.

Abstract #109

THE PREVALENCE OF OBESITY AND ITS ASSOCIATIONS AMONG TYPE 2 DM IN NIGERIA

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Objective: Obesity is a chronic metabolic disease with attendant cardiovascular problems and a key feature
of metabolic syndrome. Obesity and diabetes is increasing worldwide. There is therefore, the need to estimate the prevalence of obesity and its associations among type 2 DM in Nigeria.

Methods: In this cross-sectional study, 200 DM subjects were randomly selected in LASUTH. Their clinical characteristics and the occurrence of cardiovascular events (CV) were documented through interviewer-administered questionnaires. Fasting blood samples were collected for biochemical analysis and urine samples for persistent albuminuria. ECG was carried out. Test Statistics used were t-test, χ2. A p value of <0.05 is significant.

Discussion: The prevalence of obesity in type 2 DM (BMI ≥ 30kg/m²) was 27%. 71% of Female (F) and 37% of Male (M) had waist circumference >88cm and >102cm respectively by risk stratification. The mean age of the study group 56.7 ± 11.1yrs, F and M are comparable (F=56.5 ± 10.8yrs vs 56.9 ± 12.2yrs, p=1.0) with their mean FBS = 158.4 ± 73.24mg/dl. The mean duration of DM is 7.7 ± 5.3yrs. The frequency of abnormality in their fasting lipid fractions were: Elevated levels of Total-C 40%, LDL-C 70%, TG 14% and reduced HDL-C 63%. The prevalence of hypertension (HT) and microalbuminuria was significantly high in obese DM compared with non-obese DM (72% vs 28%, P=0.001 and 77.5%vs22.5%, P=0.001). Symptomatically, 76% had history of intermittent claudication, 72% had ECG abnormalities and 58% had clinical evidence of non-fatal cardiovascular event (stroke).

Conclusion: Obesity in type 2 DM Nigerians has significant association with hypertension, dyslipidaemia, microalbuminuria, and high rate of cardiovascular events. Improved measures to reduce the burden of cardiovascular morbidity and mortality are advocated in this group of patients.

Abstract #110

PHEOCHROMOCYTOMA: A CHALLENGING DIAGNOSIS

Simona Ioja, MD, Ioana Fat, MD, Ben Tsao, MD, Debra Howard Schusheim, MD, Nancy J. Rennert, MD, FACE, FACP

Objective: To report a case of a histologically confirmed pheochromocytoma (Pheo) with inconsistent biochemical and atypical radiologic findings.

Case Presentation: A 67 year-old female with hypertension presented with severe episodes of palpitations, anxiety, diaphoresis and tachyarrhythmia. Blood pressure (BP) ranged 120/60 to 140/80mmHg during the symptomatic episodes. An incidental left adrenal mass was noted on CT scan, which measured 4x3.5x3.8 cm, was 8 Hounsfield units and was not hypervascular in enhancement. Biochemical evaluation: nl.24-hour-urinary free cortisol and PRA: PAC. Plasma: metanephrine <25 pg/ml (nl<57), normetanephrine 46pg/ml (nl<148), chromogranin A 30 ng/ml (nl<36.4), dopamine <10 (nl); 24 hour-urinary metanephrines highly elevated: metanephrine 1773mcg/24h(nl<140), total metanephrines 2063mcg/24h (nl<475), normetanephrine 290mcg/24h(nl<310). Lab work-up was repeated with similar results. MRI: intermediate-T1 and heterogeneous diminished T2-weighted signal, with signal drop-off and mild non-vascular enhancement. MIBG: increased uptake in the left adrenal only. Laparoscopic adrenalectomy was performed with removal of a partially cystic, well delineated mass. Pathology was consistent with Pheo. The patient had resolution of symptoms and normal urinary metanephrines post-op.

Discussion: Pheo is a rare tumor arising from catecholamine-producing cells in the adrenal medulla. Accurate diagnosis is crucial; however the evaluation may be inconsistent and atypical as in our case. There is controversy concerning the single best initial test. Some guidelines (ex NIH), suggest that plasma fractionated metanephrines should be done first, especially when the pretest probability is high and then, if positive, followed by urinary testing (higher specificity). AACE guidelines (2009) recommend either plasma or urinary testing, with no preference stated. In our case, plasma tests were negative and urinary tests positive; therefore diagnosis would have been missed by plasma tests alone. Additionally, the CT and MRI findings were atypical for pheo and very typical for adenoma.

Conclusion: This case illustrates potential pitfalls in the diagnosis of pheo and suggests that care must be taken when excluding or confirming this disorder.

Abstract #111

DULOXETINE INDUCED FALSE POSITIVE TESTING FOR PHEOCHROMOCYTOMA

Venkata G. Budharaju, MD, Joseph Dillon, MD, Amal Shibli-Rahhal, MD

Objective: To present a case of false positive testing for pheochromocytoma due to duloxetine, a serotonin-norepinephrine reuptake inhibitor.

Case Presentation: A 63 year-old obese female presented with uncontrolled hypertension and a left adrenal mass. The hypertension was diagnosed 10 years ago but became difficult to control over the past year, despite treatment with metoprolol, furosemide, olmesartan, hydrochlorothiazide, terazosin, and moexipril. In the last year, she has had intermittent drenching sweats
only involving the scalp with headaches and intermittent postural dizziness. She has history of a left adrenal mass, incidentally found on computed tomography (CT) imaging in 2005. Initially the mass measured 1.9 cm in largest diameter, but has gradually increased in size over the last 5 years, and on her most recent CT done in September 2010, it was 3.0 x 3.4 cm in size. Precontrast CT density was 10 Hounsfield units (HU) and there was a 45% contrast washout on delayed images (54 HU to 34 HU). Her past medical history was significant for depression and obstructive sleep apnea treated with continuous positive airway pressure (CPAP); and in addition to the antihypertensive medications, she was taking allopurinol, aspirin, clopidogrel, duloxetine, rabeprazole, and simvastatin. On physical examination her supine blood pressure was 176/82 with no postural drop and her heart rate was 66. She weighed 254 lb and her BMI was 33. She had no cushingoid features, and the rest of her exam was unremarkable. Her plasma renin activity was less than 0.6 (ng/ml/hr) and her plasma aldosterone was 11 ng/dL. The plasma aldosterone decreased to 4.2 ng/dL after an intravenous normal saline infusion. Her plasma potassium was 3.8 (3.5-5.0). She had a creatinine of 0.8 mg/dL (0.7-1.4 mg/dL) and an estimated GFR (by MDRD study equation) of greater than 60. Her serum calcium was 9.8 mg/dL (8.5-10.5) and TSH was 1.56 uIU/ML (0.27-4.20). Her 24-hour urinary free cortisol was 6 mcg/24h (0-50), 24-hour urinary epinephrine was 7 mcg/24 h (0-32), dopamine was 299 mcg/24 h (65-610), and fractionated normetanephrines were 125 mcg/24 h (35-460). However, her 24 hr urinary norepinephrine (NE) was 204 mcg/24 h (0-140) and fractionated normetanephrine was 1404 mcg/24 h (110-1150). Plasma free metanephrines were 47 (0-62) while plasma normetanephrines were 495 (0-145). Duloxetine was held for 8 weeks and repeat plasma free metanephrines became normal at 0.77 nmol/L (less than 0.90 nmol/L). The episodes of sweating, headaches, hypertension and dizziness improved and her mood remained stable. She was referred for surgical evaluation in view of the increasing size of the adrenal mass and is scheduled to undergo a left adrenalectomy later this year.

Discussion: When testing for pheochromocytoma, it is not uncommon to find mildly to moderately elevated levels of catecholamines and/or catecholamine metabolites. In these situations, it is important to consider possible causes of false-positive results, such as accompanying medical conditions and medications prior to performing additional testing. In our patient, the mild and isolated elevation of NE and its metabolite normetanephrine led us to consider potential interferences, and since duloxetine decreases NE reuptake by neuronal cell membrane transporters we elected to repeat the tests after stopping it. Interestingly, duloxetine has been reported to cause symptoms similar to those seen with pheochromocytoma, including headache, dizziness, anxiety, sweating, palpitations and worsening hypertension, possibly as a result of the NE elevation. In our patient, these symptoms improved after discontinuation of duloxetine.

Conclusion: While the older NE reuptake inhibitors such as the tricyclic antidepressants are well known to cause elevations of norepinephrine and its metabolites, it is important to realize that the newer class of serotonin-NE reuptake inhibitors, that duloxetine belongs to, can lead to similar false positive testing for pheochromocytoma. This is particularly important given the widespread use of these medications for treatment of depression as well as other common conditions such as fibromyalgia and neuropathic pain.

Abstract #112

**PHEOCHROMOCYTOMA DIAGNOSED 1.5 YEARS FOLLOWING AN ACUTE CORONARY EVENT**

Celeste Cheryll Lopez Quianzon, MD, Pamela R. Schroeder, MD, PhD

**Objective:** To report a case of pheochromocytoma diagnosed 1.5 years following an acute coronary event.

**Case Presentation:** A 66 year-old female with a two-year history of hypertension, acute coronary syndrome 1.5 years ago, and impaired fasting glucose was experiencing episodes of pounding headaches, palpitations, diaphoresis, pallor, nausea and anxiety for the past two years that were associated with severe elevations in her blood pressure (~200/130). Her symptoms were attributed to panic disorder. One and a half years ago she was diagnosed with coronary vasospasm, minimal coronary atherosclerosis, and possible Takotsubo syndrome when she developed chest pain, headache, palpitations, perspirations and sensation of near syncope along with elevation in her blood pressure (SBP=190) while visiting her hospitalized father-in-law. She had a mild troponin I elevation (peak 0.56 ng/mL), and an inferolateral T-wave inversion on ECG. She had a normal 2D echocardiogram and non-critical coronary artery obstruction without major wall motion abnormality by cardiac catheterization both performed 3 days later. She continued to experience these symptoms intermittently and did not notice worsening of symptoms over the years. Pheochromocytoma was confirmed by marked elevations in her urinary metanephrines, normetanephrine, epinephrine and norepinephrine and plasma metanephrines. A CT abdomen and pelvis revealed a large complex cystic mass measuring 15 x 11 x 14 cm with mass effect in to the right lobe of liver. She underwent right adrenalectomy without complication following appropriate blockade with phenoxybenzamine and

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addition of propranolol and amlodipine. Post-operatively, blood pressure medications were discontinued. Pathology revealed an 18 cm pheochromocytoma with extensive associated necrosis and hemorrhage without definite vascular invasion. She has not had an attack or severe elevations in her blood pressure and a repeat plasma free metanephrines and normetanephrines were undetectable.

Discussion: Coronary artery disease leading to acute coronary syndrome is common in hypertensive, middle-aged or older individuals. Anxiety and panic symptoms are also highly prevalent conditions. These common conditions confound a medical provider’s ability to recognize pheochromocytoma.

Conclusion: Pheochromocytoma is a rare neuroendocrine tumor, which may produce significant cardiovascular morbidity. A high degree of clinical suspicion may reduce delays in diagnosis.

Abstract #113

A RARE FORM OF SYNDROMIC PHAEOCHROMOCYTOMA

Adedayo David Adegite, MBBS, Ian Ross, MD
Dinky Levitt, MD

Objective: To describe this rare form of syndromic phaeochromocytoma.

Case Presentation: A 50 year old gentleman with a background history of neurofibromatosis-1(NF-1) from childhood presented with recurrent early morning headache, palpitations and excessive sweating. General examination revealed multiple neurofibromas, cafe au lait spots, axillary freckling, mild scoliosis and left hemi-hypertrophy of the tongue. His blood pressure was 130/90mmHg, having been on Norvasc 5mg dly and Cardural XL 4mg dly. His four urine samples for total metanephrine/creatinine ratio were 2.8, 1.8, 2.0, and 1.9(0.035-0.45), and chromogranin A was 46.7Iu/L(0.0-23.0Iu/L). CT of the abdomen revealed an homogeneous, well circumscribed left adrenal mass measuring 40mm in diameter. Post contrast measurement was 45 HU in early arterial and 70 HU in late arterial/portal venous phase. Blood tests to exclude multiple endocrine neoplasia were unremarkable [PTH 4.4pmol/L (1.6-6.9pmol/L). Corrected calcium 2.42 mmol/L (2.05-2.56mmol/L), inorganic phosphate 1.09mmol/L (0.80-1.40mmol/L) and TSH was 1.37mIU/L (0.27-4.20)] all within normal reference range. Laparoscopic surgical excision revealed a soft ruptured left adrenal mass weighing 45g and measuring 55 x 40 x 40mm and its histology showed a tumor that is restricted to the medulla and composed of nests of cells with abundant amphophilic cytoplasm and variable nuclei. No tumor necrosis, vascular invasion or capsular penetration. Six months postoperatively his symptoms had disappeared. BP was 120/80 off antihypertensive and three 24hr fractionated urine normetanephrine/creatinine ratio were 142, 144, 146 (26-200) and metanephrine/creatinine were 49, 49 and 44 (5-90) respectively.

Discussion: Up to 15-20% of patients with catecholamine secreting tumors have germ line mutations in genes associated with genetic disease. NF-1 occurs in 1 out of 3,000 individuals but only 2% of these would develop catecholamine secreting tumors, our patient represent one of these group. Phaeochromocytoma associated with NF-1 is often a solitary and benign adrenal but may very rarely occur as a bilateral phaeochromocytoma.

Conclusion: We have described a rare and subtle form of phaeochromocytoma occurring in a patient with NF-1. Surveillance for development of the condition is very necessary as some of these patients may be asymptomatic or rather have mild symptoms. Diagnosis and surgical excision of the adrenal mass often result in a cure.

Abstract #114

ADRENOCORTICAL FUNCTION IN NIGERIAN PERSONS WITH HUMAN IMMUNODEFICIENCY VIRUS (HIV) INFECTION

Ifeayo Adeola Odentiy, MBBS, Olufemi Fasanmade, MBBS, FWACP, Micheal Ajala, FMCP, Augustine Efedaye Ohwovoriole, MD, MSc

Background: Human Immunodeficiency Virus (HIV) infection is a recognized cause of impaired adrenocortical function. No report on the relationship of HIV infection to adrenocortical function in Nigerians has been published. Subclinical adrenocortical failure in HIV infection should be considered as responsible for unexpected sudden death in this category of patients.

Objective: This study sets out to determine the prevalence of subclinical adrenocortical failure in persons with HIV infection by determining the response to low-dose (1μg) ACTH stimulation.

Methods: Forty-three newly diagnosed and treatment naive persons with HIV (23 males and 20 females) completed the study. One μg of Synacthen was given intravenously after basal blood had been collected for basal cortisol levels. Blood tests to exclude multiple endocrine neoplasia were unremarkable [PTH 4.4pmol/L (1.6-6.9pmol/L). Corrected calcium 2.42 mmol/L (2.05-2.56mmol/L), inorganic phosphate 1.09mmol/L (0.80-1.40mmol/L) and TSH was 1.37mIU/L (0.27-4.20)] all within normal reference range. Laparoscopic surgical excision revealed a soft ruptured left adrenal mass weighing 45g and measuring 55 x 40 x 40mm and its histology showed a tumor that is restricted to the medulla and composed of nests of cells with abundant amphophilic cytoplasm and variable nuclei. No tumor necrosis, vascular invasion or capsular penetration. Six months postoperatively his symptoms had disappeared. BP was 120/80 off antihypertensive and three 24hr fractionated urine normetanephrine/creatinine ratio were 142, 144, 146 (26-200) and metanephrine/creatinine were 49, 49 and 44 (5-90) respectively.

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Conclusion: We have described a rare and subtle form of phaeochromocytoma occurring in a patient with NF-1. Surveillance for development of the condition is very necessary as some of these patients may be asymptomatic or rather have mild symptoms. Diagnosis and surgical excision of the adrenal mass often result in a cure.

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Objective: This study sets out to determine the prevalence of subclinical adrenocortical failure in persons with HIV infection by determining the response to low-dose (1μg) ACTH stimulation.

Methods: Forty-three newly diagnosed and treatment naive persons with HIV (23 males and 20 females) completed the study. One μg of Synacthen was given intravenously after basal blood had been collected for basal cortisol levels. Blood was again collected 30 min after the injection. Cortisol was assayed using an ELISA system. Adrenocortical insufficiency was defined as patients with normal basal cortisol levels but attenuated peak stimulated and increment in cortisol levels and without classical signs of Addison’s disease. Results are presented as average values (mean (SD)) and as percentages. Significance of differences is set at p≤ 0.05.
**Results:** The mean basal cortisol (0-minute) was 154.9±35.5 nmol/L while the 30-minute post ACTH test cortisol level was 354.8±19.9 nmol/L in HIV group. The basal cortisol level, 30-minute post ACTH test cortisol level and increment were significantly lower in persons with HIV than healthy subjects.

**Discussion:** The abnormal response may be attributable to minimal degree of adrenal damage recognized in cases from autopsy studies. The amount of adrenal gland tissue remaining functional, however, is apparently enough to provide a satisfactory glucocorticoid production in the basal state. None of the patients with HIV had hyperpigmentation. There was no postural drop in blood pressure measurement in those with impaired adrenal response to ACTH test. None of the persons with HIV infection had hyperkalaemia seen in adrenal insufficiency.

**Conclusion:** Adrenocortical insufficiency, at the subclinical level, is common in persons with HIV infection, occurring in about 35% of patients studied. Clinically evident adrenocortical insufficiency is uncommon in persons with HIV. Adrenocortical reserve is impaired in persons with HIV evident by subnormal response to ACTH test. Basal cortisol levels should not be used to elicit adrenocortical insufficiency; rather stimulation tests should be used to exclude or confirm suspected adrenocortical insufficiency in persons with HIV.

**Abstract #115**

**A CASE REPORT OF ADALIMUMAB-ASSOCIATED ADRENAL INSUFFICIENCY**

Saleh A. Aldasouqi, MD, FACE, ECNU, Deepthi Rao, MD, Ved Gossain, MD, FACE, FACP, Srujan Ameda, MD, Nazish Ismail, MD, Lily Kristine Sunio, MD

**Objective:** Introduced into the market in 2002, Adalimumab (brand name, Humira®, Abbott), is a tumor necrosis factor (TNF)-alpha inhibitor used in the treatment of chronic autoimmune disorders, such as rheumatoid arthritis (RA). To our knowledge, no prior reports of adalimumab-induced adrenal insufficiency have been published. We report a case of adrenal insufficiency (AI) in a patient with RA treated with adalimumab, which resolved after stopping adalimumab, and review relevant literature, to raise awareness about this possible medication adverse effect (AE).

**Case Presentation:** A 49 year old female was evaluated for an incidental pituitary tumor. Her main symptom was fatigue. Other medical problems included hypothyroidism and RA. Medications included adalimumab, teriparatide, levothyroxine and estrogen. She reported no significant exogenous steroid medications. Work up revealed very low levels of AM serum cortisol, 1.4 mcg/dL (4.3-22.4) and 24-hour urinary free cortisol, < 1.0 mcg/24 hours (3.5-45), and a low concomitant AM serum ACTH, 7.2 pg/dL (10-60). Her thyroid function tests were normal on levothyroxine, and her other pituitary axes were appropriate. Adalimumab was discontinued, and she was started on oral hydrocortisone. Her fatigue improved markedly. She stopped hydrocortisone 3 weeks later. Repeated serum cortisol and ACTH became normal, and an ACTH stimulation test was normal. She remained well upon follow up. Subsequently, her rheumatologist adjusted her RA treatment, off adalimumab. The case was reported to the FDA and the manufacturer, as a possible newly recognized AE to adalimumab.

**Discussion:** Adalimumab is an FDA-approved TNF-alpha blocker for the treatment of RA and other autoimmune diseases. Multiple AE’s have been associated with this medication, including multiple autoimmune modulations, infections and malignancy. An extensive literature search revealed no published cases of adalimumab-induced or adalimumab-associated AI. Our case fulfills criteria for a possible medication AE, except for a re-challenge with the medication. However, we are not certain if this association implies causation. Similarly, should a causation exist, we are not certain of the mechanism(s) involved, but we propose an immune modulation mechanism, directed against the hypophyseal or hypothalamic regions, in view of low ACTH (central AI).

**Conclusion:** We propose that our patient had adalimumab-associated AI, but we are not certain of causal association. We recommend that physicians be aware that adalimumab may cause adrenal insufficiency. This adverse effect should be kept in mind in patients on this medication. Further evaluation of this observation is proposed.

**Abstract #116**

**CASE OF DISSEMINATED HISTOPLASMOSIS IN IMMUNOCOMPETENT PATIENT WHO DEVELOPED ADRENAL INSUFFICIENCY WHEN TREATED WITH ITRACONAZOLE**

Kelah Kumar, MD

**Objective:** In this case report we describe disseminated Histoplasmosis in an immunocompetent patient from a non endemic area without lung involvement who developed adrenal insufficiency after treatment with Itraconazole.

**Case Presentation:** We report a case of Disseminated Histoplasmosis with iatrogenic adrenal insufficiency in a 41 y/o male with past medical history of hepatitis C, recently emigrated from Bangladesh with an extensive
travel history to western countries, presented with weight loss, intermittent loose watery stools, generalized weakness and anorexia for 4 months. On P/E the patient was noted to have generalized wasting, dry oral mucosa with a few mucosal papular lesions on the tongue. His labs were notable for hyponatremia: Low Na 126 meq/l (135-145 meq/l), hypoalbuminemia: 1.7g/dl (3.4-5.4 g/dl) and prealbumin: 3.3mg/dl (normal 16-35mg/dl), AST 115 U/l, ALT 53 U/l, GGT 102, Alkaline phos: 489(30-115 U/l) and PT/INR: 12.8/1.15 and HIV negative. Chest x-ray was normal. His stools studies & C.difficile were negative. The Contrast CT scan of chest/abdomen/pelvis obtained to r/o an occult malignancy, revealed bilateral adrenal enlargement. Bacterial and fungal cultures were negative. The serum IgG for Histoplasma was positive. Biopsies of the skin, liver and colon revealed Histoplasma organisms and were consistent with disseminated Histoplasmosis. The patient was started on the intravenous Amphotericin B for two weeks, with improvement in appetite and resolution of diarrhea. The patient was discharged home on Itraconazole 200mg PO daily. Two months after the discharge the patient readmitted from medical clinic on his follow up, with the hyponatremia, hyperkalemia, acidosis, and generalized weakness. ACTH stimulation test revealed cortisol levels: 0.3Ug/dl at baseline & 0.6Ug/dl at 30 minutes, consistent with primary adrenal insufficiency. The patient responded on hydrocortisone and fludrocortisone as per endocrinology recommendations with resolution of weakness, wt gain and normalization of electrolytes.

Discussion: Fungal infections are rare causes of unexplained generalized systemic symptoms and should be suspected even in low risk patient group. Itraconazole can cause adrenal insufficiency by inhibiting CYP3A in less than 2% of patients. This medication adverse effect may be due to subclinical adrenal insufficiency caused by Histoplasma infestation of adrenals with addition of Itraconazole inducing full blown adrenal insufficiency. The presence of bilateral adrenal enlargement raised the possibility of Disseminated Histoplasmosis while biopsies of the skin, colon and liver confirmed this diagnosis.

Conclusion: Patients with disseminated Histoplasmosis, treated with Itraconazole, should be closely monitored for adrenal insufficiency both at the time of diagnosis as well as during follow up since systemic Histoplasmosis can involve adrenal gland in 80-90% of the patients with or without adrenal insufficiency. Treatment of Histoplasma infection with Itraconazole can adversely affect adrenal hormonal synthesis and lead to adrenal insufficiency; however this occurs in minority of cases (2%).
Abstract #118

PROFOUND HYponatraemia; CAUSES, OUTCOME, AND CLINICIANS APPROACH TO MANAGEMENT

Tarik A. Elhadd, MD, FRCP, Supriya Mather, MBBS, Sujoy Ghosh, MRCP, Iqbal A Malik, MD, FRCP, AJ Collier, MD, FRCP, S Ferguson, MD, FRCP, VE MacCaully, MD, FRCP, F Davidson

Objective: Severe hyponatraemia is well documented to be associated with excess morbidity, mortality and longer hospital stay. There is no consensus in the management of severe hyponatraemia and significant disparity exists among clinicians. However, outcome and clinicians approach to more radical cases of severe hyponatraemia has not been explored per se.

Methods: A hospital based retrospective analysis of cases of profound hyponatraemia (serum Na+ <115 mmol/l). Case-notes of 59 patients randomly selected from the computer database covering the period between 1996-2008 were used.

Results: Patients were found to be mainly females (72%), older subjects (mean age, years ± SD) of 72 ± 6 years, who usually presented with acutely (51%), with florid symptoms of hyponatremia (76%). The Clinicians approach to investigations reflected more tendency to assess serum and urine osmolality (78% & 71% respectively), testing for hepatic and thyroid dysfunction (81% & 61%), and for random cortisol testing (32%). However clinicians performed less sophisticated tests for adrenal dysfunction (only 3.4% had ACTH stimulation test ‘short synacthen test’). Further less than 50% of patients had tests for pseudohyponatraemia.

Conclusion: Overall management of cases were conflicting, with mortality of 19% and longer hospital stay of 18 ±19 days. In contrast to findings from previous studies of severe hyponatraemia, the clinicians approach to management of cases of profound hyponatraemia appears to be more proactive.

Abstract #119

MINERALOCORTICOID THERAPY IN ADDISON’S DISEASE-NOT ALWAYS A NECESSITY

Richard W. Pinsker, MD, FACE, Narinder Kukar, MD, Abhay Vakil, MD, Kelly L. Cervellione, MA, MPH, ABD

Objective: To report an unusual case of primary adrenal insufficiency not requiring mineralocorticoid replacement therapy.

Case Presentation: A 36 year-old male with no significant past medical history presented to ER with gradually progressive fatigue, weakness, and increased skin pigmentation on the abdomen over the last 3 weeks. He also reported an unintentional 15 lb weight loss over the last month. On admission he was hypotensive and hyperkalemic. Patient was started on IV dexamethasone and saline with subsequent normalization of blood pressure and potassium. Further evaluation showed ACTH=747 pg/ml; cortisol at 0 min and 60 min after 250 mcg Cosyntropin was < 2.5 and 2.5 mcg/dl respectively. Causes of secondary adrenal insufficiency, including tuberculosis, were ruled out. Patient was diagnosed with autoimmune primary adrenal insufficiency and discharged on oral hydrocortisone 20 mg in AM and 10 mg in PM with fludrocortisone 0.1 mg daily. The patient continued to be normotensive and clinically “euadrenal” on this regimen for more than 6 years. Subsequently he developed hypertension (HTN) and was started on antihypertensive medication. He continued to be hypertensive and developed hypokalemia with increased skin pigmentation. Plasma renin activity (PRA) was low. Skin pigmentation worsened. Nelson’s Syndrome was considered but MRI failed to show any increase in size of the sella. Fludrocortisone was discontinued. He became normotensive with additional BP medication and normokalemic with a rise in PRA.

Discussion: Primary adrenal insufficiency consists of glucocorticoid and mineralocorticoid deficiency. Some Addisonian patients do not require mineralocorticoid therapy. Most of these patients have underlying essential HTN or the mineralocorticoid activity in the glucocorticoid replacement is sufficient. In this case, mineralocorticoid replacement was required for 6 years. Patient had no history of essential HTN before his illness. Initial response to antihypertensives was poor. Low PRA suggested mineralocorticoid excess. The exact cause of apparent mineralocorticoid excess after being stable for 6 years on same dose of hydrocortisone and fludrocortisone is unknown.

Conclusion: Underlying essential HTN or mineralocorticoid excess should be suspected in patients developing HTN who are on mineralocorticoid replacement therapy as part of adrenal replacement. Excess mineralocorticoid activity presents with hypokalemia and low PRA with HTN. Mineralocorticoid dose should be reduced or eliminated to keep PRA at upper limits of normal if no electrolyte imbalance is present.
Abstract #120

ADRENAL CRISIS SECONDARY TO BILATERAL ADRENAL HEMORRHAGE IN A PATIENT WITH BLUNT ABDOMINAL TRAUMA AND ANTIPHOSPHOLIPID ANTIBODY SYNDROME

Anuritha Reddy Marumganti, MD, Sartaj Sandhu, MBBS, Castro Bali, MD, Kinan Dalal, MD, Sandeep Dhindsa, MD

Objective: To report a case of bilateral adrenal hemorrhage after blunt trauma in a patient with antiphospholipid antibody syndrome, causing adrenal insufficiency.

Case Presentation: A 51-year-old Caucasian male with antiphospholipid antibody syndrome on warfarin therapy presented to the emergency department after a motor vehicle accident with left-sided abdominal pain. He had been off warfarin for two weeks prior to the accident for an elective surgical procedure. He was afebrile with pulse rate of 67 beats per minute (bpm) and blood pressure of 158/100 mm Hg. His white cell count, hemoglobin, hematocrit and platelets were 12.6 x 10^9 /L, 15.2 g/dL, 44.4% and 121 x 10^9 /L; sodium was 136 mmol/L and INR 1.2. CT imaging of the abdomen revealed ‘mild inflammation’ adjacent to the left adrenal gland/body of pancreas which was likely post-traumatic. Patient was discharged on analgesics. One week later he presented with complaints of generalized fatigue, and weakness. Vital signs and laboratory values at presentation included pulse rate of 98 bpm, blood pressure of 108/70 mm Hg, with decrease in hemoglobin to 12.4g/dL, hematocrit to 34% and platelets to 52 x 10^9 /L; sodium was 114 mmol/L and a potassium of 3.8 mmol/L. Intravenous contrast-enhanced abdominal CT imaging was repeated and demonstrated high attenuation, non enhancing enlargement of both adrenal glands which measured approximately 6 cm in maximal dimension, consistent with bilateral adrenal hemorrhage. A random cortisol was low at <1 mcg/dL supporting the clinical impression. Adrenal crisis from bilateral adrenal hemorrhage was diagnosed. He was treated acutely with saline infusion and hydrocortisone with clinical improvement, and discharged on maintenance doses of glucocorticoid and mineralocorticoid replacement.

Discussion: Bilateral adrenal hemorrhage has been reported as a complication of sepsis, hypotension, anticoagulant therapy, trauma, hypotension, bleeding disorders and some surgical procedures. Failure to recognize this presentation can lead to misdiagnosis or a significant delay in diagnosis and treatment which can be potentially life threatening.

Conclusion: This case illustrates the need to have a high clinical suspicion for adrenal insufficiency, in patients with antiphospholipid antibody syndrome presenting with abdominal complaints and thrombocytopenia particularly after trauma.

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Abstract #121

THE DIFFERENT FACES OF HYPERALDOSTERONISM

James Young, MD, Reynaldo F. Rosales, MD, Michael L. Villa, MD

Objective: We describe three remarkable patients who were clinical adventures for us and provided several important lessons. This report aimed to present cases of PA presenting with unusual manifestations and to present state-of-the-art diagnostic and therapeutic management.

Case Presentation: Case 1, a 51 year-old male with episodic paralysis. Lower extremity paralysis was noted for three years with cramps and pain, hypokalemia and poorly controlled hypertension. Work-up showed elevated PAC (16.45ng/dL), suppressed PRA (0.01ng/mL/hr), high PAC/PRA ratio, increased of PAC by 52% post-postural aldosterone test and bilateral adrenal gland enlargement with multiple nodules on abdominal MRI. Adrenal venous sampling (AVS) done and the “cortisol-corrected ratio” favors the diagnosis of PA of bilateral adrenal hyperplasia (BAH). Patient was managed with Spironolactone and condition improved. Case 2, a 58 year-old male presenting with poorly controlled hypertension (despite triple anti-hypertensives) with hypokalemia and lower extremity weakness. Work-up showed elevated urine metanephrine, high PAC (35.92ng/dL) and suppressed PRA (<0.1ng/mL/hr) and PAC/PRA ratio of 359.2. Saline loading test failed to suppress PAC. CT scan of the abdomen showed 2x1.8x1.7cm left adrenal nodule and nodular right adrenal gland. AVS done and the “cortisol-corrected ratio” favors lateralization to the left adrenal. He was diagnosed of PA secondary to left adrenal adenoma associated with pheochromocytoma. Patient underwent laparoscopic left adrenalectomy. Histology identified adrenal cortical adenoma. Condition resolved post operatively. Case 3, a 39 year-old woman with symptomatic hypocalcemia presenting with hypokalemia and hypertension. Work-up showed low serum calcium, elevated TTKG and 24 hour urine calcium. PAC was elevated (20.1ng/mL) and PRA was suppressed (<0.1ng/mL/hr) with PAC/PRA of 201.2. Saline loading test failed to suppress the PAC. A 2.27x1.62cm nodule noted at right adrenal gland on abdominal CT. Spironolactone was started and patient underwent successful laparoscopic right adrenalectomy. Histologically, the tumor was identified as adenocortical adenoma. Condition improved post-adrenalectomy.

Conclusion: PA is the most common cause of secondary hypertension. PA is confirmed by lack of aldosterone suppressibility with sodium loading. Subtype evaluation is achieved with high resolution CT scanning and AVS. In PA patients with unilateral aldosterone...
hypersecretion, laparoscopic adrenalectomy is the treatment of choice. Patients with BAH are best managed with a mineralocorticoid antagonist.

Abstract #122

HORMONAL FEATURES OF INCIDENTALOMAS

Zulfiya Shafigullina, MD, Ludmila Velikanova, PhD, Ann Vydrych, PhD

Objective: The aim of this study was to investigate the clinical and hormonal features of patients with adrenal incidentalomas (AI).

Methods: 97 patients (80 women and 17 men), age 25-76 years (median 54.7 ±1.3) with adrenal incidentalomas underwent hormonal evaluation for: circadian rhythm of plasma cortisol and ACTH secretion, low-dose (2mg) dexamethasone suppression test, aldosterone level and PRA. Corticosteroids were assessed by means of high-performance liquid chromatography including measurement of blood levels of cortisol (F), cortisone (E), corticosterone (B), 11-deoxycorticosterone (DOC), 11-deoxycortisol (S) and urinary excretion levels of free cortisol and free cortisone. 52 patients underwent operation and surgical samples studied for histology.

Results: In 52 AI patients with adrenalectomy the histological findings were as follows: adenomas (n=36), adrenocarcinomas (n=8), cysts (n=8). In these patients arterial hypertension was revealed in 16, obesity in 13 and 8 had type 2 diabetes (T2DM). Hypersecretion of hormones was revealed in 52% of the patients with adenomas and 25% with adrenocarcinomas, particularly with significant elevation of 11-deoxycortisol and 11-deoxycorticosterone levels. Subclinical Cushing syndrome, defined as abnormal response to at least 2 standard tests of the hypothalamic-pituitary-adrenal function was detected in 8 patients with adenomas. Half of these patients were significantly obese (mean BMI 35.5 Kg/m²), 7 (87.5%) had hypertension and 3 (37.5%) T2DM. These patients were found to have low baseline ACTH, lack of cortisol suppression after 2mg dexametasone, disturbed circadian cortisol rhythm, increased urinary excretion of free cortisol, 3 patients had elevated blood levels of DOC and 4 with elevated S. Marginal plasma aldosterone elevation with suppressed orthostatic PRA and significantly increased levels of 11-deoxycorticosterone was revealed in 4 patients with adenomas.

Conclusion: One third of the operated patients with AI had increased steroidogenesis which was more frequently observed in patients with adrenal adenomas compared with adrenocarcinomas and cysts. Apparent silent hypersecretion of the adrenal hormones were not completely asymptomatic and was highly associated with hypertension, T2DM and obesity the main component of the metabolic syndrome.

Abstract #123

ANTENATAL THYROID FUNCTION ASSOCIATES WITH MOOD DISTURBANCES AFTER DELIVERY

Eleni Armeni, MD, Demetrios Rizos, PhD, Paraskevi Pliatsika, MD, Angeliki Leonardou, MD, John Argeitis, MD, Georgia Spentzou, MD, Dimitrios Hasiakos, MD, Ioannis Zervas, MD, Constantinos Papadias, MD, Irene Lambrinoudaki, MD

Objective: Thyroid function is known to be affected during pregnancy. Both hyperthyroidism and hypothyroidism, even if subclinical, may lead to depressive symptomatology. On the other hand, mood disturbances are relatively common following childbirth, with maternat blues and postpartum depression occurring in up to 44.5% and 19.8% of cases, respectively. The present study aimed to investigate whether peripartum thyroid function within the normal range affects the incidence of postpartum mood disturbances.

Methods: This cross-sectional study included 57 adult, married women with a gestational age of 35-38 weeks. The subjects were free of obstetrical complications, acute or chronic psychiatric disorders, eating disorders or thyroid disease. The patients were evaluated for postpartum mood swings, using the Edinburgh Postnatal Depression Scale and the Maternity Blues Questionnaire, on admission for delivery and on the first and sixth week postpartum. We measured serum concentrations of thyroid hormones (Free T4, Free T3 and TSH) as well as Thyroglobulin and Thyroid peroxidase antibodies, before delivery and daily until the fourth postpartum day. The association between hormone and antibody levels, and scores in the two scales was examined in order to evaluate postpartum mood disturbances.

Results: Women with lower FT3 and FT4 levels belonged to the high scoring group (high scoring group: FT3=1.22pg/ml, FT4=0.66ng/dl; low scoring group: FT3 =1.64pg/ml, FT4 =0.73ng/dl). Antenatal serum FT3 and FT4 correlated negatively with blues scores (blues on day 4: with FT3, r = -0.44, p≤0.01; with FT4 r = -0.36, p≤0.01) and with the mean blues score (with FT3, rho = -0.29, p-value < 0.05; with FT4: rho= -0.3, p-value < 0.05). Prepartum serum FT3 levels showed a negative independent correlation with postpartum blues scores in the first postpartum days. No association was found between thyroid antibody levels and mood scores.

Discussion: Even in this small sample, our findings support the presence of an association between the occurrence of postpartum mood disorders and antenatal thyroid function. Within normal limits, lower levels
of serum FT3 and FT4 are associated with increased incidence of mood disturbances in the first postpartum week. No correlation has been found between thyroid measures postpartum or the presence of thyroid antibodies and the occurrence of the blues.

Conclusion: If these findings are confirmed in larger prospective studies, screening of thyroid function during a routine antenatal visit might prove useful in assessing the risk for postpartum depression.

Abstract #124

A RARE NON ISCHEMIC CARDIOMYOPATHY CAUSED BY ACTH-INDEPENDENT MACRONODULAR ADRENAL HYPERPLASIA

Xiaoyan Song, MD, Qinghua Zhu, MD,
Saka Kazeem, MD, Ronak Chaudhari, MD

Objective: This report describes a rare case of ACTH-independent macronodular adrenal hyperplasia (AIMAH).

Case Presentation: A 25 year old female has been suffering from weight gain, amenorrhea, generalized weakness, purplish abdominal and arm marks and swelling of the legs bilaterally for 2-3 years. She has also been diagnosed with high blood pressure for 3 months. Physical examination revealed classic Cushingoid features. Laboratory tests showed 24 hour urine free cortisol is elevated. Adrenal vein sampling showed the increased cortical concentration in both adrenal veins. Patient developed the non ischemic cardiomyopathy showing the severe decline in the ejection fraction (EF: 25-30%) and pulmonary edema while waiting for the adrenalectomy. However, after patient received unilateral adrenalectomy, the non ischemic cardiomyopathy was resolved (EF: 55%). Patient is currently on medical treatment with Ketoconazole 200mg daily with the relief of the symptoms. (Laboratory: 24 hour urine free cortisol: 243.9, Post 2 mg dexamethasone suppression test serum cortisol level: 37.4, Serum ACTH<5, Left adrenal vein Aldosteron: 34 ng/dl, right adrenal vein aldosteron 16 ng/dl, FSH <0.2 mIU/ml, LH <0.2 mIU/ml, TSH 0.87, Free T4 1.1, T3, total 120 Cholesterol total 258, HDL 58, LDL cholesterol 160 Triglycerides 199).

Discussion: AIMAH appears to have a bimodal age distribution. Most patients present in the 5th and 6th decade, with a subset of patients presenting in the first year of life. However, in the majority of cases AIMAH appears to be sporadic. In our case, patient presents in her 20’s with overt Cushing’s syndrome, with complication of hypertension and secondary DM, dyslipidemia and congestive heart failure complicated with acute pulmonary edema. Serum and urine cortisol level significantly elevated and FSH and LH were suppressed by endogenous adrenal cortex hormone secretion. The bilateral adrenalectomy by overt or laparoscopic approach has been the most useful treatment in patients with AIMAH and hormonal hypersecretion. However, in patients with moderately increased hormonal production, unilateral adrenalectomy has been proposed as a safe and effective alternative combined with medical treatment.

Conclusion: Early detection of AIMAH and application of the prompt medical and surgical treatment can avoid the severe complications of AIMAH.

Abstract #125

PARAGANGLIOMA OF THE ORGAN OF ZUCKERKANDL

Shamsa Ali, MBBS, Mohamed Abdel Khalek, MD,
Nicholas Avitabile, MD, Ajaz Banka, MD,
Tina Thethi, MD, Emad Kandil, MD

Case Presentation: A 21-yr old man with history of resistant hypertension, episodic diaphoresis and headaches. ROS and physical examination otherwise was unremarkable. Plasma electrolytes and urinalyses were normal. Normal plasma aldosterone (5.9 ng/dL, normal below 21 ng/dL) and renin levels (2.0 ng/mL, normal 1.9-3.7 ng/mL). Free plasma metanephrines were elevated (2.92 nmol/L, normal below 0.89 nmol/L). 24-hour urine catecholamines showed elevated norepinephrine (501 mcg/24hr, normal 15-80 mcg/24hr), dopamine (327mcg/24hr, normal 65-400mcg/24hr) and epinephrine (12mcg, normal below 20.0mcg). Plasma catecholamine levels showed dopamine (37 pg/mL, normal below 142 pg/mL) and epinephrine (43 pg/mL, normal below 99 pg/mL) with elevated norepinephrine (2560 pg/mL, normal below 142 pg/mL). MIBG scan showed an increased uptake in a small region adjacent to the junction of the abdominal aorta and the inferior mesenteric artery. CT scan showed a 2.5cm mass at the junction of the inferior mesenteric vessels and the aorta, same region indicated by the MIBG scan. Preoperative diagnosis of paraganglioma was made and an exploratory laparotomy and surgical resection of the paraganglioma was performed. The paraganglioma was dissected off the inferior mesenteric artery and aorta. Pathology revealed a 2.0 x 2.0 x 1.8 cm well circumscribed, tan nodule. On microscopic evaluation, tumor cells have an organoid pattern of growth with prominent vascular network. At the periphery, a well-defined capsule is present. Neoplastic chief cells arranged in a nested/organoid/zellballen pattern along intervening fibrovascular septae. No significant mitotic figures, areas of necrosis, or vascular invasion are identified. Immunohistochemical staining showed tumor cells to be positive for neuron specific enolase (NSE), synaptophysin and chromogranin. S100 is positive in sustentacular cells. Proliferation index assessed by Ki-67 stain is low and is approximately 1.5
Discussion: The vast majority of pheochromocytomas are located within the adrenal gland, but approximately 10-15% is extra-adrenal paragangliomas. Paragangliomas almost exclusively occur in the abdomen (98%), with the Organ of Zuckerkandl at the aortic bifurcation being the predominant location. Functional secretory tumors make up 77% of paragangliomas of the Organ of Zuckerkandl, producing the aforementioned symptoms of excess catecholamines. Paragangliomas are of particular importance due to their rates of malignancy and recurrence.

Abstract #126

ACTH-INDEPENDENT MACRONODULAR ADRENAL HYPERPLASIA: AN UNUSUAL PRESENTATION OF CUSHING’S SYNDROME

Deepashree Gupta, MD, Guido Lastra Gonzalez, MD

Objective: To describe a case of ACTH-independent macronodular adrenal hyperplasia (AIMAH), a rare cause of Cushing’s syndrome.

Case Presentation: The patient is a 56 year-old caucasian female who was referred to our clinic for further evaluation of possible Cushing’s syndrome. She had had symptoms of diaphoresis and dyspnea for almost 3 years and an imaging study for the workup of the same had revealed bilateral adrenal tumors. Biopsy showed benign tumor but as it was rapidly growing, she was offered adrenalectomy; she opted out of surgery at the time. Over the past 5-6 months, she developed uncontrolled hypertension, skin atrophy, easy bruising, hirsuitism, central obesity, diaphoresis, irritability and weakness especially of her proximal muscles so much so that she was unable to get up from a sitting position without support. Blood pressure at presentation was 166/78. Workup for Cushing’s syndrome revealed an 8 AM cortisol of 21.79 mcg/dl after 1 mg and 20.51 mcg/dl after 8 mg overnight dexamethasone suppression (normal <1.8 mcg/dl), 24 hour urine free cortisol of 29.1 mcg/day (normal <=45 mcg/d) and 11 PM salivary cortisol level of 0.331 mcg/dl (normal <0.01 - 0.090 mcg/dl). ACTH levels were checked on three separate occasions and were less than 2 pg/ml (normal 6-58). DHEA sulfate was 247 mcg/dl (normal 26-200). Urine metanephrines were within normal range. CT abdomen was ordered and showed markedly enlarged right and left adrenal glands measuring approximately 3.4 x 6.1 and 3.9 x 5.1 cm respectively. MRI brain did not show a pituitary adenoma.

Discussion: AIMAH is an infrequent cause of endogenous Cushing’s syndrome, representing less than 1% of these cases; however, as 10% of incidentally found adrenal lesions are bilateral, AIMAH with subclinical cortisol and sometimes mineralocorticoid and sex steroid secretion is being increasingly recognized. The aberrant adrenal expression and function of one or several G-protein-coupled receptors has been implicated in cell proliferation and abnormal regulation of steroidogenesis in this disorder.

Conclusion: This is a case of AIMAH presenting with overt Cushing’s syndrome. Pathophysiology involves aberrant adrenal receptors and identification of these can offer specific pharmacological approach to control abnormal steroidogenesis and prevent progression of the disease in selected patients; the efficacy and safety of medications in this disease however is still under investigation. Unilateral or bilateral adrenalectomy remains the definitive treatment.

Abstract #127

MEGACE INDUCED ADRENAL INSUFFICIENCY

Priyanka Gauravi, MD, Khalid Bannan, MD, Allan Tachauer, MD

Objective: To describe a case of adrenal insufficiency caused by Megesterol acetate (MA) and emphasize the importance of weaning patients off Megace by slowly tapering the medication.

Background: Megestrol acetate has been used to improve appetite in the malnourished population. Megestrol acetate is a synthetic progestin that has been used since the 1970s for the treatment of advanced cancer and subsequently to treat anorexia, cachexia and weight loss in AIDS patients.

Case Presentation: A 79 yr old male was transferred from the geropsych unit for persistent tachycardia and shortness of breath. Patient was admitted to geropsych unit for major depressive disorder. He lost 30 pounds in the last 6 months due to his depression. A search for the etiology of sinus tachycardia, including investigations to rule out an acute coronary syndrome, pulmonary embolism, thyrotoxicosis, anemia and sepsis, was fruitless. Patient was also found to have orthostatic hypotension which prevented his physical therapy. A cosyntropin stimulation test was done to rule out adrenal insufficiency. His baseline cortisol level was 1.4 mcg/dl. Cortisol level 30 min and 60 minutes after the test was 8.0 mcg/dl and 9.8 mcg/dl. The results showed adrenal insufficiency. MA was held and patient was started on hydrocortisone supplementation. His tachycardia and orthostatic hypotension subsequently resolved.

Discussion: Failure to thrive in elderly is a common cause of increased morbidity and mortality. Its complication included increased decubitus ulcers, falls, hip fracture, poor wound healing and infection. Management requires multiple modes of treatment, one of which is MA supplementation. The exact mechanism of action of MA is unknown. It has been proposed that MA binds to the
glucocorticoid receptor and acts as a weak agonist initially but later acts as an antagonist. It is a synthetic derivative of naturally occurring steroid hormone progesterone. It stimulated the appetite by antagonizing the metabolic effect of cytokines. A potentially under recognized but serious side effect is the suppression of HPA axis and adrenal insufficiency.

**Conclusion:** Physicians should look for symptoms of hypoadrenalism in patients on MA therapy and patients and their families should be informed of the symptoms of adrenal crisis and urgent need of stress dose of steroids in patients receiving chronic MA therapy. It is important to consider a diagnosis of adrenal insufficiency in patients with symptoms of fatigue, hypotension, and asthenia who have been treated with megestrol. It is recommended that a short course of steroid replacement be given to those who are on MA therapy and are being discontinued.

**Abstract #128**

**ADRENAL CORTICAL CARCINOMA: EXPERIENCE AT KING FAISAL HOSPITAL & RESEARCH CENTRE**

*Dania Alkhafaji, MBBS, Mohammed Ahmed, MD*

**Objective:** We report data on a group of adrenal cortical carcinoma (ACC) patients at presentation, treatment rendered and f/u information in order to improve natural history of disease at our center.

**Case Presentation:** We selected 10 ACC patients who met minimum f/u of 10 months (mean 46.4, range 10-138). Their ages ranged 15-63 years. There were 5 males and 5 females. Their presenting symptoms: wt. loss in 3, hirsuitism and acne in 3, HTN in 2, myopathy in 2, and glucose intolerance in 2. There were 6 nonfunctioning and 4 functioning tumors. Of the latter, there were 2 with combined cortisol and androgen-producing, one each with cortisol and androgen-producing. Imaging modalities done: CT adrenal/chest/Pelvis in all 10, MRI in 5, PET-CT in 2, and US abdomen in 2. Histopathology confirmed diagnosis in all. All underwent open surgical removal of the tumor that weighed 72-2600 (mean 867 G) and were 6-17 (mean 14 cm) large. One patient had a 2nd surgery for local recurrence. Two had post surgical complications of pneumothorax in 1, and stricture of IVC in 1. Following surgery nine patients received mitotane and ketoconazole was added for 2. No drug toxicity was witnessed. One patient had resection of lung metastasis followed by chemo Rx but had persistent disease. At last f/u: 3 are deceased, 2 are in complete remission 29 and 48 mos. Of the 5 alive patients, lung metastasis is present in 4, lung and liver metastasis in 1.

**Discussion:** ACC is a rare aggressive disease with an incidence of 1-2 million/yr. They can present as rapidly growing abdominal masses without hormonal disturbance. Of the functional ones about 60% present with Cushing’s disease, 45% combined with androgen-production. Majority present or develop metastases later in course. Metastases are commonly encountered in lungs, liver and bones. The primary Rx modality is surgery. There are no uniform standards for administration of adjuvant mitotane Rx. The best evidence from a retrospective study of 177 patients from 55 European centers with stage 1-111 indicates longer recurrence-free survival and fewer deaths in mitotane treated patients compared to controls. Others recommend it only when tumor is larger than 8 cm, with microscopic invasion, and Ki-67 of >10%. Several other centers recommend it to all patients soon after surgery. There is no agreement on duration of Rx. But up to 5 years is considered reasonable. Role of radiation Rx remains unsettled.

**Conclusion:** We encountered large ACC with 60% showing metastases at presentation. 60% were nonfunctional. Lung metastases were commonest (40%). Majority (90 %) received mitotane post surgery. At a mean f/u of 46 mos. 30% are deceased. 20% are in remission. 40% are alive with persistent metastases while on mitotane maintenance.

**Abstract #129**

**ADRENAL MASS**

*Kanakasabai Narasimhan, MD, FACP, ECNU*

**Objective:** To demonstrate the workup and management of Adrenal mass, namely a Pheochromocytoma.

**Case Presentation:** A 68 year old man presented to the ED with headaches, chest pain, and hypertension and was admitted to the hospital. He had no prior history of HTN and was not on any medications. He was worked up for his chest pain and an adrenal mass was discovered on the right side incidentally. He was started on Hydralazine and discharged from the hospital to be followed by Endocrinology for work up of this adrenal mass. The patient was seen in our office and his blood pressure was 226/110 mm Hg with a heart rate of 76 bpm and was asymptomatic. He admitted to headaches intermittently but no other symptoms. His exam otherwise was unremarkable. His workup for his adrenal mass included a 24 hr urine collection for fractionated metanephrines, catecholamines, cortisol, and creatinine. A plasma metanephrines, aldosterone, plasma renin activity, and a metabolic panel was ordered as well. On reviewing his CT abdomen a solid mass 10/10 cms on the right side with
an area of central necrosis and calcification and a normal appearing left adrenal gland were noted. He was started on calcium started blockers in addition to hydralazine and his blood pressure was monitored twice daily. His laboratory data showed a 24 hr urine normetanephrines more than 8000 mcg/24 hrs (normal- 44-540 mcg), metanephrines of 2294 mcg/24 hrs (normal 26-230mcg), catecholamines 737 mcg (26-121 mcg), and a normal cortisol, aldosterone and renin activity. He was then started on Phenoxybenzamine 10 mg b.i.d and gradually increased to 60 mg daily. His blood pressure was well controlled and was then referred to surgery for excision of the mass. He was admitted and was hydrated for 24 hours and his alpha blocker was continued and underwent surgical resection of the adrenal mass. Surgical pathology confirmed a right adrenal pheochromocytoma. The patient was followed up after surgery and his blood pressure was 118/84 mm Hg not on any antihypertensive and felt well. His repeat 24 hr urine showed a normetanephrine 504 mcg/24 hr, metanephrine 149 mcg with normal catecholamines.

**Discussion:** Catecholamine-secreting tumors that arise from chromaffin cells of the adrenal medulla and the sympathetic ganglia are referred to as “pheochromocytomas” and “catecholamine-secreting paragangliomas” respectively. Classic triad - The classic triad of symptoms in patients with a pheochromocytoma consists of episodic headache, sweating, and tachycardia. About half have paroxysmal hypertension; most of the rest have what appears to be essential hypertension. Familial pheochromocytoma - When pheochromocytoma is associated with the multiple endocrine neoplasia type 2 (MEN2) syndrome, symptoms are present in only about one-half of patients and only one-third has hypertension. 97%-abdomen, and only one-third has hypertension. 97%-abdomen, symptoms are present in only about one-half of patients with multiple endocrine neoplasia type 2 (MEN2) syndrome, 24-hour urine catecholamines and metanephrines — At Mayo Clinic, the most reliable case-finding method for identifying catecholamine-secreting tumors is measuring fractionated metanephrines and catecholamines in a 24-hour urine collection (sensitivity=98%, specificity=98%). If clinical suspicion is high, then plasma fractionated metanephrines, should also be measured. CT and MRI both detect sporadic tumors and are helpful. Medical preparation for surgery- Once a pheochromocytoma is diagnosed, all patients should be operated on after appropriate medical preparation. The preoperative medical therapy is aimed at controlling hypertension (including preventing a hypertensive crisis during surgery) and volume expansion. Some form of preoperative pharmacologic preparation is indicated for all patients with catecholamine-secreting neoplasms. However, no randomized controlled trials have compared the different approaches. All patients with pheochromocytoma need to undergo pre-operative alpha-adrenergic blockade. After adequate alpha-adrenergic blockade has been achieved, beta-adrenergic blockade is initiated. Monitoring of hypertension is essential during and after surgery.

**Conclusion:** Pheochromocytoma, the symptoms of which are not very specific and during which hypertension is present in only half the patients, is a disease that remains rare. The incidence of this disease is about 800 new cases/year. Correct diagnosis and management of this rare disease is essential to prevent multiorgan complications.

**Abstract #130**

**CRH STIMULATION TESTING CAN HELP DISTINGUISH BETWEEN PITUITARY OR ADRENAL SOURCES OF CUSHING SYNDROME IN INDETERMINATE CASES**

Donny Wynn, MD, Muneer Khan, MD, Sailatha Padmanabhan, MD, Lubna Wani, MD, Jeffrey Bender, MD, Madona Azar, MD

**Objective:** To detail a case of using CRH stimulation testing to help differentiate from adrenal versus pituitary sources of Cushing syndrome.

**Case Presentation:** Clinical suspicion for Cushing syndrome should prompt evaluation because of the significant morbidity and mortality associated with the condition. Adrenal incidentalomas also require work-up for hypercortisolism since the manifestations can be subtle. We present the case of a 37 year-old woman with symptoms of fatigue, hirsutism, depression, and an incidentally discovered left adrenal mass. Initial work-up for hyperfunctioning nodule included 24 hour urinary catecholamines and metanephrines, plasma DHEA-S, morning plasma renin activity and aldosterone levels, all of which were normal. However, her morning cortisol after overnight suppression with 1 mg of dexamethasone was 28.9 mcg/dL (NI<1.8), and a 24h urinary cortisol was measured at >500 mcg/24h (NI<50) which confirmed hypercortisolism. A peripheral ACTH level was obtained, and the patient’s level was indeterminate at 10 pg/mL. A Corticotropin Releasing Hormone (CRH) stimulation test was subsequently performed. Neither cortisol nor ACTH levels increased, signifying that the hypercortisolism most likely originated from the adrenals. The patient was referred for surgical resection, and a left adrenalectomy was performed, revealing a 4.6 cm cortical adrenal adenoma by pathology. Her post-operative cortisol level was low at 3.5 mcg/dL, whereas pre-operative levels averaged 30 mcg/dL. She was discharged home on tapering dose of hydrocortisone.
ABSTRACT – Adrenal Disorders

Discussion: In order to determine whether hypercortisolism is pituitary-driven or adrenally-driven, ACTH levels can be obtained. ACTH levels less than 5 pg/mL suggest an ACTH-independent cause, usually adrenally-sourced, and levels greater than 15 pg/mL suggest an ACTH-dependent cause, usually from a pituitary source. If the ACTH level is in between 5 - 15 pg/mL, a CRH stimulation test can help distinguish between the two causes. After administration of CRH, cortisol and ACTH levels can be measured every 15 minutes for one hour. An increase of both ACTH > 35% and cortisol > 20% suggests pituitary dependent hypercortisolism whereas static levels suggest adrenal dependent hypercortisolism.

Conclusion: Work-up for Cushing syndrome can be challenging. Thorough and accurate evaluation and meticulous source determination can help avoid useless, invasive procedures and can guide definitive therapy. In certain clinical scenarios in which there is difficulty in localizing between pituitary or adrenal sources of Cushing syndrome, the CRH stimulation test can be a valuable tool to distinguish the two etiologies.

Abstract #131

CEREBELLAR HEMANGIOBLASTOMA AND RECURRENT PHEOCHROMOCYTOMA PRESENTING IN THE 8TH DECADE IN A PATIENT WITH VON HIPPEL LINDAU SYNDROME

Pooja Sherchan, MD, Yousef Altowaireh, MD, Kamal Shoukri, MD

Objective: To describe a case of VHL syndrome with an unusual course, presenting with hemangioblastoma and recurrent pheochromocytoma 53 years following bilateral adrenalectomy.

Case Presentation: A 72 year old gentleman presented to our hospital with sudden onset of dizzy spells and unsteady gait in 2009. Given this presentation, MRI of the brain was obtained which showed a mass in his left cerebellum. The mass was resected and the histology revealed hemangioblastoma. He had a previous history of bilateral adrenalectomy for pheochromocytoma in 1957. He required steroid replacement for a few years following which he was successfully weaned off them. CT of the abdomen obtained at some point for abdominal pain following the surgery showed recurrent left adrenal mass. Biochemical testing for pheochromocytoma was not revealing, although he continued to have difficulty controlling hypertension following his initial adrenal surgery. MIBG scan showed an increased uptake in the left adrenal gland. In 2010, he had laparoscopic surgery of his left adrenal mass, the histology of which revealed pheochromocytoma. Following the surgery, his blood pressure improved by an average of 50 points reduction in the systolic and 20 points reduction in the diastolic value. Genetic testing was obtained and revealed a mutation in VHL tumor suppressor gene.

Discussion: Hemangioblastomas are the most common lesions associated with VHL disease, affecting 60 to 84 percent of patients. Patients with VHL-associated hemangioblastomas tend to be younger than those with sporadic hemangioblastomas with a mean age at diagnosis in one series of 29 years. Because hemangioblastomas often first develop in the second decade, routine screening with magnetic resonance imaging (MRI) of the brain and spinal cord for hemangioblastoma is recommended in patients with VHL disease, starting after the age of ten.

Conclusion: This case emphasizes the importance of genetic screening in patients with bilateral pheochromocytomas. Testing for VHL and radiological screening in our patient earlier in his life may have allowed us to detect his hemangioblastoma before it became symptomatic. This case also reminds us of the indolent course of pheochromocytomas that can occur in the setting of VHL syndrome.

Abstract #132

MYOCARDIAL INFARCTION WITH NORMAL CORONARY ARTERVES

Sandra Barrow, MD, Harsha Karanchi, MD, Dale Hamilton, MD

Case Presentation: A 63 year-old woman presented to the hospital with generalized muscular weakness, fatigue and epigastric pain. While waiting on test results she became progressively short of breath. The patient reported that she had experienced three similar episodes in the past 15 months. Each usually began with the same nonspecific symptom pattern, but quickly progressed to acute shortness of breath and chest pain. During the first episode, she required intubation following respiratory failure, and shortly thereafter was resuscitated from cardiac arrest.

Discussion/Results: On physical exam the patient was found to be hypertensive (179/83 mmHg). Cardiac exam was normal but auscultation of her lungs revealed bibasilar crackles. There were no other signs of congestive heart failure and the remainder of her exam was unremarkable. Laboratory results were significant for elevated cardiac enzymes. Her EKG showed ST depressions in the anterolateral leads. Chest X-Ray displayed bilateral diffuse interstitial infiltrates consistent with pulmonary edema. Echocardiography showed impaired left ventricular function with an ejection fraction of 28%.
fraction of 45%. In addition to standard treatment for acute coronary syndrome, she received noninvasive ventilation and diuretic therapy. However, two normal cardiac catheterizations that were performed following her previous episodes suggested a diagnosis other than coronary artery disease. Outside hospital records contained a report of a right sided adrenal incidentaloma. A CT of the abdomen confirmed that finding and showed bilateral adrenal masses. 24-hour urine catecholamine analysis revealed a predominantly epinephrine secreting tumor and the PET/CT- scan was consistent with a right sided pheochromocytoma. After preoperative alpha and beta blockade the patient underwent successful bilateral adrenalectomy. Following the operation, she showed complete recovery of the left ventricular function with an EF of 65%.

Conclusion: Pheochromocytoma are catecholamine producing tumors that arise from chromaffin cells. If they become clinically apparent they usually present with palpitations, diaphoresis, headaches, hypertension and flushing. A rare clinical presentation in the absence of the classic signs and symptoms is a diagnostic challenge. This report illustrates a case in which a patient first presented with catecholamine-induced cardiotoxicity mimicking acute coronary syndrome and non-cardiogenic pulmonary edema. Failure to diagnose a pheochromocytoma under these circumstances might lead to sustained cardiomyopathy and even death; however early diagnosis and treatment can reverse the adverse toxic effects described above.

Abstract #133

ADRENOCORTICAL CANCER: A RARE CAUSE OF HORMONE EXCESS

Shuchi Gulati, MBBS, David Lu, MD

Objective: Adrenocortical cancer (ACC) is a rare, aggressive tumor. It accounts for 0.2% of all malignancies and 70% diagnosed patients have distant metastasis at initial presentation. Up to 60% patients with ACC present with clinical evidence of hormone excess. We discuss a patient who presented with symptoms of virilization and Cushing’s syndrome.

Case Presentation: A 65 year old female was admitted to the hospital with multiple pulmonary emboli diagnosed on a routine CT scan of her chest done for a 6-8 week history of dry cough. She was incidentally found to have multiple lung nodules on chest X-ray and a 7cm x 7cm left adrenal mass. She had noted a recent significant weight gain, development of facial hair and new onset hoarseness of voice. Examination revealed high blood pressure of 170/96 mm of Hg (of new onset), excessive facial hair, Cushingoid facies and a buffalo hump. Laboratory evaluation revealed total Testosterone 145 ng/dL (nl 8-60 ng/dL), dihydroepiandrosterone (DHEA) 172.9 mcg/mL (nl <5 mcg/mL), Androstenedione 326 ng/dL (nl 30-200 ng/dL), PM cortisol of 22 mcg/dL (nl <10 mcg/dL), 24-hour urinary cortisol 234 mcg/24 hr (nl 3.5-45 mcg/ 24 hours). Adrenal mass was biopsied and histopathology confirmed an adrenocortical neoplasm; while lung biopsy confirmed metastatic adrenal cancer. She was started on mitotane therapy, but died within six months from metastatic disease.

Discussion/Conclusion: With improving diagnostic techniques, recognition of adrenal incidentalomas has improved. Up to 0.4% incidentally discovered adrenal masses on CT scans of the abdomen end up being diagnosed as ACC. On imaging studies size of adrenal mass > 4 cm, heterogeneous appearance, central necrosis, calcifications and density > 20 Hounsefield units suggest malignancy rather than a benign adenoma. Recognition of ACC is important to facilitate early diagnosis as the tumor can be resectable in early stages.

Abstract #134

A TALE OF TWO SISTERS

Michael Gonzalez, MD, Jagdeesh Ullal, MD, Donald Richardson, MD, David Lieb, MD

Objective: To present a case of two siblings with Autoimmune Polyglandular Syndrome (APS) type II with different manifestations and few shared features.

Case Presentation: The first sibling is a 52 year-old female who was diagnosed incorrectly with type 2 diabetes mellitus (DM) when she was 20 years-old. She had vitiligo, a thin body habitus and a poor response to oral anti-diabetic agents, requiring insulin therapy. In her thirties she had frequent bouts of nausea, vomiting, and abdominal pain with weight loss, resulting in a cholecystectomy and a psychiatric admission. She also had hot flashes, cessation of menses, and an elevated FSH, consistent with premature ovarian failure. In her forties, she was seen by an endocrinologist, who noted areas of hyperpigmentation surrounding her known vitiligo. Adrenal insufficiency was confirmed after she failed a cosyntropin stimulation test and with an ACTH of 895 pg/mL. Physiologic steroid replacement improved her symptoms dramatically. At age 45 she was diagnosed with APS type II. Two years later she developed celiac disease and patchy graying of her hair. Her younger sister was diagnosed with type 1 DM at age 23 after having marked weight loss. Unlike her sister she never had malaise or skin pigmentation changes. After a decade, she developed celiac disease and alopecia universalis. Their youngest
brother developed type I DM at age 30 but has yet to manifest other autoimmune endocrine disorders.

**Discussion:** APS are rare endocrinopathies characterized by the coexistence of at least two endocrine gland insufficiencies having autoimmune mechanisms. Associations with non-endocrine immune diseases may occur. The two major subtypes of APS are distinguished according to age at presentation, patterns of disease combinations, and modes of inheritance. APS II is the most common APS and is typically found in adulthood. It is characterized by primary adrenal failure with autoimmune thyroid disease and/or type 1 DM and can be associated with celiac disease but less so with primary ovarian failure. It is notable that both patients have not yet developed thyroid disease as it is the most common primary manifestation in APS II. The combination of type I DM and adrenal insufficiency is rare. APS type II is associated with HLA DR3 and DR4 and is inherited polygenically. It has an autosomal dominant mode of inheritance with incomplete penetrance, which could explain the distinctive presentation in those affected.

**Conclusion:** For those suspected as having APS, long term follow up with functional screening is recommended in light of the long interval between 1st and 2nd endocrinopathies.

**Abstract #135**

**CHALLENGES OF DIAGNOSING ECTOPIC ACTH DEPENDANT CUSHING’S SYNDROME IN A PATIENT**

Jorge Rohena, MD, Marielba Agosto, MD, Margarita Ramirez, MD, Meliza Martinez, MD, Myriam Allende-Vigo, MD, MBA, FACP, FACE

**Objective:** Report a case of a female with ectopic ACTH dependent Cushing’s syndrome and its difficulty in diagnosing.

**Case Presentation:** 53 y/o female with history of Diabetes Mellitus type II, hypertension that presented with 4 months of weight gain, acne, darkening of the skin, hirsutism, and weakness of proximal extremities. She denied use of glucocorticoids preparations in any form. Physical examination showed moon shaped face, acne, hyperpigmentation of the skin, buffalo hump, increased abdominal girth but no striae, supraclavicular fat pads, and proximal muscle weakness. On laboratories plasma cortisol was 45 ug/dL (4.3-22.4), free urine cortisol >2310 ug/24hrs (28.5-213.7), ACTH 323 pg/mL (5-27), 1 mg dexamethasone suppression test 42.25 ug/dL. Pituitary MRI was normal. Inferior petrosal sinus sampling (IPSS) was done and ratio after CRH administration was <3.0. Chest and abdomen CT were done; on chest CT an area at the head of the pancreas suggestive of a mass with high vascularity was found. Patient was taken to OR for removal of the mass. Pathology was consistent with an ACTH producing adenoma. After surgery plasma cortisol was 14.08 ug/dL and ACTH 22 pg/mL.

**Discussion:** The most common endogenous cause of Cushing’s syndrome is an ACTH secreting pituitary adenoma but other causes include ectopic secretion by nonpituitary tumors and primary adrenal tumors. The nonspecific nature of clinical signs and symptoms coupled with limitations of laboratory tests makes the diagnosis of Cushing’s syndrome a challenging one. After determining the patient has hypercortisolism the second stage of workup involves differentiation of ACTH dependent from ACTH independent. If it is ACTH dependent it needs to be determined if the patient has Cushing’s disease or ectopic ACTH syndrome. IPSS is used to establish this difference. If there is no conclusive central to peripheral gradient after IPSS, the search for an ectopic ACTH source must continue. Octreotide or pentetreotide scintigraphy can detect some ectopic ACTH secreting tumors, although neither is specific for ACTH secreting tumor. Chest and upper abdominal CT or MRI should be performed to confirm any positive pentetreotide scans and to identify masses not detected by scintigraphy. Tumors that can be localized by imaging studies should be removed surgically as it was done in this patient.

**Conclusion:** Determining the cause of Cushing’s syndrome requires an understanding of the patophysiology of hypercortisolism which, in turn, is critical to accurately diagnose, treat and overcome diagnostic challenges.
SUBCUTANEOUS INSULIN INJECTIONS – ARE MOST NEEDLES TOO LONG?

Laurence J. Hirsch, MD, Michael Gibney, RN, Karen Byron, MS

Objectives: Study 1 - Determine skin and subcutaneous thickness (ST, SCT) at four common insulin injection sites. Study 2 - Determine the safety, efficacy and patient ratings of a new 4mm x 32G pen needle (PN) vs two longer PNs (31G, 5mm + 8mm)

Methods: Two related, separate studies. First - measured ST, SCT in 388 diverse U.S. adults with diabetes (3 BMI groups: <25; 25-29.9 and ≥ 30 kg/m²) by ultrasound at injection sites. Second - a prospective, controlled, 2-period non-inferiority crossover trial in subjects with T1 or T2 DM using insulin pens ≥ 2 mos, BMI 18-50 kg/m², A1c 5.5-9.5% at 4 U.S. centers. Subjects randomly assigned to compare either 4/5 mm or 95% CI for % absolute

Results: 4mm PN was less painful than 5mm

Discussion: Knowledge of injection site ST and SCT is essential to select appropriate needle lengths for insulin therapy. ST is very consistent in subjects with diverse demographics, including BMI. Needles ≥ 8mm are not needed for SC injections, even in obese subjects, and increase IM injection risk.

Conclusion: ST at insulin injection sites is thinner and much less variable than commonly thought. A 4mm PN penetrates the skin and consistently delivers insulin into SC tissue with minimal risk of IM injection. It provides equivalent glycemic control vs longer PNs with less pain, no increase in leakage, and is preferred.

CASE SERIES OF DIABETIC MASTOPATHY

Matheni Sathananthan, MD, Steven A. Smith, MD, Carol Reynolds, MD

Objective: Diabetic (DM) mastopathy, also known as sclerosing lymphocytic lobulitis, is strongly associated with type I diabetes mellitus. It is characterized by lymphocytic lobulitis, keloid-type fibrosis and perivascularitis. The purpose of this study is to describe our institution’s experience of those evaluated and treated at Mayo Clinic, Rochester, MN with a diagnosis of DM mastopathy from 1990-present.

Case Presentation: Seventeen patients with pathology suggestive of DM mastopathy were identified through a search of our medical records. Charts were reviewed for type and duration of diabetes, complications, presentation, imaging, pathology, treatment and follow up. Data was abstracted from the Mayo Clinic medical record and reports from local providers.

Discussion: All patients were female ranging in age from 30-64 years at time of presentation. Sixteen were type 1 diabetics. Average duration of diabetes at time of DM mastopathy presentation was 33 years (range 16-52 years) with an average hemoglobin A1c of 8.2% (range 5.5-11.3%). Patients were on varying treatment regimens with either multiple daily injections or use of insulin pump. The majority of patients presented with self-detected breast lumps, and three presented with painful breast lumps. Use of imaging modalities varied with 14 patients undergoing both mammography and ultrasonography, two underwent both of these in addition to magnetic resonance imaging, and one patient underwent mammography only. None were biopsied solely for suspicion of DM mastopathy. Thirteen patients had diabetic complications (retinopathy, nephropathy, neuropathy or some combination). Two patients had concomitant breast cancer. One underwent a right simple mastectomy which revealed DM mastopathy and non-comedo ductal carcinoma in situ. The other patient underwent bilateral excisional breast biopsies which revealed DM mastopathy, and had an abnormal left axillary node fine needle aspiration. She subsequently underwent left modified radical mastectomy which revealed grade III infiltrating ductal carcinoma. None of the patients received specific treatment for the DM
Conclusion: DM mastopathy is a clinical entity that is yet to be fully elucidated. The majority of our patients presented with self-detected breast lumps. Varying imaging modalities were used in evaluation. Two patients were found to have concomitant breast cancer, although this does not imply that DM mastopathy is a premalignant condition.

Abstract #202

SITAGLIPTIN IN THE TREATMENT OF STEROID INDUCED HYPERGLYCEMIA

Hector Eloy Tamez Perez, MD, Maria Gomez, MD, Alejandra Tamez, MD, Dania Quintanilla, MD

Objective: To determine the effectiveness of sitagliptin in a series of patients with steroid-induced hyperglycemia.

Methods: This study is a case series of patients seen in the outpatient clinic of the “Dr. Jose Eleuterio Gonzalez” University Hospital in the city of Monterrey, Mexico during 2009. We included adult patients of both sexes with normal fasting blood glucose at the start of steroid treatment who during follow-up by their physician had fasting blood glucose levels diagnostic of type 2 diabetes. Pregnant patients and those with less than six months of steroid therapy were excluded. Sitagliptin was used (100 mg orally every 24 hours) over a period of six months. The primary objective was to determine the efficacy of sitagliptin by measuring fasting blood glucose and glycated hemoglobin (A1c) before and after treatment.

Results: We evaluated 19 patients. Gender distribution was as follows: 5 men and 14 women with a mean age of 42 ± 7 years and a BMI of 31 ± 1.37 kg/m2. All patients used prednisone at a dose of 15 ± 10 mg and had more than one year with this treatment strategy. Drug tolerance and compliance was adequate and no serious adverse effects were documented. The average fasting glucose level and glycated hemoglobin prior to the start of treatment was 184 ± 16 mg/dl and 8.1 ± 0.84%, respectively. These values changed after treatment with levels of 124 ± 13 mg/dl (P < .001) for fasting glucose and 6.1 ± 0.18% (P < .001) for glycated hemoglobin.

Discussion: Steroids are widely used drugs for the treatment of a variety of diseases. One of the best known consequences is its deleterious effect on carbohydrate metabolism with the appearance of postprandial hyperglycemia. Despite this being a major problem, there are no specific recommendations for screening and treatment of this entity. In our country, since 2006, we have a new type of treatment for type 2 diabetes mellitus based on incretins sitagliptin. These drugs cause increased serum concentrations of the GLP-1 hormone, promoting greater postprandial glucose-dependent insulin release, inhibition of glucagon secretion, and improvement in glucose uptake in peripheral tissues.

Conclusion: Treatment with DPP-4 inhibitors should be considered an effective strategy for treatment of steroid-induced hyperglycemia.

Abstract #203

A CASE OF STIFF-PERSON SYNDROME AND DEVELOPMENT OF TYPE 1 DIABETES OVER 2 YEARS

Patchaya Boonchaya-anant, MD, Alan Burshell, MD

Objective: Stiff-person syndrome (SPS) is a rare neurological disease. The disorder is thought to result from an immune-mediated deficiency of γ-aminobutyric acid (GABA). Autoantibodies against glutamic acid decarboxylase (GAD), the enzyme responsible for the synthesis of GABA, is used to help diagnosis SPS. Anti-GAD antibodies (GAD-Ab) are well recognized in the pathophysiology of type 1 diabetes mellitus (DM1). We report a case with SPS and the development of DM1 over 2 years follow up.

Case Presentation: A 35-year-old African American female presented with tremors and progressive rigidity of lower extremities. Extensive neurological work up was done but could not reveal the cause of her symptoms. She was initially diagnosed with panic disorder. Two years later she presented with polyuria, polydipsia and weight loss. Her random blood sugar was 466 mg/dl and HbA1c was 9.6%. The diagnosis of diabetes mellitus was made. Her C-peptide level was 2.5 (0.9-4.3) ng/ml. As part of her diabetes work up, GAD-Ab was done, and the level was 3,202 (0-0.02) nmol/L. This led to the diagnosis of DM1 and SPS. With her progressive neurological symptoms, plasmapheresis was started. Her symptom of stiffness improved with the treatment and GAD-Ab trended down to 609 nmol/L. For diabetes treatment, she was initially started on multiple daily insulin injections with insulin glargine 12 units daily and insulin aspart 2-4 units with meals. Her HbA1c continued to improve and her insulin requirement decreased substantially. Eight months later her HbA1c was down to 5.8% with the need of insulin glargine 4 units per day and insulin aspart as needed. Despite the declining of GAD-Ab level, her C-peptide level continued to fall. She continued to do well for two years after plasmapheresis. Upon recent follow up, she developed worsening of stiffness in her lower extremities, polyuria and polydipsia. GAD-Ab went up to 2,190
nmol/L, C-peptide was down to 0.5 ng/ml and HbA1c was 8.1%. Her insulin dosage was adjusted accordingly. Due to neurological symptoms, plasmapheresis was then restarted.

**Discussion/Conclusion:** SPS and DM1 share underlying pathophysiology with GAD-Ab. SPS rarely occurs in patients with DM1, while DM1 is relatively common in SPS. There are two isoforms of GAD-Ab, GAD65 and GAD67. Only GAD65 is present on pancreatic cell. Antibodies to GAD67 in SPS can target GAD65 as well. Plasmapheresis in our patient reduced GAD-Ab level, and was associated with improvement of her neurological symptoms. She had some improvement of her glycemic control and decrease insulin requirement. This could be due to honeymoon phase or effect of plasmapheresis.

**Abstract #204**

**DAPAGLIFLOZIN IMPROVES HYPERGLYCEMIA AND BETA-CELL FUNCTION WITHOUT INCREASING HYPOGLYCEMIC EPISODES IN PATIENTS WITH TYPE 2 DIABETES MELLITUS**

Afsih Salsali, MD, Arnaud Bastien, MD, Traci Mansfield, PhD, Lisa Ying, PhD, Shoba Ravichandran, MD, FACE, James F. List, MD, PhD

**Objective:** Impaired insulin secretion and insulin resistance are among the main defects in patients with type 2 diabetes mellitus (T2DM) and hyperglycemia can worsen these pathologies, a phenomenon called glucotoxicity. Dapagliflozin (DAPA), a selective inhibitor of the renal sodium-glucose co-transporter 2 (SGLT2), lowers glucose levels in an insulin-independent manner by inhibiting renal glucose reabsorption. DAPA also preserved β-cell function and pancreatic islet morphology in animal models. Our aim was to assess if DAPA, by lowering blood glucose, improves β-cell function without causing hypoglycemia.

**Methods:** Patients with T2DM received DAPA 2.5, 5 or 10 mg or placebo as monotherapy (Study 13, NCT00528372, N=274) or as an add-on to metformin (Study 14, NCT00528879, N=546). The primary end point for both trials was change from baseline in HbA1c at week 24. β-cell function (measured by Homeostasis Model Assessment 2 [HOMA-β%]) was assessed at baseline and week 24. Hypoglycemic episodes were recorded throughout the study period and were defined as major if patients were symptomatic with plasma glucose <54 mg/dL and required assistance.

**Results:** Mean HbA1c at baseline ranged from 7.84%–8.01% in Study 13 and from 7.92%–8.17% in Study 14. The adjusted mean change from baseline in HbA1c at week 24 showed reductions of 0.58% to 0.89% with DAPA vs 0.23% with placebo in Study 13 and reductions of 0.67% to 0.84% with DAPA vs 0.30% with placebo in Study 14 (unadjusted P value ≤ 0.02 for all). The placebo-corrected mean improvement (95% CI) in HOMA-β% for DAPA groups ranged from 13.2% (2.7%–23.8%) to 17.3% (7.1%–27.4%) in Study 13 and from 8.3% (1.3%–15.3%) to 13.4% (6.4%–20.5%) in Study 14. There were no reports of major episodes of hypoglycemia in DAPA or placebo groups in either study, and no hypoglycemic episodes led to discontinuation of study medication. All other hypoglycemic events were non-major episodes reported in Study 13 by 2 patients (2.7%) in the placebo arm, 1 (1.5%) at DAPA 2.5 mg, 0 at 5 mg and 2 (2.9%) at 10 mg. Non-major episodes in Study 14 were reported by 4 patients (2.9%) in the placebo group, 3 (2.2%) at DAPA 2.5 mg, 5 (3.6%) at 5 mg, and 5 (3.7%) at 10 mg.

**Conclusion:** DAPA as monotherapy or add-on to metformin improved hyperglycemia in patients with T2DM. Improvements in β-cell function were also observed, most likely due to relief of glucotoxicity. However, the HOMA-β model has not been fully validated in patients treated with SGLT2 inhibitors. Episodes of hypoglycemia were infrequent and occurred in a similar proportion in DAPA and placebo groups. There were no major episodes of hypoglycemia with DAPA.

**Abstract #205**

**A PILOT STUDY ON TREATMENT EFFECT OF LYCOPENE AND ISOFLAVONES ON INSULIN RESISTANCE**

Himara Davila Arroyo, MD, Wengton Pan, MD, Manish Saraf, PhD, Geetika Saraf, MS, Manisha Chandalia, MD, Nicola Abate, MD

**Objective:** Lycopene and Isoflavones derivatives have been suggested to increase insulin sensitivity in cell cultures and improve insulin resistance in animal models. The aim of this study was to obtain pilot translational data in humans to assess the effects of Lycopene and Isoflavones administration on insulin resistance in normoglycemic subjects.

**Methods:** This was a pilot study with an open-label design which included 31 normoglycemic volunteers of age between 18 and 45 years. The aim of the study was to obtain pilot translational data in humans to assess the effects of Lycopene and Isoflavones administration on insulin resistance in normoglycemic subjects.

**Results:** Mean HbA1c at baseline ranged from 7.84%–8.01% in Study 13 and from 7.92%–8.17% in Study 14. The adjusted mean change from baseline in HbA1c at week 24 showed reductions of 0.58% to 0.89% with DAPA vs 0.23% with placebo in Study 13 and reductions of 0.67% to 0.84% with DAPA vs 0.30% with placebo in Study 14 (unadjusted P value ≤ 0.02 for all). The placebo-corrected mean improvement (95% CI) in HOMA-β% for DAPA groups ranged from 13.2% (2.7%–23.8%) to 17.3% (7.1%–27.4%) in Study 13 and from 8.3% (1.3%–15.3%) to 13.4% (6.4%–20.5%) in Study 14. There were no reports of major episodes of hypoglycemia in DAPA or placebo groups in either study, and no hypoglycemic episodes led to discontinuation of study medication. All other hypoglycemic events were non-major episodes reported in Study 13 by 2 patients (2.7%) in the placebo arm, 1 (1.5%) at DAPA 2.5 mg, 0 at 5 mg and 2 (2.9%) at 10 mg. Non-major episodes in Study 14 were reported by 4 patients (2.9%) in the placebo group, 3 (2.2%) at DAPA 2.5 mg, 5 (3.6%) at 5 mg, and 5 (3.7%) at 10 mg.

**Conclusion:** DAPA as monotherapy or add-on to metformin improved hyperglycemia in patients with T2DM. Improvements in β-cell function were also observed, most likely due to relief of glucotoxicity. However, the HOMA-β model has not been fully validated in patients treated with SGLT2 inhibitors. Episodes of hypoglycemia were infrequent and occurred in a similar proportion in DAPA and placebo groups. There were no major episodes of hypoglycemia with DAPA.
events. Each subject received a combination of Lycopene 7mg and Soy Isoflavones 50mg in 1 tablet by mouth, daily. Insulin sensitivity was measured by a euglycemic hyperinsulinemic clamp, using an insulin infusion protocol of 80 mU/m²/min. Twenty-five of the 31 participants completed clamp studies before and after treatment. The main outcome variable was change in insulin-mediated total body glucose disposal rate (Rd-value).

**Results/Discussion:** Plasma concentrations of the Isoflavones ganistein and daidzein, but not Lycopene, increased significantly after treatment (p-value <0.001 for both). Isoflavones bind the β-isoform of the estrogen receptor and activate the Peroximal Proliferator Activated Receptor-γ (PPAR-γ). Through this mechanism, systemic insulin resistance could improve. Lycopene can also improve insulin resistance by reducing oxidation and tissue inflammation. In the 25 participants who completed the clamp studies, the response was different based on baseline Rd-value. In those participants who were insulin resistant with a baseline Rd-value below 6 mg/min/kg of body weight (n=19) there was a 9% increase in glucose disposal rate with an average post-treatment Rd-value of 4.21±1.45 vs baseline Rd-value of 3.86±1.26 mg/min/kg of body weight (paired t-test p-value=0.04). In the remaining 6 participants who were insulin resistant at baseline (Rd-value ≥6 mg/min/kg), we did not detect any improvement. There were no changes in body mass index and no adverse events during the study.

**Conclusion:** Oral administration of the combination of Lycopene 7mg and Isoflavones 50mg daily induces clinically significant improvement of glucose metabolism in normoglycemic insulin resistant people. If the findings of this study are confirmed by a randomized placebo-controlled trial, Lycopene/Isoflavones combination could be proposed as a safe and effective non-pharmacological treatment to improve insulin resistance and prevent its metabolic complications, including diabetes and cardiovascular disease.

**Abstract #206**

RECURRENT DIABETIC KETOACIDOSIS IN INNER-CITY POPULATIONS: BEHAVIORAL, SOCIOECONOMIC, AND PSYCHOSOCIAL FACTORS.

Lori Randall, MD, Megan Hudson, Jovan Begovic, Dawn Smiley, MD, Guillermo Umpierrez, MD, Limin Peng, PhD

**Objective:** Poor treatment adherence is a major precipitant of DKA. To understand what drives poor compliance, we analyzed socioeconomic and psychological factors in 164 patients with DKA admitted to Grady Hospital in Atlanta from 7/2007 to 8/2010. Of them, 91 patients had multiple admissions for DKA and 73 had a first-time event upon enrollment.

**Methods:** Questionnaires and medical records were used to obtain patient demographics, outpatient follow-up, DM education, mental illness, substance abuse, and lab values. The PHQ-9 and SF-36 surveys screened for depression and assessed quality of life.

**Results:** The cohort had a mean of 3.54 admissions prior to index case and 0.99 admissions subsequently. The mean age was 41±13 yrs; BMI: 27±9; and length of stay: 4.2 ± 3 days (±SD). Discontinuation of insulin was the precipitating cause in 84.6% of the 141 patients on insulin before admission. Among those who quit insulin, 32.5% gave no reason or did not feel like taking it, lack of money: 27.6%, feeling sick: 18.7%, away from supply: 14.6% and stretching supply: 4.9%. The mean PHQ-9 score was 9.8 ± 7.4, 46% had a history of depression, 26% had schizophrenia or bipolar, and 36% had taken antidepressants. A total of 7.3% were married, 15.9% had a history of homelessness, and 27.8% had health insurance. Compared to those with recurrent DKA, patients with first-time had higher BMI (p = 0.05), older age of DM onset (p=0.04) and shorter duration of DM (p<0.001). Those with recurrent DKA had received DM education more often than those with first-time (p=0.001) but were not more likely to know the meaning of A1C (p=0.06). Those with recurrent DKA were more likely to have a history of drug abuse (p<0.001), homelessness, and/or incarceration.

**Conclusion:** Poor adherence to insulin therapy is the leading precipitating cause of DKA in inner-city patients, related to multiple behavioral, socioeconomic, and psychosocial factors. Identifying such factors and intervening with support groups and education could decrease recurrence and high costs associated with DKA.

**Discussion:** DKA represents an important financial and healthcare problem in inner city hospitals in the United States. Poor compliance with treatment and recurrent admissions for DKA relate to common inner-city challenges: lack of money, substance abuse, no insurance, unemployment, and mental health issues. A comprehensive approach including more engaging and repeated DM education, medication check-in calls, and case workers to help patients obtain insurance could improve compliance and reduce DKA admissions.
COAGULATION ABNORMALITIES IN DIABETES ARE ASSOCIATED WITH INCREASED RISK OF MICROVASCULAR COMPLICATIONS

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Objective: Diabetes is known to be associated with coagulation and fibrinolysis pathway disturbances making it a procoagulant state. The role of hypercoagulability in development of diabetic microvascular complications is unknown. Aim of this study was to evaluate if there was any correlation between hypercoagulability and development of diabetic retinopathy, nephropathy and neuropathy.

Methods: Sixty non-insulin dependent diabetics were enrolled in the study. In the study group, 40 patients had retinopathy, nephropathy, neuropathy or a combination of these and 20 patients did not have any of these complications. Both groups were demographically similar. Platelet count, prothrombin time, activated partial thromboplastin time, serum fibrinogen and PAI-1 levels were measured. Assays for vWF, protein C, protein S, factor V, VIII, IX, and antithrombin III activity were carried out using standardized kits.

Results: Statistical analysis was done using student’s t-test. Plasma PAI-1 levels (37.15 ± 15.18 vs 48.65 ± 22.29, p=0.0) and vWF activity (123.19±29.63 vs 155.57 ± 34.61, p=0.007) were significantly higher in diabetic patients with microvascular complications compared to those without microvascular complications while protein S activity (63.05 ± 16.85 vs 51.59 ± 10.7, p=0.002) was significantly lower in diabetics with microvascular complications. On subgroup analysis, diabetics with retinopathy had decreased protein S activity (63.05 ± 16.85 vs 48.48 ± 8.72, p=0.005) and increased vWF activity (123.19 ± 29.63 vs 151.85 ± 29.74, p=0.009) compared to those without retinopathy. Patients with diabetic nephropathy had increased PAI-1 levels (39.55 ± 13.20 vs 51.69 ± 26.53, p=0.02) and vWF activity (134.99 ± 32.54 vs 157.57 ± 37.37, p=0.007) when compared to those without nephropathy.

Discussion/Conclusion: Studies have suggested the role of hypercoagulation in development of major vessel disease in diabetes but very few studies have been done assessing the role of hemostatic abnormalities in development of microvascular disease. This study suggested that diabetics with microvascular complications have significantly more disturbances in coagulation pathways consistent with procoagulant state compared to diabetics without microvascular complications. A prospective randomized trial may be necessary to establish an etiological role of procoagulant state of diabetes in development of microvascular complications.

INSULIN-ANTIBODY ASSOCIATED HYPOGLYCEMIA: A CASE REPORT OF THE OLDEST KNOWN PATIENT

Brittany Bohinc, MD, Paul Whitesides, Jr, MD, John C. Parker, MD, FACE

Objective: To present a rare case of hypoglycemia caused by anti-insulin antibodies in a Caucasian woman of advanced age.

Case Presentation: This is a 97-year-old woman with history of hypertension, coronary artery disease, and osteoarthritis who was discovered to have hypoglycemia (glucose of 50 mg/dL) during emergency department evaluation for syncope with possible seizure. Subsequent testing revealed a nonfasting insulin measurement of >1000.0 (0-24.9 uU/mL), C-peptide 8.9 (1.1-4.4 ng/mL), proinsulin 75.5 (0-10.0 pmol/L). Computed tomography demonstrated no pancreatic abnormalities. She remained asymptomatic during a modified 18-hour supervised fast; at time of termination: glucose 76, cortisol 6.1 (3.1-16.7 ug/dL), C-peptide 5.2, insulin >1000.0, growth hormone 0.2, glucagon 127 (40-130 pg/mL), insulin antibodies (Ab) 2255 (<5.0 uU/mL). About 9 hours after the fast was ended, she had a syncopal episode with capillary glucose of 34 upon arrival of emergency medical services; measured glucose of 211 following intravenous 50% dextrose and insulin was associated with improved level of consciousness.

Discussion: Hypoglycemia caused by an autoimmune etiology ranks as the third most common cause of hypoglycemia in Japan, but it is extremely rare in a non-Asian population. When encountered in non-Asian subjects, it is most commonly associated with hematologic disease, other autoimmune disease or medications. Her recent medication exposure included celecoxib (a sulfonamide; clear relation between sulfhydryl compounds and this syndrome has been shown in Japanese but not non-Asian patients) and ciprofloxacin (type 2 diabetes on therapy with sulfonylurea has been associated with autoimmune hypoglycemia, and ciprofloxacin has been reported to have sulfonylurea-like activity). Whether the anticardiolipin Ab was drug-induced or causative in the autoimmune hypoglycemia is unclear.
**Conclusion:** This is the 59th reported non-Asian patient with hypoglycemia caused by insulin Ab and she is also the oldest patient to be recognized as having (age range 10 months through 84 years) this condition. Insulin-Ab mediated etiology must be considered in any case of hypoglycemia, regardless of patient’s ethnicity.

**Abstract #209**

**TYPE 2 DIABETES MEN WITH SEXUAL DYSFUNCTION: PERCEPTION ABOUT AETIOLOGY, HEALTH SEEKING BEHAVIOR AND TREATMENT PRACTICE**

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**Objectives:** 1. To determine the perception of type 2 diabetes (T2DM) men about aetiology of their sexual dysfunction (SD). 2. To assess the health seeking behavior and treatment practice of these men with regard to their SD.

**Methods:** Male T2DM patients from a diabetes clinic in Nigeria were interviewed with the aid of a questionnaire to determine the presence or absence of SD (disorder of libido, erectile dysfunction(ED), retrograde ejaculation and premature ejaculation). In addition, the international index of erectile function (IIEF) - 15 was used to assess erectile function. Information regarding their perception of aetiology, health seeking behavior and treatment practice of SD was also obtained.

**Results:** Information was obtained from 66 patients. The patients’ age (mean ± SD) was 56 ± 8.8 years, while the mean diabetes duration was 7 years. SD of any form was reported in 53(80%). Prevalence of reported ED was 52% but 88% with IIEF-15 questionnaire. Median duration of SD was 3 years. Sixteen (30%) had developed SD before they were diagnosed with diabetes while SD was the reason for screening for diabetes in 3(6%) participants. While 53% reported diabetes as the culprit, 22% did not know the cause. Anti-diabetic therapy, antihypertensives, hypertension, old age and evil forces were among the perceived aetologies by the rest of the participants. Individuals that perceived diabetes as the cause were more likely to have been diagnosed with SD before diabetes p=0.024 and more likely to have hope of improvement in their sexual function p=0.005. About 49% of the participants had tried one form of treatment or the other while the rest did not try for a number of reasons including ignorance of what to use (21%).

**Conclusion:** Sexual dysfunction is a common but underreported complication of diabetes and its onset may predate the diagnosis of diabetes. Significant number of male diabetics either lack understanding or have wrong perception about the aetiology of their SD. Societal inhibition, norms on issues that border on sexuality and caregivers’ reluctance to discuss these issues may all contribute to the apparent poor health seeking behavior among these patients. There is a serious dearth of understanding of treatment options and coping strategies for T2DM men with various forms of SD.

**Abstract #210**

**PROTECTIVE EFFECTS OF TRECULIA AFRICANA SEED EXTRACT ON SPERM QUALITY OF DIABETIC RATS**

Abraham Adewale Osinubi, MBBS, MSc, FACE, Victor Ukwenya, MSc

**Background:** Diabetes has been associated with reproductive impairment in both men and women. A large body of evidence has demonstrated that men with diabetes appear to have lower sperm quality compared with healthy controls. There is, therefore, a great need for continued efforts at sourcing for agents that will not only lower blood glucose but will also preserve normal reproductive functions. We have earlier demonstrated that aqueous seed extract of Treculia africana (SETA) contains hypoglycemic agent(s).

**Objective:** The aim of present study was to investigate the protective effects of 400 mg/kg of SETA on sperm quality in alloxan-induced diabetic Sprague-Dawley rats.

**Methods:** Thirty-two adult male Sprague-Dawley rats were randomly divided into 4 groups (I-IV) of 8 rats each. After 8 weeks of been diabetic, group I, II and III rats were treated for 8 weeks with 400 mg/kg/day of SETA, 10 mg/kg/day of glibenclamide and distilled water, respectively. Group IV rats were normal non-diabetic rats administered distilled water. Body weight and blood glucose levels were evaluated. At the end of 16 weeks all animals were sacrificed. Caudal epididymal fluid was collected, sperm count, motility and morphology assessed, and testicular weight determined. A p value less than 0.05 was considered to be significant.

**Results:** SETA caused significant (p<0.001) blood glucose reduction comparable to that of glibenclamide. The weight of the testes, sperm count and motility of SETA-treated rats showed significant increase when
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compared with the untreated diabetic group. Eight weeks after the onset of diabetes, the rats given distilled water only became azoospermic, the diabetic rats treated with SETA for 8 weeks had sperm count of $60.67 \pm 10.51 \times 10^6$/ml comparable to that of glibenclamide-treated group ($62.55 \pm 11.33 \times 10^6$/ml). The mean sperm count of the non-diabetic group ($84.34 \pm 11.12 \times 10^6$/ml) was, however, significantly better than the other groups. The mean sperm motility for non-diabetic, diabetic-SETA-treated and diabetic-glibenclamide-treated groups were $82.63 \pm 17.74$, $70.67 \pm 14.73$ and $74.33 \pm 15.47\%$, respectively, while their % sperm abnormalities were $0.56 \pm 0.35$, $3.07 \pm 1.01$ and $5.12 \pm 1.81\%$, respectively. The cross-sections of seminiferous tubules of the diabetic rats treated with distilled water showed atrophic tubules containing a higher ratio of Sertoli cells: spermatogonia when compared to those of the non-diabetic rats and SETA-treated diabetic ones. In addition, the Leydig cells were very few in the cross-sections of diabetic rats treated with distilled water when compared to those of the diabetic animals treated with SETA.

Discussion: Maturation arrest within the seminiferous tubules has been reported in studies conducted in human and animal diabetics. This has been attributed to hyposecretion of testosterone which is made evident by the reduction in Leydig cell population. The TAE-treated animals showed seminiferous tubules lined by Sertoli cells with ongoing spermatogenesis suggesting the ability of the extract in reversing the cytotoxic effects of diabetes on the testes. The semen parameters of the rats treated with the extract also appreciably compared with the diabetic control. We observed that the process of spermatogenesis was restored in the TAE-treated animals. This suggests that diabetes may not necessarily cause a permanent damage to the testes if intervention is initiated on time, and that the extract aided in the recovery of the testes and restored reproductive capacity. This makes TA a most desirable adjunct with standard drugs of choice in the treatment of diabetes.

Conclusion: SETA would be a good adjunct in the treatment of diabetes mellitus, especially in men to minimize the adverse effects of the condition on fertility.

Abstract #211

IS THE METABOLIC SYNDROME AN ACCURATE PREDICTOR OF CARDIOVASCULAR RISK IN PERSONS WITH TYPE 2 DIABETES MELLITUS

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Objective: The objective of this study was to calculate the absolute cardiovascular risk in persons with type 2 DM and to compare the values in persons with the metabolic syndrome and in those without.

Methods: Three hundred forty patients with type 2 DM who satisfied the inclusion criteria were recruited into the study by consecutive sampling. Anthropometric measurements (weight, height, and waist circumference) were taken and blood samples were obtained for analysis of fasting plasma glucose, fasting lipid profile and glycated haemoglobin. All patients also had their blood pressure checked twice and the average was recorded. Laboratory analysis was carried out while the cardiovascular risk score was calculated using the United Kingdom Prospective Diabetes Study (UKPDS) risk engine. The diagnosis of the metabolic syndrome was by the International Diabetes Federation Criteria. The results obtained were analyzed using SPSS package version 16.

Results: Two hundred twenty five (66.3%) of these persons with type 2 DM had the metabolic syndrome. The calculated absolute cardiovascular risk score stratification for coronary heart disease, stroke, fatal coronary heart disease, fatal stroke was found to be similar in people with type 2 DM with and without the metabolic syndrome, with no statistically significant difference between the two groups.

Discussion: The presence of the metabolic syndrome in addition to type 2 DM has been associated with an increased risk of development of cardiovascular disease. Studies carried out to determine if the diagnosis of the metabolic syndrome actually conferred a higher cardiovascular risk have shown conflicting results. Cardiovascular risk engines are usually a composite of several cardiovascular risk factors and good control of these factors may result in attenuation of the patient’s global cardiovascular risk.

Conclusion: The absolute cardiovascular risk score was similar in type 2 DM patients with or without the metabolic syndrome. The above findings suggest that
Despite the high prevalence of the metabolic syndrome using the IDF definition, this did not necessarily imply a higher cardiovascular risk. Therefore, the absolute cardiovascular risk score may be a more reliable method to accurately stratify cardiovascular risk in persons with type 2 DM.

**Abstract #212**

**A 24 WEEK, DOUBLE-BLIND, PLACEBO-CONTROLLED, MULTICENTER STUDY OF METANX® IN PATIENTS WITH DIABETIC PERIPHERAL NEUROPATHY (DPN)**

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**Objective**: To assess the efficacy and safety of Metanx® (L-methylfolate calcium 3mg, pyridoxal-5′-phosphate 35 mg, and methylcobalamin 2mg) in patients with DPN in a multi-center, randomized, controlled trial.

**Methods**: 214 outpatients [66 women (30.8%), mean age 62.6 ± 8.85] with DPN were enrolled in a multicenter, double-blind, placebo-controlled trial and randomized 1:1 to receive either Metanx or identical placebo for 24 weeks. Inclusion criteria required a documented diagnosis of type 2 diabetes and a baseline vibration perception threshold (VPT) of 25-45 volts. Excluded were peripheral vascular disease, previous surgery with residual neurologic deficit, concomitant opiate use, and A1C >9% or other unstable medical illness. Subjects were allowed to use concomitant DPN medications (other than opiates), but the doses were kept constant during the study. The primary outcome measure was change in VPT, and secondary measures included validated instruments testing a range of patient-related parameters affected in such patients, including the Neuropathy Total Symptom Score-6 (NTSS-6), the Neuropathy Disability Score (NDS), Short Form-36 (SF-36) Health Survey, Visual Analog Scale for pain (VAS), and the Hospital Anxiety and Depression Scale (HADS).

**Results**: There was no difference between the two groups at baseline in age, race, and ethnicity, length of diabetes and neuropathy history, or baseline outcome measures. Subjects reported having diabetes for a mean 12.0 ± 8.6 years with symptoms of neuropathy present for a mean 5.1 ± 5.0 years. At 24 weeks, change in VPT with Metanx was no different than with placebo. Mean NTSS-6 scores in the Metanx group improved more at 16 weeks (-0.90 ± 1.42 vs. -0.40 ± 1.72, p=0.013) and 24 weeks (-0.96 ± 1.54 vs. -0.53 ± 1.69, p=0.033) compared to the placebo group, the reduction being clinically meaningful. NDS improvement with Metanx was greater than placebo at 16 weeks (p=0.027), but the trend was non-significant at 24 weeks (p=0.354). Significant improvement was observed with Metanx in the Mental Component subscale of the SF-36 survey (p=0.0306). Medication compliance was >95% in both groups. Adverse events were infrequent, with those reported occurring in <2% of all subjects.

**Conclusion**: These findings suggest that Metanx may be a safe and effective therapy for patients with symptomatic DPN. While VPT was not affected in the present study, significant improvements with Metanx were observed in measures of neuropathic symptoms (NTSS-6), health-related quality of life (SF-36), and neuropathy-focused physical exam (NDS), improving parameters that may have a greater impact on patient’s well being.

**Abstract #213**

**EFFICACY OF 3 DAY BLINDED CONTINUOUS GLUCOSE MONITORING SYSTEM ON HBA1C IN CHILDREN AND ADOLESCENTS WITH TYPE 1 DIABETES MELLITUS**

*Douglas George Rogers, MD, Jami Klein, RN, CDE, Ramachandra Aswini, MBBS, Sara Worley, MS*

**Objective**: We assessed the impact of 3 day continuous glucose monitoring (CGMS) on HbA1c levels in children and adolescents with T1DM.

**Methods**: Forty patients (age 3-18 years) with T1DM were placed on the I-Pro (Medtronic, Northridge CA) CGMS for 3 days. HbA1c levels obtained within 0 – 1 month prior to using the I-Pro were compared with HbA1c levels obtained 2 - 6 months after using the I-Pro CGMS. Pre and post CGMS HbA1c levels were compared using Wilcoxon signed rank test.

**Results**: HbA1c levels typically decreased after CGMS, mean -0.45% (95% confidence: -6.5 to 1.5) P<0.001. Improvement was most apparent in patients with higher initial HbA1c levels.

**Discussion**: The efficacy of continuous glucose monitoring (CGMS) in children and adolescents with Type 1 diabetes mellitus (T1DM) is controversial. One article found no beneficial effect from CGMS on HbA1c levels in patients less than 24 years of age while another found significant benefit in children aged 7-18 years.

**Conclusion**: We have demonstrated that children and adolescents may benefit with lower HbA1c levels from the use of a 3 day CGMS. This benefit was seen mostly in patients with initial HbA1c levels above 8.0%.
Abstract #214

VACCINATION AGAINST STREPTOCOCCUS PNEUMONIAE IN ADULT PATIENTS WITH DIABETES: A SIMPLE INTERVENTION SIGNIFICANTLY IMPROVED DOCUMENTATION

Jennifer Joanne Miranda, MD, Marc J. Laufgraben, MD

**Background:** Pneumococcal polysaccharide vaccine (Pneumovax-23) is recommended for all diabetic patients 2 years of age. Pneumovax helps protect against invasive pneumococcal disease such as pneumonia, meningitis, and febrile bacteremia (1). Diabetic patients, due to common associated issues of cardiovascular and renal dysfunction, are at increased risk for severe pneumococcal illness (2). However, utilization rates for Pneumovax are poor.

**Case Presentation:** We performed a project to improve documentation and awareness of Pneumovax by placing a 1” x 2.5” “sputum-green” sticker consisting of the word “Pneumovax” and a line to write the date that Pneumovax was given on each patient’s medical chart. We first examined the charts of all diabetic patients seen in our clinical practice in one designated week prior to our intervention. Our purpose was to attempt to locate documentation of Pneumovax administration status within ten seconds of opening the chart (i.e., by looking at front of the chart, the first divider, and the last note). Next, our office staff placed the sticker on the first divider of every chart patient seen between our intervention times of September 2010 through December 2010. At the end of our intervention time, we examined the charts of all diabetic patients seen for one week in December 2010. Prior to intervention, 33 of 125 (26%) charts of diabetic patients had documentation of Pneumovax. Following the intervention, 47 of 85 (55%) charts of diabetic patients had documentation of Pneumovax. Thus, the rate of documentation of Pneumovax improved more than 50%, which is clinically important as well as statistically significant at P < 0.001 by chi square analysis.

**Conclusion:** We have used a simple intervention to markedly improve documentation and awareness of Pneumovax status. We believe this is an appropriate and necessary step toward improving adherence.

Abstract #215

EFFECTIVENESS OF INSULIN PUMP THERAPY ON POORLY CONTROLLED TYPE 2 DIABETES MELLITUS

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**Objective:** To evaluate for effectiveness of insulin delivered by continuous subcutaneous insulin infusion (CSII) in patients with poorly controlled type 2 diabetes mellitus.

**Methods:** In this retrospective study, charts of patients with inadequately controlled type 2 diabetes who were placed on CSII therapy from January, 2008 to December, 2009 at Albany Medical College Endocrinology and Metabolism Division were reviewed. The reason for starting CSII therapy on type 2 diabetes patients included: diabetes poorly controlled despite intensive insulin therapy with or without oral agents for at least 3 months. Effectiveness was assessed by hemoglobin A1C measurement on intensive insulin therapy and six months after insulin pump therapy.

**Results/Discussion:** Fifty-eight adults were identified (mean age 53 ± 11; mean body mass index 36 ± 7, mean insulin requirement 0.49 U/kg per day; and mean hemoglobin A1C, 8.75%). Treatment with U100 (n=51) or U500 (n=7) via insulin pump significantly reduced HgA1C by 1.02% (P< 0.001). This improvement was associated with a decreased insulin requirement with both U100 and U500 necessary to maintain adequate glucose homeostasis (- 0.063U/kg per day), (P=0.014). When comparing calculated bolus using pump software to manual bolus, there was no difference in six month hemoglobin A1C improvement observed (P= 0.58).

**Conclusion:** Continuous subcutaneous insulin infusion is an effective method to treat poorly controlled type 2 diabetes mellitus, and lead to lower insulin requirement. No therapeutic benefit was observed when comparing calculated bolus with manual bolus dosing.
Abstract #216

PREVALENCE AND DETERMINANTS OF GLUCOSE INTOLERANCE AMONG HIV/AIDS PATIENTS IN NORTH-CENTRAL NIGERIA

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Andrew E. Uloko, MD

Objective: To determine the prevalence of glucose intolerance and associated risk factors in HIV/AIDS patients.

Methods: Consenting adult HIV patients at the HIV clinic of Jos University Teaching Hospital, Plateau, North-Central Nigeria were evaluated. Clinical characteristics and anthropometry were obtained. Laboratory tests for each patient; fasting plasma glucose (FPG), fasting plasma insulin (FPI), oral glucose tolerance test (OGTT) with 75g glucose, serum lipids, CD4 cell count and viral load. Glucose Intolerance (GI) was defined as Impaired Fasting Glucose (IFG) =FPG > 6.1mmol/l; Impaired Glucose Tolerance (IGT) =FPG= 6.1mmol and 2hrs post-glucose load (PGL) 7.8 – 11.0mmol/l; and Diabetes Mellitus (DM) =FPG≥7.0 and/or 2hr PGL ≥ 11.1 mmol/l.

Results: Of 584 patients studied, 384 (130 males and 254 females) with mean age (range) of 38 (20-64) years were HAART-treated; while 200 (61 males and 139 females) with mean age (range) of 33 (18-62) years were HAART-naïve. Overall, the prevalence of GI was 40.4% (IFG 19.5%, IGT 11.5% and DM 9.4%). Prevalence rates of IFG (27.1%) and DM (11.2%) in HAART-treated patients were significantly higher than those in HAART-naïve patients (IFG 5.0%, DM 6.0%), p<0.005. Conversely, IGT was more prevalent in HAART-naïve than in HAART-treated patients (19.5% and 7.3% respectively), p<0.05. The proportions of patients with GI were higher in overweight and obese HAART-treated patients with moderate CD4 cell count (200–500x10^6 cells/L); while in the HAART-naïve patients, GI was more prevalent in underweight subjects with CD4 cell count (<200x10^6 cells/L). The mean FPI in HAART-treated patients (41±4.1µU/ml) was similar to that of HAART-naïve patients (39.9±3.5µU/ml), p>0.05. FPI increased in HAART-treated patients with increasing treatment duration. Determinants of GI were age, increasing BMI, low CD4 cell count, metabolic syndrome and HAART treatment duration. Strong independent risk factors were, low CD4 cell count and HAART treatment duration.

Discussion: HIV/AIDS is a big health problem in Sub-Saharan Africa. The advent of free HIV treatment programs in Nigeria offers many persons with HIV/AIDS the benefit of HAART and longer life, thus constituting a ‘high-risk’ group for developing glucose intolerance (IFG, IGT and DM). Expectedly, HIV/AIDS patients on HAARTS were found to be three times more likely to develop GI than in the general population. Glucose intolerance and its associated risk factors among HIV patients have not been extensively studied in Nigeria and require a close review.

Conclusion: The prevalence of GI among HIV/AIDS patients in this region is high. Treatment with HAART and low CD4 cell count are strong determinants.

Abstract #217

MICROALBUMINURIA AND ITS RELATION TO METABOLIC FACTORS AND CORONARY HEART DISEASE IN A CAUCASIAN POPULATION WITH DIABETES: A CASE CONTROL STUDY

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Objective: To ascertain the relation between microalbuminuria and the metabolic factors that influences the development of coronary heart disease in a caucasian population with diabetes.

Methods: We studied 137 caucasian patients with microalbuminuria (ACR; males > 2.5 mg/mmol and females > 3.5 mg/mmol) and 274 age and sex matched Caucasian controls. Prevalent CHD was defined with diagnosis of angina or heart attack and/or ischemic changes (q waves/LBBB) in ECG. Comparative analysis was done between microalbuminuric patients and those with normal albumin excretion. Student’s “T” was used for parametric and chi-square test was used for non-parametric data. Odds ratio was calculated to establish association between CHD and albumin excretion.

Results: Patients with microalbuminuria had lower BMI (29.48 ± 5.40 vs 33.24 ± 7.51 kg/m2, p=0.00). These patients also had higher levels of SBP (134.99 ± 25.42 vs 132.46 ± 17.87 mmHg, p=0.24), DBP (76.07 ± 10.73 vs 73.90 ± 11.32 mmHg, p=0.06), cholesterol (4.58 ± 1.03 vs 3.98 ± 1.02 mmol/L, p=0.00) and HDL (1.32 ± 0.34 vs 0.93 ± 0.21 mmol/L, p=0.00) but lower levels triglycerides (2.35 ± 1.54 vs 2.46 ± 1.65 mmol/L, p=0.51) LDL (1.84 ± 1.27 vs 2.14 ± 1.28 mmol/L, p=0.02) as compared to controls. No difference was noted in glycaemic control between the groups. Linear regression analysis with ACR (albumin creatinine ratio) as dependant variable in between microalbuminuric patients and those with normal albumin excretion.
Discussion: Microalbuminuria is a surrogate marker of underlying endothelial dysfunction and it not only predicts the development of clinical albuminuria in diabetes patients but also is a well-established risk factor for cardiovascular morbidity and mortality. Subclinical vascular damage in the kidneys and other vascular beds in combination with dysmetabolic factors play a significant role for development of CHD hence periodic screening for microalbuminuria in patients with diabetes help to identify vascular disease and reduce the risk of future complications. Our study demonstrates that patients with microalbuminuria had higher traditional risk factors like blood pressure and lipids with strong statistical correlation. Surprisingly, the case population had lower BMI as compared to the controls. Our findings also suggest that these patients also have a higher risk of CHD as compared to their normoalbuminuric counterparts. These results suggest that targeted therapy should be aimed at reducing microalbuminuria and prevent its progression in diabetes population to prevent adverse cardiovascular outcome in the future.

Conclusion: Microalbuminuria has been increasingly recognised as a marker of atherogenic milieu. Our study shows that there is a strong association between albumin excretion in caucasian diabetes population with the traditional risk factors that significantly influence development of CHD. A positive urine albumin excretion warrants an intensive multifactorial interventional strategy like behaviour modification and targeted pharmacotherapy aimed at reducing albuminuria and thereby improving the overall CHD risk factor profile.

Abstract #218

GASTRIC BYPASS SURGERY: IS IT REALLY A “CURE” FOR DIABETES?

Akshay Bhanvarlal Jain, MD, Mariana Marin, MD, Marilyn Konezny, CDE, Krishnakumar Rajamani, MD

Objective: To determine the extent of glycemic control in patients who have undergone gastric bypass surgery for morbid obesity.

Methods: We studied glycemic control in 4 patients who were experiencing hypoglycemic symptoms after undergoing Roux-en-Y surgery. These patients had been advised by their surgeons that they had been cured of diabetes and prediabetes. Interstitial fluid glucose levels were monitored using a Medtronic iPro™ Continuous Glucose Monitor (CGM). CGM data was obtained over 72-111 hours for each patient. Pre and post-operative levels of hemoglobin A1c (HbA1c), fasting blood glucose (FBG) and hemoglobin (Hb) were obtained for each patient. CGM recordings were analyzed for total duration of high readings (>180 mg/dL) and low readings (<70 mg/dL), regardless of prandial status.

Results: The mean age of the patients (A,B,C,D) was 45.8 years. Time since surgery ranged from 12 to 72 months. Except for patient C (insulin pump), none of the patients was on insulin or oral hypoglycemic agents at the time of CGM. Preoperative/postoperative HbA1c and FBG values were as follows: A 8.2/5.2%, 170/94 mg/dL; B 6.7/5.1%, 177/87 mg/dL; C 6.1/9.1%, 120/252 mg/dL; D 5.9/5.4%, 109/52 mg/dL. Patients A and B were advised by the surgical team that their diabetes was cured. Patient C was advised that her prediabetes had resolved following surgery, but was then admitted 2 months later with diabetic ketoacidosis and started on insulin therapy. Patient D was advised that her prediabetes had resolved following surgery. Percentage of high (H) and low (L) glucose levels during CGM were as follows: A 19%H, 11%L; B 3%H, 7%L; C 56%H, 6%L; D 0%H, 0%L. Patient D had postprandial BG elevations in the 140-180 mg/dL range and experienced hypoglycemic symptoms when BG dropped from >140 mg/dL to 85 mg/dL.

Conclusion: Gastric bypass surgery is often touted as a cure for type 2 diabetes mellitus. All four patients were informed that their diabetes or pre diabetes had been “cured” post-operatively, based on their HbA1c and FBG values. This study shows that patients who appear to be “cured” of diabetes mellitus may still have periods of hyperglycemia and hypoglycemia, possibly accounting for the normalization of HbA1c. Current diagnostic criteria for diabetes mellitus may not apply to patients who have had gastric bypass surgery. Criteria to define cure or remission of diabetes mellitus in these patients, possibly utilizing CGM, need to be established. Further studies using CGM in a larger group of patients may show the actual prevalence of this phenomenon and the true incidence of cure or remission of diabetes mellitus.

Abstract #219

INCIDENCE OF CEREBRAL EDEMA WITH RAPID BLOOD GLUCOSE CORRECTION IN THE TREATMENT OF DIABETIC KETOACIDOSIS IN ADULT POPULATION

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Objective: Cerebral edema (CE) is a life-threatening complication resulting from rapid correction of hyperglycemia in Diabetic Ketoacidosis (DKA). Current guidelines for the rate of glucose correction in patients with DKA are based on studies in pediatric populations.
Methods: A retrospective chart review was conducted of patients diagnosed and treated for DKA at Providence Hospital between January of 2000 and December of 2006. Over 800 charts were reviewed. Inclusion criteria included adult patients who presented with DKA and had an average glucose correction rate greater than 75 mg/dL per hour. The rate of correction was defined as the change of average glucose measurement per hour, from the time of presentation until the blood glucose measurement reached 250 mg/dL. Patients were excluded if they had any of the following: concurrent steroid use, alcohol abuse, or presence of an eating disorder.

Results: A total of 94 patients met the inclusion criteria. The mean patient age was 42 ± 16 years. The etiology of precipitating factors included: noncompliance with insulin therapy (41%), infection (19%), other causes (e.g. pancreatitis, and myocardial infarction) (32%) and idiopathic (8%). The average blood glucose measurement on presentation was 751 mg/dL. All patients were treated with intravenous insulin, with an average rate of blood glucose correction of 107 mg/dL per hour. The rate of correction was defined as the change of average glucose measurement per hour, from the time of presentation until the blood glucose measurement reached 250 mg/dL. Patients were excluded if they had any of the following: concurrent steroid use, alcohol abuse, or presence of an eating disorder.

Discussion: CE is a rare but serious complication that may result from overcorrection of blood glucose during treatment of Diabetic Ketoacidosis. Multiple studies have implicated rapid rate of glucose correction to CE in pediatric population. In this study, rapid rate of glucose correction in our adult population above the recommended rate did not increase the risk of developing CE.

Conclusion: In addition to the presumed reduction in healthcare costs, based on our observations, rapid rate of glucose correction in the treatment of DKA could be feasible in adult population.

Abstract #220

AN ASSESSMENT OF 16-WEEKS OF INSULIN PUMP THERAPY IN ELDERLY PATIENTS WITH TYPE 2 DIABETES

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Objective: Assess insulin pump therapy in patients ≥65 yo with suboptimally controlled T2DM.

Methods: In this sub-analysis of a 16-wk, open-label study, 13 insulin pump naïve patients ≥65 yo (9 male/4 female, age 68±3 y, DM duration 17±5 y, C-peptide 1.62±1.48 ng/ml, A1C 8.1±1.0%, body weight 99±16 kg, BMI 34±4 kg/m², mean±SD) treated with either ≥2 oral agents (OA) (n=3), basal insulin±OA (n=2) or MDI±OA (n=8) discontinued all DM medications except MET and initiated pump therapy (Animas® 2020) with 1 daily basal rate and bolus doses at each meal. Insulin doses were titrated to safely optimize glycemic control. Outcomes included insulin dose and dosing patterns, A1C, patient reported outcomes (PRO, Insulin Delivery System Rating Questionnaire [IDSRQ]) and hypoglycemia.

Results: A1C improved significantly after 16 wks of pump therapy (Baseline: 8.1 ± 1.0%, Wk 16: 7.3 ± 1.0%, change: -0.8 ± 1.0%, P=0.01). 38% of patients reached an A1C ≤7.0% and 85% achieved an A1C ≤ 7.0% and/or an absolute A1C reduction of ≥0.5%. There was no severe hypoglycemia and non-severe hypoglycemia was reported by 85% of patients at least once during the study. At Wk 16, the mean daily basal, bolus, and total insulin doses were 58 ± 42U, 49 ± 35U, and 107 ± 76U (1.1U/kg), respectively, and 92% of patients were treated with ≤2 daily basal rates. Weight increased by 1.6 ± 3.3kg (P<0.09). 5 of 7 IDSRQ domains improved (Treatment satisfaction: 64 ± 15 vs 82 ± 10, P<0.001; Clinical efficacy: 40 ± 15 vs 63 ± 13, P<0.005; Diabetes worries: 43 ± 24 vs 37 ± 20, P<0.05; Diabetes social burdens 46 ± 19 vs 31 ± 13, P<0.05; Overall treatment preference: 48 ± 19 vs 72 ± 25, P<0.01; Scale of 0-100, Mean ± SD), with no worsening in the remaining 2 domains.

Discussion: Limited data exist about pump therapy in elderly patients with T2DM, a population less likely to be experienced with devices/technology. Even so, patients in this analysis safely improved glycemic control and had favorable PROs. Improved patient experience may result in enhanced persistence and adherence, leading to improved outcomes. Although this is a post-hoc analysis of an uncontrolled study, it suggests that pump therapy may be an effective therapeutic option for selected elderly patients with T2DM.

Conclusion: Insulin pump therapy using a simple dosing regimen safely improved glycemic control in elderly patients with T2DM. Patients experienced moderate weight gain, no severe hypoglycemia and preferred pump therapy to baseline treatment. Our analysis suggests that in otherwise appropriate pump candidates, advancing age should not deter from considering this form of therapy. Controlled trials are needed to further assess the benefits of pump therapy in T2DM.
ABSTRACTS – Diabetes Mellitus

Abstract #221

CGM TRAINING METHODOLOGY AND PATIENT SATISFACTION

David Price, MD, FACE, Keri Weindel, MS, RD, CDE

Background: Continuous glucose monitoring (CGM) is a proven technology that when used continuously, improves clinical outcomes. However, physician recommendations for personal use CGM remain sporadic. One of the potential barriers to prescribing CGM is the perceived complicated initial training needed for successful CGM use. Many clinicians equate CGM training to the time-intensive and often complicated CSII trainings. Depending upon individual CGM manufacturer training guidelines, training time has been documented to be up to 1.5-3 hours. Different methods of device training have been used in successful adult training programs - guided self-training, group education, phone trainings and individual patient trainings. These trainings have been performed by the manufacturer representative, physician office staff, or at diabetes centers.

Objective: To understand current training processes of new CGM users and compare these to patient satisfaction.

Methods: In this study, 565 patients responded to an on-line survey from April – September, 2010 after initial purchase of the Dexcom™ SEVEN® PLUS (Dexcom Inc., San Diego, CA). The survey looked at the initial training methods used for the Dexcom CGM and corresponding patient satisfaction and training time.

Results: 46% of surveyed patients participate in a self-training method; 17% trained in the physician office or diabetes center, 3.5% trained in a group setting by the manufacturer, 3.5% trained over the phone by the manufacturer and 30% trained on an individual basis by the manufacturer. Patient satisfaction was evaluated and stratified by training method and patients reported an equally high level of satisfaction, regardless of training method - self-training (77%), individual training done by the manufacturer (81%) and trainings done in the physician office or diabetes center (74%). 87% of the Dexcom trainings took ≤ 60 minutes while maintaining a high degree of patient training satisfaction.

Discussion: Many patients can successfully initiate Dexcom CGM through an innovative, self-guided training program. These results challenge the preconceived idea that most patient need and want individualized initial device training. The 17% of patients trained in physician offices or diabetes centers is surprisingly low as there is widespread reimbursement for CGM training through CPT code 95250. The short training time in this study is significantly different than that reported for other CGM systems. Whether CGM training methodology impacts ongoing CGM utilization or outcomes requires further study.

Conclusion: This survey suggests that CGM training does not have to be a burden for the physician office.

Abstract #222

GLYCEMIC CONTROL ACHIEVED WITH LIRAGLUTIDE REGARDLESS OF BASELINE HBA1C LEVELS

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Objective: To assess the effectiveness of once-daily liraglutide (1.8mg) in achieving glycemic control as compared to other anti-diabetic therapies.

Methods: A meta-analysis across seven phase 3 studies was performed to determine the observed mean changes in HbA1c from baseline to week 26 by baseline HbA1c category (≤ 7.5%, >7.5-8.0%, >8.0-8.5%, >8.5-9.0%, >9.0 %). In addition, logistic regression was used to compare the percentage of subjects achieving the AACE target HbA1c of ≤6.5% by baseline HbA1c category.

Result: All diabetes therapies improved glycemic control across all baseline HbA1c categories, with greater reductions at higher baseline HbA1c levels as compared to placebo (added to background therapy). The greatest reductions were observed in the liraglutide group and ranged from 0.7% in the ≤7.5% category to 1.8%, in the >9.0% category. These reductions were followed by insulin glargine (0.5-1.7%) and exenatide (0.5-1.4%). Subjects taking sulfonylureas (SUs) and sitagliptin had a narrower margin of reduction from 0.1% in the ≤7.5% category to 1.3%, in the >9.0% category. Thiazolidinediones (TZDs) had the narrowest margin of reduction, from 0.2% in the ≤7.5% category to 0.5%, in the >9.0% category. Sixty-two percent (62%) of subjects on liraglutide in the ≤7.5% category achieved HbA1c ≤6.5% as compared to 23-44% of subjects taking other anti-diabetic therapies; p-values from <0.001 to 0.030. About 10-12% of subjects on liraglutide and insulin glargine in the >9% category achieved HbA1c ≤6.5% as compared to 0-6% of subjects taking other anti-diabetic therapies; p-values from <0.0001 to 0.2036 with 4 out of 6 comparisons being statistically significant (p<0.05).

Conclusion: Liraglutide consistently showed benefit compared to other commonly used anti-diabetic therapies in subjects across all baseline HbA1c categories as evidenced by number of subjects achieving the AACE target HbA1c of ≤6.5%.
**Abstract #223**

**LATE ONSET HYPERSENSITIVITY REACTION WITH SUB-CUTANEOUS INSULIN IN TYPE 1 DIABETIC – A CASE REPORT**

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**Background:** Human insulin allergy-immediate or late type III reaction is a rare event. It is suspected upon noticing immediate symptoms following insulin injections ranging from urticaria and simple rash to dyspnea, angioedema and hypotension.

**Case Presentation:** We report a 32 year old patient, suffering from type 1 diabetes for the past 15 years, well controlled on Humolog Mix 25 (NPH 75%, Lispro 25%). The patient presented with allergic skin reaction at injection site for 20 days with Humolog Mix 25. He initially changed the pen, but the reaction persisted. He was advised to shift back to Humulin 70/30, which he had used in the past with good tolerance but same reaction occurred. He was then tried on all the different brands and types of insulin, including Humulin R, Humulin N, Lispro, Glulisine, Aspart, Detemir and Glargine, in combination and separately. He was also advised to take antihistamines, followed by oral prednisolone, but the allergic reaction continued to increase in severity. Finally, it was then decided to admit him for glycemic control and possible desensitization. In hospital, glycemic control was achieved through use of intravenous insulin to which he had no allergic reaction. Once this was done, he was started on subcutaneous Humulin R at a rate of 0.012 units/hour (166% dilution with normal saline). This was increased at a rate of 0.012 units/hour reaching to a maximum of 0.288 units/hour at 24 hours. The patient tolerated this regime well. The concentration of subcutaneous insulin was gradually increased over the next 48 hours to a maximum of 4.8 units/hour (at 10% dilution). No reaction occurred during this time. He was then switched to undiluted Humulin R pre-meal three times daily and adjusted accordingly. Once this was achieved, Glargine was added as a basal bolus with 4mg of Kenacort (triamcinolone acetonide). Patient was discharged home on pre-meal 16 units of Humulin R and 30 units of bedtime Glargine with Kenacort 4 mg. At one week follow up he was still allergy free and maintaining his sugars.

**Discussion:** Insulin allergy is a life threatening condition for type 1 diabetics. If no insulin is administered patient may soon go to diabetic ketoacidosis. The immediate management is the control of sugar and a possible fluid and electrolyte balance. Fortunately, almost all the reported patients were allergic to subcutaneous insulin administration only. The first step is to start insulin infusion and normalization of sugars. Once patient’s condition is stable, subcutaneous injection of a very low dose of insulin on hourly basis with a gradual increase in the dose and decrease in dilution can desensitize the patient. Sometimes addition of anti histamine and steroid can give an added advantage on fastening of desensitization at the cost of steroid induced increase in sugars.

**Conclusion:** Insulin allergy is a rare but severe condition, especially in Type 1 diabetics, that calls for immediate management. Patient may respond well to continuous intravenous infusion followed by gradual desensitization.

**Abstract #224**

**INSULIN RESISTANCE CORRELATES WITH THROMBOTIC AND INFLAMMATORY FACTORS**

Rozalina Grubina, MD, Rickey E. Carter, PhD, K. Sreekumaran Nair, MD, PhD

**Objective:** Type 2 diabetes mellitus (T2DM) is a cardiovascular disease (CVD) equivalent, while the related metabolic syndrome (MetS) is a cluster of risk factors that independently increase CVD risk. Although both T2DM and MetS are known to be pro-thrombotic states, the mechanism of this association is elusive and controversial. Because atherosclerosis is the result of thrombotic and inflammatory events, both pathways contribute to CVD risk. Moreover, because they are also characterized by altered hepatic insulin signaling, insulin sensitivity may in fact be the missing link behind the high rate of thrombotic events in patients with T2DM and MetS.

**Methods:** Forty two volunteers with a wide range of insulin sensitivities were recruited, including Asian Indians with (I-D; n=14) and without (I-C; n=14) diabetes, and Northern European Americans without diabetes (C-C; n=14). Insulin sensitivity was measured as the mean glucose infusion rate (GIR) using the euglycemic-hyperinsulimic clamp. Multiple regression analysis was used to quantify the association of between GIR and inflammatory events in patients with T2DM and MetS.

**Results:** Insulin sensitivity was uniformly lower in diabetic (I-D) than non-diabetic (I-C and C-C) subjects regardless of race (p<0.001). It was also lower in Indian (I-D and I-C) than Northern European (C-C) participants regardless of diabetic status (p<0.001). Insulin sensitivity correlated positively with adiponectin (r = 0.62; p<0.001) and HDL cholesterol, CRP, TNFα, and interleukin-6 (IL-6), while adjusting for age, sex, and BMI (presented as correlation coefficient, r).

**Conclusion:** In the setting of T2DM and MetS, insulin resistance is associated with elevated inflammatory markers and reduced insulin sensitivity.
Importantly, there was no association between insulin sensitivity and fibrinogen, CRP, or non-HDL cholesterol.

**Discussion:** We systematically quantified and correlated key inflammatory and thrombotic factors with insulin resistance across a wide range of insulin sensitivities, establishing for the first time a direct relationship between inflammation, thrombosis, and metabolic dysfunction. Thus, insulin sensitivity is associated with lower levels of pro-inflammatory (IL-6, CRP, TNFα) and pro-thrombotic (PAI-1, TG) factors, and higher levels of HDL-C and adiponectin.

**Conclusion:** Additional studies are currently under way to establish possible causality of this relationship and ultimately disrupt it, paving the way toward focused treatment of thrombosis in patients with T2DM, MetS, and other inflammatory and insulin-resistant states.

**Abstract #225**

**PREPONDERANCE OF CARDIOMETABOLIC RISK FACTORS IS DETERMINED BY OBESITY, BUT NOT PARENTAL HISTORY OF DIABETES IN NORMOGLYCEMIC SUBJECTS**

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**Objective:** Cardiometabolic risk factors (CRF) are associated with increased prevalence of diabetes and cardiovascular disease. In comparison with subjects without metabolic syndrome, the risk of cardiovascular death is increased about twofold; while incident diabetes is increased fivefold in people with metabolic syndrome. Some studies have reported a genetic basis for the aggregation of CRF in some subjects. Given that family history of diabetes constitutes a genetic proxy for metabolic disease, we sought to compare the prevalence of CRF in offspring of diabetic or non-diabetic parents.

**Methods:** Forty-four offspring of diabetic parents were matched in a case-control fashion for age, gender, race and BMI with 44 offspring of non-diabetic parents. Anthropometry and blood chemistry were done to determine metabolic risk status. Subjects then underwent 75 g OGTT after overnight fasting, with blood sampling for glucose and insulin at 0, 30 and 120 minutes. Insulin resistance and β-cell function were estimated using Homeostatic Model Assessment (HOMA-IR and HOMA-B respectively). Urine microalbuminuria was determined. Metabolic syndrome was defined by a modified NCEP criteria (all subjects were normoglycemic). Subjects with IFG and IGT were excluded from the study. Statistical analyses were performed by paired t-test, Chi square and multiple logistic regression methods using SPSS statistical package.

**Results:** Subjects were aged 39 ± 10 years with mean BMI was 29 ± 6 Kg/m². BP, waist circumference, triglyceride, HDL, and microalbuminuria were similar between the two groups (p>0.06), but HOMA-IR and HOMA-B were significantly higher in offspring of diabetic parents (1.10 ± 0.97 vs 1.49 ± 0.76; p<0.02 and 67.4 ± 51.2 vs 90.3 ± 67.1 p<0.04 respectively). The prevalence of CRF and metabolic syndrome was comparable in the two cohorts (p>0.3). Irrespective of parental history of diabetes, obese subjects showed significant (>3-fold) preponderance of CRF when compared with non-obese individuals in the same cohort; but subjects in the same BMI category exhibited similar risk status in the two cohorts. Multivariate analysis showed that BMI was the only independent variable associated with the prevalence of CRF (p<0.0001), while parental history of diabetes, age, race, HOMA-IR and HOMA-B were not (p>0.2).

**Conclusion:** In comparison with subjects without parental history, normoglycemic offspring of diabetic parents show evidence of diminished insulin action and compensatory augmentation of insulin secretion. The influence of genetic traits which predispose to CRF, diabetes and cardiovascular disease may be modulated by obesity. Therefore, maintaining a healthy body weight could extinguish the effect of unfavorable heredity on metabolic risk.

**Abstract #226**

**LINAGLIPTIN IMPROVES GLYCEMIC CONTROL INDEPENDENT OF BODY MASS INDEX IN PATIENTS WITH TYPE 2 DIABETES**

Angelina Lee Trujillo, MD, FACE, Marc Rendell, Steven G. Chrysant, Angela Emser, Maximilian von Eynatten, Sanjay Patel, Hans-Juergen Woerle

**Objective:** Three randomized, double-blinded, placebo-controlled, phase 3 trials for the DPP-4 inhibitor linagliptin examined its safety and efficacy of glycemic control as monotherapy, as add-on to metformin, or as add-on to metformin + sulfonylurea in patients with type 2 diabetes (T2D). Identical endpoints, linagliptin dosing, and a large cohort size (N=2,258) facilitate subgroup analyses using the pooled dataset. Given the need for evaluation of the safety and efficacy of new antidiabetic agents on a background of other medications and patient comorbidities, we analyzed pooled patient data to evaluate the effect of key patient characteristics on the safety and
efficacy of linagliptin. Some research studies have shown a reduced treatment response in obese individuals with T2D, thus we determined the response to linagliptin treatment in overweight and obese patients.

**Methods:** The primary efficacy outcome in all three pooled studies was mean change from baseline in HbA1c at 24 weeks. The incidence of any adverse events (AE) were recorded. Patients were categorized according to baseline BMI: normal weight (<25), overweight (25 to <30), or obese (>30).

**Results:** The mean (±SD) patient age and baseline BMI were 57 ± 10 years and 29.0 ± 4.9kg/m2, respectively. Patients were predominantly White (58%) and Asian (42%), with an equal gender distribution. 57% of patients had a mean disease duration of >5 years, 40% of patients were overweight (mean BMI 27.5±1.4), and 38% were obese (mean BMI 34.1 ± 3.0). Mean baseline HbA1c (±SD) and HOMA-IR were 8.1% (±0.8) and 4.7 ± 5.3 mU/L•mmol/L, respectively. In the pooled analysis of efficacy, linagliptin showed significant reductions in HbA1c levels in all 3 groups with no significant difference based on BMI. Mean change from baseline in HbA1c levels among obese patients was -0.61% (±0.79), compared to a similar reduction of -0.60% (±0.85) in overweight patients and -0.66% (±0.93) in patients with normal BMI. The overall AE rate did not differ significantly between the 3 groups, and the most commonly observed AE was hypoglycemia; however the overall hypoglycemic event rate with linagliptin in monotherapy and add-on to metformin therapy was very low (≤1.0%). A higher rate of hypoglycemic events only occurred in the study that used a background therapy with metformin and a sulfonylurea; this was expected due to the combination with SU.

**Conclusion:** Treatment with linagliptin provided clinically meaningful HbA1c reductions in patients with T2D independent of BMI category, with a safety profile comparable to placebo. The reductions in HbA1c were consistent with results from the primary phase 3 trials.

**Abstract #227**

**IN SEARCH OF A SINGLE GLYCEMIC METRIC TO BENCHMARK INSTITUTIONAL DIABETES PERFORMANCE: THE PERFECT DIABETIC DAY**

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*Brett MacLaren, MBA*

**Objective:** Develop a single glycemetic metric which can be used to benchmark institutional diabetes care that also conveys clinical meaning to hospital caregivers.

Since 2002 at our four community hospital system, all BGs in the electronic record of patients with a secondary diagnosis of diabetes are collected in a database. Diabetes improvement initiatives were started in 2003. We developed a family of glucometrics. In 2010, we measured the fraction of perfect diabetic days (PDDs) over 8 years. We defined PDDs as days during which all BG’s per patient per day are between 70-180 mg/dl. The yearly improvement and the rate of change of PDDs was determined. We compared PDDs to all of our other glucometrics.

**Results:** 1.8 million BGs on ½ million diabetic days are included in this analysis. The database is growing by 25,000 BG/month. Prior to the improvement projects, PDDs in the system ranged from 20%-34%. After 8 years, this increased to 40%-47%. Two phases of improvement are evident. During the first 3-4 years a 7%-10% yearly improvement was achieved. Subsequently the rate decreased to 1-2% per year. We found that compared to other glucometrics (e.g., average BGs or BG distributions) the PDDs metric is readily accepted by the hospital staff and it provides more clinical relevance than other metrics.

**Discussion:** AACE and ADA recommend that BGs be maintained at least between 70-180 mg/dl for all hospitalized diabetic patients. Levels outside this range are felt to be potentially harmful. While a variety of metrics have been proposed, no single metric has emerged as “the standard” to compare institutional performance, set institutional targets, and help balance the drive to improve control with resources available for diabetes care. We propose that the PDDs is such a metric. This single metric takes into account desirable glycemia, permits a reasonable degree of patient care variation, and is easily understood by hospital staff. The optimal level of PDDs needs to be determined. Our results suggest that 50% PDDs is attainable with sustained improvement efforts. As inpatient diabetes care matures, PDDs above 50% can be expected.

**Conclusion:** The PDDs can serve as single metric to benchmark institutional diabetes care. PDDs of 20%-30% represents poor institutional performance. A 7%-10% improvement rate can be expected during the first 3-4 years of an improvement project. Subsequently, the rate will slow to below 2% per year. A 50% PDDs level is achievable; greater than 50% may be difficult to reach and sustain.
Abstract #228

COMPARISON OF INSULIN DELIVERY SYSTEM RATING BY PEOPLE WITH DIABETES USING FINESSE™ INSULIN BOLUS-PATCH WITH THEIR USUAL PEN/SYRINGE/PUMP FOR DELIVERY OF MEALTIME INSULIN

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Objective: We compared subjects’ rating of insulin delivery systems when they used a novel insulin bolus-patch (Finesse™) versus usual device (pen/syringe/pump) to deliver mealtime insulin under simulated use.

Methods: A total of 169 subjects with diabetes (113 type 1, 56 type 2) ages 7 to 85 years (mean 41 years) were evaluated with respect to their responses to a validated insulin delivery system rating questionnaire (IDSRQ) when they used their usual device versus the bolus-patch under simulated use. Entry in the study required subjects to inject insulin ≥ 2 times a day or use an insulin pump. For usual device, subjects used a pen (21%), syringe (52%) or pump (27%) for a median of 6 years with a mean of 3 injections of insulin per day. The bolus-patch is wearable for up to 3 days, allows manual delivery of mealtime insulin subcutaneously through a soft cannula, holds up to 200 units of insulin, and administered in 1 or 2 unit increments by actuating buttons on the device. The bolus-patch was worn on the abdomen (83%), arm (10%), thigh (6%) and gluteal region (1%). The IDSRQ responses were coded on scales from 1 to 4 or 1 to 5 and summary measures were made for 6 subscales. This analysis combined data from 11 human factors studies conducted from 2007-2010. Repeated measures ANOVA with the grouping category of study were performed for the summary scale measures to justify pooling the data over studies. Delivery systems were then compared using Wilcoxon signed rank tests for paired data. Interactions of gender, age, type of diabetes and usual device on method comparisons were performed by repeated measures ANOVA.

Results: Subjects scored the bolus-patch better versus their usual device on 6 of 6 subscales on the IDSQR during simulated use. The bolus-patch interfered less with daily activities (p<0.001), helped better adherence to insulin dosing regimen (p<0.001), created less worry about diabetes (p<0.001), improved feelings about oneself (p<0.001) and was associated with improved device satisfaction (p<0.01). Subjects rated the bolus-patch as very easy to use (average rating 5.2 on a scale of 1-6; 1 = extremely difficult; 6 = extremely easy) and preferred the bolus-patch overall (p<0.001). Pen and syringe users had more favorable responses to the bolus-patch than did pump users. The bolus-patch was preferred by females and males, children and adults and subjects with type 1 or type 2 diabetes.

Conclusion: Under simulated use conditions, the bolus-patch had significantly more favorable ratings than the usual device for delivery of mealtime insulin. Learnings from these studies were used to iterate the design of the product to improve safety and usability.

Abstract #229

AUTOMATIC VERSUS MANUAL CALIBRATION OF CONTINUOUS GLUCOSE MONITORING SENSORS

Scott Winfred Lee, MD, Francine Kaufman, MD, John B. Welsh, MD, PhD, John Shin, MBA, PhD

Objective: Sensors for continuous glucose monitoring (CGM) must be calibrated to ensure fidelity with blood glucose values. Optimal sensor accuracy was assumed to be related to calibration occurring during stable glycemic periods, when glucose levels are neither rising nor falling. The automatic calibration algorithm uses every available blood glucose value, regardless of glucose trend.

Methods: STAR 3 was a 1-year, multi-center, randomized, controlled trial. We compared the efficacy of sensor-augmented pump therapy (SAP) with that of a regimen of multiple daily insulin injections (MDI) in 485 patients (329 adults and 156 children) with inadequately controlled type 1 diabetes. Post-hoc analysis of sensor accuracy in patients using SAP was performed comparing automatic calibration and manual calibration.

Results: Automatic sensor calibration was performed 272,043 times (89.8%) and manual calibration was performed 30,774 times (10.2%) in SAP arm. Sensor accuracy (MARD%) comparison between automatic calibration and manual calibration revealed no significant differences between either method. Sensor accuracy was consistent at different rates of change of sensor glucose values. At 1 year, the baseline mean glycated hemoglobin level (8.3% in the two study groups) had decreased to 7.5% in the SAP arm, as compared with 8.1% in the MDI arm (P<0.001). The rate of severe hypoglycemia in the pump-therapy group (13.31 cases per 100 person-years) did not differ significantly from that in the injection-therapy group (13.48 per 100 person-years, P=0.58).

Discussion: There was no significant difference in CGM sensor accuracy when either automatic calibration or manual calibration was employed. Sensor accuracy was insensitive to the rate of change of sensor glucose values.

Conclusion: Adult and pediatric patients in the STAR 3 trial primarily using automatic calibration had a significant improvement in glycated hemoglobin levels, without an increase in hypoglycemia.
Abstract #230

INSULIN SENSITIZERS AND DIABETIC CONTROL DECREASE THE RISK OF COLON POLYPS

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**Background**: Patients with diabetes mellitus have an increased risk for the development of colon cancer and colon polyps. Since majority of colon cancers originate from colon polyps, identifying factors that reduce the occurrence of polyps may help reduce the risk of colon cancers among diabetic patients.

**Methods**: We conducted retrospective analysis on all outpatient colonoscopies performed at ten Veterans affairs (VA) VISN representing half of all VA medical centers, obtained from VA national datasets, the medical SAS and Decision support system from 2002 to 2008. We included all adult patients with diabetes mellitus receiving first VA documented colonoscopy. We excluded patients with concomitant malignancy or human immunodeficiency virus infection. Patients were defined as having polypectomy if they had (a) polyp diagnosis and biopsy, or (b) colonoscopy with polypectomy or (c) colonoscopy with hot biopsy. Logistic regression analysis was used to estimate adjusted odds ratio for polypectomy.

**Results**: This study evaluated 132,354 patients, comprising one of the largest cohorts of patients with diabetes undergoing a colonoscopy. Of these, 54,741 (41.4%) had polypectomy. The mean age was 62.79 (± 8.87), 96.9% male. After adjusting for age, gender, race, obesity, charlson comorbidity score, anti diabetic medications, diabetic control, aspirin, NSAID, statin, tobacco abuse, alcohol abuse we found use of insulin sensitizers (metformin (OR = 0.94) and thiazolidinediones (OR = 0.83)) and Hemoglobin A1c (Less than or equal to 6.5 vs. greater than 6.5 (OR = 1.06)) to be significantly associated with decreased occurrence of colon polyps. These independent predictors were in addition to previously established significant predictors of polyps such as age (OR = 1.01), obesity (OR = 1.11) aspirin use (OR = 0.92) and NSAIDs (OR = 0.63). Additionally we found that African American race (OR = 0.77 compared to caucasian), female sex (OR = 0.65) and Hispanic ethnicity (OR = 0.82) to be significantly associated with decreased occurrence of colon polyps. Interestingly in this well powered national diabetic cohort, post adjusted analysis we were not able to detect a significant relationship between insulin and statin use with the occurrence of colon polyps.

**Conclusions**: Diabetic control and use of insulin sensitizers may decrease risk of colon polyps and possibly reduce risk of colon cancers among diabetic patients.

Abstract #231

ETHNIC AND REGIONAL VARIATIONS IN ANTHROPOMETRY AMONG NIGERIANS

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**Background/Objective**: Obesity is widely accepted as a major factor driving the pandemic of diabetes and metabolic syndrome. Genetic and ethnic factors largely account for variations in anthropometry measures worldwide. This consideration accounts for the differences in recommended cut-points for anthropometry measures for different ethnic/racial groups. International diabetes Federation (IDF) recommends that European figures be extrapolated for Africans. The Nigerian state is multi-ethnic, hence may not even have fairly homogenous anthropometry attributes. Presently there are no nationwide data on anthropometry indices in Nigeria. The aim of this study was to determine regional/ethnic distribution of anthropometry among diabetic and apparently healthy non-diabetic Nigerians.

**Methods**: A cross-sectional survey was designed and all members of AACE-Nigeria across the country were requested to collect and return data using a pre-agreed simple protocol. The protocol essentially contained demography and anthropometry [weight in kg, height in meters, body mass index (BMI) and waist circumference (WC) in cm]. By consensus, the WC were measured at the level of widest abdominal girth. Data were consecutively collected from diabetic patients attending the hospitals and apparently healthy, non-diabetic hospital workers where members practiced. Data were captured on excel and analysed using SPSS version 16; significant p-value was set at <0.05.

**Results**: Data were received from all 6 geo-political zones in the country: Calabar (South-South), Enugu (South-East), Lagos and Ibadan (South-West), Kano (North-West), Ilorin (North-Central) and Maiduguri (North-East). A total of 1299 subjects comprising 711 diabetics and 588 apparently healthy non-diabetics were recruited. There were 383 (54%) female diabetics and 263 (44.7%) female non-diabetics. The mean ages for diabetics and non-diabetics were 42.3 (SD 18.2) and
Abstract #232

BETA CELL RESPONSE TO A MIXED MEAL IN PATIENTS WITH TYPE 2 DIABETES

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Chioma Unachukwu, BSc, MBBS, FWACP, FACE

Objective: To assess the response of the beta cell to a standardized mixed meal and its relationship with glycemic control in patients with type 2 diabetes.

Methods: Ninety patients being managed for type 2 diabetes were recruited consecutively as they attended the diabetic clinic for follow-up. The patients were assessed with questionnaires to obtain demographic data. Weight, height, body mass index and waist circumference was measured. Blood samples were collected for analysis of fasting plasma glucose and fasting C peptide. Patients were given their usual diabetic drugs and then served with a standard meal calculated to contain 50g of carbohydrate, providing 500kcal. Blood samples were collected 2 hours after the start of the meal for postprandial glucose (PPG) and postprandial C peptide levels. Fasting and postprandial beta cell responsiveness was calculated. Data were analyzed with SPSSv17 and p value < 0.05 considered significant.

Results: The mean age, duration of diabetes, and body mass index of the patients were 57.7 ± 10.8 years, 6.77 ± 6.53 years and 27.54 ± 6.01 kg/m² respectively. The mean fasting plasma glucose and 2 hour postprandial glucose were 7.51 ± 3.39 mmol/l and 11.02 ± 4.03 mmol/l respectively while the mean HBA1c was 9.0 ± 2.5%. The mean fasting C-peptide was 1.44 ± 1.80 µg/ml. Many of the patients (56.7%) had low fasting C-peptide levels. The mean fasting C-peptide was 1.44 ± 1.80 µg/ml. Many of the patients (56.7%) had low fasting C-peptide levels. The mean fasting C-peptide was 1.44 ± 1.80 µg/ml. Many of the patients (56.7%) had low fasting C-peptide levels. The mean fasting C-peptide was 1.44 ± 1.80 µg/ml. Many of the patients (56.7%) had low fasting C-peptide levels. The mean fasting C-peptide was 1.44 ± 1.80 µg/ml. Many of the patients (56.7%) had low fasting C-peptide levels. The mean fasting C-peptide was 1.44 ± 1.80 µg/ml. Many of the patients (56.7%) had low fasting C-peptide levels. The mean fasting C-peptide was 1.44 ± 1.80 µg/ml. Many of the patients (56.7%) had low fasting C-peptide levels. The mean fasting C-peptide was 1.44 ± 1.80 µg/ml. Many of the patients (56.7%) had low fasting C-peptide levels. The mean fasting C-peptide was 1.44 ± 1.80 µg/ml. Many of the patients (56.7%) had low fasting C-peptide levels. The mean fasting C-peptide was 1.44 ± 1.80 µg/ml. Many of the patients (56.7%) had low fasting C-peptide levels. The mean fasting C-peptide was 1.44 ± 1.80 µg/ml. Many of the patients (56.7%) had low fasting C-peptide levels. The mean fasting C-peptide was 1.44 ± 1.80 µg/ml. Many of the patients (56.7%) had low fasting C-peptide levels. The mean fasting C-peptide was 1.44 ± 1.80 µg/ml. Many of the patients (56.7%) had low fasting C-peptide levels. The mean fasting C-peptide was 1.44 ± 1.80 µg/ml. Many of the patients (56.7%) had low fasting C-peptide levels. The mean fasting C-peptide was 1.44 ± 1.80 µg/ml. Many of the patients (56.7%) had low fasting C-peptide levels.

Discussion/Conclusion: There were a large proportion of patients with low fasting C peptide levels suggesting low beta cell reserve. This has been reported in similar studies demonstrating low beta cell reserve in African patients with type 2 diabetes. There was poor glycemic control in the patients. Beta cell responsiveness correlated significantly with glycemic control. The poor beta cell function may have resulted in the poor glycemic control in the patients. These patients may have required insulin for proper glycemic control.

Conclusion: The patients had low C peptide levels.
with poor beta cell response to the meal. Fasting and postprandial beta cell responsiveness were significant determinants of blood glucose levels.

Abstract #233

HIGH PREVALENCE OF SELF-REPORTED HYPOGLYCEMIA RATES FOR DIABETES MEDICATIONS AMONG ADULTS WITH TYPE 2 DIABETES MELLITUS

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Objective: Hypoglycemia can cause significant morbidity, but has not been well investigated in a real world setting, especially for oral antidiabetic drugs (OADs). We assessed the rate of hypoglycemia among adults with type 2 diabetes mellitus (T2DM) based upon their diabetes treatment regimen.

Methods: Respondents to the 2008 U.S. Study to Help Improve Early evaluation and management of risk factors Leading to Diabetes (SHIELD) survey reported the number of times they experienced hypoglycemia (low blood sugar) in the past 4 weeks and past 12 months and their current medications as indicated on their prescription bottles.

Results: Of 2,801 respondents with T2DM, 15% were not currently on diabetes therapy; 64% received OADs in combination or as monotherapy; 8% received insulin alone; and 13% received a combination of insulin and OADs. About 43% of respondents who received insulin alone (n = 221) self-reported hypoglycemia in the past 4 weeks; with an average of 6.2 episodes. Of 361 respondents who received insulin + OADs, 40% reported hypoglycemia in the past 4 weeks, with an average of 6.4 episodes. Among those receiving OADs, hypoglycemia rates were higher among users of sulfonylureas (n=1,045). Seventeen percent of those indicating no current treatment with a sulfonylurea (n=1,109) reported hypoglycemia in the past 4 weeks versus 24% in the past 4 weeks for sulfonylurea users (p<0.001). Sulfonylurea users reported an average of 6.3 episodes in the past 4 weeks compared with an average of 5.7 episodes for non-sulfonylurea OAD users (p >0.05). Similar rates of hypoglycemia were reported over 12 months.

Conclusion: Risk of hypoglycemia is substantially increased in patients with T2DM who receive either sulfonylureas or insulin, compared with other OADs. Consideration should be given for using classes of medication with lower rates of hypoglycemia when treating T2DM adults to reduce the potentially serious adverse outcomes associated with hypoglycemia.

Abstract #234

USE OF STRUCTURED SMBG IMPROVES GLYCEMIC CONTROL AND PROMOTES EARLY AND AGGRESSIVE TREATMENT IN NON-INSULIN TREATED DIABETES

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Objective: The American Association of Clinical Endocrinologists (AACE) supports use of self-monitoring of blood glucose (SMBG) to detect glucose patterns, assess current glycemic control and monitor therapy. We assessed the value of structured SMBG in a prospective, cluster-randomized, multi-centered clinical trial.

Methods: We recruited 483 poorly controlled (HbA1c ≥7.5%), insulin-naïve T2DM patients who were randomized to structured testing (STG) or active usual care (ACG). STG subjects used the Accu-Chek® 360° View Blood Glucose Analysis System to collect/interpret 7-point glucose profiles (before/after meals and bedtime) over 3 consecutive days. STG patients completed the tool quarterly and brought it to medical visits. STG patients and physicians received standardized instruction in SMBG pattern recognition/interpretation. All patients received free blood glucose meters/test strips.

Results: At 12 months, intent-to-treat (ITT) analysis revealed that STG subjects evidenced significantly greater mean improvement in HbA1c than ACG subjects over the 12 months (-1.2% vs. -0.9%; ∆=-0.3%; p=0.04), significantly lower average preprandial and postprandial glucose levels at all meals and bedtime (P<0.001) and significant reductions in mean amplitude of glucose excursions (MAGE), from a mean (SE) 38.5 mg/dL (0.9) at month 1 to 34.3 mg/dL (1.0) at month 12; P=0.0003. Significantly more STG physicians recommended a medication change (60% vs. 23%, p<0.0001), lifestyle change (41% vs. 9%, p<0.0001) and a medication change and/or lifestyle change (76% vs. 28%, p<0.0001) compared with ACG physicians. All subjects (ACG and STG) who had a treatment change recommended at month 1 achieved significantly greater HbA1c reductions at 12 months than those that did not (-1.3 vs. -0.8, ∆=0.5, p<0.002); however, significantly more STG patients received a treatment change recommendation at the month 1 visit compared to ACG patients, regardless of the patient’s baseline HbA1c level: 179 (75.5%) vs. 61 (28.0%); P<0.0001.

Discussion: The greater frequency of therapy change recommendations indicates a more aggressive treatment strategy by STG physicians. Improvement in HbA1c associated with month 1 interventions demonstrates that early therapeutic intervention is important.
**Conclusion:** An intervention that encourages the collection and collaborative use of structured SMBG data facilitates improved glycemic control and promotes more timely and aggressive treatment changes in poorly controlled, non-insulin-treated type 2 patients. This finding directly supports AACE recommendations regarding periodic, comprehensive SMBG in T2DM patients as the standard of care.

**Abstract #235**

**SUBANALYSES OF SMBG IN THE ACT (ACTIONS WITH THE CONTOUR BLOOD GLUCOSE METER AND BEHAVIOR IN FREQUENT TESTERS) TRIAL**

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**Background/Objective:** Self monitoring of blood glucose (SMBG) is a behavioral tool for patients with diabetes. Features on BG meters, such as meal markers for pre- and post-prandial BG levels and reminders for post-prandial testing, may prompt more focused self management, especially at mealtimes. This 6 month randomized, multicenter study evaluated if use of a BG meter (Bayer’s CONTOUR) with meal marker + audible reminder and diabetes education maintains or increases frequency of postprandial testing in frequent testers compared to diabetes education and standard features alone. The impact of the trial conditions on patients’ SMBG information, motivation and behavioral skills (IMB) on SMBG practice and decision-making, were evaluated from baseline to completion via IMB survey.

**Methods:** Subjects (n=211) had type 1 (n=120) or type 2 (n=90) diabetes, used prandial insulin at least 1x/day and tested BG at least 3x/day. Subjects received diabetes education and were randomized to Basic (no meal marker or reminder) or Advanced (meal marker + reminder) and instructed to record BG levels in their logbook. Subjects were seen at baseline, 6 weeks, 3 months, and 6 months. Baseline testing frequency was self-reported and meters were downloaded at visit 2-4. There were no mandated therapeutic actions between visits.

**Results:** As reported previously, for the primary endpoint of frequency of post-prandial testing, the Advanced testing group had significantly more frequent weekly post-prandial tests, and significantly more paired pre and post-prandial tests than the Basic group at each follow-up, as well as demonstrating significant improvement in understanding pre and post-meal results over time. Both groups had significant declines in A1c values (Basic 8.3% to 7.9 % and Advanced 8.0% to 7.8%). The decrease in the basic group compared to advanced group was statistically significant. Hence, subanalyses were performed to further explore correlations between SMBG behaviors and glycemic control, including A1c. Patients in practice may bring either a logbook or a meter for download, a correlation coefficient of the frequency of results recorded was computed, and found to be 73%. Correlation analysis of postprandial testing frequency and A1c show that in both treatment groups, A1c decreases significantly (p = 0.0062) as post-prandial testing frequency increases.

**Conclusion:** In this study, there is strong agreement between frequency of BG results recorded in logbooks versus meter downloads. Additional subanalyses of SMBG behaviors and glycemic control show that postprandial testing is correlated with a significant decrease in A1c levels.

**Abstract #236**

**DIABETIC STIFF HAND SYNDROME A COMMONLY OVERLOOKED DIAGNOSIS**

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**Objective:** Musculoskeletal complications are most often seen in patients with a long-standing history of diabetes. Some of the complications have a direct association with diabetes, while others have a suggested but unproven association. These complications involve the joints of the hand, shoulder and feet.

**Case Presentation:** This is a 28 year old Hispanic woman with a 12 year history of poorly controlled type 1 DM complicated by non proliferative retinopathy. She is on an insulin pump for four years and developed pain and stiffness in both hands for the past one year. Pain is described as dull about 5/10, aggravated by movements and constant throughout the day, worsening at night. Stiffness is worst in the morning, lasting about 5 to 10 minutes. She also has limitation of movements of all joints in her hands with associated tightening of the skin. She didn’t have skin color changes with cold exposure and difficulty of swallowing and dry mouth or eyes. Physical examination: Bilateral boggy swelling of the PIP joints with limited ability to make full fist, more pronounced on the left hand is noted. She has “prayer sign” and limited right shoulder movement because of pain. Sensation and muscle power are normal. Laboratory data revealed HbA1C of 8.9%, LDL of 76 mg/dl and ESR of 1mm/hr and no microalbuminuria. All rheumatologic work up is
negative. X-Ray of the shoulders and hands didn’t reveal any pathology except for mild prominence of the bilateral PIP joints and soft tissue bilaterally. 

**Discussion:** Diabetic cheiroarthropathy (DCA), known as diabetic stiff hand syndrome or limited joint mobility syndrome, has a prevalence of 8 to 50%, with most studies identifying the prevalence rate of 30%. Prevalence increases with duration of diabetes and poor glycemic control. The possible pathogenesis is hyperglycemia-induced glycosylation of collagen in the skin and periarticular tissue. This results in increased cross-linking of collagen and thickening of tendon sheaths, joint capsules and skin. In advanced stage flexion contractures of the fingers may develop leading to “prayer sign” and “tabletop sign”. There is a strong correlation with microvascular complications, particularly retinopathy consistent with our patient’s history. The treatments of DCA include optimizing glycemic control, analgesics and stretching exercises.

**Conclusion:** Clinicians should be aware of the possible musculoskeletal complications of diabetes. Asking patients about their symptoms and monitoring for signs of musculoskeletal complications can be an invaluable part of overall diabetes care.

**Abstract #237**

PROLONGED AMNESIA DUE TO HYPOGLYCEMIA

Archana Reddy, MD, Kenneth Rosenman, MD, G. Matthew Hebdon, MD, PhD, Ved Gossain, MBBS, MD

**Objective:** To report a case of prolonged amnesia due to hypoglycemia.

**Case Presentation:** A 58 year old male with a 19 year history of Type 1 Diabetes mellitus (DM1) was seen in an occupational clinic for clearance to return to work after an episode of prolonged amnesia. Historically, his diabetes had been poorly controlled on a regimen of NPH, regular insulin and pre-meal insulin lispro. About 3 months prior to the episode of amnesia, this was revised to insulin detemir in AM with pre-meal insulin lispro, and his HbA1C decreased from 10% to 6.9 %. He experienced queasiness 4 hours post dinner, which resolved with a bedtime snack. He did not check his blood glucose when symptomatic but denied other changes in sensorium. He worked as a gardener during spring and summer, typically from 6AM to 2:30 PM. On the day of the episode, his morning blood glucose was 90 mg/dL. He took detemir 54 units at 5AM, skipped his breakfast and did not take lispro. He began work at 6AM raking leaves until 9AM when he felt “queasy.” He did not check his blood sugar but got onto his tractor to drive to a nearby parking lot where he planned to eat a snack. He has only vague recollection of subsequent events. He drove 5-6 miles, ending up parked in a residential neighborhood. At around 5PM his wife called and he realized where he was. He then remembers eating a banana, yogurt and a sandwich. She picked him up; finding him still disoriented. His blood glucose was 130 mg/dL, about 20 minutes after the snack. For 7 hours he had been lost, with no recollection of events; we attribute this disorientation to hypoglycemia. He saw his physician the following day, his insulin was decreased, and he has had no similar episodes.

**Discussion:** Hypoglycemia is a limiting factor in achieving optimal glycemic control. For patients with DM1 on intensive insulin therapy, the risk of hypoglycemia is increased more than 3 fold. Typically, 2 episodes of symptomatic hypoglycemia per week and one temporarily disabling hypoglycemia occur per year. Classic symptoms of hypoglycemia include anxiety, palpitations, tremor, sweating and hunger. Neuroglycopenic symptoms including confusion, cognitive dysfunction, seizures, coma and death, are reported. Amnesia associated with hypoglycemia is usually transient. However, in this case, amnesia, most likely due to hypoglycemia, lasted 7 hours. Prior “too tight” a glycemic control might have resulted in hypoglycemia unawareness in our patient.

**Conclusion:** Although transient neurological impairment is common with hypoglycemia, episodes of prolonged amnesia can occur with serious consequences.

**Abstract #238**

NON-ISLET CELL TUMOR HYPOGLYCEMIA (NICTH) WITH HIGH IGF-1 IN LYMPHOMA

Peter Dahl, MD, Ulrick Espelund, David J. Straus, MD, Marcia F. Kalin, MD

**Objective:** To report the first known case of NICTH with high IGF-1 in a patient with lymphoma.

**Case Presentation:** The patient is a 68-year-old woman with recurrent follicular B-cell lymphoma diagnosed and treated with chemotherapy and radiation in 1987. In 1988, lymphoma recurred, and she was retreated with radiation. In 2004, lymphoma recurred again, but she remained under observation until 2009. In 2005, she had lung adenocarcinoma, treated with surgery; she currently has no evidence of disease. In 4/2008, she was hospitalized elsewhere for confusion and hypoglycemia; her fasting blood sugar (FBS) was 24 mg/dL. She was treated with diazoxide but hypoglycemia recurred. Fasting labs at our institution on 5/1/08 revealed FBS 34 (70-99 mg/dL), undetectable insulin (0-17 mcU/mL), undetectable beta hydroxybutyrate (0-43.9 mcg/mL),
Discussionproinsulin 4.0, IGF-1 99, IGF-2 293, pro-IGF-2 178. on 5/3/09 without recurrence of hypoglycemia. Fasting labs and has remained stable. Steroids were discontinued on induction rituximab and during maintenance rituximab rituximab 1/12/09-12/7/09. Adenopathy decreased after need for steroids to maintain euglycemia. She received trial of rituximab was initiated because of the continued she did not require treatment for lymphoma perse, but a trial of rituximab was initiated because of the continued for steroids to maintain euglycemia. She received rituximab 1/12/09-12/7/09. Adenopathy decreased after induction rituximab and during maintenance rituximab and has remained stable. Steroids were discontinued on 5/3/09 without recurrence of hypoglycemia. Fasting labs on 10/9/09 revealed FBS 93, insulin 4.6, C-peptide 2.2, proinsulin 4.0, IGF-1 99, IGF-2 293, pro-IGF-2 178.

Discussion: NICHT with high IGF-2 and high pro-IGF-2 has been well documented. This patient had high IGF-1, normal IGF-2, and normal pro-IGF-2 during hypoglycemia. Prior to this case, there has been only one report of NICHT with high IGF-1, in a patient with metastatic large-cell lung cancer; this report is the first known case of NICHT with high IGF-1 in a patient with lymphoma. As in the previously reported patients with NICHT and high IGF-1 or high IGF-2, this patient maintained euglycemia with steroid treatment. Treatment of the lymphoma with rituximab resulted in decreased adenopathy and resolution of hypoglycemia.

Conclusion: This report is the first known case of NICHT with high IGF-1 in a patient with lymphoma. IGF-1 normalized and hypoglycemia resolved with effective treatment of the lymphoma, suggesting that excess IGF-1 caused the hypoglycemia.

Abstract #239

GLUCOSE VARIABILITY AMONG ADMITTED TYPE 2 DIABETIC PATIENTS ON BOLUS ENTERAL FEEDING VERSUS CONTINUOUS ENTERAL FEEDING: A PILOT STUDY

Zarina Guevarra Lorenzo, MD, Jo-Anne Ponce, MD, Flordeluna Mesina, MD

Background: Glucose variability is associated with increased hospital morbidity and mortality. Enteral alimentation is the preferred modality of nutritional support administered as intermittent bolus or continuous tube feeding. Continuous tube feeding has been shown to improve glucose control in diabetic patients. Recent studies show that diabetes-specific formula reduces insulin requirements with lower mean amplitude of glycemic excursions (MAGE) and 24-hour glycemic variability. It is therefore hypothesized that continuous tube feeding using a diabetes-specific formula will decrease the glucose variability in diabetic patients requiring enteral alimentation.

Objective: To compare the glucose variability in two modes of enteral alimentation: continuous tube and bolus tube feeding using diabetes-specific formula.

Methods: Eight type 2 diabetic in-patients on enteral tube feeding were randomized to intermittent bolus tube feeding given every 4 hours for the first 3 days followed by continuous tube feeding for the next 3 days (Group 1) versus continuous feeding for the first 3 days followed by bolus feeding (Group 2). Each patient received 30 Kcal/kg/day of diabetes-specific formula. A long–acting insulin analog was given once daily for basal insulin coverage and a rapid–acting insulin analog given as correction insulin to target capillary blood glucose (CBG) of 140-180mg/dL. CBG was measured every 2 hours using the same glucose meter for 6 days. Baseline characteristics were recorded. Glucose variability was determined in terms of SD and MAGE.

Results: There were 6 males and 2 females with mean age of 64 years, BMI of 23 kg/m² and HBA1C of 7.5%. Both groups were similar at baseline. There was a clear pattern of variability when under bolus feeding with well-defined peaks and nadirs. The readings from the continuous feeding were also visibly variable but with lesser fluctuations between readings and smoother transitions. ANOVA for repeated measures during the continuous tube feeding did not differ significantly across the observation period (p=0.413) but differed significantly during bolus tube feeding (p<0.001). There was no significant difference with the mean glucose between two groups (p=0.24). There was a trend of greater total daily insulin dose received while in intermittent bolus feeding compared with continuous tube feeding (p=0.20). There was no significant hypoglycemia noted in the two groups.

Conclusion: Glucose variability was seen in both modes of enteral alimentation using diabetes-specific formula. However, there were lesser fluctuations and smoother transitions between readings in continuous tube feeding.

Abstract #240

SOME GLYCEMIC INDICES ARE RELATED TO NON TRADITIONAL CARDIOVASCULAR RISK FACTORS IN DIABETES MELLITUS

Anthonia Okeoghene Ogbera, MBBS, FMCP, FACE, Alfred Azenabor

Background: The excess risk for cardiovascular disease (CV) in type 2 diabetes mellitus (DM) may be explained by non-traditional risk factors.
**Objective:** The objective of this report is the evaluation of some non traditional CV risk factors and possible relationship with indices of glycemic control in DM.

**Methods:** The study design is cross sectional in nature and involved 200 patients with type 2 DM and 100 age and sex matched healthy controls. Glycemic control was assessed using fasting blood glucose, fructosamine and glycosylated haemoglobin tests. The non traditional risk factors studied included C reactive protein (CRP), Lipoprotein a (Lp (a), serum uric acid (SUA), microalbuminuria and fibrinogen.

**Results:** The overall prevalence rate of hyperfibrinoginaemia, elevated CRP, LP (a), microalbuminuria and hyperuricaemia in type 2 DM patients were 3.5%, 65%, 12%, 6% and 57% respectively. The mean levels of these CV risk factors were significantly higher in subjects with type 2 DM than that of the Control subject. There was a positive and significant correlation between HbA1c and FBS (r=0.46, p=0.0001) and HbA1c and fructosamine. (r= 0.49, p=0.0001). Using multiple regression analyses after adjustment for age and sex, fibrinogen and SUA levels were found to be significantly and linearly associated with HbA1c levels and microalbuminuria and CRP levels were significantly associated with FBS.

**Conclusion:** Glycosylated hemoglobin and fasting plasma glucose but not fructosamine are significantly associated with microalbuminuria, fibrinogen SUA and CRP in type 2 DM.

Abstract #241

**RELATIONSHIP BETWEEN ADMISSION BLOOD GLUCOSE AND THE TYPES OF STROKE**

Akinleye Taofiq Akinlade, MBBS, Anthonia Okeoghene Ogbera, MBBS, FMCP, FACE

**Objective:** To determine if there is a relationship between the admitting blood glucose (ABG) and the types of stroke in patients with stroke.

**Methods:** Fifty-one subjects consecutively admitted into the emergency ward of a tertiary hospital in Lagos, Nigeria for acute stroke, confirmed with brain computerized tomography (CT) scan were studied over a year period. Subjects’ clinical history and blood glucose were recorded at admission and analyzed.

**Results/Discussion:** Mean age (and standard deviation, SD) of study subjects was 60 (12) years, ranging between 28 and 85 years. The male-female ratio was 1:1. No statistically significant difference in the ages of the male and female subjects (p=0.20). Nine (18%) of the subjects had prior history of diabetes mellitus (DM) with a mean duration (SD) of 7(6) years. Most subjects (65%) had prior history of systemic hypertension with an average duration (SD) of 8 (7) years. The mean ABG was 134 (58) mg/dl, ranging between 37 and 320mg/dl. While 32 (63%) of the subjects had infarctive stroke, 16 (31%) had hemorrhagic stroke and 3 (6%) had both. All the subjects with ABG 200mg/dl or more had an infarctive stroke. However, of those with ABG less than 200mg/dl, 36% had hemorrhagic stroke, 58% had infarctive stroke while 7% had both. No statistically significant relationship between the ABG and stroke types (p=0.13). Also, mean ABG was higher in infarctive than in hemorrhagic stroke (138 Vs 130mg/dl) but difference is not statistically significant (p=0.064).

**Conclusion:** Patients with ABG ≥200mg/dl are more likely to have an infarctive stroke.

Abstract #242

**CENTRALITY INDEX AND METABOLIC CONTROL IN AMBULATORY TYPE 2 DIABETES SUBJECTS IN LIMA, PERU**

Alberto Alejandro Teruya Gibu, MD

**Objective:** To correlate visceral obesity assessed by DEXA body composition with metabolic control in subject with type 2 diabetes.

**Methods:** Body composition by DEXA was assessed in subjects with type 2 diabetes (DM) to measure visceral obesity defined as centrality index (CI) according to Ley et al. Blood samples were drawn at fast to measure glucose, glycosylated hemoglobin (HbA1c) and lipid profile. Anthropometric parameters were measured in light clothes including weight, height, waist and hip circumferences. Body mass index (BMI) and waist to hip ratio (W/H) were calculated from those measurements. Centrality index was correlated with biochemical and anthropometric parameters. Non diabetic subjects assessed for obesity related comorbidities were considered as a control sample (NODM).

**Results:** 22 DM subjects (F:M 13:9; 51.3 ± 17.2 years) and 35 NODM (F:M 26:14; 42.3 ± 19.2 years) were included in the analysis. Mean BMI were similar (27.25 ± 4.9 vs 28.64 ± 5.4, t-test: p=0.33) in both groups. Mean CI was higher in DM than NODM (1.28 ± 0.26 vs 1.15 ± 0.18, t-test: p=0.04). A better correlation was seen between IC and W/H than for BMI in both groups. In DM group according to sex, IC positively correlated with biochemical and anthropometric parameters. Non diabetic subjects assessed for obesity related comorbidities were considered as a control sample (NODM).

**Discussion:** Central obesity is a key anthropometric condition related to risk, development and evolution of type 2 diabetes and dyslipidemia. Clinical trials have demonstrated that pharmacological interventions
of hyperglycemia and dyslipidemia reduce the risk of cardiovascular events but an important proportion of subjects remain at risk in spite of those interventions. The evolution of abdominal obesity by a non invasive, costless and specific method such as DEXA could be an important clinical tool in order to evaluate the variation of abdominal fat mass as a predictive parameter of therapeutic interventions.

**Conclusion:** Centrality index measured by DEXA seems to be a good non invasive method to assess visceral obesity in type 2 diabetic subjects. Further studies deserve to consider a better therapeutic strategy to control both glucose and lipid metabolism in subjects with type 2 diabetes.

**Abstract #243**

**GRAVIDITY AND AGE OF ONSET OF TYPE 2 DIABETES MELLITUS**

Andrew Efosa Edo, MBBS, FMCP, Gloria Edo, OD, Steve Obanor, MBBS, Ahanuwa Eregie, MBBS, FMCP

**Background/Objective:** It has been hypothesized that increasing gravidity will predispose to development of type 2 diabetes mellitus (DM) in an earlier age in women. We investigated the association between the age of onset of type 2 diabetes mellitus (AODM) and gravidity.

**Methods:** Hospital records of women with type 2 DM seen over a 2-year period at Faith Medical Centre, Benin City were retrieved. Data extracted included age of patients, age at diagnosis of DM and gravidity of patients. Women that used hormonal contraceptives were excluded from the study. Gravidity was defined as number of pregnancies irrespective of whether it resulted in live birth. Group A was defined those as having less than 5 pregnancies and Group B were those having more than 4 pregnancies. The data was analyzed using SPSS version 16. Significant level was set at p < 0.05.

**Results:** 241 women with type 2 DM were included in the study. Their mean age and AODM were 58.2 ± 10.1 and 53.5 ± 10.0 years respectively. Mean gravidity was 6.5 ± 2.8 pregnancies/woman (range 0 – 16). The mean AODM was significantly lower in Group A than in Group B, 49.2 ± 13.1 vs 53.7 ± 9.8 years, p=0.008. There was a significant positive correlation between AODM and gravidity, r = 0.306, p = 0.001; AODM and age at the last pregnancy, r = 0.315, p = 0.001.

**Conclusion:** AODM is associated with gravidity and occurs earlier in women who had less than 5 pregnancies compared to those who had more than 4 pregnancies.

**Abstract #244**

**LIVER FUNCTION IN TYPE-2 DIABETIC NIGERIANS**

Adamu Girei Bakari, MBBS, FWACP, FACE, Lawal Nasiru, MSc, Akuyam Shehu Abubakar, PhD, Anaja, PO, PhD, Ahmad Mohammed Bello, MSc

**Background:** Patients with type 2 DM have two times the risk of developing liver diseases and possibly three times the risk of developing liver cancer than their healthy counterparts. Liver disorders among diabetics are similar to that of alcoholic liver disease including fatty liver (steatosis), steatohepatitis, fibrosis and cirrhosis. Elevated serum activities of the liver enzymes such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP) and gamma glutamyltrasferase (GGT) are the most frequent indicators of liver disease. As opposed to the vast literature on the relationship between DM and liver disease in technically advanced regions of the world, there is paucity of published materials in Nigeria in particular and Africa in general.

**Objective:** The aim of the present study was to assess the liver function status in type 2 diabetic patients in Zaria.

**Methods/Results:** The study comprised of 170 type-2 diabetic patients whose sera are negative for hepatitis B Surface antigen (HBsAg) attending the diabetic clinic of Ahmadu Bello University Teaching Hospital, Zaria. A concise history of the patients, physical examination and laboratory findings were recorded on a proforma. Serum bilirubin concentrations, Serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), Serum alkaline phosphatase (ALP) and Serum gamma glutamyl transferase (GGT) activities were measured using standard methods. The concentrations of serum FBG and RBG were measured using glucose oxidase method. The mean values of serum ALT, AST, GGT, ALP activities and bilirubin in diabetic patients were 36 ± 2.2 IU/L, 35 ± 2.9 IU/L, 36 ± 4.4 IU/L, 89 ± 4.9 KAU/L and 11 ± 0.8 µmol/L respectively. The mean values for serum liver enzymes activities in diabetic patients were significantly higher than those in non-diabetic individuals (p<0.01). Whereas the mean values for serum total bilirubin in diabetic patients was found to be similar with those in non-diabetic controls (p>0.05).

**Conclusion:** It is concluded that there is derangement in liver function in diabetic patients in this study.
Abstract #245

TO STUDY THE IMPACT OF AN ELECTRONIC MEDICAL TEMPLATE ON PHYSICIANS’ ADHERENCE TO GUIDELINES FOR MANAGEMENT OF DIABETES

Vishal Mundra, MBBS, Viet Nguyen, MD, Shadi Yaghubian, MS3, Nemer Dabage-Forzoli, MD, Stephen Avallone, Jr, MD, Jose Muniz, MD, Darby Sider, MD, Carmen V. Villabona, MD

Background: Diabetes was the seventh leading cause of death in 2006. The number of patients with diabetes is expected to double by 2050. Physicians’ adherence to guidelines for management of diabetes is very poor.

Objective: To study the impact of an electronic medical record (EMR) template on physicians’ adherence to guidelines for management of diabetes.

Methods: We designed a template based on ADA guidelines for management of diabetes including: 1) HbA1c 2) BP control 3) Lipid control 4) Smoking cessation counseling 5) Feet exam 6) Pneumonia vaccination 7) Renal assessment 8) Annual Eye exam. We randomly selected 154 patients from the database of a community teaching hospital and “pre-intervention” data was collected. Physicians used the template for 6 months, then, we randomly selected 212 patients and “post-intervention” data was collected. The data was analyzed using Fisher method and statistical significance was set at p value less than 0.05.

Results: Subsequent analysis is discussed below for each parameter separately. HbA1c measurement: In the pre-intervention group, HbA1c was checked periodically in 57.5 % of patients vs. 94.1% of patients in the post-intervention group (p<0.001). Blood Pressure Control: In the pre-intervention group, blood pressure was at goal in 53.3% of patients vs. 89.1% in the post-intervention group (p<0.001). Lipid control: In the pre-intervention group, the LDL was at goal in 65.6% vs. 90.0 % in the post-intervention group (p<0.001). Smoking cessation counseling: It was documented in 97.3% in the pre-intervention group, vs. 100% in post-intervention group (p 0.578). Feet Examination: In the pre-intervention group 88.3% of patients had feet examination vs. 99.1% in the post-intervention group (p 0.001). Pneumonia Vaccination: In the post-intervention group about 92.9% received a pneumococcal vaccine. No pre-intervention data was collected. Renal assessment: It was done in 92.8% of patients pre-intervention vs. 92.9% in the post-intervention group (p 0718). Annual eye exam: In the pre-intervention group, 38.3% had documented eye exam vs. 94.8% in the post-intervention group (p<0.001). Limitations: The template had to be used voluntarily, which affected the compliance. Same patients were not followed in pre and post intervention group.

Conclusion: Utilization of a template in the EMR showed a significant improvement in diabetes care including HbA1c assessment, BP control, lipid control, feet examination and annual eye examination. EMR use can improve physician’s adherence to guidelines and may be useful for all chronic and complicated disease.

Abstract #246

SEVERE DIABETIC KETOACIDOSIS AND PANCREATITIS ASSOCIATED WITH ARIPIPRAZOLE TREATMENT

Kemisha Key, MD, Mais Trabolsi, MD, Rachanon Murathanun, MD, Tahira Yasmeen, MD, FACE, Farah Hasan, MD, FRCP, FACE

Objective: Aripiprazole as a new antipsychotic medication has become the mainstay in the treatment of schizophrenia due to its favorable side effect profile compared to other atypical antipsychotics. Hyperglycemia, diabetes mellitus (DM) and pancreatitis have been commonly associated with other atypical antipsychotic. Very few cases of aripiprazole induced pancreatitis or diabetic ketoacidosis (DKA) have been reported. We describe a case of profound DKA coexistent with severe pancreatitis associated with aripiprazole use.

Case Presentation: A 35-year-old male with schizophrenia presented to the ED with complaints of nausea, vomiting and abdominal pain. He reported having polyuria, polydipsia and progressive weight gain. He denied any fever, dysuria, alcohol use or history of DM or gallstones. He denied any family history of DM or gallstones. Physical examination was remarkable for BMI of 46.7 kg/m², tachypnea, dry mucus membranes and tenderness to palpation on abdominal exam. Patient was found to have a blood glucose of 710 mg/dL, anion gap of 36 mmol/L, serum osmolality of 332 mOsm/kg, C0₂ 4 mmol/L, creatinine 2.1 umol/L, PH <6.96, PCO₂ 19 mmHg, P0₂ 120 mmHg, HCO₃⁻ 2 . Further investigations found amylase 440 IU/L, lipase 9777 IU/L and triglycerides 191 mg/dL. CBC was normal except for WBC of 20.7 x 10⁹/L. Toxicology screen, salicylate, and ethylene glycol levels were negative. HbA1c 15.8, islet cell antibodies, c peptide and glutamic acid antibodies were negative. Diagnosis of severe DKA associated with pancreatitis was made. He was started on DKA protocol with aggressive hydration, insulin infusion and electrolyte replacement. Ultrasound of abdomen was negative for gallstones. CT abdomen demonstrated an atrophic pancreas with peripancreatic inflammatory changes. A
few days after aggressive treatment DKA and pancreatitis resolved and the patient was discharged home on oral metformin.

**Discussion:** Aripiprazole is a commonly used antipsychotic medication for schizophrenia due to its safety profile and has rarely been associated with DKA and/or pancreatitis. Incidence of diabetes mellitus is lowest with aripiprazole and the onset was estimated to be few days up to 4 years. The pathophysiology of aripiprazole induced DKA or pancreatitis is not completely understood, but alterations in insulin sensitivity and weight gain associated insulin resistance have been postulated as possible mechanisms precipitating DKA in patients taking aripiprazole. Pancreatitis is believed to be due to elevated triglyceride levels caused by this medication. To the best of our knowledge this is the first case of severe DKA coexistent with acute on chronic pancreatitis in a patient taking aripiprazole. In our patient evidence of pancreatitis on imaging suggests that elevated lipase and amylase levels were not solely due to DKA.

**Conclusion:** Despite aripiprazole’s favorable side effect profile cases of diabetic ketoacidosis and pancreatitis have been found with its use. Physicians should monitor for potential adverse effects when prescribing antipsychotic agents. Patients on long term antipsychotic medications including aripiprazole should be screened for diabetes and have their triglyceride levels monitored.

Abstract #247

**INSULIN EDEMA**

Nicolas Lazio Kissell, MD, Manmeet Kaur, MD, Michael Radin, MD

**Objective:** Discuss a rare presentation of insulin induced edema and review the pathogenesis behind it.

**Case Presentation:** A thirty two year old caucasian female diagnosed with type 1 diabetes mellitus eight years prior with an initial weight of 250 lbs. She was previously on and off insulin therapy. She has not taken her insulin for five months and had not been hospitalized. She had a glycosylated hemoglobin of 17.4%. Physical examination revealed a woman with a BMI of 20 kg/m2 and a weight of 125 lbs. Basal and bolus insulin was restarted and increased on the succeeding days. There was significant improvement in her blood glucose levels. One week after insulin treatment began she noticed swelling in her feet that ascended to her legs and abdomen. The swelling did not improve with diuretics. Two weeks after the initiation of insulin, she had a weight gain of 60 pounds, for which she sought help at the emergency department. Physical examination revealed a puffy face and bilateral lower extremity pitting edema up to the abdomen. Lung, cardiovascular and abdominal examination was normal. Laboratory data showed normal electrolytes with slightly elevated blood glucose. Chest X-ray, echocardiogram, abdominal ultrasound, liver function, renal function and thyroid function tests were within normal limits. The patient was placed on a sodium and fluid restricted diet. She continued her insulin and was diuresed with furosemide. Her edema significantly decreased and she lost 15 pounds on the third day. The patient remained on insulin therapy and was seen at the clinic two months later. Her weight remained stable with no recurrence of edema.

**Discussion:** The pathogenesis of insulin edema involves the following two effects of insulin treatment: anti-natriuresis and increased capillary permeability. Our patient was in a severe catabolic state given her insulin non-compliance with the majority of her weight loss from protein breakdown. This resulted in a hypo-proteinemic state with capillary wall damage. When insulin was reintroduced, there was sodium and fluid retention directly caused by insulin. Her low protein state and leaky capillary vessels allowed for third spacing. Treatment of insulin induced edema is conservative with continuation of insulin therapy and use of diuretics.

**Conclusion:** Insulin edema is a rare and benign complication of insulin therapy. It is a syndrome of unidentified origin with exclusion of all other causes of edema. It occurs in patients with either type 1 or type 2 diabetes after the introduction or intensification of insulin treatment. It is characterized by weight gain, mild to moderate edema, and rarely generalized edema.

Abstract #248

**CARDIOVASCULAR RISK FACTORS IN GAD AUTOANTIBODY POSITIVE TYPE 2 DIABETIC SUBJECTS**

Olufunmilayo Olubusola Adeleye, MD, A. O. Ogbera, MBBS, FACE, FACP, FMCP, A. O. Dada, FMCP, A. O. Ale, MD, O. Abatan

**Background/Objectives:** Diabetes mellitus (DM) is a risk factor for cardiovascular disease. Subjects with slowly progressive autoimmune DM have been reported to have fewer cardiovascular risk factors compared to autoantibody negative type 2 DM. This study is to determine the frequency of cardiovascular risk factors in glutamic acid decarboxylase autoantibody (GADA) positive (+ve) type 2 DM subjects in southwestern Nigeria.

**Methods:** A descriptive study involving 235 type 2 diabetic subjects, recruited by systematic random sampling. Subjects with severe comorbidities, GDM and those on steroids were excluded. Demographic and anthropometric indices were obtained. Blood samples
were taken for GADAs. Subjects positive for GADAs were matched with those negative for GADAs in age, gender, duration of DM. Parameters of age, gender, duration of DM, history of hypertension and medication, stroke, dyslipidemia, myocardial infarction, and dialysis were obtained through interviewer based questionnaire and hospital records. Fasting blood samples were taken for glucose, lipids and C-peptide. Early morning urine samples were analyzed for macro and microalbuminuria.

**Results:** 13.6% were GADAs positive. Mean age of GADAs positive and negative was 53.9 ± 6.0 and 52.00 ± 7.4 respectively, mean duration of DM 6.8 ± 4.7 and 7.5 ± 7.3 respectively. 47% of GADAs positive were already on insulin, while 22% GADAs negative had commenced insulin. Mean body mass indices (BMI) was 27.2 ± 6.3 and 27.2 ± 5.1, mean waist circumference 91.7 ± 16.1 and 91.7 ± 10.4, mean waist/hip ratio 0.913 ± 0.07 and 0.91 ± 0.05. Mean systolic blood pressure 137 ± 20.6 and 137 ± 23, mean diastolic BP 84 ± 11.2 and 81 ± 10. Microalbuminuria -47.1% and 52.1%. Mean glycosylated hemoglobin 8.4 ± 1.85% and 7.3 ± 2.0%. Total cholesterol, 180 ± 34mg/dl and 203 ± 50mg/dl, LDL-C 118.3 ± 34.4 and 132 ± 41.2, TG 85 ± 31.74 and 104 ± 78 respectively. 60% of GADAs positive and 59.2% GADAs negative had a history of hypertension. Both groups had one individual each with history of stroke, and there was no occurrence of myocardial infarction in both groups.

**Discussion:** Waist circumference, waist/hip ratio, waist circumference, hypertension were comparable between the two groups, lipid parameters were however lower amongst GADAs positive subjects. There’s a higher prevalence of microalbuminuria amongst GADAs negative individuals.

**Conclusion:** GAD autoantibody positive type 2 DM subjects have comparable cardiovascular risk factors with GAD autoantibody negative type 2 DM subjects.

**Abstract #249**

**RISK OF CORONARY HEART DISEASE AND STROKE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS**

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**Background:** Patients with type 2 diabetes have increased risk of developing coronary heart disease (CHD) and stroke. There is paucity of data on the estimated risk of developing these complications in Nigeria.

**Objective:** To estimate the risk of coronary heart disease and stroke in Nigerian patients with type 2 diabetes.

**Methods:** We studied sixty-four patients (forty females and twenty-four males) with type 2 diabetes mellitus in an outpatient setting. Data obtained included age, gender and time since diagnosis. Heart rate (beats/min), blood pressure (mmHg), weight (kg), height (m), waist and hip circumference (cm) were recorded. Results of glycated hemoglobin and fasting lipid profile of the patients were obtained. The United Kingdom Prospective Diabetes Study risk engine v 2.0 was used to calculate their risk of developing CHD and stroke which was expressed as a percentage. Average values are expressed as means ± S.D. p value less than 0.05 was considered significant. Data were analyzed using SPSS version 17.

**Results:** The mean age, time since diagnosis, body mass index, and glycated hemoglobin of the patients were 56.11 ± 12.9 years, 4.81 ± 3.88 years, and 28.2 ± 6.3 kg/m², and 7.8 ± 2.1% respectively. Hypertension was present in 30 (46.9%) of the patients. The mean 10 years CHD risks in males and females were 10.8 ± 1.9% and 4.5 ± 0.5% respectively (p<0.05) while the stroke risk was 10.5 ± 2.1% and 6.8 ± 1.7% respectively (p=0.18).

**Discussion:** Traditionally, CHD had been said to be rare in Africans. Increasing westernization and the rising prevalence of diabetes have led to reports of increased prevalence in Sub-Saharan Africa. The estimated risk of stroke was higher than that of CHD and this is in keeping with previous studies which have shown that the incidence of stroke is higher than CHD in our patients. The estimated risk of CHD and stroke in this study showed that males had a higher risk for both conditions and this mirrors previous findings by Kolawole and co-workers.

**Conclusion:** The 10 year CHD and stroke risk in our patients appears to be low. There is need to determine the appropriateness of this risk engine in Africans.

**Abstract #250**

**FOOTWEAR UTILIZATION - KNOWLEDGE AND PRACTICE OF PERSONS LIVING WITH TYPE 2 DIABETES MELLITUS**

Stephen Onesi Ogedengbe, MD, Mariam Adediran, MD, Anthony Anyanwu, MD, Olusegun Sheyin, MD, Jide Aderoba, MD, Abimbola Ajayi, MD, Olufemi Fasanmade, MBBS, FACE, Augustine Efedaye Ohwovoriole, MD, MSc

**Background:** Foot ulceration is a major cause of amputation among people with diabetes mellitus worldwide. An important risk factor of ulceration is the use of inappropriate footwear.

**Objective:** To determine knowledge and practice of footwear utilization among persons living with type 2 diabetes mellitus.
Abstracts – Diabetes Mellitus

Methods: Questionnaires on knowledge and practice of foot wear utilization were administered by doctors on a clinic day. Footwear worn to the clinic that day were inspected and categorized into inappropriate and appropriate footwear by both the attending physicians and patients. Data were entered into Excel 2007 and further analyzed by SPSS 16.0.

Results: Forty-one patients with type 2 DM (14 males and 27 females) were studied. The mean age was 57.8 ± 10.4 years. About 90.2% had foot wear education, 82.9% wash and dry their feet while 51% do routine self foot-examination. About 56% either always or occasionally walk without shoes at home while about 14.6% either always or occasionally walk without shoes outside their home. On inspection of foot wear in the clinic, 68.2% of foot wears were found to be inappropriate, however, from the patients’ perspective 73.1% were thought to be appropriate. There was a 46.3% discordance (X²= 3.551, p=0.06)

Discussion: The knowledge of footwear education appears to be fair; however, there appears to be a disconnection between the knowledge and practice.

Conclusion: The disconnection between the patients’ knowledge and practice may be a contributing factor to the high prevalence of diabetic foot ulceration and high rate of amputation in our locale. There is therefore an urgent need to review and reinforce our diabetes education.

Abstract #251

ARTIFICIALLY LOW HEMOGLOBIN A1c MEASUREMENTS IN A MULTI-ETHNIC GROUP OF DIABETICS: A SIMPLIFIED CORRECTION FACTOR (A1c DIVIDED BY 0.65) ACCURATELY ADJUSTS FOR FALSELY NORMAL A1c MEASUREMENTS

John A. Tayek, MD, JoHanna Parker, MD

Objective: To identify artificially low A1c concentrations in an multi-ethnic group of diabetics. The gold standard for the glucose management of diabetes is the A1c measurement. The A1c reflects average blood glucose over the prior 120 days by measurement of the amount of glycosylation that occurs on the valine residue at the NH2-terminus of one or both of the beta chains of hemoglobin.

Case Presentation: Approximately 6 years ago, a patient with diabetes was charted by the residents to be under “excellent control” with an A1c of 4.7% yet his fasting blood glucose concentrations were in the 300-400 mg/dl range. Evaluation of the hemoglobin demonstrated hemoglobin SC. The 4.7% A1c result was due to his fetal hemoglobin co-migrated to the same area used in the measurement of hemoglobin A1c. Based on this test case, patients with a diagnosis of diabetes and a low A1c were screened to identify how common and what types of hemoglobin abnormalities occur at an LA County Internal Medicine Clinic. A total of 48 patients were identified with hemoglobin electrophoresis to identify normal A1c concentrations in patient that had otherwise poorly controlled diabetes based on blood glucose measurements. Approximately 80% (37 of 47) had sickle trait. Sickle trait patients have approximately 65% hemoglobin A and the A1c measurement does not correct for the 35% loss in hemoglobin A. Other abnormalities included approximately 5% with Beta thalasemia and 2% with hemaglobulin C other rare hemoglobins. The measured A1c in sickle trait patient and other hemaglobulinopathys can be adjusted upward by dividing the % hemoglobin A concentration by 0.65 (Parker Correction Factor) to get a corrected A1c. In patients who also had multiple blood glucose concentrations recorded an estimated A1c was also determined using the formula: mean blood glucose = 31.7 x A1c-66.1. The plot below demonstrates the corrected, measured and expected A1c measurements.

Conclusion: When there is a mismatch between the blood glucose measurements and the reported A1c, a hemoglobin electrophoresis should be considered to identify those patients where the A1c is not a accurate reflection of glucose control. Since Sickle trait occurs in 10% of African Americans and in hemaglobulin C in 20% of Vietnamese American, both resulting in falsely lower A1c concentrations. More attention should be paid to clinical blood glucose concentrations when the A1c look “too good” to believe.

Abstract #252

HEMOGLOBIN FUKUAKA CAUSING A FALSELY LOW HBA1C VALUE MEASURED BY IMMUNOASSAY

Deepti Rawal, MD, Kinan Dalal, MD, Mehul Vora, MD, Ajay Varanasi, MD, Sartaj Sandhu, MD, Castro Bali, MD, Antoine Makdissi, MD, Monica Galilivan, MD, Paresh Dandona, MD

Objective: To present a rare case of hemoglobin Fukuaka causing a falsely low HbA1c value.

Case Presentation: A 50 year-old white man with type 2 diabetes mellitus (DM-2) for 20 years, diabetic retinopathy, nephropathy and neuropathy presented for evaluation and management of his diabetes. He reported elevated blood glucose (BG) values between 200-300 mg/dL throughout the day, measured using his glucometer.
He denied any hypoglycemic episodes. Patient was on metformin 850 mg three times a day, glyburide 10 mg bid and glargine insulin subcutaneously at night. HbA1c (point of care testing [POCT]) was 5.4%, Hemoglobin (Hgb) of 15.3 g/dl and creatinine 1.29 mg/dl. The dose of glargine insulin was increased and glulisine insulin was added before meals. During follow up visits, the patient was noted to have a persistent discrepancy between elevated BG values measured at home and near-normal HbA1c values of 5.2% and 5.8% done as POCT and at the reference laboratory respectively. Further laboratory evaluation revealed elevated levels of fructosamine at 360 umol/L (190-270), and total glycohemoglobin at 10.8% (5.4-7.4%). Hgb electrophoresis showed that patient has a rare variant of Hgb known as Hgb Fukuaka.

Discussion: Fukuaka Hgb has a substituted amino acid (AA) residue at the 2nd position of the ß-Globin chain [B2 (NA2) His+Tyr]. Immunoassays used in different laboratories and POCT instruments for measuring HbA1c usually target the first 4-10 AAs of the ß-Globin chains. Factors preventing glycosylation or identification of these AAs by the used antibodies lead to inaccurate results, as were the case in our patient where the value of HbA1c was falsely low. Other Hgb variants potentially affected are: Hgb E, Hgb D, Hgb Philadelphia and Hgb Raleigh. In addition to the conditions causing analytic interference with the method used to measure HbA1c, several conditions affecting the lifespan of red blood cells such as uremia and hemolytic anemia can also lead to inaccurate values. These should be considered especially when there is a discrepancy between the measured glucose concentrations and HbA1c values.

Conclusion: This case illustrates the importance of knowing the characteristics and limitations of the assay used to measure HbA1c. It also highlights the potential pitfalls of using HbA1c as the sole measure of glycemic control. A lack of understanding of such discrepancies may lead to inadequate diabetic control in the long term.

Abstract #253

IMPROVING RETINOPATHY SCREENING RATES AMONG AN URBAN PATIENT POPULATION

Tracy Susan Tylee, MD, Brent Wisse, MD

Objective: Recent review of the retinopathy screening rates at Harborview Medical Center (HMC), a county hospital in Seattle, WA, revealed rates of 37% compared to 60% for the region. The low rates of retinopathy screening at HMC could be due to a number of factors, both provider and patient centered. Prior to instituting any intervention geared toward improving screening rates it is important to know what factors are at play in order to best target the intervention. We undertook a quality improvement project to determine the barriers to screening, with a goal of developing interventions to improve compliance.

Methods: We reviewed 120 charts from diabetic patients identified using ICD-9 codes. The index clinic visit was the most recent visit that had one full year follow up. We reviewed chart notes for one year following the index visit for 1) documented ophthalmology visit, 2) if no visit, documentation of scheduled visit, 3) if no scheduled visit, documentation of clinic referral, or 4) if none of the above, documentation of exam by outside provider.

Results: Among patients with diabetes, only 42% had a documented eye exam in the year following their index visit. However, 67% of patients were appropriately referred for exam. One-third of patients referred for screening failed to follow through with the referral.

Discussion: Diabetic retinopathy is an important cause of blindness. Annual exam has been shown to be cost effective and beneficial, but many patients fail to get the recommended screening. Our study showed that patients are being referred for screening, suggesting providers are making appropriate referrals. The main barrier is patient compliance with follow up appointments. This is a particular challenge with the HMC patient population. They face significant social challenges limiting access to care, including unemployment, language barriers and homelessness. The results indicate that an appropriate intervention would provide retinopathy screening at a primary care visit, eliminating the need for a separate appointment. Based on these results office based retinal imaging, which has been shown to be an effective means of retinopathy screening, has been implemented in the adult medicine clinic. We are currently collecting follow up data and hope to show that this intervention will improve our screening rates.

Conclusion: Low screening rates among our urban patient population are due to challenges with scheduling and follow-up appointments. Implementing retinal photography at primary care clinics should improve screening rates and overall care of diabetic patients.
Abstract #254

EFFECTS OF PIOGLITAZONE OR SITAGLIPTIN IN TYPE 2 DIABETIC PATIENTS INADEQUATELY CONTROLLED WITH METFORMIN MONOTHERAPY

Hans Tandra, MD, FACE, Audrey Amelia, MD, Olivia Handayani, MD, BMedSc

Objective: To compare the efficacy of additional oral hypoglycemic agents (OHAs), Pioglitazone (PIO) or Sitagliptin (SIT), in patients with type 2 diabetes (T2D) who were inadequately controlled with metformin (MET) monotherapy.

Methods: The 24-week study was performed in male and female patients, aged 20 – 80 years, with inadequately controlled T2D (HbA1c 6.8 – 9.7%) on MET regimen (1500 – 2000 mg/d for ≥ 3 months). We have been using PIO 30 mg/d and SIT 100 mg/d in the study. The primary efficacy variable was the change in HbA1C from baseline to week 24.

Results: There were 208 patients who completed the study, with 150 randomized: PIO (n=75), SIT (n=75). At baseline, there were no significant differences between the groups. After 24 weeks, PIO and SIT significantly reduced HbA1c, -1.24% (-0.56 - -1.63) and -1.19% (-0.65 - -1.88), respectively; (p <0.05), whereas 36% PIO and 33% SIT of the subjects attained HbA1c <6.5%. Fasting plasma glucose and 2 hour postprandial glucose significantly decreased in all groups. Overall, PIO and SIT were well tolerated as the major adverse reactions were mild in severity.

Conclusion: The OHAs Pioglitazone and Sitagliptin significantly improved the glycemic control, and well tolerated when used in combination with Metformin.

Abstract #255

TOPICAL THYROID HORMONE IN MODULATION OF DIABETIC WOUND HEALING

Karen Choong, MD, Joshua Safer, MD

Objective: To examine the role of topical thyroid hormone as an adjunctive treatment modality in the management of diabetic wounds and to assess the mechanisms involved by which thyroid hormone modulates wound healing.

Methods: The db/db mouse is a well-accepted diabetic mouse model for the study of wound healing. For our pilot experiment, 6 db/db male mice, aged 8 weeks, were purchased. On day 1, two wounds, one on each side of the midline, was created on the shaved dorsum of each mouse using a sterile 6cm punch biopsy tool. Each mouse is its own control; half the wounds were treated with placebo cream while the remaining wounds were treated with inert cream containing triiodothyronine. Digital photographs were taken daily from Day 1 to Day 14 for wound area assessment and for comparisons of wound closure rate.

Results: Administration of topical thyroid hormone accelerated wound closure by 15-20% in the T3 treated wounds than placebo. Topical T3 administration appears to achieve complete wound closure by 24-48 hours earlier than placebo-treated wounds.

Discussion: Wound healing is impaired in diabetes. This is largely due to a multitude of causes including impairments in keratinocyte and fibroblast proliferation, altered cytokine levels and growth factor levels, and impairment in angiogenesis. Thyroid hormone is a main regulator of skin homeostasis and has been shown to have stimulatory effects on skin cell growth through keratinocyte and fibroblasts proliferation. Topical administration T3 hormone derivative, TRIAC, increases the dermal thickness and restores collagen levels in glucocorticoid-induced skin thinning. In vivo, wound closure was accelerated in wounds treated with topical T3. Previously, we demonstrated that topical T3 improved wound healing in wild-type mice. In this preliminary study, we noticed a trend towards accelerated wound healing with topical T3 application in the diabetic mouse model. An improvement in both wound area size and in wound closure rate was appreciated. We postulate that these improvements are associated with enhanced skin cell proliferation.

Conclusion: The identification of new treatment agents in the management of wound healing in diabetes continues to be an area of intense research. We aim to establish a mechanistic pathway integral to thyroid hormone action on diabetic skin and thereby provide therapeutic targets for enhancing wound healing. Local skin manipulation by thyroid hormone may prove a novel and cost-effective strategy for the treatment of cutaneous pathology; particularly in the multi-dimensional approach to diabetic wound management.

Abstract #256

SUCCESSFUL MANAGEMENT OF POSTPRANDIAL HYPOGLYCEMIA WITH ACARBOSE AND METFORMIN

Rami Mortada, MD, Gail Wong, MD

Objective: To describe successful management of the under-recognized syndrome known as reactive hypoglycemia (RH). Patient 1: 27-year-old caucasian
female with BMI of 28 kg/m² and no past medical history has been complaining of nausea, dizziness, tremor and anxiety happening 2-3 hours after meals for more than 15 years. She was diagnosed as having “dumping syndrome”. Treatments with metoclopramide, meclizine and alprazolam failed to relieve the symptoms. Prior to Endocrinology referral, serum glucose and insulin measured 1 h after oral glucose load were 87 mg/dl and 17 uIU/ml, respectively. Hgb A1c was 4.8%. Home glucose monitoring showed postprandial glucose of 50 mg/dl with associated symptoms. Five hour OGTT showed exaggerated insulin response 93.6 uIU/ml at 3 hours with BG of 62 mg/dl, again with symptoms. In order to reduce hyperinsulinemia, she was placed on a low glycemic index diet and metformin 500 mg BID with complete resolution of symptoms, in 6 months period.

Patient 2: 34-year-old caucasian female with BMI of 37 kg/m² and history significant for esophagitis had history of fatigue and anxiety since her teenage years. She had a hypoglycemic event at work with blood sugar of 24 mg/dl. Her Hgb A1c was 4.6%. Sulfonylurea screen was negative. 48 hour fasting did not result in hypoglycemia. Home glucose monitoring showed postprandial glucose 46 mg/dl with corresponding symptoms. Five hour glucose tolerance test showed impaired glucose tolerance with a 2 hour value of 163 mg/dl, delayed hypoglycemia of 57 mg/dl with serum insulin of 56.9 uIU/ml. She was started on a low glycemic index diet and acarbose. Acarbose titrated to 100 mg P.O., TID resulting in symptoms resolution in 1 year.

Discussion: Postprandial or RH is a clinical syndrome describing recurrent episodes of symptomatic hypoglycemia occurring 2-5 hours after a high carbohydrate meal or oral glucose load. It is usually the consequence of exaggerated insulin response that extends beyond the digestion and metabolism of the glucose derived from the meal.

Conclusion: Reactive hypoglycemia, a postprandial hypoglycemic state, occurs within 2–5 h after food. The cases presented here had disabling symptoms and were undiagnosed or misdiagnosed for more than 10 years. Pathogenesis involves a mismatch between insulin secretion and glycemia. Loss of the early insulin response followed by exaggerated late insulin response both are associated with RH, which is also considered a risk factor for development of diabetes mellitus. Once diagnosed, adequate diet and medication can improve symptoms.

Abstract #257
ASESEMENT OF GLOMERULAR FILTRATION RATE AND HEMATOLOGICAL PROFILE IN DIABETIC SUBJECTS IN INDIA

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Background: Diabetic nephropathy affects 25–40% of diabetic patients. It is the leading cause of end-stage renal disease (ESRD) in developed countries. Serum creatinine concentration is widely used as an indirect marker of GFR, but it is influenced by muscle mass and diet. GFR can be directly measured by infusion of external substances such as inulin, 51Cr-EDTA or 99m Tc DTPA but these methods are expensive and time consuming. In the Modification of Diet in Renal Disease (MDRD) study, patients with renal dysfunction underwent GFR measurements by 125I-iothalamate renal clearances. From these data, several equations were derived, including a four-variable MDRD equation that has been the most widely accepted and used. The more recent MDRD equation seems more accurate, but it has not been validated in diabetic kidney disease in India. Its superiority over the Cockcroft-Gault formula has been mentioned in some, but not all recent reports.

Objective: 1. Comparison of Cockcroft-Gault formula and MDRD equation of GFR with Tc-DTPA measurement in diabetic subjects by correlation between both estimations and isotopic measurement of GFR. 2. Observing the hematological status of patients with relation to GFR.

Methods: The study group consisted of 100 consecutive diabetic patients attending outdoor of Diabetic OPD of SSKM Hospital and willing to participate in the study. Subjects with nephrotic proteinuria (>3 g/24 h) were excluded. No subject was treated by dialysis at the time of the study. Clearance of the radionuclide marker was measured after intravenous injection of Tc-DTPA.

Results/Discussion: Both sexes (58 men and 42 women) and types of diabetes (24 type 1 and 76 type 2) were represented. Mean ± SD HbA1c was 8.42 ± 1.2 %. Mean isotopic GFR was 35.44 ± 1.84 ml · min⁻¹ whereas mean MDRD GFR was 32.25 ± 1.73 m²⁻¹. GFR by isotope method correlated with GFR calculated by MDRD method (r = 0.823, p = 0.00) and with CG method (r = 0.719, p = 0.000). It also correlated well with urinary creatinine clearance. (r = 0.735, p = 0.00) So, MDRD method has better correlation than CG method and urinary creatinine...
clearance. Patient’s hemoglobin value also showed good correlation with GFR by all methods. \( r = 0.534, p = 0.00 \). GFR values also correlated well with TIBC \( r = 0.401, p = 0.002 \) and Serum Iron \( r = 0.455, p = 0.00 \)

**Conclusion:** GFR calculated by Both MDRD and CG formula correlate well with Isotope scan and may be used. However MDRD has better correlation in diabetic patient. Fall in Hb gm% has moderate correlation with GFR.

### Abstract #258

**STIFF-PERSON SYNDROME IN A DIABETIC PATIENT IN ZARIA: A CASE REPORT**

_Innocent Onoja Okpe, MBBS, Joseph Ovosi, MBBS, Damian Ogoina, MBBS, FWACP, R.O. Obiako, MBBS, FMCP, FWACP_

**Objective:** To highlight the occurrence of stiff-person syndrome, a rare autoimmune neurological disorder characterized by muscle rigidity and spasms that wax and wane sometimes associated with type 1 diabetes.

**Case Presentation:** A 55-year-old Teacher presented with a 14-month history of progressive muscle stiffness, painful spasms and recurrent falls. He had been previously diagnosed diabetic 6 months prior to the onset of the symptoms. Examination revealed a late middle aged man, who was fully conscious and alert, with generalized tightening and tethering of skin over joints, generalized hypertonia and hyperreflexia with provocation of spasms at examination. He was diagnosed of stiff-person syndrome and was managed with antispasmodics, steroid and subcutaneous insulin with good improvement of symptoms and was discharged home after 5 months of hospitalization but was however, lost to follow-ups.

**Discussion:** Stiff-person syndrome is a rare autoimmune neurological disorder characterized by muscle rigidity and spasms that wax and wane. It is an extremely rare condition with an estimated incidence of 1:1,000,000 people and a 2:1 female preponderance. No gender predilection in the severity of the illness and no racial bias in its occurrence. The syndrome results from the loss of GABAergic central inhibition of the spinal neurons leading to uncontrollable spontaneous discharge. Auto antibodies to Glutamic Acid Decarboxylase, GAD, an enzyme responsible for the synthesis of Gamma-Amino butyric acid, GABA, is found in 50-90% of this patient and is also linked to type 1 DM.

**Conclusion:** Stiff-person syndrome, though rare, could pose a diagnostic dilemma to physicians. It requires a high index of suspicion and its unique symptomatology makes it unforgettable to a first time observer.

### Abstract #259

**CAN NEW IDF CRITERIA ON METABOLIC SYNDROME DETECT NEWLY DIAGNOSED DIABETICS WITH MULTIPLE METABOLIC DERANGEMENTS AND PREDICT THE FUTURE CARDIOVASCULAR RISK?**

_Gamage Jagath Chaminda Garusinghe, MD, Nadisha Dissanayake, MBBS, Tharanga Amarasinghe, MBBS, Upali Illangasekera, MBBS, MD, FRCP_

**Objective:** The lifestyle changes, resulted by industrialization and urbanization coupled with reduced physical activity and intake of energy dense food are believed to increase the prevalence of metabolic syndrome (MS) in developing countries which is a strong predictor of cardiovascular (CVD) risk. Its prevalence in an unselected urban population in India was found to be as high as 26% while Sri Lankans have 20% risk of dysglycemia. This study was designed to see the applicability of MS based on International Diabetic Federation (IDF) criteria in detecting groups with multiple metabolic derangements among newly diagnosed diabetics, and to see its ability to predict high CVD risk, calculated by Framingham Risk Score (FR).

**Methods:** 661 newly diagnosed (within 3 months) diabetics were studied. Exclusion criteria were gestational diabetes, type 1 diabetes and prior lifestyle measures to avoid diabetes. Waist circumference (WC), height, weight and blood pressure measured with calibrated instruments in standard manner. Lipid profile and Fasting Blood Sugar were measured with semi-automated Riele Photometer 5010 V5+ analyzer. MS was detected by IDF 2006 criteria for Asians. CVD risk was assessed by FR.

**Results:** Out of 661 participants 173 (m=84,F=89) qualified based on exclusion criteria. MS was diagnosed in 33% (N=57, M=37, F=20). 58 did not qualify merely for lack of obligatory WC criterion. An equal number (58) subjects with required waist circumference and dysglycemia did not qualify as they fulfilled no additional criteria. WC correlated well with BMI \( r=0.73, \text{sig.0.00} \). ROC curves at BMI of 23,25,30 against MS showed no discriminatory value of BMI in diagnosis of MS. Based on FR, 28.9% of subjects(n=43, with MS 18, without MS 25) were having general CVD risk of more than 20% for the next 10 years. It also showed that males with MS have significantly higher risk of CVD events than those without MS (Chi sq. 1.92, p-0.166). In females those with MS were not at a significant excessive CVD risk compared to those without MS (Chi sq. 7.63, p-0.005).

**Discussion/Conclusion:** Both MS and FR identified similar proportion (33% and 28.9% respectively) of
newly diagnosed diabetics positively. Majority of subjects positively identified by FR were actually not qualifying for MS mealy due to obligatory WC criterion in MS. Though MS is common in newly diagnosed diabetics the magnitude of problem is underestimated as many with multiple metabolic abnormalities still do not qualify due to obligatory WC. Earlier studies have also shown the inferiority of IDF criteria in detecting metabolically abnormal but non-obese groups.

Abstract #260

PREVALENCE AND RISK FACTORS FOR 2° ORAL HYPOGLYCEMIC AGENT FAILURE IN NIGERIANS WITH TYPE 2 DIABETES MELLITUS

Felicia Ohunene Anumah, MBBS, MWCP, FMCP, FACE, Muazu Salisu, MBBS, FMCP, Bola Musa, PhD

Background: Secondary oral hypoglycaemic agent (OHA) failure is common among T2DM patients taking oral agents particularly late into the disease. It is one of the many challenges of diabetes management in Nigeria, the consequence of which is poor diabetes control and early development of chronic complications.

Objective: The purpose of this study was to determine the prevalence and risk factors for 2°OHA failure among T2DM Patients in northern Nigeria.

Methods: Two hundred consecutive T2 diabetic Patients on OHA (glibenclamide and metformin) for at least one year were recruited from the diabetes clinic and their consent was sought for the study. Parameters studied included age, sex, age at diagnosis, duration of DM, type of OHA and dosage, BMI, WC, WH ratio, FBG, 2HPP, Lipid profile, anti – GAD autoantibody positivity and HbA1c. 2°OHA failure was defined as FBG >8.0mmol/l, 2HPP >10.0mmol/l despite maximum doses of OHA. Average values of indices studied are expressed as mean (SD), comparison of group means was by student’s t-test, P value =0.05. Comparison of proportions by the chi-squared test.

Prevalence rates were calculated as percentages while odd ratio estimation was used to determine the risk for OHA failure.

Results: A total of 200 patients were studied. The mean (SD) age of the subjects was 53.2(8.9) years (range 34-75 years). The prevalence rate of secondary OHA failure was 36% with a female preponderance 46(63.9%); males 26(36.1%). The mean (SD) BMI [22.9(5.4)kg/m²] and mean WC for both males and females [87.7(11.3) cm and 90.3(7.9)cm] were significantly lower in subjects with OHA failure than those without OHA failure [27.2(4.8) kg/m² , 93.5(10)cm and 95.7(6.8)cm respectively ], p<0.05. The mean (SD) FPG [11.7(2.6) mmol/L], 2hr PPG [14.5(3.7)mmol/L] and HbAlc [8.3(1.42)%] of those with OHA failure were significantly higher than in those without OHA failure [5.7 (1.5)mmol/L,11.1 (2.8)mmol/L and 7.0(2.07)% respectively], p<0.05. The prevalence of anti-GAD positivity generally among the study subjects was 14.5% while in those with and without OHA failure were found to be 31.4% and 3.1% respectively. Risk factors that were associated with secondary OHA failure included early age at diagnosis of diabetes, duration of diabetes, WC, BMI, FPG, 2hr PPG, and HbAlc level.

Conclusion: The prevalence of OHA failure appears to be high among T2DM patients in this study. Low BMI, WC and duration of diabetes have been found to be risk factors resulting in poor glycaemic control in these patients

Abstract #261

INSULIN AUTOIMMUNE SYNDROME IN A NON DIABETIC INDIAN PATIENT

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Objective: The aim of this study was to describe the occurrence of profound hypoglycemia due to insulin autoantibody in a non diabetic patient.

Case Presentation: A 59-year-old woman with frequent severe hypoglycemia was admitted to the emergency room, presenting with loss of consciousness. In the emergency room, her blood glucose level was 45 mg/dl. She had been in good general health, except for hypertension for 12 years before admission. She has no evidence of other diseases associated with altered immunity nor had taken exogenous insulin ever in her life. Although she had had intravenous glucose injections, she had frequent hypoglycemic attacks, such as disorientation, loss of consciousness, palpitation, and diaphoresis. Her blood glucose levels had been <50 mg/ dl on every hypoglycemic event, especially during fasting hypoglycemia. Physical examination revealed normal vital signs. Her HbA1c was 6.3% (range 3–6%), plasma glucose 40 mg/dl, insulin >18000 μU/ml and >30,000 μU/ml on two occasions, C-peptide 19.5 ng/ml. Her thyroid, liver, and adrenal function studies were normal. IGF 1 and IGF BP3 were also normal. She had a hemoglobin level of 13.4g/dl. Her creatinine level was 0.9 mg/dl. Tests for anti-nuclear antibody, anti-DNA antibody, anti-smooth antibody, and anti-microsomal antibody were all negative. Insulin antibody levels were >300 U/ml (normal range <12 U/ml, measured by EIA). Endoscopic ultrasound to rule out pancreatic mass, turned out to be normal. Dual phase
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Multi slice CT scan abdomen reveals no abnormality. PET CT and Ga-DOTATOC scan also didn’t found any abnormality. Pt was put on prednisolone 60mg/day and within week, she stopped having hypoglycemic episodes. Insulin antibody level came down to 15.3 U/ml (equivocal range).

Discussion: There are two types of autoimmune hypoglycemia, one due to autoantibodies acting against the insulin receptor and the other due to autoantibodies acting against insulin itself in individuals who have or have never received exogenous insulin, respectively. Both types are rare and can produce fasting and postprandial reactive hypoglycemia. Insulin Autoimmune Syndrome was first described by Hirata et al in 1970 and there have been only 200 cases of insulin autoimmune syndrome reported over the past 30 years. Most cases of insulin autoimmune hypoglycemia described in Asian races have shown a strong correlation with certain HLA systems, suggesting the existence of a predisposing genetic component. Autoimmune hypoglycemia is associated with certain HLA systems, such as DR4 and DQw3, and especially DRB1*0406/DQA1*0302/DQB1*0302. It is noteworthy that HLA-DRB1*0406 is quite prevalent in Japanese patients. Several types of insulin antibodies have been reported and are most frequently seen in patients who receive insulin injections, but there have also been reports of them in nondiabetic patients with such autoimmune disease. Postprandial hypoglycemia is more common with this syndrome than fasting hypoglycemia and the course of this condition is benign and self-limited, with remission usually occurring within 1 year.

Conclusion: Insulin autoimmune syndrome, though very uncommon clinically, should be one of the differential diagnosis n patient with hyperinsulinemic hypoglycemia. Our patient had historical serum insulin level, to our knowledge most cases reported had levels around 3 to 4,000 only, while it was >30,000 u/ml in our case.

Abstract #262

IMPACT OF A RESIDENT-RUN QUALITY IMPROVEMENT PROJECT IN IMPROVING PHYSICIAN COMPLIANCE WITH ADA RECOMMENDATIONS IN AN ACADEMIC SETTING

Akshay Bhanwarlal Jain, MD, Leela Mary Mathew, MD

Objective: To determine if practice patterns of physicians change, 12 months after releasing results of a quality improvement (QI) project assessing compliance with American Diabetes Association (ADA) goals for reducing vascular disease risk in patients with diabetes mellitus type 2 (DM-2).

Methods: A retrospective chart review (pilot project) was performed on all patients coded for diagnosed DM-2 in a 7-member faculty group practice of internists in 2009. Levels of glycohemoglobin (HbA1c), low density lipoprotein (LDL) and blood pressure (BP) for 6 months preceding data collection were used for analysis. Results were then shared with the internists and their residents. A follow-up analysis was done after 12 months and the 3 parameters were reanalyzed in the same patient group.

Results: Of the 244 patients in the initial study (mean age 64), 21 were either lost to follow-up or died. Out of the remainder, 124 (56%) had HbA1c<6.9%, 146 (65%) had LDL<99mg/dl and 132 (59%) had BP<130/80. Comparatively, the clinic average values in 2009 were 54%, 59% and 34% respectively. National averages were 37%, 49% and 36% respectively, according to the National Health and Nutritional Examination Survey (NHANES) 1999-2000. Overall, 49 adults (22%) met ADA recommendations on all 3 parameters, compared to 12% in 2009 and the national estimate of 7%.

Discussion: Multiple studies have emphasized the importance of adequate glycemic, cholesterol, and BP control to prevent or delay the micro and macrovascular complications of diabetes. 85% of the study population in 2009 were already on either an angiotensin converting enzyme inhibitor (ACEI) or angiotensin II receptor blocker (ARB). Although HbA1c and LDL levels in our patients in 2009 were better than the national average, BP was not. The faculty physicians and their residents were notified of this deficiency. Follow-up comparison shows significant improvement in BP control.

Conclusion: Adequate steps were taken by the faculty physicians and their residents after the initial study to ensure vigilant follow-up and optimum titration of antihypertensive medications, resulting in significantly better results. This led to a higher proportion of patients with DM-2 meeting the tri-pronged ADA goals. Resident-run QI projects are important tools to increase awareness of latest guidelines and to monitor and improve practice patterns. With the nation veering towards a pay-for-performance model for healthcare, these efforts will help to reduce vascular complications in the study population.
**Abstract #263**

**PRESCRIBING PATTERNS IN A DIABETES CENTER: ALGORITHMS AND PHYSICIAN PREFERENCES**

Celeste Cheryll Lopez Quianzon, MD, Karezhe Mersha Mansur Shomali, MD, CM

**Objective:** The ADA/EASD and AACE have provided guidelines for management of type 2 diabetes mellitus emphasizing lifestyle changes and use of metformin as the initial intervention. Recommendations for combination therapy if goals are not met are more complicated with multiple options. We wanted to look at patterns of type 2 diabetes management using combination therapy among four endocrinologists.

**Methods:** A chart review was performed on 100 type 2 diabetes patients with at least 2 recent visits for each endocrinologist (n=400). A patient was included in the review if type 2 diabetes was present for at least 2 years, on at least 1 diabetes medication, the interval between visits is not longer than one year, and there are two A1C determinations. Data on patient demographics, A1C, and diabetes medications were obtained.

**Results:** Four hundred charts were identified; 100 from each physician. Majority of the patients were females (238). The mean patient age was 62, weight was 215 lb and A1C was 7.3. The overall adherence to the ADA/EASD guidelines was 54%. The overall adherence to the AACE guidelines was 56%, 24%, and 15% for the A1C categories 6.5-7.5, 7.6-9, and > 9, respectively. Metformin was most commonly prescribed and mixed insulin was least prescribed. With regards to addition of another agent, physician A and B prescribed more sulfonylureas, physician C favored basal and bolus insulin and physician D preferred GLP-1 agonists and TZDs.

**Discussion:** Considerable variation exists in prescribing patterns for each physician with regards to add-on therapy to metformin. Despite the differences in the pharmacotherapy for type 2 diabetes mellitus, patient A1Cs among the 4 physicians were similar. The treatment guidelines may be more relevant for primary care physicians rather than endocrinologists.

**Conclusion:** In this group of patients treated for type 2 diabetes by 4 community-practicing endocrinologists, adherence to the ADA/EASD and AACE guidelines was low. Individual physician prescribing preference may determine the patients’ prescription. Further study is needed to determine health outcomes of patients treated with different medications who achieve similar glycemic goals.

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**Abstract #264**

**EFFICACY OF POLYURETHANE FOAM DRESSING IN TYPE 2 DIABETIC PATIENTS WITH DEBRIDED WOUNDS**

Hans Tandra, MD, FACE, Audrey Amelia, MD, Olivia Handayani, MD, BMedSc

**Objective:** The aim of this study was to assess the effectiveness of polyurethane foam dressing for wound healing in debrided wounds of patients with diabetes.

**Methods:** Type 2 diabetic patients with foot ulcer or infections were included in this study. The study was conducted between August 20, 2010, and November 20, 2010. Twenty patients were randomly assigned to a study group (10 patients) and a control group (10 patients). In the study group, we used Wundres, Polyurethane Foam Dressing from Korea, with a size of 10 cm x 10 cm x 0.5 cm. No topical antibiotics were used. Dressings were changed every 1 – 2 days, and bedside debridement was also performed. Controls were dressed with conventional techniques using local antibiotics. Wound healing was calculated as the number of days from the date of the first debridement to the date the wound was detected as completely epithelized.

**Results:** A total of 20 patients were studied. The mean duration for wound healing was 15.2 ± 11.5 days in the foam group and 32.4 ± 20.6 days in the control group (P < 0.001). Polyurethane Foam Dressing had less pain, more comfortable, easier handling, and more rapid wound healing.

**Conclusion:** Sterile and non-medicated Polyurethane Foam Dressings significantly reduced the time taken for wound healing, compared to conventional dressings.

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**Abstract #265**

**SCREENING FOR HYPOGONADISM IN TYPE 2 DIABETIC MALES: A COMPARISON OF PRIMARY CARE AND ENDOCRINOLOGY PRACTICES**

Dana Patrick Houser, MD, Elena Christofides, MD, FACE

**Background/Objective:** Greater than fifty percent of males with type 2 diabetes have comorbid hypogonadism. Hypogonadism refers to a state of absolute or relative androgen deficiency. Review of the endocrine literature shows that testosterone therapy has a positive impact on insulin resistance and the cardiovascular sequelae inherent in diabetes. However, greater than ninety percent of diabetics are currently managed by primary care physicians. It is suspected that male patients with type
2 diabetes are screened less frequently in primary care than in an endocrine practice. The purpose of this study is to determine the difference in screening adult male type 2 diabetics for hypogonadism between endocrine and primary care physicians in outpatient care settings.

**Methods:** This is a retrospective chart review evaluating the rates of screening for hypogonadism in two endocrine practices versus two primary care practices in central Ohio. Charts with diabetes related ICD-9 codes were examined. Screening for hypogonadism would, therefore, be defined as ordering blood tests for one or more of the following: total testosterone, free testosterone, bioavailable testosterone and sex hormone binding globulin. Data will be analyzed using non-parametric statistical methods.

**Results:** Rates of screening for hypogonadism in adult male type 2 diabetics by endocrinologists match those found in the literature. Rates of screening by primary care physicians fall short. Results of the analysis will be the focus of this poster presentation.

**Conclusion:** There is scant literature in this topic area despite growing evidence for the linkage between hypogonadism and type 2 diabetes in males. This is the first study to evaluate differing rates of screening in the specialist versus the primary care setting. A change in practice standards may be warranted in order to ensure no health disparities in the current health care reform climate. A larger scale study to further explore these differences and their outcomes will be necessary to inform any practice changes.

**Abstract #266**

**HYPOGLYCEMIA IN PATIENTS ON ANTI-DIABETIC MEDICATIONS WHO FAST FOR LABORATORY TESTS**

Saleh A. Aldasouqi, MD, FACE, ECNU, Ahmad Sheikh, MD, ECNU, Pam Klosterman, RN, NP, CDE, Sheila Kniestedt, LPN, Lisa Schubert, LPN, Rosie Danker, RN, MS, CDE, Mary Austin, MA, RD, CDE, FAAD

**Objective:** Hypoglycemia is a major obstacle in diabetes management. Every now and then, physicians’ offices are notified by laboratories of patients’ critically low glucose results (typically after patients who showed earlier for fasting tests have already left the laboratory). This may create nervousness about patients’ safety, and could be potentially harmful. To our knowledge, diabetes education programs lack instructions about precautions for overnight fasting for laboratory tests. We undertook this study to evaluate this overlooked, potentially serious, problem.

**Methods:** We asked our central laboratory, which does not keep a record of patients’ fasting status, to track all morning patients’ glucose results below 70 mg/dL between January 2008 and September 2009 (representing a practice of 3 diabetes clinicians). We then identified those who were on anti-diabetic medications, and contacted them for telephone interviews, verifying their recollections of these abnormal results, including questions about: the state of fasting, the presence of symptoms, and whether they made adjustments in their anti-diabetic medications.

**Results:** Of 55 patients who had AM glucose < 70 mg/dL, 39 were on anti-diabetic medications. Of these, 15 patients recalled being fasting, 20 were uncertain, and 4 recalled being non-fasting. The range of hypoglycemia in patients who recalled being fasting or possibly fasting (n=35) was 69-31 mg/dL: 6 results < 40, 5 < 50, 12 < 60, and 12 < 70 mg/dL (17, 15, 34, 34%, respectively). Seven patients recalled having autonomic hypoglycemic symptoms, but none had change in level of consciousness, and none needed assistance. No patient recalled making adjustments to their anti-diabetic medications, the night before, nor the morning of the test.

**Discussion:** Extensive literature search retrieved no guidelines regarding educating patients on how to prepare for overnight fasting for laboratory tests. We believe this is the first study to evaluate this apparently overlooked educational piece in diabetes. Patients on insulin or sulfonylurias may have lingering effects of the medications if they do not interrupt the overnight fast when glycogen stores begin to wane, and the risk of hypoglycemia increases.

**Conclusion:** We believe that hypoglycemia resulting from fasting for laboratory tests is an overlooked problem. This potential serious harm to patients should be of particular interest to risk managers, laboratories, clinicians and diabetes educators. Clinicians and diabetes educators should instruct their patients about preparation for fasting for laboratory tests, including close glucose monitoring and adjustment of anti-diabetic medications.

**Abstract #267**

**OUTCOME OF THE HISPANIC PATIENTS WITH DIABETES MELITUS WHO WERE ADMITTED TO GENERAL MEDICAL AND SURGICAL FLOORS**

Soe Naing, MD, MRCP, Jagrati Mathur, MD, Tushar Acharya, MD, Swapna Busa, MD, Jaynesh Patel, MD

**Objective:** To determine the outcome of the Hispanic patients with diabetes mellitus (DM) who were admitted to general medical and surgical floors and to compare their outcome with caucasians.
Methods: Hispanic and caucasian patients with known DM type 1 or type 2, who were admitted to medical or surgical floors during the month of March 2009 and stayed in the hospital for at least 24 hours, were included in this retrospective study. The medical records were reviewed and the outcome measures were compared between these 2 groups. An infection is considered hospital-acquired if clinical symptoms that required antibiotic therapy originated in our hospital and were not clinically apparent at the time of admission.

Results: 133 Hispanic and 107 caucasian patients were included in the study. Of Hispanic patients, 38% were men with the mean age of 61.8 years, mean BMI 30.6, mean HbA1c 8.3%, mean admitting blood glucose (BG) 231 mg/dl and mean LDL cholesterol 82.3 mg/dl. Of white patients, 46% were men with the mean age of 66.4 years, mean BMI 30.9, mean HbA1c 7.4%, mean admitting BG 177 mg/dl and mean LDL cholesterol 79.8 mg/dl. Mean bed-side BG during hospital stay was 183 mg/dl in Hispanics compared with 177 mg/dl in caucasians. Rate of mild and severe hypoglycemia were 12% and 3% in Hispanics and 15% and 1.9% in caucasians, respectively. Mortality rate, hospital acquired infection and length of stay were 3%, 3% and 5.01 days in Hispanics and 2.8%, 1.9% and 6.6 days in caucasians, respectively.

Discussion: Mean admitting HbA1c (p 0.029) and BG (p 0.001) were significantly higher in Hispanics than in caucasians, indicating poorer pre-admission diabetes control in Hispanics. However, there was no significant difference in mean bed-side BG and rate of hypoglycemic episodes during hospital stay. It was previously reported that Hispanic diabetic patients had shorter length of stay than caucasians; and we observed a similar outcome in our study (5.01 vs 6.6 days: p 0.0689). There was no significant difference in mortality rate and hospital acquired infection between two groups.

Conclusion: Mortality rate, hospital acquired infection and length of stay were 3%, 3% and 5.01 days, respectively, in Hispanic patients with DM who were admitted to general medical and surgical floors. Diabetes control was poorer in Hispanic patients prior to admission. However both groups achieved similar diabetes control during hospitalization and there was no significant difference in clinical outcome between two groups. Further studies with larger number of cases are needed to validate the result.

Abstract #268

SEVERE HYPOGLYCEMIA AND AUTOPSY-PROVEN ISLET CELL HYPERPLASIA IN A NON-DIABETIC DIALYSIS PATIENT

Brittany Bohinc, MD, Sarah Larson, DO, John C. Parker, MD, FACE

Objective: Case report.

Case Presentation: A 77-year-old white man with bilateral renal cell carcinoma (RCC) s/p bilateral nephrectomy on hemodialysis (HD) for 13 years presented with recurrent episodes of hypoglycemia. For 6 months he had multiple episodes of daily symptomatic hypoglycemia as low as 19 mg/dl. His symptoms were associated with Whipple’s Triad and responded to glucagon. Most of his hypoglycemic episodes occurred in the fasting state, but postprandial episodes did occur, both on HD and non-HD days. Medications were gabapentin, methadone, Percocet, buspar, and sevelamer. Vital signs were stable. He was placed on IV infusion of 10% dextrose (D10) due to continued episodes of symptomatic hypoglycemia. Laboratory data: Glucose 38 mg/ml, c-peptide 16.5 mg/ml (1.1-4.4 mg/ml), insulin 16.6 uIU/ml (0-24.9), proinsulin 13.5 pmol/L (0-10), and beta-hydroxybutyrate suppressed at 0.5 mg/dl. Sulfonylurea screen and insulin antibodies were negative. IGF-II, adrenal, thyroid, and liver function tests were normal. Endoscopic ultrasound and MRI pancreas failed to reveal a pancreatic source of endogenous hyperinsulinemia. On day 12 of hospitalization, after recurrent hypoglycemic episodes despite a D10 drip, he experienced a fatal arrhythmia. Autopsy examination revealed enlarged islets (0.3 to 1.1 mm) compared to age matched control (0.2 mm). There was beta-cell atypia and occasional ductulo-insular complexes intermixed with normal appearing islets. Thorough examination of the pancreas and the bowel showed no ectopic pancreatic foci or insulinoma. He was diagnosed with autopsy-proven islet cell hyperplasia as a cause of his persistent hypoglycemia.

Discussion: Adult-onset islet cell hyperplasia (ie. nesidioblastosis or non-insulinoma panceatogenous hypoglycemic syndrome) is a rare diagnosis. Although described most frequently in children it has been described in adults post-gastric bypass, in MEN, idiopathically, and in Von-Hippel-Lindau (VHL). Despite RCC, he did not have clear-cell morphology nor other findings to suggest VHL. There has only been one other reported case describing similarly expanded and erratically-shaped islet cells in a patient with chronic kidney disease (CKD) and hypoglycemia. It was fatal. In both cases of CKD and endogenous insulin production, laboratory data was
difficult to assess because of decreased renal clearance of insulin and its metabolites. Similar issues with laboratory interpretation have been encountered in the very rare circumstance of insulinoma in CKD.

**Conclusion:** In addition to other purported contributors to hypoglycemia in patients with ESRD, causes of endogenous hyperinsulinism should also be considered.

**Abstract #269**

**WEIGHT LOSS AND METABOLIC BENEFIT WITH THE ADDITION OF GLUCAGON-LIKE PEPTIDE AGONIST AND PIOGLITAZONE TO TYPE 2 DIABETES MELLITUS ADOLESCENT TREATMENT**

Nouhad Raissouni, MD, Sheila Perez, MD, Fatma Ahmed, MD, Amrit Bhangoo, MD, Sonal Bhandari, MD, Svetlana Ten, MD

**Background:** Glucagon-Like Peptide agonists has been shown to stimulate insulin secretion from the β cell and inhibit β cell apoptosis. Pioglitazone is known to improve insulin sensitivity as well as inhibit β cell apoptosis. We used Glucagon-Like Peptide agonists with Pioglitazone in newly diagnosed adolescents with Type 2 diabetes mellitus (DMT2) to induce remission.

**Objective:** Evaluate whether Glucagon-Like Peptide agonists use with Pioglitazone in newly diagnosed adolescents with DMT2 will induce remission. To analyze the safety and effectiveness of GLP-1 agonists and Pioglitazone in newly diagnosed adolescent with DMT2.

**Methods:** Nine Overweight adolescent’s with DMT2 and BMI >24 kg/m² were studied. GLP-1 agonists 5mcg subcutaneous was prescribed twice daily once patients were clinically diagnosed with DMT2 and then increased to 10 mcg twice daily one month later. Lantus average 30 units daily with Actoplus Met 15mg/850mg once daily was used. Anthropometric parameters, metabolic parameters, gastrointestinal and neurological complications assessment were obtained at the baseline and 6 months after treatment.

**Results:** Anthropometric and biochemical characteristics of 9 adolescents with DMT2, Base Line and post 6 months treatment.

**Conclusion:** After 6 months of therapy 75% of patients showed a remission of DMT2 based on improved Hba1c. Lantus therapy was discontinued after one month of use only. Short acting insulin use was not necessary. BMI %was decreased in all patients. All patients showed improvement in there lipid panel and in there liver enzymes. No documented gastrointestinal or neurological complications were notified.

**Abstract #270**

**WHAT BLOOD SUGAR SHOULD BE TARGETED TO ACHIEVE HBA1C GOAL IN YOUR PATIENT?**

Gamage Jagath Chaminda Garusinghe, MD, Thilak Weeraratna, MD, Sarath Lekamwasam, MD, FRCP

**Objective:** In previous studies, compared to PPBS, FBS shows a stronger correlation with HBA1c in poorly controlled diabetics (PCD). In well controlled diabetics (WCD), however, PPBS correlated better with HBA1c than FBS. Exploration of this relationship will cast light on the exact method of achieving target Hba1c in both groups. The objective was to find out the correlations of FBS and PPBS with HBA1c among diabetics with different degree of glycemic control.

**Methods:** Consecutive 584 type 2 diabetics were studied and patient and disease related factors were recorded. FBS, 2-hour PPBS (glucose oxidase method) and Hba1c (immunoassay for direct photometric determination of Hb A1c) were estimated. Patients were categorized to PCD (HBA1c>7%) and WCD (HBA1c<7), based on their HBA1c level.

**Results:** Mean duration of diabetes was 6.7 (SD=5.5) years. In the entire group, mean FBS, PPBS and HbA1c were 14 (SD=5.2) mmol/L, 10.2 (SD=4.6) mmol/L and 6.9 (SD=0.8) %, respectively. PCD (n=206) had mean HbA1c, FBS and PPBS of 7.7% (SD=0.47), 17.5 (SD=5.0) mmol/L, and 12.4 (SD=4.0) mmol/L, respectively. Among them, HbA1c showed a marginally better correlation with FBS (r=0.54, r²=0.29) than with PPBS (r=0.49, r²=0.24). Among WCD (n=311) mean HbA1c, FBS and PPBS were 6.4 % (SD=0.50), 12 (SD=3.5) mmol/L and 8.9 (SD=3.2) mmol/L, respectively. Among WCD, HbA1c showed a better correlation with FBS (r=0.47, r²=0.22) than with PPBS (r=0.3, r²=0.09).

**Conclusion:** Among these diabetics, FBS showed a stronger correlation with HBA1c than PPBS and FBS can be considered a surrogate of HBA1c as well as a treatment target of glycemic control. It was shown that it is still FBS needed to be targeted in all diabetics to aim for tight control in terms of HBA1c reduction. However, the correlation between FBS and HBA1c in WCD was slightly lower than that of PCD group. This study strengthens the common knowledge that lowering FBS yield better HBA1c reduction. At the same time, it has cast doubts as to whether PPBS should be done at all especially in fairly controlled diabetics.
Abstract #271

EFFECTS OF SITAGLIPTIN OR PIOGLITAZONE ON GLYCEMIC CONTROL IN TYPE 2 DIABETIC PATIENTS RECEIVING INSULIN

Hans Tandra, MD, FACE, Audrey Amelia, MD, Olivia Handayani, MD, BMedSc

Objective: To compare the benefits of additional oral hypoglycemic agents (OHAs), Sitagliptin (SIT) or Pioglitazone (PIO), in patients with type 2 diabetes mellitus (T2D) receiving insulin.

Methods: The 12-week study was performed in 20 patients, aged 40 – 65 years, with inadequately controlled T2D (HbA1c 6.8 – 8.1%) on Insulin. We have been using SIT 100 mg/d and PIO 30 mg/d in the study. The primary efficacy variable was the change in HbA1C from baseline to week 12.

Results: Twenty patients were completed in the study, 10 SIT and 10 PIO. At baseline, there were no significant differences between the groups. After 12 weeks, additional SIT and PIO significantly reduced HbA1c, -1.46% (-0.72 - -1.89) and -1.42% (-0.68 - -1.81), respectively; (p <0.05), whereas 42% SIT and 39% PIO of the subjects attained HbA1c <6.5%. Fasting plasma glucose and 2 hour postprandial glucose significantly decreased in all groups. Overall, Sitagliptin and Pioglitazone were well tolerated as the major adverse reactions were mild in severity.

Conclusion: Additional oral hypoglycemic agents Pioglitazone and Sitagliptin significantly improved the glycemic control, and well tolerated when used in combination with Insulin.

Abstract #272

ASSESSMENT OF PANCREATIC BETA CELL FUNCTION OF PATIENTS WITH HYPERGLYCEMIC EMERGENCIES

Akinyele Taofiq Akinlade, MBBS, Anthonia Okeoghene Ogbera, MBBS, FMCP, FACE, Olufemi Fasanmade, MBBS, FWACP, FACE

Objective: To assess level of pancreatic beta cell function in patients with hyperglycemic emergencies (HE), using serum C-peptide.

Methods: Ninety-seven patients consecutively admitted for HE were recruited. Each patient’s data were collated using an investigator-administered questionnaire. All patients had their serum C-peptide, glucose, electrolytes, urea, creatinine and urinary ketones done at admission using appropriate laboratory methods. Statistical analysis was done and results expressed as mean ± standard deviation (SD). A p value <0.05 was regarded statistically significant. Correlation between levels of serum C-peptide and age of subjects and duration of DM respectively was done.

Results/Discussion: The mean age of the patients was 51 (16) years and comparable in both sexes, with most between 40 and 60 years, with prior history of DM and on oral anti-diabetic drugs. The mean duration of DM was 6.5 (7.1) years. Thirty five percent were newly diagnosed at the time of admission. A quarter of the subjects were hypertensive and majority had been so for 10 years or less. The types of HE in this study are: DKA (24.7%), NHS (36.1%), and HHS (39.2%). It was highest in HHS and lowest in NHS, a difference that was statistically significant. Mean serum C-peptide level was 1.6ng/dL. It was 0.9ng/dL in patients with DKA and NHS while 2.7ng/ dL for HHS. Differences were not statistically significant. There was no significant correlation between serum C-peptide and either the age of subjects or duration of DM respectively.

Conclusion: About 70% of the study subjects, cutting across all HE types, had poor pancreatic beta cell function.

Abstract #273

EXERCISE PATTERNS AND GLYCEMIC CONTROL IN PERSONS WITH DIABETES MELLITUS IN BENIN CITY, NIGERIA

Aihanuwa Theresa Eregie, MBBS, FMCP, Andrew Efosa Edo, MBBS, FMCP

Background: Exercise is a major therapeutic tool in diabetes care, with proven benefits in terms of improved metabolic indices and physical wellbeing, amongst others. This report details the exercise patterns and levels of glycemic control in persons with diabetes mellitus (DM) seen in a tropical tertiary health facility.

Methods: Consenting persons with DM seen over a 4-week period in the Diabetes Clinic of the University of Benin Teaching Hospital, Benin City, Nigeria were recruited for the study. Socio-demographic, clinical and laboratory data were recorded in questionnaires by the authors. The type(s), frequency and duration of exercise were documented and mean fasting plasma glucose (FPG) values over the preceding year were utilized in the determination of glycemic control.

Results: Ninety DM persons were recruited into the study. Type 2 DM was present in 92.2% of subjects. The mean (SD) values for age, body mass index (BMI), waist circumference (WC) and FPG were 25.6(4.7), 91.6 (15.8) cm and 6.1(2.6) mmol/L respectively. Sixty (66.6%) DM persons were engaged in
some form of exercise, the most common being walking (24.4%) and aerobics (10%), and the least common being table tennis, swimming and weightlifting (1.1% each). The frequency of exercise was ≥3 times a week in 66.6% of the exercising DM persons (p < 0.001). The mean duration of exercise was 25 (10) minutes. The mean FPG of 8.6mmol/L in non-exercising DM persons was significantly higher than the value of 5.2mmol/L in exercising DM persons (p < 0.005).

**Discussion:** Exercise therapy is a major aspect of management of diabetes mellitus, and DM persons who exercise regularly enjoy the benefits, including improved metabolic control. The finding of better glycemic control in exercising DM persons in our locale is similar to previous reports from elsewhere.

**Conclusion:** Sizeable proportions of DM persons in our centre exercise regularly and have better glycemic control than their non-exercising counterparts. More DM persons should be encouraged to exercise regularly, for at least 30 minutes duration in order to benefit maximally from this intervention.

Abstract #274

**SOCIO-ECONOMIC AND RACIAL DISPARITY IN HBA1C, LDL AND SELF-CARE OF DIABETES**

Akshay Bhanwarlal Jain, MD, Ajmal Kazman, MD, Saadia Sherazi, MD, Jean Bauch, RD, CDE, Krishnakumar Rajamani, MD

**Objective:** This study aimed to determine differences in the self-care of diabetes and its correlation with hemoglobin A1c (HbA1c) and LDL cholesterol levels (LDL) in patients from different socioeconomic and racial groups. We hypothesized that non-caucasians with diabetes would have worse self-care and glycemic control than caucasian patients due to unfavorable socioeconomic conditions.

**Methods:** A survey of 3,197 patients with diabetes was conducted from August 2009 to October 2009 in Rochester, NY. The Summary of Diabetes Self Care Activities (SDSCA) questionnaire (maximum score=42), which is a validated instrument to assess a patient’s practices regarding diet, exercise, blood glucose testing, and foot care, was mailed to the survey group. HbA1c and LDL values were obtained from electronic medical records. SDSCA scores, HbA1c levels, and LDL levels were compared using student-t and chi-square tests. The median household income (MHI) corresponding to zip codes of the responders was obtained from civic records, to estimate the socioeconomic status (SES) of these patients.

**Results:** Of the 705 responses returned, 411 (58.2%) were female and 584 (82.9%) were caucasian. The mean age was 65.6 (±13.1) and the mean SDSCA score was 23.6 (95% CI=23.2 to 24.1). A total of 294 patients (41.7%) had MHI below the national average of $49,777. Within this lower income group, the mean HbA1c of non-Caucasians (7.79 ± 1.79) was higher than that of Caucasians (6.97 ± 1.29, p=0.0001). Mean SDSCA scores (23.2 ± 7.3 vs. 24.1 ± 6.9, p=0.32) and LDL levels (94.6 ± 30.6 vs. 88.7 ± 26.8, p=0.11) were not significantly different. In a comparison of different socioeconomic groups, the mean HbA1c of patients below the MHI national average (7.21 ± 1.48) was higher than that of patients above it (6.84 ± 0.97, p=0.0002). Mean SDSCA scores (23.5 ± 7.2 vs. 23.7 ± 6.2) and LDL levels (90.41 ± 28.03 vs. 89.8 ± 27.89, p=0.77) were not significantly different.

**Conclusion:** SDSCA scores were generally in the mid-range and few people reported high levels of self-care. Despite similar levels of reported self-care, a significant difference was seen in HbA1c levels between patients of different SES. In patients from the same SES, significant disparity existed between caucasian and non-caucasian populations, despite comparable SDSCA scores. Similar SDSCA scores may underestimate the need to intensify measures to improve HbA1c levels in non-caucasians, regardless of their SES.

Abstract #275

**DIABETIC MYONECROSIS**

Hassan Shawa, MD

**Objective:** To report a case of diabetic myonecrosis.

**Case Presentation:** Fifty one year-old patient with a history of poorly controlled type-2 diabetes, presented with a complaint of severe right knee pain and swelling for 4 days which limited his activity. Physical exam was significant for a firm, warm, and severely tender swelling in the super medial aspect of the right knee. MRI of the right lower extremity and a biopsy confirmed the diagnosis of diabetic myonecrosis. The patient was treated conservatively, his symptoms improved during the course of the hospital stay.

**Discussion:** Diabetic muscle infarction (also known as diabetic myonecrosis) is a rare disorder which was initially described in 1965. Pathogenesis is unclear but it is most likely related to diffuse microangiopathy and atherosclerosis. The diagnosis is clinical and a MRI can confirm the diagnosis. A muscle biopsy is often not needed but it can show typical findings of muscular tissue necrosis. Other diagnostic tests (imaging, laboratory investigations) can be used to rule out other causes. Slow,
spontaneous resolution usually occurs in 4-8 weeks. Conservative management is recommended; surgery can delay recovery.

**Conclusion:** Diabetic myonecrosis is a rare disorder which affects patients who have relatively longstanding diabetes, many of whom have other micro or macrovascular complications. Since the incidence of this disorder is likely to increase because of the increasing global prevalence of diabetes, clinicians should have high index of suspicion of this often underdiagnosed/misdiagnosed disorder to make a timely diagnosis and to avoid the unnecessary use of steroids, antibiotics or surgical intervention.

**Abstract #276**

**IMPACT OF A PROJECT RENEWAL SHELTER ON DIABETIC MANAGEMENT**

_So-Young Kim, MD, Amit Seth, MD, Ilias M Almakaev, MD, Adrienne M Fleckman, MD_

**Objective:** To report a case of a homeless man whose poorly controlled diabetes (DM) was dramatically improved with the help of Project Renewal Shelter.

**Case Presentation:** A 62-year-old homeless man with T2 DM, hypertension, hyperlipidemia, peripheral neuropathy, chronic low back pain, and depression was non-compliant with diet and unable to pay for prescriptions or doctors. After moving into a Project Renewal shelter, comprehensive health care, including medications, was provided under supervision of the shelter physician. He was then referred to endocrine clinic with a packet including medical history, medication list (humalog 75/25, metformin, sitagliptin), and labs. He did not bring his fingerstick glucose (FSG) log and did not know his medications. He took his medicine, but was unable to follow a diet. BMI was 24 kg/m2, blood pressure normal, skin intact, and monofilament sensation absent on his feet. A1c was 12.5%; LDL 132mg/dL. He was referred to podiatry and asked to return with FSG log and new labs. Recommendations were provided to his shelter. The next visit, he did not bring a log, recall medications, or have labs. He reported symptomatic hypoglycemia. Insulin was lowered, and sitagliptin stopped. He was referred to a nutritionist. On his last visit, he again did not bring a log, nor recall medications. He now limited his carbohydrate intake and checked his feet daily. A1c was now 7.4%, and LDL 60mg/dL.

**Discussion:** Chronic disease is prevalent among the homeless, with DM being the most frequently diagnosed. DM management requires medical care, education, drug therapy, diet modification, exercise, glucose self-monitoring. Three-quarters of homeless patients report difficulty in managing DM; half are poorly controlled. Common barriers are diet and scheduling medication with meals. Lack of food choice limits the ability to eat a diabetic diet. Other barriers include mental illness, substance abuse, and poverty. Our patient was diabetic and homeless with no available medical care. After moving into a Project Renewal shelter, he had ready access to medical care through in-house physician visits, specialty referrals, and medication administration. Despite diet non-adherence and poor knowledge or insight, this patient quickly achieved marked improvement in glycemic control.

**Conclusion:** Uncontrolled DM is widespread among the homeless. Excellent care and follow up can be provided to this population. It is important for health care providers to recognize the difficulties in managing DM in homeless patients, and direct these patients to shelters that can provide services to optimize diabetic care.

**Abstract #277**

**ISOLATED NON-TRAUMATIC CRANIAL NERVE SIX PALSY AS PRESENTING SYMPTOM OF DIABETES MELLITUS**

_Gaurav Gulati, MD, Richard Alweis, MD_

**Objective:** Diabetes mellitus is a known cause of new onset Abducens nerve palsy in the population. The relative risk is 23.7% higher in the diabetic population than the general population, but it is a very rare presenting symptom for its new diagnosis. We present here a case of a middle aged man who presented with Abducens nerve palsy as the first sign of Diabetes Mellitus.

**Case Presentation:** A 58-year-old male with no significant past medical history and who had not been under a physician’s care for many years presented with a two day history of blurry vision, dizziness and headache. His headache was frontal, associated with left ear pressure and some blurring of vision. There was associated subjective unsteadiness of gait. This was reported to improve when he would walk with closed eyes. He denied any recent trauma to the head or ears, earaches, fevers or chills, neck stiffness, black spots or floaters in his field of vision. His sister reported him to be a bit “cross eyed” in appearance, which was new. On his physical examination, he had an elevated BP of 162/95, and a Right esotropia of about 15 deg. with ipsilateral lateral gaze palsy. Pupils were symmetrical and bilaterally equally reactive, with no papilledema and his physical exam including a detailed ear and extra-aucular exam was otherwise unremarkable. In the emergency department, he had an extensive workup including a normal head CT and normal CBC with differential, electrolytes, ESR, TSH, thiamine, folate and...
B12 levels, but he did have a random blood sugar of 274. This was repeated and was again elevated at 258 mg/dL. Urinary glucose levels were greater than 250 mg/dL. An autoimmune workup was unrevealing. Glycohemoglobin HA1C was 7.5%. The patient was diagnosed as a diabetic and persistent hypertensive and outpatient treatment was initiated.

**Discussion/Conclusion:** There is a 6-fold increase in odds of having diabetes in cases of sixth nerve palsy over controls, whereas systemic hypertension does not seem to be associated with increased odds. In contrast, there is an 8-fold increase in odds of having coexistent diabetes and hypertension in cases of sixth nerve palsy over controls. This case reinforces the importance of keeping in mind diabetes and possibly coexistent systemic hypertension as causative factors in non-traumatic sixth cranial nerve palsy. Additional diagnoses of exclusion include: restrictive diseases of the orbit (e.g., from thyroid disease or orbital tumors), spasm of the near reflex, neuromuscular diseases (e.g., myasthenia gravis), pseudotumor cerebri, Posterior Inferior Cerebellar Artery (PICA) aneurysms, and the congenital Duane Syndrome Type I. A focused work-up should be performed to rule out these phenomena in the appropriate clinical setting. However, treatment of diabetes and hypertension should not be withheld while this work-up is ongoing.

Abstract #278

**MICROALBUMINURIA IN TYPE 2 DIABETES IN NIGERIA**

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**Background/Objective:** Albuminuria is a strong independent predictor of all-cause of CVD mortality in American Indians with diabetes. Early assessment and targeted interventions are necessary to treat and prevent all risk factors associated with diabetic complications. This study is to determine the prevalence of microalbuminuria and its clinical profile in type 2 DM subjects in Nigeria.

**Methods:** This is a cross-sectional study in which 200 DM subjects were randomly selected in LASUTH. Interviewer administered questionnaires, biochemical and urine analysis were carried out. All the study subjects had ECG done to assess their cardiovascular status and statistical analysis done. P value of <0.05 is significant.

**Results/Discussion:** The prevalence of microalbuminuria was 31%. The total mean age of subjects with microalbuminuria 59.7 ± 11.02yrs, Female(F)=55.1 ± 12.9yrs, Male(M)=64.3 ± 10.6yrs, p=0.01. This showed that the mean age of M is higher than F with a sex distribution, F:M =2:1. The mean BMI of the subjects was 28.2 ± 4.7kg/m². The mean BMI of the F and M was comparable F= 28.9 ± 4.6kg/m² vs. M= 26.3 ± 4.7kg/m²; P=0.1. 76% of these subjects have BMI >25.

The mean duration of DM and mean RBS were comparable in subjects with and those without microalbuminuria except that the HBA1C=9.3% ± 4.2 and the proportion of hypertensives (43%) was significantly high in the microalbuminuria group, p<0.05. Lipid fractions analysis showed that LDL-C was significantly high in microalbuminuria group compared to without (135.76mg/dl ± 45.37 vs. 117.68mg/dl ± 43.13, p=0.03) while Total-C, HDL-C, TG are comparable p<0.05. A significant proportion of subjects with microalbuminuria showed significant ECG abnormalities compared to subjects without (80% vs. 20% p=0.04).

**Conclusion:** There are strong clusters of cardiovascular risk factors-hypertension, poor glycemic control, elevated LDL-C with microalbuminuria. Having defined the associated risk factors, it is therefore important to sensitize healthcare personnel on the need to regularly screen DM patients and institute appropriate treatment.

Abstract #279

**PREVALENCE OF NON ALCOHOLIC FATTY LIVER DISEASE (NAFLD) IN MULTIETHNIC DIABETIC POPULATION OF UAE & ITS CORRELATION WITH CARDIOVASCULAR RISK FACTORS**

Satendra Kumar Multani, MD, FACE, Meenakshi Jain, MD

**Background/Objective:** Non Alcoholic Fatty Liver Disease (NAFLD) is an important metabolic disorder in patients with Type 2 Diabetes Mellitus (T2DM). It is a marker of insulin resistance and is also a cardiovascular risk factor. It is the most common cause of chronic liver disease & Cryptogenic Cirrhosis in the United States. United Arab Emirates has the 2nd highest prevalence of T2DM in the World but there is a dearth of data on the prevalence of NAFLD in this population. This retrospective observational study was carried out in Ras Al Khaimah emirate of UAE to assess the prevalence of NAFLD in multiethnic T2DM population & to find it’s correlation with other cardiovascular risk factors like hypertension, dyslipidemia & microalbuminuria.

**Methods:** 500 subjects with T2DM were randomly selected and divided in NAFLD & Non NAFLD groups. Their phenotypic features and relevant biochemical parameters were recorded.

**Results:** Out of 500 subjects (Male-413, Female-87),...
Abstract #280

ISOLATED POSTPRANDIAL HYPERGLYCEMIA IN TYPE 2 DIABETIC PATIENTS IN A TERTIARY HEALTH CENTER

Ekechukwu Esther Young, MD,
Sonny Chineny, MBBS, FWACP,
Chioma Unachukwu, MBBS, FWACP, FACE

Objective: To estimate the prevalence of isolated postprandial hyperglycemia in patients with type 2 diabetes.

Methods: Ninety patients being managed for type 2 diabetes were recruited consecutively as they attended the diabetic clinic for follow-up. The patients were assessed with questionnaires to obtain demographic data. Clinical assessment of BMI was also carried out. Fasting blood samples were collected for analysis of fasting plasma glucose and glycated hemoglobin. Patients were given their usual drugs for diabetes and then served with a standard meal calculated to contain 50g of carbohydrate, providing 500kcal. Blood samples were collected 2 hours after the start of the meal for postprandial glucose levels.

Results: The mean age of the patients was 57.7 ± 10.8years with a male: female ratio of 2:3. The mean duration of diabetes was 6.77 ± 6.53years. The mean body mass index was 27.54 ± 6.01kg/m2. The mean fasting plasma glucose and 2hour postprandial glucose were 7.51 ± 3.39mmol/l and 11.02 ± 4.03mmol/l respectively, while the mean Hba1c 9.0 ± 2.5%. The prevalence of isolated postprandial hyperglycemia was 24.4%. The mean Hba1c in these patients was 7.9%. Elevated postprandial glucose was seen in 41.7% of the patients at target glycated hemoglobin levels (≤7%).

Discussion: Postprandial hyperglycemia has been shown to be an independent cardiovascular risk factor. Postprandial hyperglycemia is common and can occur even in patients with normal fasting glucose levels. This has been referred to as isolated postprandial hyperglycemia (IPPH). Excessive glycemic surges occur after meals in these patients and this leads to oxidative stress and thrombosis. Postprandial hyperglycemia can only be identified in these patients by monitoring of postprandial glucose (PPG) levels. Elevated PPG occurs more when patients are approaching target glycated hemoglobin levels. Studies have reported that PPG is the major contributor to Hba1c when the latter is about 8.4%. This was seen in this study as the mean Hba1c of the patients with IPPH was 7.9%. Though glycemic control was generally poor in these patients, as much as 41.7% at target Hba1c still experienced excessive elevation in PPG levels, while the prevalence of IPPH was 24.4%. There is a need to search for elevated PPG in patients who are close to target and treat appropriately with drugs which specifically lower postprandial glucose.

Abstract #281

HBA1C LEVELS IN A DIABETIC COSTA RICAN COHORT

Chih Hao Chen Ku, MD, Rodrigo Lizano-Montoya, MD, Fabián Carballo-Ortiz, MD

Background: In Costa Rica, prevalence of type 2 diabetes has been reported to be 6-8% but we have no clear data on diabetes control. Previously we reported data on Hba1c values in a cohort patients in Oreamuno, Costa Rica. From 2006 to 2008, Hba1c improved significantly. We collected the 2009 Hba1c data to see if this trend continues.

Objective: To evaluate Hba1c levels in a cohort of diabetic population in Costa Rica.
Methods: All patients with an Hba1c measurement during 2009 were identified in the Clinical Laboratory Department of the Oreamuno Health Area; this area is basically a primary care that is part of Costa Rica’s Social Security System. Hba1c values were collected as well as their demographic data. Statistics were analyzed using SPSS 18.0

Results: 1645 patients with at least one Hba1c measurement were analyzed. Mean Hba1c was 7.34 ± 0.4%, (95% confidence interval 7.26-7.42) with a median of 6.95%. Average age 61.27 ± 13.66 years. 34.6% of patients are males. There were no statistically significant differences in Hba1c between males (7.36 ± 1.70) and females (7.32 ± 1.64). 47.2% of patients achieved an Hba1c less than 7%; these values were similar in males and females. There were some differences regarding town of residence, the lowest being Cipreses (mean hba1c of 7.04%) and the highest San Rafael 1 (8.73%, p=0.014). Oreamuno Health Area has an adult population of about 33507 persons. If we assume that all patients with an Hba1c measurement are diabetic, this would render a diabetes prevalence of 4.9%. 50% of the population lives in a rural zone, there is no statistical significant difference in Hba1c when compared to urban population.

Discussion: Previously we reported the hba1c control in this population from 2006 to 2008. Over the years there has been a reduction in Hba1c and this trend continues in 2009 (7.95% in 2006, 7.72% in 2007, 7.60% in 2008 and 7.34% in 2009). This shows an improvement in diabetes care due to physician and patient education. All patients are being controlled in the Social Security System and there has been no change in diabetes medications in our formulary. National Guidelines set a goal of 7% in Hba1c, and almost half of our patients reach that goal. Compared to other Latin American countries, Costa Rica is the country where more patients achieve a goal of less than 7%. The prevalence is very similar to that reported in Costa Rica. A drawback in the present study is that all these patients are being treated by primary care physicians, so we can expect that patients with complications are referred to a tertiary care center and are not included in the present evaluation. This is the largest cohort of Costa Rican diabetic patients where Hba1c is reported.

Conclusion: In a large cohort of diabetic patients in Costa Rica, mean Hba1c is 7.34%. Almost half of patients achieve a goal of Hba1c less than 7%.

Abstract #282

VITAMIN B LEVELS IN TYPE I DIABETES PATIENTS

Grace Sun, DO, Amir Hamrahian, MD, Vinni Makin, MD, Krupa Doshi, MD, Charles Thomas, Betul Hatipoglu, MD

Objective: Water-soluble B vitamins are metabolic cofactors integral for carbohydrate metabolism and gluconeogenesis. Our aim is to see if lower vitamin B levels occur in type 1 diabetes (T1DM).

Methods: In this retrospective chart review, three groups were examined. Group 1 (n=34) had labile T1DM chosen by kidney-pancreas or pancreas-alone transplant status and all but four were on B multivitamins (MVIs) included in renal supplements. Group 2 (n=37) had non-labile T1DM. Group 3 (n=59) had non-T1DM; 26 had T2DM and 33 had no known glycemic issues at time of B-vitamin labs with medical history of thyroid or pituitary disorders. Subjects were consecutively chosen based on an outpatient encounter at Cleveland Clinic Foundation, and those with known gastrointestinal malabsorptive disease were not included. B-vitamin levels were done in commercial labs by the following methods: vitamin B1 (VB1), vitamin B2 (VB2), vitamin B6 (VB6) were assayed by high-performance liquid chromatography and vitamin B12 (VB12) was performed by electrochemiluminescence immunoassay. Chi-square analyses were done with 95% confidence levels with a p-value obtained for each B-vitamin for the groups overall; if the p-value was <0.05, then comparisons between groups were done.

Results: Overall group analysis showed p = 0.002 for VB2 and further results showed that group 2 had significantly lower levels compared to groups 1 & 3 with means of 45, 15 & 31 and medians of 21, 9, & 14, respectively for each group (normal = 6.2-39 nmol/L). Groups 2 & 3 had significantly lower VB1 compared to group 1. There was no statistical difference between the groups for VB6, and groups 2 & 3 had significantly lower VB12 than group 1. Group 1 had the highest percent of neuropathy (53%), gastroparesis (29%) and retinopathy (74%).

Discussion: VB1 and VB12 were elevated in group 1 compared to groups 2 & 3, which is likely due to group 1 MVI use. VB2 is a key intermediary in cellular oxidation-reduction reactions key in carbohydrate breakdown, yet there is a paucity of data in the literature regarding low VB2 in T1DM. VB2 along with other B-vitamins may be consumed more rapidly in T1DM, and repletion may impact development of diabetes complications.
Conclusion: In our patients, we found a statistical difference in lower VB2 in T1DM not on B-complex MVIs compared to non-T1DM and T1DM on MVIs. More studies are needed to confirm this observation of low VB2 and further evaluate the clinical impact on diabetes.

Abstract #283

RELATION BETWEEN GLYCEMIA AND HOSPITAL STAY AMONG VARIOUS SYSTEMIC INFECTED DIABETIC SUBJECTS

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Objective: To establish a relationship between the control of blood glucose levels and the severity of infection in a retrospective review of medical records of patients with diabetes admitted with fever and to assess the potential correlation between the number of days of hospitalization and the baseline and in-hospital glycemic status.

Methods: Medical records were reviewed to identify patients with diabetes admitted to a tertiary care center with symptoms and signs of infection (fever, cough, dysuria, abdominal pain, leukocytosis, etc). Patients in whom any new complications developed that could have prolonged the hospitalization were excluded from the study. The number of days of hospitalization attributable to infection were noted and statistically correlated with the glycemic control.

Results: Data on 185 patients included in the study are presented. Male 74 (40%) and Female 111 (60%). Age was 14-90 years (Mean 52 ± 16.2). According to the site of infection UTI 41.6%, RTI 16.3%, GIT 9.9%, and others 32.2%. The duration of hospitalization ranged from 3 days to 63 weeks (mean, 11.75 ± 8.30 days). The in-hospital glycemic control strongly correlated positively with the number of days of hospitalization (r = 0.455; 95% confidence interval [CI], 0.325 to 0.643). The admission blood glucose level also showed a strong positive correlation with the days of hospitalization (r = 0.577; 95% CI, 0.426 to 0.720). The mean hemoglobin A1c (HbA1c) correlated positively with the number of days in the hospital (r = 0.653; 95% CI, 0.508 to 0.764). The 147(79.45 %) patients with uncontrolled diabetes (HbA1c > 7%) were hospitalized for a mean period of 11.3 ± 3.2 days, in comparison with a mean duration of 6.7 ± 1.9 days for the 38(20.55%) patients with good outpatient glycemic control (HbA1c ≤ 7%).

Discussion: For diabetic subjects with systemic infection, period of hospital stay depends on glycemic control status, represented by FBG and HbA1c.

Conclusion: Patients with diabetes admitted with infection who have poor glycemic control and HbA1c > 7% needs prolonged hospitalization than the infective patients with good glycemic control (HbA1c < 7%).

Abstract #284

IS ROUTINE PREOPERATIVE ASSESSMENT FOR DIABETES MELLITUS NECESSARY IN PATIENTS WITHOUT FAMILY HISTORY?

John Adi Ashindoitiang, MBBCh

Background/Objective: This to determine the clinical value of blood sugar testing in patients undergoing elective general surgical procedures. Diabetes is a very common disorder and is often encountered in surgical patients that have not been previously diagnosed with the disorder. Again surgical procedures are more common in diabetes than non diabetes because eighty percent of diabetics are over 40 years and surgical procedures are more common in this age group. Furthermore diabetes and its complications predispose to a variety of surgical disorder such as foot gangrene, renal insufficiency cataract and cardiovascular disease.

Methods: We studied 75 consecutive patients with various surgical disorders that underwent elective surgery within a period of 12 months. Each patient had fasting blood sugar testing before surgery. In addition patients were asked about family history of DM. The weight, height, waist size and hip size were obtained and entered into proforma. The BMI and waist /hip ratio were then calculated.

Results: A total of 75 patients were recruited. Patients below the age of 16 years were excluded. There were 54 males (72%) and 21 females (28%) giving M:F 2.5:1. The age range was between 18 years to 80 years with a mean of 48.7. A total of 21 patient (28%) had fasting blood sugar >126mg/dl. Hyperglycemia > 126mg/dl increases with age. It was found to be 23% in the age range 18-40years but increases to 35% in the age range between 40-80years. 16 patients (21%) in this study had BMI above 30, that is obese. Out of the 16 patients, 11 of them accounting for 68.8% had FBS >126mg/dl. Hyperglycemia > 126mg/dl increases with age. It was found to be 23% in the age range 18-40years but increases to 35% in the age range between 40-80years. 13patients (17.3%) had positive family history of DM, 9 patients out of the 13 with positive family history of DM accounting for 69.2%. The waist/hip ratio did show any significant value in predicting patients with disorder blood sugar.

Discussion: There is increasing evidence that hyperglycemia increases the risk of poor outcome in cardiac surgery. Some observational studies also show poor outcome in non cardiac surgery with evidence that patients with pre or per operative hyperglycemia have increase hospital stay, increase resource utilization, increase
infection and increase morbidity and mortality. It also observed that about a third of hospitalized patient or those going for surgery with diabetes have not been diagnosed with the disorder before, therefore it is necessary to screened at risk patient before surgery. However not all patients need screening as it is not cast effective. Accordingly, from this study, patients with family history, overweight and obese individuals and patients above the age of 40 years need to be screened before undergoing elective surgery.

**Conclusion:** Diabetes is common disorder and is frequently encountered in surgical patients without previous history. Hyperglycemia affects surgical outcome. Controlling blood sugar reduces the poor outcome. Hence it is important to screen high risk patients. Individuals with family history of obesity and increasing age (40 years and above) should be screened before surgery. Also patients that present with unusual infection in surgical practice should be screened.

**Abstract #285**

**PRE-DIABETES & CARDIOVASCULAR RISK FACTORS IN MULTIETHNIC HYPERTENSIVE POPULATION OF UAE**

Satendra Kumar Multani, MD, FACE, Meenakshi Jain, MD, Fuad K Hassan, MBBS

**Background/Objective:** Approximately one third of adult population of United Arab Emirates is hypertensive. In addition, UAE has the 2nd highest prevalence of Type 2 Diabetes Mellitus (T2DM) in the World. This retrospective observational study was carried out in Ras Al Khaimah emirate of UAE to assess the prevalence of Pre-diabetes & cardiovascular risk factors like dyslipidemia and microalbuminuria in multiethnic hypertensive population of UAE.

**Methods:** 301 hypertensive subjects were randomly selected and their phenotypic features and relevant biochemical parameters were recorded.

**Results:** Out of 301 subjects (Male-251, Female-40), 234 subjects were of South-Asian origin, 19 were of Far Eastern origin & 48 subjects were of Arab origin. The mean age of the study population was 45.56 ± 8.42 yrs. The mean BMI and WC were 27.87 ± 4.17kg/m2 & 96.39 ± 8.95cms. In terms of hypertension control 101/297 (34%), 126/297 (42.5%), 70/297 (23.5%) subjects required one drug, two drug & three or more drugs respectively to control their blood pressure. Only 4 subjects were exclusively on life style modification. 161/267 (60.30%) subjects had Fasting Plasma Glucose (FPG) levels >100mg %. 234/301(77.75%) subjects had dyslipidemia. 84.30% of subjects had LDL >100mg %, 38.3 % had hypertriglyceridemia % and 37.95% had low HDL. 12.5% & 26.3% subjects had microalbuminuria and NAFLD respectively.

**Discussion/Conclusion:** A very high prevalence of pre-diabetes & dyslipidemia was found in the multiethnic hypertensive population of UAE which predisposes this population to future development of diabetes and cardiovascular complications at an early stage of their productive life. More than two thirds of the subjects required multiple agents to control their hypertension. Intensive life style modification along with aggressive control of hypertension & dyslipidemia can contribute to the prevention of diabetes & cardiovascular morbidity / mortality in this population.

**Abstract #286**

**USE OF INSULIN PUMP THERAPY IN DIABETES PATIENTS UNDERGOING SURGERY**

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**Objective:** To better define current practice, we reviewed insulin pump use in diabetes patients undergoing surgery.

**Methods:** Preoperative, intraoperative, postanesthesia care unit (PACU), and inpatient medical records (if applicable) were retrospectively reviewed. The Mayo Clinic Institutional Review Board approved this study.

**Results:** A total of 33 insulin pump treated diabetes patients comprised 45 unique surgical cases. Mean age was 56 years, diabetes duration 29 years, duration of insulin pump therapy 6 years, with mean hemoglobin A1c of 7.7%. Eighteen were men, 32 were white, and 27 had type 1 diabetes. Overall, 13 surgical procedures were orthopedic, 11 general surgical, 6 urologic, 6 were solid organ transplant, and the remaining 9 cases were comprised of other surgical procedures. Average anesthesia time was 175 minutes, procedure time 134 minutes, and PACU time 172 minutes. The Endocrinology service was contacted beforehand in 30 of the planned surgeries and guidelines regarding perioperative insulin pump use were provided to these patients. The history of insulin pump use was documented in the anesthesia medical history in 32 cases. The presence of the pump was documented in 28 cases in the preoperative area, 26 cases in the PACU, and in only 6 cases intraoperatively. Glucose values were recorded in 42 cases in the preoperative area and in 43 cases in the PACU, but in just 24 cases intraoperatively. Mean PACU glucose (186 mg/dl) was significantly (p=.039) higher than the average preoperative glucose (165 mg/dl). Of 37 cases admitted post-surgery, 32 remained on insulin pump therapy during the hospital stay.
Abstract #287

QUALITY OF GLYCEMIC CONTROL AND CHRONIC COMPLICATIONS OF DIABETES MELLITUS IN NORTH-WESTERN NIGERIA

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Objective: To determine the quality of glycemic control and prevalence of chronic complications of diabetes mellitus (DM) in Kano.

Methods: In a descriptive cross-sectional study at the diabetes clinic of Aminu Kano Teaching Hospital (AKTH) Kano spanning six months, the quality of glycemic control in terms of clinical characteristics, blood pressure (BP), fasting plasma glucose (FPG), 2-hour post-prandial (2-hr pp) glucose, and glycated hemoglobin (HbA1c) was assessed.

Results: A total of 121 patients; males 56(46.3%), females 65(53.9%) participated. The mean age of the patients was 52.47 ± 13.73 years; male 51.57 ± 13.51 years, female 53.25 ± 13.98 years. The mean duration of diabetes, FPG, 2-hr pp glucose and HbA1c of the patients were 7.5 ± 4.3 years, 9.54 ± 10.15mmol/L, 10.98 ± 4.17mmol/L, and 8.93 ± 2.59% respectively. The chronic complications of DM found included peripheral neuropathy 46(38.0%), retinopathy 28(23.1%), nephropathy 20(25.6%), stroke (CVA) 3(2.5%), DM foot syndrome 15(12.5%), and cataract 16(13.2%). The quality of glycemic control was good (HbA1c < 6.5%) in 31(25.6%) patients, fair (HbA1c 6.5–7.5%) in 22(18.2%) and poor (HbA1c > 7.5%) in 68(56.2%) patients. Poor glycemic control was mostly (73.2%) seen in those with chronic complications of DM. Coexisting systemic arterial hypertension was seen in 90(74.4%) patients; 41 (73.2%) males, 49(75.4%) females. Most patients (68.7%) with abnormal anthropometry had poor glycemia.

Conclusion: More data on current practices regarding use of these devices in the surgical setting is needed, and guidelines should be developed for safe insulin pump use during the perioperative phases of care. The effectiveness of insulin pumps versus alternative methods of controlling perioperative hyperglycemia should be further studied. We discuss guidelines developed at our institution for the use of insulin pumps during surgery.

Abstract #288

PUMP BASED INTENSIVE CONTROL OF SUGAR IN HOSPITALS (PICS)

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Objective: To control inpatient diabetes intensively and to study its impact on overall hospitalization time, incidence of complications, morbidity indices and cost.

Methods: Current standards of care for inpatient diabetes management were compared and found that most hospitals like to follow ‘sliding scale’ based insulin regimens for inpatient diabetes control. We compared the standard Stanford Protocol for intensive insulin management in hospital floors in a control group of 25 patients in three different hospital floors (medical stepdown unit, surgical stepdown unit and cardiothoracic stepdown unit) with another group of 25 patients in similar nursing floors on a basal bolus regimen of insulin via continuous infusion by pumps, with blood sugar monitoring by CGMS devices. We propose to collect data in these two groups and compare them by using standard statistical analysis tools for significance. Study group: on insulin pump, using regular insulin or analog, standard regimen of ‘low’ = 0.5 units hourly basal, bolus at 2 units pre breakfast, 3 units pre lunch and 4 units pre dinner. ‘Medium’ = 1.0 units hourly, 3 units pre breakfast, 4 units pre lunch and 5 units pre dinner.
Caloric utilization may predict impaired glucose tolerance and diabetes. Study may reveal that correction of hyperinsulinemia will correct caloric utilization and promote weight loss. Measurement of caloric utilization may predict diabetes.

Abstract #290

SELF BLOOD GLUCOSE MONITORING PRACTICE AMONG PATIENTS WITH DIABETES

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Objective: This study set out to evaluate the knowledge and practice of self glucose monitoring in our patients.

Methods: Ninety diabetic patients attending the diabetic clinic of the hospital were assessed with self-administered questionnaires. The data obtained were analyzed using simple statistical methods.

Results: There were 36 (40%) males and 54 (60%) females. Eighty-one had type 2 diabetes while nine had type 1. The mean age was 53.6 ± 23.3 years. The mean duration of diabetes was 7.6 years. Of the type 2 patients 14 (17.3%) were on insulin treatment alone, 46 (56.8%) on oral drugs alone while 21 (25.9%) were on combination. Of the 86 patients who knew about SBGM, 52 knew only about using glucometers for SBGM, 30 knew about using both glucometers and urine dip-sticks, 4 did not know of any method. Only 24 (26.7%) patients had glucometers. None of the type 1 patients had a glucometer. The highest frequency of monitoring was once daily in 6 patients. None of the patients practised urine monitoring.

Discussion: A large percentage of the patients knew about SBGM, however only a small percentage owned glucometers and also the frequency of monitoring was low. Since patient awareness was high, economic reasons is the most likely cause of poor SBGM practice. In the absence of health insurance, patients have to provide their own glucometers and strips and in our resource-poor environment, this is not easy for them to do. It is worrisome that none of the patients with type1 DM owned a glucometer despite the fact that they are on insulin. The introduction of health policies to help patients own and use glucometers is advocated.

Conclusion: This study has shown that the practice of SBGM is in our patients is inadequate despite adequate knowledge. This is most likely due to scarce resources. The importance of SBGM should be emphasized more in our practice especially in patients with type1 DM.
Abstract #291

DIABETES MUSCLE INFARCT, A RARE PRESENTATION

Manash Pratim Baruah, MD, Pranjal Goswami, MD

Objective: We present a case of acute onset diabetic muscle infarction in a long standing diabetic who initially presented with acute onset pain and features of inflammation and distinctive MR imaging features.

Background: The patient, a 62-year-old male, had a background of T2DM for the previous 12 years. He was a heavy smoker for a long time. The presentation was dramatic with acute onset excruciating pain and swelling on anterior aspect of the right thigh, which lasted for 1 week before presentation, partly responding to usual NSAIDs. Laboratory investigations revealed mildly elevated erythrocyte sedimentation rate. His fasting and post-prandial blood glucose levels were 210 mg/dl and 340 mg/dl respectively. The creatine kinase level was normal. Urine analysis revealed glucosuria and trace of albumin. All other relevant laboratory parameters including total and differential cell counts were within normal limits. Magnetic resonance imaging of the right thigh confirmed the swelling in the quadriceps muscles with blurring of muscle margins and hyperintense signal on T2 weighted and hypo to isointense signal on T1 weighted images reflecting muscle edema along with inflammatory changes. Subcutaneous fat tissue also showed moderate edema. Fine needle aspiration cytology showed features of aseptic inflammation only.

Results: A diagnosis of diabetic muscle infarction was made considering the patient’s long standing diabetic status, clinical presentation, laboratory findings and MRI features. The patient was treated symptomatically and showed remarkable resolution of the pain and swelling over next one month duration. Follow up MRI was performed after approximately a three month interval which revealed remarkable resolution of the inflammatory changes with mild residual edema and swelling of the vastus lateralis muscle.

Discussion/Conclusion: Diabetic muscle infarction is a rather rare aseptic complication of long standing diabetes mellitus, seen mostly around second week of onset of the disease. The quadriceps are the commonest site of involvement followed by calf muscles and the condition is bilateral in approximately 8% of cases. The possible causes include atherosclerosis, diabetic microangiopathy, atheroembolic phenomenon and alteration in the coagulation-fibrinolysis system. In the absence of specific systemic sign or a definitive laboratory investigation, MRI turns out to be the modality of choice in the radiological evaluation of the patients with diabetic muscle infarct. Muscle biopsy is rarely indicated when the clinical features or MRI findings is atypical or when the recovery is delayed.

Abstract #292

A METHOD FOR RAPID OUTPATIENT INSULIN DOSE-FINDING IN A PATIENT WITH POORLY CONTROLLED TYPE 2 DIABETES MELLITUS AND SEVERE INSULIN RESISTANCE - A CASE REPORT

Laura Emily Trask, MD, Richard Comi, MD

Objective: To describe an approach for quickly estimating a patient’s insulin needs using outpatient administration of IV insulin.

Case Presentation: A 56 y/o man with a 4 year history of type 2 diabetes, presented for evaluation of worsening diabetes control. His HbA1c had risen from 8 to 14% over the last year despite treatment with pioglitazone, metformin, mealtime glulisine, and escalation of his lantus dose to 160 units/day. No inciting factor for his insulin resistance was identified. He was not obese.

To determine appropriate insulin dosing the following outpatient protocol was devised: volume repletion with 1 L normal saline, then IV insulin at 10 units (U)/hr with fingerstick blood glucose every 30 minutes. After one hr blood glucose had only decreased from 245 to 199 mg/dL and insulin was increased 50% to 15 U/hr. Thirty minutes later the patient developed a blood sugar of 61 mg/dL with mild symptoms. Insulin was held for 1 hour and then restarted at 10 U/hr which maintained glucose between 72 and 163 mg/dL. This was converted to the equivalent 240 units a day using U500 insulin: 0.16 ml (80 units) at breakfast, dinner and bedtime. Over the next three months, by monitoring his fasting glucose, his U-500 insulin dose was reduced to 90 units per day as his HbA1c fell to 8.5%. He was also found in this period to have a right coronary artery lesion which underwent stenting.

Discussion: Marked insulin resistance can be multifactorial, including overeating, inflammation/infection, or underlying coronary artery disease. This can be confounded by chronic volume depletion due to glucosuria and glucose toxicity. The method described here for outpatient use seeks to remove these confounders by restoring volume and rapidly determining the effective dose of intravenous insulin. The long-acting subcutaneous insulin dose chosen at the end of this 4 hour protocol is based on the infusion rate of insulin required for non-meal glucose control. Since the total daily insulin is a combination of non-meal insulin plus meal-associated insulin, this dose is conservative. However, due to progressive relief from glucose toxicity, there must be frequent adjustment of the insulin dose downward over time. This case nicely illustrates the effect that alleviating glucose toxicity can have on a patient’s diabetes control.
Abstract #293

PREVALENCE OF METABOLIC SYNDROME IN DIABETIC PATIENTS

Hans Tandra, MD, FACE, Olivia Handayani, MD, BMedSc, Audrey Amelia, MD

Objective: To determine the prevalence of metabolic syndrome (MS) in type 2 diabetic patients using the International Diabetes Federation (IDF) definition.

Methods: 400 patients were randomly selected and recruited. The clinical data and anthropometric indices were collected during interview and examination. Fasting serum lipid profile, blood glucose and blood pressure were done for all subjects. 120 randomly selected patients had their glycosylated hemoglobin (HbA1c) levels checked. Prevalence rate of MS was determined using the IDF definition.

Results: Mean age of the subjects was 56.7 ± 12.2 years and 233 (58.3%) of whom were females. The male-female ratio was 1:1.4. 219 (54.75%) of the subjects were hypertensive, and 77.3% were women. The mean systolic blood pressure (SBP) was 140.3 ± 24.5 mmHg and mean diastolic blood pressure (DBP) was 86.2 ± 11.7 mmHg. 296 (74%) of the subjects had a SBP ≥ 130 mmHg while 128 (32%) subjects had a DBP ≥ 85 mmHg. Mean waist circumference (WC) was 94.8 ± 11.1 cm. By the IDF definition, 72 (18%) of the men and 167 (41.8%) of the women had central obesity. Mean serum HDL of the subjects was 43.8 ± 14.5 mg/dl. 134 (33.5%) of the women had HDL ≤ 50 mg/dl unlike 41 (10.3%) of the men with HDL ≤ 40 mg/dl. Mean serum triglyceride (TG) of this study was 142.1 ± 34.4 mg/dl with the value for either sex within normal limits. There are 35 (15%) of women and 12 (7.1%) of men has a TG ≥ 150 mg/dl. Only 12.6% of the subjects had prior history of dyslipidemia. Mean values of fasting blood glucose were 159.8 ± 12.3 mg/dl and mean HbA1c were 7.3 ± 1.2%, and almost the same for either sex. According to IDF definition, 198 (49.5%) of the subjects had MS. Of these 62 (31.3%) were men and 136 (68.7%) were women.

Conclusion: Metabolic syndrome is found in almost half of diabetic patients. It was significantly related to poor regulation of blood glucose, especially in female diabetics.

Abstract #294

ASSOCIATION BETWEEN CORONARY ARTERY DISEASE RISK FACTORS AND MODE OF THERAPY OF DIABETES MELLITUS WITH OCCURRENCE OF OBSTRUCTIVE CORONARY ARTERY DISEASE IN AFRICAN AMERICANS WITH DIABETES

Theresa Adadzewa Fynn, MD, Gail Nunlee-Bland, MD, Wolali Odonkor, MD, Vijaya Ganta, MD, Cherqaoui Rabia, MD, Abdelwahab Suliman, MD, Tadele Dejalew, MD, Selasie Samuel Mortoti, MD, Onyekachi Egyiw, MD, Oluwakemi Banjo, MD, Steven N. Singh, MD, Marlon Daniel, MPH, MHA

Background: Cardiovascular disease, particularly Coronary Artery Disease (CAD), is the leading cause of death in the United States for Americans of all racial and ethnic backgrounds. African Americans have a greater burden of diabetes, with a higher incidence of vascular complications than whites and highest overall CAD mortality rate of any ethnic group in the US.

Objective: The aim of this study is to determine whether there are any associations between CAD risk factors and the mode of therapy of diabetes mellitus with the severity of CAD in African Americans.

Methods: The charts of 345 African American patients with diabetes who underwent coronary angiography at Howard University Hospital, in Washington, DC, spanning a period from 2003 to 2008 were reviewed. Demographic data was analyzed in addition to data identified as risk to coronary artery disease. Risk factors included: age in males > 45 years and in females > 55 years, family history of early CAD in first-degree relatives, smoking, hypertension, and hypercholesterolemia. Other risk factors were: obesity, defined as BMI ≥ 30; sedentary life style; and use of birth-control pills. The severity of coronary artery disease was assessed by reviewing coronary angiography reports for number of diseased epicardial vessels. Coronary arterial stenosis of more than 50% was regarded as significant disease and any disease less than 50% was regarded as non-obstructive coronary disease. Severity of coronary artery disease was determined by the presence of obstructive versus non-obstructive disease. Diabetic treatment regimens were also reviewed. The SAS version 9.2 (Cary, NC) for statistical analysis Simple and Multivariable logistic regression model was used to determine adjusted and unadjusted effects of each treatment modality and risk factor in the prevalence of obstructive CAD. Simple and Multivariable logistic regression was employed to determine adjusted and unadjusted effects of each patient with diabetes treatment modality and CAD risk factor in the development of obstructive CAD.
Results: Of a total of 345 patients, 201 (61.85%) had obstructive CAD. The mean age of the total group analyzed was 60.02 years with 51.3% being female. The variables studied were age, sex, BMI, blood pressure, family history of CAD, lipids, smoking and hemoglobin A1c. Age was found to have a very strong relationship with the occurrence of obstructive CAD among patients with diabetes in our study population (OR = 1.10; 95% CI = 1.061-1.138).

Conclusion: Our study results revealed a strong association between age and the occurrence of obstructive CAD in the studied African American population with diabetes but failed to demonstrate a statistically significant relationship between other CAD risk factors and the mode of therapy of diabetes mellitus with severity of coronary artery disease.

Abstract #295

THE EFFICACY OF MULTIPLE DAILY INSULIN INJECTION (MDI) AND PATIENT’S SATISFACTION WITH MDI REGIMEN AMONG FILIPINOS

James Young, MD, Gerry H. Tan, MD, Maria Gabriela Gonzalez-Gallenero, MD, Evangeline P. Costelo, MD

Background: The long term complications of diabetes lead to diminished quality of life. As a means to avoid these complications, insulin therapy had evolved into a specialized regimen to achieve physiologic control of blood glucose, the so-called Multiple Daily Insulin (MDI) regimen which is a relatively new technique in the Philippines.

Objective: To study the efficacy of Multiple Daily Insulin regimen in controlling plasma glucose and to evaluate patient’s satisfaction with MDI regimen among Filipino type 2 diabetics who have been on MDI for at least 2 months.

Methods: Filipino patients (n= 107) with uncontrolled diabetes were included in the study protocol. The majority was male, more than 60 years old, and was diabetic for more than 6 years duration. The mean body mass index was 27 kg/m² and the mean baseline HbA₁c was 9.2% ± 2.65. Efficacy was evaluated by HbA₁c and treatment satisfaction was assessed with the Diabetes Treatment Satisfaction Questionnaire (DTSQ). Enrolled patients were followed up at week 12, 24 and 48.

Results/Discussion: Mean HbA₁c fell by 2.43 ± 2.68 at week 12, 2.03 ± 2.35 at week 24 and 1.73 ± 2.23 at week 48 showing a statistically significant decrease of HbA₁c within the 3 time period (p = 0.001). The difference in the mean change of HbA₁c among the 3 groups was not statistically significant (p = 0.52). The proportion of patients achieving an HbA₁c of ≤ 7% at week 12, 24, and 48 were 42%, 52% and 42%, respectively. Treatment satisfaction improved significantly (p = <0.001) with the MDI regimen using the DTSQ at the end of the study.

Conclusion: Multiple Daily Insulin Regimen is an effective treatment modality based on a significant lowering of HbA₁c among the study population with uncontrolled type 2 diabetes mellitus. Patients were satisfied with the regimen based on the positive treatment satisfaction. This, however, is contrary to popular belief that patients’ quality of life is affected by insulin administration.

Abstract #296

THE PREVALENCE OF OBESITY AND ITS ASSOCIATIONS AMONG TYPE 2 DM IN NIGERIA

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Background/Objective: Obesity is a chronic metabolic disease with attendant cardiovascular problems and a key feature of metabolic syndrome. Obesity and diabetes is increasing worldwide. There is therefore, the need to estimate the prevalence of obesity and its associations among type 2 DM in Nigeria.

Methods: In this cross-sectional study, 200 DM subjects were randomly selected in LASUTH. Their clinical characteristics and the occurrence of cardiovascular events (CV) were documented through interviewer-administered questionnaires. Fasting blood samples were collected for biochemical analysis and urine samples for persistent albuminuria. ECG was carried out. Test Statistics used were t-test, χ². A p value of ≤0.05 is significant.

Results/Discussion: The prevalence of obesity in type 2 DM (BMI ≥ 30kg/m²) was 27%. 71% of female (F) and 37% of male (M) had waist circumference > 88cm and > 102cm respectively by risk stratification. The mean age of the study group 56.7 ± 11.1 years, F and M are comparable (F=56.5 ± 10.8 years vs. 56.9 ± 12.2 years, p=1.0) with their mean FBS = 158.4 ± 73.24mg/dl. The mean duration of DM is 7.7± 5.3 years. The frequency of abnormality in their fasting lipid fractions were: Elevated levels of Total-C 40%, LDL-C 70%, TG 14% and reduced HDL-C 63%. The prevalence of hypertension (HT) and microalbuminuria was significantly high in obese DM compared with non-obese DM (72% vs 28%, P=0.001 and 77.5% vs 22.5%, P=0.001). Symptomatically, 76% had history of intermittent claudication, 72% had ECG abnormalities and 58% had clinical evidence of non-fatal cardiovascular event (stroke).
**Conclusion**: Obesity in type 2 DM Nigerians has significant association with hypertension, dyslipidaemia, microalbuminuria and high rate of cardiovascular events. Improved measures to reduce the burden of cardiovascular morbidity and mortality are advocated in this group of patients.

**Abstract #297**

**CLINICIANS PREFERENCES IN DIAGNOSIS AND FOLLOW-UP OF PATIENTS WITH TYPE 2 DIABETES MELLITUS**

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**Objective**: To determine the preferences in diagnosis and follow-up of diabetic patients by a group of medical specialists according to international criteria.

**Methods**: We carried out this study during a diabetes update session at a private clinic in Monterrey, Mexico. We performed an observational cross-sectional study applying an invalidated eight-item survey to internal medicine physicians from public and private institutions, collecting demographic data (age and gender), type of institution where they work, number of years practicing medicine, and type 2 DM diagnostic procedures and control methods most frequently used in their clinical practice. We included two questions to identify knowledge of the term eAG and if it was useful to them.

**Results**: We applied a total of 28 surveys. Distribution by gender was 8 (28%) women and 20 (72%) men. Average age was 47 ± 10.4 years. Seven (25%) of the specialists were from a private institution, nine (32%) were from a public institution and 12 (43%) were from both types. The average number of years practicing medicine was 21 ± 11.

For diagnosis, 82% use fasting glucose, 61% use HbA1c, 25% postprandial glucose, 14% the glucose tolerance test with a 75 g dose and 4% use a random glucose sample. For follow-up, the preferences were the following: 75% use HbA1c, 43% use fasting glucose, 29% use postprandial glucose, 4% the glucose tolerance test with a 75 g load, and 4% use a random glucose sample. Thirty nine percent of the specialists knew the term eAG and 100% confirmed that it was useful for follow-up of patients with DM.

**Discussion**: The management of Diabetes Mellitus has always been considered a major medical challenge because adequate glycemic control reduces the incidence and progression of microvascular disease in both Type 1 DM and Type 2 DM. The diagnostic criteria for DM are well standardized. HbA1c is currently the most reliable test for long-term monitoring of patients with type 2 DM, since this is the main mediator of diabetes complications. The concept of estimated average glucose (eAG), which correlates with HbA1c in terms of mg/dl, has been recently proposed. This new determination will facilitate the patient’s understanding of diabetes control and lead to improved management.

**Conclusion**: The variability that exists with regard to the diagnosis and follow-up of patients with DM reflects the importance of promoting training for specialists about these criteria. Global harmonization of eAG and HbA1c is desirable; however, we still have methodological and information issues in our country about its usefulness.

**Abstract #298**

**THE CORRELATION OF LIPID PROFILE AND TYPE 2 DIABETES PROGRESSION**

Hans Tandra, MD, FACE, Olivia Handayani, MD, BMedSc, Audrey Amelia, MD

**Objective**: Lipid profile holds an important role in type 2 diabetes (T2D) prognosis. This report is to determine the correlation of poor lipid profile and blood glucose regulation in T2D patients in Surabaya, Indonesia.

**Methods**: This is a prospective study involving 70 patients with T2D attending the diabetes clinic in Surabaya, Indonesia. Data collected included demographic, anthropometric indices, lipid profile (LDL, HDL and triglyceride) and DM complications. Quantitative data are presented as mean and standard deviation, with p value of <0.05 indicated statistical significance.

**Results**: The mean age of the subjects recruited for the study was 57.5 ± 13.2 years and 65% of the subjects were female. The mean age of the females was 58.9 ± 11.1 years and that of the males was 54.7 ± 12.4 years. The ages of the females and males were comparable 59.3 ± 10.2 vs 51.1 ± 9.4 years, (P>0.05). The mean LDL cholesterol was 123.1 ± 31.1 mg/dl, the mean HDL cholesterol was 37.2 ± 12.1 mg/dl in men and 45.2 ± 11.1 mg/dl in women, respectively, and the mean TG was 167.2 ± 12.4 mg/dl. 45 of the subjects had poorly controlled of blood sugar, mean HbA1c was 8.4 ± 2.1%.

**Conclusion**: Poor lipid profile is related to poor regulation of blood glucose in diabetic patients. The better diabetes management should involved lipid lowering therapy. Diabetes education and lifestyle intervention are required to achieve a better quality of life in patients with diabetes.
Abstract #299

**BEetter GLYcemic OUTcome DEPENDS ON GOOD DIABETIC EDUCATION WHICH INFLUENCE IN DELAYING OF DIABETIC COMPLICATION**

Mohammad Feroz Amin, MD, Tofail Ahmed, PhD, Faruque Pathan, MD, Zafar A Latif, FCPS, S. M. Ashraful Hassan, MD

**Objective:** The present study was undertaken to explore the glycemic status and frequency of diabetes related complications among the type 2 diabetic patients in respect to their knowledge about the disease.

**Methods:** One hundred and seventy five patients, duration ≥5 years, were consecutively selected from the out-patient department BIRDEM, the central institute of diabetic association of Bangladesh. Their knowledge about diabetes and its management was assessed by a predesigned questionnaire. Subjects were subgrouped on the basis of their level of knowledge; Group 1 scored ≤ 40 % (n=123) and Group 2 scored >40 % (n=52). Variables considered; age, sex, BMI, patients formal education, fasting and postprandial glucose, HbA1C, blood pressure, lipids, urine for albumin, creatinine, signs of neuropathy and retinopathy.

**Results:** Mean (±SD) age (years) and BMI in two groups were 46.1 ± 8.9 years and 43.8 ± 8.1 (p=ns) and 24.9 ± 3.7 and 24.3 ± 3.1 (p=ns) respectively. Male/ female distribution of the study subjects were 34% vs. 66% in Group 1 and 61.5% vs. 38.5% in Group 2. Mean (±SD) duration (yrs) of diabetes was similar in two groups [10.2 ± 4.6 and 10.6 ± 4.1 respectively]. Formal education up to grade 10 in Group 1 and Group 2 36.5% and 73% respectively (p<0.01) and others had different level of higher education. Group 2 had significantly better glycemic control compared to their counterpart [FBG: p=0.006; and PPG: p=0.374; HbA1C; p<0.001] and at evaluation [FBG: p=0.007; and PPG: p<0.001; HbA1C: p<0.001]. Frequencies of different complications in the Group 1 and Group 2 were as follows: nephropathy; 11.4% vs. 7.6% (p=ns); retinopathy; 56.1% vs. 46.2% (p=ns); neuropathy; 78.9% vs. 69.2% (p=ns). Vibration and neurological test revealed neurological abnormalities in 43.9% and 30.7% of cases in the Group 1 and Group 2 respectively (p=ns). Proportion of patients with cataract were 44.7% and 17.8% (p=0.01) and proliferative diabetic retinopathy 8.9% and 7.6% in the two groups respectively.

**Conclusion:** Data reconfirmed that better knowledge about diabetes among the patients has profound effect in their glycemic control. This might have possibly been confounded by the patient’s formal educational status. Diabetologists and policy makers need to think about taking measures to improve patient’s knowledge about diabetes and management.

Abstract #300

**A COMPARISON OF THE CHARACTERISTICS OF SUBJECTS WITH SEVERE INSULIN RESISTANCE VERSUS THOSE ON MORE TYPICAL INSULIN REQUIREMENTS IN TYPE 2 DIABETES (T2DM)**

Alina Khan-ghany, MD, Angela Szeto, PhD, Jay Sosenko, MD, Armando Mendez, PhD, Ronald Goldberg, MD

**Objective:** There is a group of obese subjects with T2DM that have severe insulin resistance (SIR) the nature of which is not understood. It is unclear whether these individuals belong to the continuum of “common” T2DM or form a distinct pathophysiologic group. This study was aimed at characterizing those with SIR among a group of insulin-requiring subjects with T2DM referred to our diabetes clinic with difficult to control diabetes.

**Methods:** 72 patients with T2DM receiving insulin therapy were identified after referral to our diabetes clinic and data was collected by interview and from electronic records. They were divided into 2 groups based on the distribution of total daily dose of insulin (TDD): those taking <180 units (U) (controls, n=56) or ≥180 U (SIR, n = 16). Comparisons were made between demographic, anthropometric and clinical data in the 2 groups using t tests for continuous variables and Mann-Whitney tests for categorical variables.

**Results:** Mean (±SEM) age for the sample population was 57.0 ± 1.2 years, BMI 33.4 ± 0.9 kg/m2, HbA1c 9.2 ± 0.3%, duration of diabetes 15.9 ± 1.1 years, duration of insulin treatment 8.0 ± 1.0 years and TDD 105 ± 10.7 U. BMI was higher in the SIR group (38.4 ± 2.1 vs. 31.9 ± 0.8 kg/m2; p=0.001) as was TDD (247.8 ± 19.8 U [2.5 ± 0.2 U/kg] versus 64.6 ± 5.0 U [0.7 ± 0.1 U/kg]; p=0.001). There was a positive correlation between BMI and TDD in both control (r=0.357, p=0.009) and SIR (r=0.541, p=0.03) groups. Based on regression analyses, for a given BMI the TDD required by the SIR group was 204, 231, 256 and 282 U respectively.

**Discussion:** Although the SIR group was more obese than the controls, and BMI was positively correlated with TDD in both groups, based on the regression analyses the
TDD at a given BMI was almost 3-fold greater in the SIR group. Therefore, SIR in those subjects receiving ≥180 units of insulin daily cannot be explained simply by their degree of obesity.

**Conclusion:** These findings suggest that subjects with T2DM and SIR form a distinct subgroup whose very high insulin requirements are not simply related to their degree of obesity. The results provide the rationale for a more detailed characterization of the nature of their insulin resistance and its clinical implications.
HYPOGLYCEMIA

None submitted.
LIPID DISORDERS

Abstract #400

INVESTIGATION OF LIPIDS IN FIRST YEAR MEDICAL RESIDENTS

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Mitra Shah-Hossein, MD

Objective: We sought to examine the change in lipid levels in PGY-1 house staff, with the hypothesis that drastic changes in physical activity, diet, stress level, and sleep habits will adversely affect cardiovascular risk factors in these young physicians.

Methods: Participants were first year medical residents at Georgetown University Hospital. We used CARDIA questionnaires to assess stress, sleep, physical fitness, and nutrition. Fasting blood draws were performed to measure HDL, LDL, total cholesterol, and CRP. In addition, participant's weight was measured and BMI calculated. These values were obtained at enrollment and again at the end of the intern year. Data was analyzed using one sample t-test. The study was designed to detect a 5.0mg/dL difference in mean with power of 99% for 60 participants.

Results: 57 people were recruited for the baseline examination, however only 26 people returned for the one year examination, 62% male and 38% female. After one year of internship, there was a statistically significant decrease in total cholesterol by 16 points (p=0.0007) and statistically significant decrease in LDL by 10 points (p=0.0172). There was statistically significant decrease in both LDL and total cholesterol after one year of internship. In addition we found a statistically significant decrease in exercise units after intern year. The exercise units after intern year may have had a significant increase which was hypothesized to occur after a year of internship. Finally CRP levels had a statistically significant increase within the normal range of unknown significance.

Conclusion: The Investigation of Lipids in First Year Medical Residents found a statistically significant decrease in total cholesterol, LDL and exercise units after one year of internship. These results indicated that interns continue to have time to maintain a healthy lifestyle during residency.

Abstract #401

INHIBITION OF APOLIPOPROTEIN A-I GENE EXPRESSION IN HEPATOCYTES BY TNF ALPHA REQUIRES THE PRO-INFLAMMATORY TRANSCRIPTION FACTOR C-JUN

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Objective: Plasma levels of apolipoprotein A-I (apo A-I), a potent anti-atherosclerotic component of high-density lipoprotein (HDL), are reduced during both acute and chronic inflammation. Prior studies have demonstrated that the master cytokine tumor necrosis factor a (TNF a) inhibits the synthesis of apo A-I in both hepatocytes and intestinal cells, and that c-jun may have an important role.

Methods: Western and Northern blot and transient transfection of HepG2 liver cells were used to assess the effects of TNF a on c-jun activity and apo A-I gene expression.

Results: TNF a treatment of HepG2 cells resulted in rapid phosphorylation of c-jun on Ser63 and phosphorylation of c-jun-N-terminal kinase-1 (JNK1), an upstream activator of c-jun, on Thr183/Tyr185, suggesting that the cytokine may suppresses apo A-I gene expression by activating c-jun. To examine this, HepG2 cells were treated with phorbol-12-myristate-13-acetate (PMA), activating endogenous c-jun DNA binding and activity. As predicted, apo A-I mRNA and protein levels were suppressed by PMA treatment. Exogenous expression of c-jun as well as its upstream activators, namely c-jun-N-terminal kinase-1 and -2 (JNK2), augmented the ability of TNF a to inhibit apo A-I expression. However, treatment of cells with SP 600125, a potent and selective inhibitor of JNK1 and JNK2 reduced the potency of TNF a to inhibit apo A-I promoter activity, while the p38 mitogen-activated kinase inhibitor SB 202474 had no effect. In addition, when JNK1 and c-jun expression was knocked out by short inhibitory RNA, TNF a was less potent at inhibiting apo A-I gene expression.

Discussion: Our results indicate that apo A-I gene expression is suppressed by c-jun in hepatocytes. TNF a levels are elevated in several forms of chronic disease,
including metabolic diseases, providing a rational explanation for the low rates of HDL synthesis in subjects with these conditions.

**Conclusion:** These results indicate that c-jun is required for inhibition of apo A-I gene expression by TNF α. Furthermore, they also indicate that anti-inflammatory therapies that target TNF α may provide a novel approach in preventing the hypoalphalipoproteinemia of diabetes, obesity, and metabolic syndrome.

Abstract #402

**INSULIN INFUSION IN THE TREATMENT OF SEVERE HYPERTRIGLYCERIDEMIA**

Rachel Baerga Duperoy, MD, Marjan Vahedi, MD

**Objective:** To describe the use of insulin in the management of hypertriglyceridemia.

**Methods:** A 41 y/o female with PMH of DM type 2, depression, obesity, asthma, hypercholesterolemia, and bipolar disorder presented to our medical clinic for regular check up. She was found to have a finger stick blood glucose of 596 mg/dL. She was referred to ER for admission. Home medications included: Actos 15 mg/d, Simvastatin 80 mg/d, Lamictal 100mg/d, Risperidal 2 mg/d and Proventil nebulizer PRN. On admission vital signs were within normal limits except heart rate 114/min. Physical examination was unremarkable except for generalized obesity and widespread eruptive popular skin lesions (xanthomas) on the back and extremities. Significant laboratory values were: Triglyceride (Tg) 9370 mg/dL, HDL 38 mg/dL and HbAlc 14%. Patient was started on insulin infusion for the treatment of extreme hypertriglyceridemia. In the first 72 hours Tg dropped almost by 7000 mg/dL. Patient was switched to subcutaneous insulin when Tg was 900 mg/dL. She was also NPO in the first 24 hours then feeding was started as the patient insisted on eating. Her blood sugars were fair on subcutaneous insulin. She was discharged with close clinic appointment. Patient was lost to follow up for a few months. Last time she was seen six months after this hospitalization, her Tg was 168 mg/dL, and HbAlc was 7.3 %. In this period she has been taking insulin 130 unit/d, gemfibrozil 600 mg twice/d, and metformin 1000 mg twice/d. Her xanthomas have completely resolved.

**Discussion:** Hypertriglyceridemia can be classified into mild to moderate (TG between 150-499 mg/dL) and severe if levels => 500mg/dL. Although short course of insulin infusion is not a widely used method for the treatment of non-complicated severe hypertriglyceridemia; this case demonstrated that it is an effective way to rapidly decrease triglyceride levels. Insulin activates the lipoprotein lipase through which it decreases triglycerides. Patients with severely increased plasma triglyceride levels are at risk of developing serious complications such as pancreatitis, coronary heart disease and stroke. Therefore it is important to rapidly decrease plasma triglyceride levels. A sufficient control of triglyceride levels with drugs like fibrates and nicotinic acid can usually only be achieved after a couple of weeks. Insulin infusion is a safe and inexpensive method for rapid reduction of serum TG. Intravenous heparin has also been used for the management of severe hypertriglyceridemia.

Abstract #403

**A CASE OF TRANSIENT MASSIVE HYPERCHOLESTEROLEMIA**

Amanda La Greca, MD, Mary Zoe Baker, MD

**Objective:** To describe a patient with massive hypercholesterolemia in the setting of acute cholestasis due to choledocholithiasis.

**Case Presentation:** A 39 y/o woman presented with ten days of abdominal pain followed by jaundice and severe pruritus. She had dark urine and light-colored stools. She was on no medications and didn’t drink alcohol. She had no family history of early coronary artery disease. Her exam was significant for scleral icterus, severe right upper quadrant abdominal tenderness and jaundice. There were no xanthomas or xanthelasmas. Her laboratory studies were: aspartate aminotransferase 145 U/L (7-40), alanine aminotransferase 249 U/L (10-45), total bilirubin 12.3 mg/dL (0.3-1.2), direct bilirubin 7.8 mg/dL (0.0-0.3), alkaline phosphatase 617 U/L (50-136), total cholesterol (TC) > 1000 mg/dL (120-200), triglycerides (TG) 568 mg/dL (35-163), HDL< 10 mg/dL (35-80). An abdominal CT scan revealed global dilatation of the intra and extrahepatic biliary tree and an abdominal ultrasound showed a 1.4 cm obstructive stone within the distal common bile duct. She was diagnosed with choledocholithiasis and underwent Endoscopic Retrograde Cholangiopancreatography with lithotripsy and placement of common bile and pancreatic duct stents. Further work-up for cholestasis revealed no evidence of autoimmune diseases such as primary biliary cirrhosis or autoimmune hepatitis. Her laboratory studies after one month of her initial presentation were: TC 272 mg/dL, TG 215 mg/dL, LDL 200 mg/dL, HDL 29 mg/dL and normal liver function tests.

**Discussion:** In patients with chronic cholestatic liver disease, cholesterol’s metabolism and excretion are impaired and hypercholesterolemia is largely due to an increased level of lipoprotein-X (LP-X), an abnormal lipoprotein particle within the LDL density region that is...
rich in free cholesterol and phospholipids. Our patient is the second case identified upon review of the literature with massive hypercholesterolemia in the setting of acute cholestasis. We believe that these abnormalities on the patient’s lipid profile were all due to choledocholithiasis resulting in cholestasis. The potential of cardiovascular diseases in these patients is probably low since LP-X lacks the surface protein constituents necessary to interact with vascular endothelium.

**Conclusion:** Clinicians should be aware that massive hypercholesterolemia can be seen in patients with acute cholestasis due to choledocholithiasis. No treatment is warranted since hypercholesterolemia associated with acute cholestasis resolves with treatment of the underlying disorder and it is not associated with atherosclerosis.
METABOLIC BONE DISEASE

Abstract #500

LONG TERM FOLLOW UP OF PATIENTS ON DRUG HOLIDAY FROM BISPHOSPHONATES

Lauren Myers, (MS2), Jim Sinacore, PhD, Pauline Camacho, MD, FACE

Background: Recent reports of atypical fractures from over-suppression of bone turnover secondary to bisphosphonate treatment of postmenopausal osteoporosis have caused the duration of therapy to come into question. The current regimen includes drug holidays after 4 to 5 years, but there is little data on its optimal duration. The FLEX study by Black et al (2006) compared fracture risk in patients who discontinued alendronate and those who stayed on the drug and found increased fracture risk in the former group at 5 years. These risk reduction data however, are difficult to apply to individual patients. Changes in bone mineral density (BMD) and bone turnover markers are more useful for clinical use and are the focus of this study.

Objective: Our aim was to identify optimal drug holiday length after bisphosphonate therapy based on changes in BMD and bone specific alkaline phosphatase (BSAP). This is a retrospective study of osteoporotic and osteopenic patients seen at Loyola University Osteoporosis and Metabolic Bone Disease Center who started a drug holiday from 2005-2010.

Case Presentation: Patient ID, bisphosphonate history, reports of fracture, Dual energy x-ray absorptiometry (DXA) scans, 25-hydroxy-vitamin D (25-OHD) and BSAP values were obtained from the patients’ medical records at the beginning of the holiday and yearly for 3 years. Comparative statistical analyses were used to compare DXA and BSAP results. Our cohort consisted of 139 patients; 123 females and 16 males with a mean age of 68±11 years and mean pretreatment length of 6.8±2.9 years. 70% of patients were on alendronate, 21% on risedronate and 9% on ibandronate. Baseline mean 25-OHD was 45ng/ml.

Discussion: Five fractures occurred during drug holidays. Over 3 years, there was no significant change in the mean lumbar spine BMD (1.07±0.25g/cm² baseline, 0.97±0.51g/cm² year 1, 1.03±0.23g/cm² year 2, 1.13±0.37g/cm² year 3.) There was also no significant change in the femoral neck BMD (0.80±0.10g/cm² baseline, 0.78±0.09g/cm² year 1, 0.77±0.11g/cm² year 2, 0.85±0.13g/cm² year 3.) There was a significant change in BSAP from 6 months to 3 years after drug holiday. BSAP was 9.0±1.75ug/L baseline, 10.9±2.78ug/L year .5, 10.5±3.06ug/L year 1, 9.907±2.77ug/L year 2, 9.55±4.17ug/L year 3.

Conclusion: Neither the type of bisphosphate nor the duration of holiday significantly affected BMD. Cessation after oral bisphosphonate use results in stable bone density for up to 3 years, but bone turnover starts to increase at 6 months. Fractures do occur during the drug holiday; however, our study is not powered to assess fracture risk. Larger prospective studies are needed to assess adequately the optimal duration of drug holiday.

Abstract #501

CASE OF VITAMIN D DEFICIENCY MASQUERADING AS OCCULT MALIGNANCY

Mohammed Ahmed, MD, FACP, FACE, Ali Al-Jubran, MD, Alyaa Elhazami, MD

Objective: Severe vitamin D deficiency (VDD) can result in extensive metabolic bone disease including “brown tumors” that may be misinterpreted as metastatic bone disease. This may cause unwarranted anxiety and costly investigations. A clear distinction between VDD-related bone disease versus metastatic skeletal lesions is crucial.

Case Presentation: 19 year-old Saudi female was referred from an outside hospital as a case of probable osteosarcoma vs metastatic tumor because of osteolytic lesions of pelvic bones. She was initially seen in the combined Orthopedic-Oncology service where following investigations were undertaken. Pelvic X-ray: multiple “lytic lesions” in pelvic rami. Bone scan: multiple “hot areas”. CT scan of chest, abdomen and pelvis: 2 cm lesion below Left thyroid lobe. 3 cm soft tissue mass symphysis pubis, multiple “lytic lesions”. BM aspiration and bone biopsy: fibrosis. Leukemia and lymphoma WU: negative yield. Patient was referred to Endocrine service. She provided us with a history of avoiding sun exposure and dairy product intake, of painful limping for 2 yrs, and lately patient was crawling on her legs. She had profound proximal myopathy. Investigations: Serum Ca++ 2.04 mmol/l(RR:2.1-2.6), albumin 44 g/l (36-48), Po4 0.57 mmol/l (0.9-1.5), ALP 960 U/l(30-135), PTH (intact)716 ng/l (10-65), 25(OH) Vitamin D 13nmol/l(50-116), creatinine 55 umol/l(RR:2.1-2.6), albumin 44 g/l (36-48), Po4 0.57 mmol/l (0.9-1.5), ALP 960 U/l(30-135), PTH (intact)716 ng/l (10-65), 25(OH) Vitamin D 13nmol/l(50-116), creatinine 55 umol/l(RR:40-90), GFR >60 ml/min, 24 h urine Ca++ 1.57 mmol/day (2.5 - 8). BMD:T& Z scores lumbar spine & hip -3.5.Celiac serology: negative. Parathyroid scan: negative. Review of X-Ray: diffuse severe osteopenia, multiple looser zones pubic bones, resorption of femoral neck bilaterally.

Discussion: Our patient had severe VDD, very high serum PTH, and AL P, hypocalciuria, osteoporosis, osteomalacia, and radiological evidence of widely dispersed “brown tumors”, with normal kidney functions, and no evidence of malabsorption. These data confirm
unequivocally the Dx of VDD-related secondary hyperparathyroidism. VDD is a common problem in Saudi Arabia. It is rather curious that with an abundance of year-round sunlight, very low levels of serum VD were observed in the kingdom. VDD in Saudi Arabia is possibly related to inadequate sun exposure based on social dressing customs and dietary habits of eating high wheat fiber containing lignin, which binds to bile acids interfering with VD absorption.

**Conclusion:** Our case is illustrative of the vagaries encountered in the Dx of VDD. Diffuse “brown tumors” are rare presenting features of VDD. When confronted with multiple osteolytic lesions, it is mandatory to exclude VDD-related hyperparathyroidism. An understanding of the unusual aspects of VDD-related bone disease will facilitate timely and accurate Dx.

**Abstract #502**

**ARE THE BENEFICIAL EFFECTS OF NITRIC OXIDE IN BONE MEDIATED THROUGH INSULIN-LIKE GROWTH FACTOR I?**

Sunil J. Wimalawansa, MD, PhD, FCCP, FRCP, FACE

**Objective:** Many therapeutic advances have been made during the past decade in the prevention and treatment of osteoporosis. However, these treatments are expensive, and some have significant adverse effects, so simple, cost-effective therapeutic options are warranted. The beneficial effect of estrogen on bone maintenance is at least in part mediated via the nitric oxide/cGMP pathway and perhaps also via insulin-like growth factor I (IGF-1). At appropriate doses nitroglycerin, as a nitric oxide donor, favorably affects osteoblasts and osteoclasts (i.e., uncoupling these two cell types) and the prevention of estrogen- and glucocorticoid-induced bone loss.

**Methods:** A 3 year randomized, doubled-blind, controlled clinical trial was conducted to assess the efficacy of nitroglycerin in preventing bone loss in early postmenopausal women. This study, Nitroglycerin as an Option: Value in Early Bone Loss (NOVEL) was funded by NIAMS. Women were randomized to receive nitroglycerin ointment or placebo ointment. All women received calcium and vitamin D supplementation. There were no differences in bone mineral density (BMD) in the treatment group compared with the calcium and vitamin D group. However, considering compliance (~75%), the dose used by the study participants was only ~50% of that intended in this study (i.e., a sub-therapeutic dose).

**Results:** Nevertheless, a significant increase of serum IGF-1 levels was observed in women who had positive BMD response after nitroglycerin therapy, but not in the placebo-treated subjects who had a gain in BMD. Nitroglycerin-treated subjects with increased BMD had increased serum IGF-1 levels (201 ± 25.6 vs. 40.2 ± 16.9 ng/mL for non-responders; \( P < 0.001 \)), and the BMD changes were significantly correlated with the change of serum IGF-1 levels from the baseline (\( r = 0.5; \) \( P < 0.01 \)). Subjects in the placebo group who had increased BMD had no change in serum IGF-1 levels (responders vs. non-responders, respectively, -2.6 ± 24.6 vs. 10.8 ± 13.5 ng/mL; NS).

**Discussion/Conclusion:** Previously, the author demonstrated that estrogenic effects on bone can be blocked with nitric oxide synthase (NOS) inhibitors, such as L-NAME. Current data suggest that nitroglycerin, in addition to being one of the key final common pathways for positive effects of estrogen in bone, may also be involved in enhancing the local production of IGF-1, thereby assisting bone formation that is observed with nitric oxide therapy.

**Abstract #503**

**DENOSUMAB TREATMENT FOR 5 YEARS OF POSTMENOPAUSAL WOMEN WITH OSTEOPOROSIS: RESULTS FROM THE FIRST TWO YEARS OF THE FREEDOM TRIAL EXTENSION**

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**Background/Objective:** FREEDOM was a pivotal, 3-year, phase 3 trial designed to establish the efficacy and safety of denosumab for the treatment of postmenopausal women with osteoporosis (Cummings;NEJM;2009;361:756). The open-label extension of FREEDOM continues to evaluate the long-term efficacy and safety of denosumab for up to 10 years. Here, we report the results from the first 2 years of the extension study, representing up to 5 continuous years of denosumab exposure. Postmenopausal women enrolled in the extension study previously completed the FREEDOM trial.

**Discussion/Results:** During the extension, all women receive denosumab (60 mg) every 6 months and calcium and vitamin D daily. For the FREEDOM denosumab group, the data reported here reflect up to 10 doses of denosumab (5 years total; long-term group). For the FREEDOM placebo group, the data reflect up to 4 doses of denosumab (2 years total; de novo group). \( P \)-values are descriptive. A total of 4550 (70.2%) women
who completed FREEDOM enrolled in the extension study (2343 long-term; 2207 de novo). During the 4th and 5th years of denosumab treatment, the long-term group had further yearly significant improvements in BMD of 1.9% and 1.7% (lumbar spine) and 0.7% and 0.6% (total hip), respectively (all P<0.0001 compared with extension study baseline). Denosumab treatment for 5 years increased lumbar spine and total hip BMD 13.7% and 7.0%, respectively. During the first 2 years of denosumab treatment, the de novo group had significant improvements in lumbar spine BMD (7.9%) and total hip BMD (4.1%) (P<0.0001 compared with extension study baseline), similar to those observed during the first 2 years of FREEDOM. CTX was rapidly and similarly reduced after the 1st denosumab dose (de novo group) or the 7th denosumab dose (long-term group). In both groups, the characteristic attenuation of bone turnover reduction was observed at the end of the dosing interval, as previously reported (Eastell;JBMRR;2010;DOI-10.1002/jbmr.251). In both groups, yearly incidences of new vertebral and nonvertebral fractures were low and below the rates observed in the FREEDOM placebo group. Reported adverse events (AEs) or serious AEs did not increase over time with denosumab treatment. There were 2 subjects with AEs adjudicated to ONJ in the de novo group and none in the long-term group. Both cases healed completely and without further complications; one subject continues to receive denosumab. There have been no cases of atypical femoral fractures observed to date.

Conclusion: 5 years of continuous denosumab treatment of postmenopausal women with osteoporosis remained well-tolerated, maintained significant reductions in bone turnover, and continued to increase BMD.

Abstract #504

KNOWLEDGE OF OSTEOPOROSIS AMONG MEN IN PRIMARY CARE SETTING

Hassan Shawa, MD, Emanuel Favela, MD, Josefina Diaz, MD

Objective: We aimed to assess knowledge of osteoporosis and its risk factors in men.

Methods: A questionnaire assessing knowledge of osteoporosis was presented to male patients in Internal Medicine and Family Practice clinics at Saint Joseph Hospital.

Results: A total of 136 men were recruited to fill the questionnaire. Only 130 patients who completed the entire questionnaire were included in the study. 23% of men surveyed had never heard about osteoporosis. 39% were unaware that osteoporosis is directly responsible for disabling hip fractures. 67% did not know that a potential outcome of hip fracture is death. Only 38% recognized that smoking is a risk factor, 20% knew that excessive caffeine intake can put them at risk, and 35% realized that excessive alcohol intake is a risk factor. Only 21% could correctly identify the calcium-rich foods among the choices. There was a positive relationship (P< 0.05) between receiving an official discussion with a physician regarding osteoporosis and the actual score on the “knowledge of osteoporosis” questionnaire.

Discussion: Osteoporosis is a leading cause for morbidity and mortality in elderly people. It has been viewed as a disease of women. However, men are at risk for osteoporosis, and the mortality after hip fracture in men older than 75 years of age is significantly higher than in women.

Conclusion: A significant percentage of men are unaware of the complications and risk factors for osteoporosis. Receiving educational information about osteoporosis from a physician should be considered at an early stage, especially for those patients with modifiable risk factors.

Abstract #505

MAST CELL (MC) ACTIVATION DISORDER (MCAD), AN UNUSUAL CAUSE OF SECONDARY OSTEOPOROSIS IN MEN

Ashwini P Gore, MBBS, Julius Sagel, MD, Jimmy Alele, MD, Lawrence Afrin, MD

Objective: To highlight the potential role of MCAD in male osteoporosis.

Case Presentation: A 39 year-old male who since age 2 had suffered numerous fractures involving his upper and lower extremities and ribs was referred for endocrinologic evaluation. Review of systems was positive for alternating non-bloody diarrhea and constipation, frequent headaches, fatigue, pre-syncope, deep bone and joint pains, episodic flushing, sweats and pruritic skin rashes that appeared without any apparent trigger and resolved spontaneously. He denied history of kidney stones or erectile dysfunction. He had smoked half a pack of cigarettes daily since age 15, drank alcohol socially, and denied family history of osteoporosis. Physical exam was unremarkable except for moderate dermatographism (Darier’s sign). DEXA scan revealed low bone density for age (Z-score -2.71 at L-spine). Procollagen gene sequencing showed no evidence of osteogenesis imperfecta, and workup for secondary causes of osteoporosis was negative except for low 25 OH vitamin D level of 17.7 ng/ml (normal 25-80) and mildly elevated serum tryptase of 13.2 ng/ml (0.4-10.9). High dose ergocalciferol was begun. Hematologic consultation confirmed only a mild elevation of tryptase
and found a normal marrow aspiration and biopsy, failing to meet criteria for systemic mastocytosis (SM), but urinary prostaglandin D2 was elevated (313 ng/24hr, normal 100-280) and small and large bowel biopsies showed increased MCs on CD117 staining, securing a diagnosis of MCAD. Histamine blockade (loratidine and famotidine) resulted in complete alleviation of headaches, pre-syncope, and rash. A bisphosphonate was recommended for bone disease.

Discussion: While secondary causes of bone loss are often implicated in male osteoporosis, the etiology remains unknown in up to 40% of cases. A potential cause of bone loss in these cases of “idiopathic osteoporosis” is MC disease, a diagnosis that can have broader therapeutic implications. In one study, SM was almost twice as common in males younger than 45 years than in older subjects. Bone loss in MC disease can result from many factors including MC infiltration of the marrow, release of osteolytic promoters (e.g., interleukin (IL)-1, IL-3, IL-6, and histamine), and intestinal malabsorption. Bone loss in our patient was multifactorial.

Conclusion: We present a case of MCAD causing secondary osteoporosis in a young man. Evaluation of the male patient with idiopathic osteoporosis should consider assorted forms of MC disease.

Abstract #506

PRIMARY HYPERPARATHYROIDISM WITH OSTEITIS FIBROSA CYSTICA IN A PATIENT WITH ECTODERMAL DYSPLASIA

Michael Gonzales, MD, David Lieb, MD

Objective: To describe a rare presentation of primary hyperparathyroidism with osteitis fibrosa cystica in a patient with ectodermal dysplasia.

Case Presentation: A 36 y/o female with ectodermal dysplasia was found to have lytic lesions in her hips and hypercalcemia after presenting with back pain. The patient had a history of non-traumatic wrist and ankle fractures, constipation, and nausea. She had no nephrolithiasis. On examination her vital signs were stable. Skin was dry and rough, nails were thick, and eyelashes were few. Mouth was narrow with rudimentary dentition. The remainder of her exam was unremarkable. A complete metabolic panel was remarkable for a calcium of 11.1 (Ref. 8.4-10.5 mg/dl), phosphorus was 2.2 (Ref. 2.4-4.7 mg/dl), and PTH was 1579 (Ref. 15.0-65.0 pg/ml). Alkaline phosphatase was 1196 (Ref. 25-115 u/L) and 25OH-vitamin D was < 4.0 (Ref. 32.0-100.0 ng/ml). 24 hour urine calcium excretion was 164 mg/24hr (Ref. 110-250mg/24hr). Renal function was normal. MRI of the pelvis revealed multiple large cystic lesions in both iliac wings. Skeletal survey revealed lytic lesions involving the ribs, right humerus, pelvis, right femur, and left tibia. Thoracolumbar spine had coarsened trabeculation and demineralization, and the skull exhibited a salt and pepper appearance with numerous lytic abnormalities. Technetium sestamibi scan demonstrated a focus of increased uptake consistent with a right inferior parathyroid gland adenoma. Cervical ultrasound confirmed an extra-thyroidal 2.5 x 5.0 cm lesion in this location. The patient was referred for surgery and a 7.4 gram right inferior parathyroid adenoma was removed. She developed postoperative hypocalcemia, and was treated with calcitriol and oral and IV calcium.

Discussion: Ectodermal dysplasia is a genetic syndrome characterized by the triad of hypohydrosis, hypotrichosis, and hypodontia. It is also a characteristic part of the APECED syndrome which involves mutations in the AIRE gene on chromosome 21q. This has been associated with autoimmune diseases including pernicious anemia, Addison’s disease, and hypoparathyroidism. To the authors’ knowledge this condition has not been described in association with hyperparathyroidism.

Conclusion: Ectodermal dysplasia is a rare condition associated with autoimmune endocrine diseases, including hypoparathyroidism. We present a patient with this condition and severe primary hyperparathyroidism, associated with osteitis fibrosa cystica. One might consider hyperparathyroidism as an associated endocrinopathy in patients with this condition.

Abstract #507

AN UNUSUAL CASE OF PARATHYROID CARCINOMA WITH EXTRAORDINARY HIGH PARATHYROID HORMONE LEVELS IN THE SETTING OF MILD HYPERCALCEMIA

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Objective: To describe the unique clinical and pathologic features in a young man with parathyroid carcinoma (PC).

Case Presentation: A 32-year-old male with history of nephrolithiasis presented with hematuria and hypertensive urgency. He had no known history of renal failure. 8 years prior he was told he had hypercalcemia, but he did not seek further diagnostic work-up. Biochemical data showed an elevated ionized calcium at 1.46 mmol/l (1.13-1.32); corrected serum calcium 11.7 mg/dl (8.4-10.4) Intact-PTH 2165 pg/ml (15-65); alkaline phosphatase 1590 U/L (40-120); Phosphorus 2.5 mg/dl (2.5-4.9); 25-OH Vit D <4 ng/ml (32-100); Bun 19mg/dl (5-23) serum creatinine 2.4 mg/dl (0.8-1.4). Radiographs revealed multiple brown tumors throughout the skeleton with erosions in the distal clavicles and subperiosteal reabsorption of
the B/L humeral heads. There was evidence of multiple nonobstructing renal stones and diffuse nephrocalcinosis. On physical exam, there was a palpable mass in the right paratracheal region. Thyroid U/S and Sestamibi scan identified an adenoma in the inferior right thyroid lobe. Intra-op PTH level decreased from 2810 to 173 pg/ml, grossly, the tumor measured 3cm, involving the thyroid gland. Histologically, capsular and vascular invasion was identified indicative of parathyroid carcinoma. No metastatic carcinoma was identified in any of the lymph nodes assessed. Postoperatively, he developed “hungry bone syndrome” requiring calcitriol and IV Calcium infusions.

**Discussion:** PC is a slow-growing but progressive disease. Surgery is the only cure for this rare malignancy, which comprises < 1-5% of primary hyperparathyroidism (PHPT) cases. The ability to distinguish between malignant and benign disease preoperatively is associated with better outcomes. A high suspicion of PC warrants a more aggressive initial surgical approach and therefore decreases the recurrence rate. Typically, PC patients have a palpable neck mass along with concomitant renal and skeletal disease. These clinical features are quite rare with benign PHPT. Most patients with PC have markedly elevated calcium and PTH levels. Our patient had relatively mild hypercalcemia in the setting of a strikingly elevated PTH level. A possible explanation for this disparity may be due to the tendency for renal failure to lower serum calcium levels.

**Conclusion:** PC can be a diagnostic challenge. Disease recurrence significantly reduces the possibility of a cure. This case highlights the importance of suspecting PC based on biochemical and clinical grounds when the patient presents initially.

**Abstract #508**

**CAROTID INTIMA MEDIA THICKNESS IN PATIENTS WITH SPORADIC IDIOPATHIC HYPOPARATHYROIDISM**


**Objective:** To compare the carotid intima media thickness (CIMT) of patients of sporadic idiopathic hypoparathyroidism with healthy controls and subjects with metabolic syndrome. CIMT was measured by B-mode ultrasonography by a single trained operator blinded to subject’s details.

**Results:** The CIMT was significantly higher in sporadic idiopathic hypoparathyroidism than in healthy controls (mean ± SD; 0.06±0.0006 Vs 0.053±0.003 mm, p<0.001) and was comparable with metabolic syndrome patients (0.06±0.0006 Vs 0.06±0.02 mm, p<0.12). Age (p=0.003) and high phosphate levels (p=0.032) were important independent predictors of increased CIMT in patients with sporadic idiopathic hypoparathyroidism using multiple linear regression analysis. No significant correlation was found between CIMT and duration of disease (r=0.193, p=0.4) and intact parathyroid hormone (PTH) levels (r=0.283, p=0.2).

**Discussion:** CIMT increases with age and higher BMI. Despite our patients with sporadic idiopathic hypoparathyroidism were lean and young and CIMT was higher. Higher CIMT in sporadic idiopathic hypoparathyroidism in our study might be attributed to increased phosphate levels as serum phosphate was an independent predictor for CIMT using multiple regression analysis (r=0.84, p=0.03). Hyperphosphatemia has been shown to be a strong and independent predictor of cardiovascular mortality in patients with chronic kidney disease. Our observation of hyperphosphatemia having a correlation with CIMT is also in consonance with earlier studies. Transient hypercalcemia occur during the course of treatment of hypoparathyroidism can promote vascular calcification however, using multiple logistic regression analysis we could not found serum calcium as a risk factor for increased CIMT. Parathyroid hormone has been shown to have variable effects on CIMT but our study found no relationship between PTH and CIMT. This is the first study that assessed CIMT in patients with idiopathic hypoparathyroidism however; the limitations of our study are small sample size and cross-sectional design and hence this finding needs to be confirmed by further research.

**Conclusion:** Sporadic idiopathic hypoparathyroidism is associated with increased CIMT compared to age and sex matched healthy controls and may be regarded as condition with cardiovascular risk.
Abstract #509

MAGNESIUM SULPHATE-INDUCED HYPOCALCEMIA IN PATIENTS WITH PREECLAMPSIA OR PREMATURE LABOR (THE MAGCA STUDY)

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Objective: Magnesium sulfate (MgSO4) is used in supraphysiological doses for the treatment of pre-eclamptic toxemia (PET) and premature labor (PML). Although significant maternal hypocalcaemia as a result of MgSO4 therapy is well known, there is a paucity of studies to evaluate its clinical significance on the mother or baby. Therefore we undertook this study to evaluate the effects of supraphysiological doses of MgSO4 on maternal serum calcium and whether these effects are clinically significant in view of maternal and fetal outcomes.

Methods: All consecutive pregnant women who received MgSO4 in our obstetric unit, between November of 2001 and October of 2003, were prospectively enrolled in this study. Their serum magnesium and calcium levels at baseline and at subsequent 6-hourly intervals following MgSO4 infusion were recorded. In addition, maternal and fetal outcomes were also recorded.

Results: Forty patients aged 18-42 years in the 3rd trimester of gestation were enrolled in the study, of whom 36 patients had complete laboratory data available. The loading dose of MgSO4 was 4 gm, and the infusion rate was 1 gm/hr. The mean serum calcium levels dropped from 2.3 mmol/l (normal 2.12 - 2.57) at baseline to 2.0 mmol/l at 6 hrs, 1.9 mmol/l at 12 and 18 hrs, 1.8 mmol/l at 24 and 30 hrs, and 1.7 mmol/l at 36 hrs. Maternal outcome: No symptoms or signs of hypocalcemia were noted, despite the significant drop of maternal calcium from 2.3 at baseline to a nadir of 1.7 mmol/L (e.g., 9.2 to 6.8 mg/dL). Fetal outcome: About 50% of newborns had complications, including one fetal loss.

Discussion: MgSO4 is a standard universal treatment for PET and a routine tocolytic agent for PML in many places around the world. The resulting maternal and fetal hypocalcaemia and the mechanisms thereof are well-established in the literature. However, literature about the significance of this maternal or fetal hypocalcaemia has been quite scarce and only scattered case reports and small studies address the severity of this phenomenon with conflicting conclusions regarding maternal or fetal outcomes. This current study is one of the largest studies to address the clinical significance of MgSO4-induced hypocalcaemia. Our findings confirmed the relative safety of MgSO4 on the mother at dosing schedules employed at our institution. However, we did not collect data on fetal magnesium or calcium, and therefore our study can not further interpret the poor fetal outcome observed in about half of the newborns.

Conclusion: MgSO4-induced hypocalcemia is not clinically significant for the mother. Given our study design, further research is warranted to evaluate relevant fetal outcomes.

Abstract #510

VITAMIN D STATUS IN HIV INFECTED PATIENTS

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Objective: Evaluating the prevalence of vitamin D insufficiency (VDI), hyperparathyroidism and associated factors for VDI in an adult HIV cohort in comparison to matched control and the response to standard dosing of vitamin D replacement.

Methods: A retrospective case control study was conducted of 82 randomly selected HIV positive (HIV+) adults, matched by age, gender and race with HIV negative (HIV-) patients enrolled in osteoporosis and diabetes databases at HFHS. 25(OH)D level (ng/mL) was classified as sufficient (≥ 30), insufficient (15-30), and deficient (<15). Serum Parathyroid hormone (PTH) levels were reported as pg/ml. Irrespective of the degree of VDI, patients were prescribed 50,000 units weekly of VD2 for 12 weeks followed by 50,000 units every month. 25(OH)D and PTH levels were studied at a median follow up of 16 weeks after treatment. Chi square, Wilcoxon-Mann-Whitney test and t-tests were used to compare 25(OH)D levels and PTH levels among HIV+ and HIV- groups. Spearman’s correlation and linear regression were used to determine relation between 25(OH)D levels and PTH.

Results: For both groups mean age was 49.1 ± 9 years, 84% were males and 62% were African American (AA). 21.4% of HIV+ were vitamin D sufficient as compare to 78% in the HIV- (P< 0.01). HIV+ had significantly higher mean PTH vs HIV- (79.6 pg/mL vs 60.4 pg/mL, p <0.0001). In both groups there was a significant (p=0.005) negative correlation between Vitamin D and PTH. Compared with Caucasians, AA HIV+ were more likely to have VDI (N=86% vs 14%) and mean PTH levels were significantly higher in AA HIV+ (80.1 pg/mL vs 53.8 pg/mL, p 0.0013). HIV+ AA had more VDI and elevated PTH (median 80.1 pg/mL vs 52.7 pg/mL) when compared...
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with HIV-AA. 25(OH)D levels did not correlate with baseline CD4 count, nadir CD4 count, baseline viral load or the highest viral load. The median increase in 25(OH)D after therapy was 17.5ng/ml (from 11 to 28.5ng/ml).

Discussion: We have demonstrated that in our location, where vitamin D deficiency is prevalent, HIV+ had a higher prevalence of VDI in comparison to patients without HIV. This was independent of the HIV viral load or CD4 counts. AA HIV infected patients had the highest prevalence of VDI. Since VDI contributes to bone disease, including osteomalacia, and DXA scans are unable to differentiate osteoporosis from osteomalacia, prospective studies that include clinical history, biochemical markers, and bone biopsy are needed to define the prevalence of osteomalacia in patients with VDI and hyperparathyroidism.

Conclusion: In our cohort VDI was nearly universal. The dose/response we observed indicates that HIV+ patients can achieve optimal vitamin D status by using weekly VD2, which does not result in a significant increase in pill burden. To our knowledge, our study is the first study that evaluates responsiveness of HIV infected patients to standard therapy for vitamin D replacement.

Abstract #512

RIGHT THIGH PAIN IN A WOMAN WITH OSTEOPOROSIS

Omar Naeem Akhtar, MBBS, Saba Faiz, MD, Tipu Faiz Saleem, MD, MS, FACE

Objective: To describe a case of atypical diaphyseal femoral fracture associated with bisphosphonates with emphasis upon associated risk factors, clinical course, prevention and management.

Case Presentation: A 66 year-old woman was referred from a rural clinic for non-traumatic right thigh pain which, persisted despite avoiding weight bearing. She had a bilateral femur shaft fracture 27 years ago in a car accident. She had history of resection of melanoma. Her brother and father died of leukemia at younger ages. She was taking alendronate 70 mg/day and esomeprazole/sucralfate for 6 years. Her base line DXA, done 6 years...
Abstract #513

RECOMBINANT HUMAN PARATHYROID HORMONE TREATMENT IN A PATIENT WITH ADULT HYPOPHOSPHATASIA

Grace Y. Kang, MD, Kimberly I. Rieniets, DO, Robert A. Vigersky, MD, Henry B. Burch, MD

Objective: To report a case of adult hypophosphatasia patient and the treatment course of recombinant human parathyroid hormone (Teriparatide) therapy.

Case Presentation: A 57 year old Caucasian man sustained multiple atraumatic recurrent metatarsal fractures (MTSF) and was found to have low serum alkaline phosphatase (SAP) ranging from 29-31 U/L (reference range 40-130). Serum calcium, phosphorus, and PTH level were within the reference range. The patient had a normal bone mineral density. Sequencing of ALPL gene confirmed the heterozygous missense mutation at exon 11 (Asn417Ser). Urine phosphoethanolamine was elevated to 364 μmol/24 hr (reference range 17-95). Teriparatide (recombinant human PTH 1-34) 20mcg subcutaneous daily injection was started for chronic boney foot pain and poorly healing metatarsal fractures in AUG 2008. Teriparatide therapy was continued for 22 months, during which time plain foot films every six months showed no new MTSF. SAP level improved to 36-45 U/L, but there was no significant change in bone turnover markers (urine N-telopeptides and osteocalcin). About four weeks after Teriparatide was stopped, the patient was diagnosed of new left 5th MTSF. Teriparatide injection was restarted in JUL2010 for 4.5 months and follow up films showed gradual healing of the left 5th MTSF.

Discussion: Adult hypophosphatasia is a rare metabolic bone disorder caused by loss-of-function mutation of the ALPL or TNSALP gene, the gene encoding tissue non-specific alkaline phosphatase. Defective skeletal mineralization and the finding of low SAP is a hallmark of the disease. There is no established treatment for adult hypophosphatasia, but the use of Teriparatide has been reported in three postmenopausal women, treated with 20mcg sc daily injection for 13-24 months. Teriparatide therapy improved SAP level and showed improvement of bone remodeling (Whyte MP 2007, Camacho PM 2008, and Gagnon C 2010). Our patient appeared to benefit from Teriparatide therapy in terms of improved fracture healing and prevention of new fractures. He had recurrent MTSF within one month of stopping Teriparatide. Previous case reports showed no sustained response off Teriparatide, with SAP returning to the baseline.

Conclusion: In this man with heterozygous adult hypophosphatasia, Teriparatide treatment was effective in prevention of recurrent fractures and improved SAP...
level, but therapeutic benefit was not sustained when therapy was stopped. Teriparatide may benefit adult hypophosphatasia patients for promoting fracture healing and possibly preventing new fractures, but the treatment response appears not to be sustained after stopping the medication.

Abstract #514

MULTICENTRIC OSTEOLYSIS WITH IGA NEPHROPATHY: AN “N OF ONE” CASE

Sergio Eduardo Chang Figueroa, MD, Stephen Brietzke, MD

Objective: To identify a rare, previously unreported association of idiopathic multicentric osteolysis with IgA nephropathy.

Case Presentation: The now 25-year-old male patient (an adoptee with no knowledge of his biological parents’ family medical history) presented with progressive deformity of the hands and feet at 10 years of age. After being treated for presumed juvenile rheumatoid arthritis (JRA) for 3 years with a regimen of experimental diet, bracing and splinting, he was diagnosed with idiopathic multicentric osteolysis (IMO) and, treated with alendronate and calcium and Vitamin D supplementation. Twelve years later, physical examination revealed facial features that included a slender nose and micrognathia, and bilateral hand deformity with camptodactyly in the right, as well as reduced extension of the elbows and hammer/claw toes. Laboratory studies were notable for estimated GFR 44 ml/min (normal for age > 60), proteinuria (2.68 mg/mg creatinine [normal = < 0.2]), intact PTH 10 pg/ml (normal = 10-55), 25-OH Vitamin D (calcidiol) 38 ng/ml (normal = 30-80), serum cross-linked N-telopeptide 22.2 nM bone collagen equivalents (normal = 5.4 - 24.2) and serum calcium 10 mg/dl (normal = 8.6-10.2). Renal biopsy demonstrated focal segmental glomerulonephritis with immunostaining positive for IgA. Dual-energy X-ray absorptiometry revealed Z-scores of +1.2 at L1-L4, and +0.7 at total hip. Skeletal X-rays demonstrated absence of carpal bones with erosion of the phalanges and marked dysplastic deformity of the right distal humerus. Ongoing management, coordinated among specialists in endocrinology, nephrology, rheumatology, and orthopaedics, includes orthoses and assistive devices, a bisphosphonate, and an ACE inhibitor.

Discussion: MON is an extremely rare condition (30 reported cases worldwide). The pattern of affected joints, facial features, absence of inflammatory markers, and presence of carpal and tarsal osteolysis differentiates MON from JRA. The role of bisphosphonates is uncertain. Current treatment options are limited, and consist of physical therapy and surgical correction when possible. Unique to this case is the biopsy-confirmed IgA nephropathy. Previous reported cases characteristically have been associated with non-immunostaining focal segmental glomerulosclerosis (FSGS).

Conclusion: Recognition of this bone and renal disease is important, so that potentially toxic anti-inflammatory treatment is appropriately withheld. Treatment of MON at this time is primarily supportive.

Abstract #515

IMPACT OF WRIST BONE MINERAL DENSITY MEASUREMENT ON MANAGEMENT RECOMMENDATIONS FOR ASYMPTOMATIC PRIMARY HYPERPARATHYROIDISM

Ejigayehu Gigi Abate, MD, Caroline Davidge-Pitts MBCh, Colleen Thomas, MS, Michael Heckman, MS, Shon Meek, MD

Objective: 1) To estimate the proportion of patients with asymptomatic primary hyperparathyroidism whose recommendations for surgery over observation is altered by results of wrist bone mineral density (BMD) measurement. 2) To evaluate the association of wrist BMD with markers of bone metabolism: vitamin D, calcium, alkaline phosphatase, intact parathyroid hormone (PTH), urine calcium, and BMD at hip, spine, femoral neck, wrist. 3) Proportion of patients with any site osteoporotic fracture and association with wrist BMD.

Methods: We conducted a retrospective study of 220 patients with a diagnosis of primary hyperparathyroidism at Mayo Clinic Florida between 1/2004 - 9/2010. From electronic medical records: age, weight, sex, BMD at the wrist, femoral neck, spine, and hip, serum calcium, PTH, creatinine, creatinine clearance, phosphorous, alkaline phosphatase, 24-hour urine calcium, 25-hydroxy-vitamin D, bisphosphonate use, history of kidney stones and osteoporotic fracture. The proportion of patients whose recommendation for surgery would be altered by results of wrist BMD measurement was estimated along with an exact binomial 95% confidence interval (CI).

Results: Recommendation for surgical parathyroidectomy based on current guidelines would have been given to 151 patients (69%). The inclusion of wrist BMD <-2.5 would increase the number of patients to 164 (75%). Thus, surgical recommendations would have been altered by the results of wrist BMD measurement for 13 patients (5.9%, 95% CI: 3.2%-9.9%). Wrist BMD was significantly associated with BMD measured at the femoral neck (r= 0.46, P<0.001), spine (r=0.43, P<0.001), and hip (r=0.56, P<0.001, creatinine clearance (r=0.46, P<0.001) and inversely associated with serum...
phosphorous ($r=-0.16, P=0.019$). Wrist BMD was lower in patients with any site osteoporotic fracture compared to those without (Median: -2.4 vs. -1.6, $P<0.001$).

**Conclusion:** The inclusion of wrist BMD measurement would alter treatment in 6% of patients with asymptomatic primary hyperparathyroidism. These patients would not have been candidates for surgery based on their femoral neck BMD indicating differential bone loss at wrist and femoral neck. Any site osteoporotic fracture is associated with lowest wrist BMD, a potential marker of severe osteoporosis. Utilizing wrist BMD in asymptomatic primary hyperparathyroidism may be useful in risk assessment of fractures and potential medical or surgical management.

Abstract #516

A CASE REPORT OF ACQUIRED HYPOPHOSPHATEMIC OSTEOMALACIA WITH PATHOLOGIC FRACTURES

Prasuna Madhavaram, MD, Fred Faas, MD, Robert S Weinstein, MD, Brendan M Colaco, MD

**Objective:** To present the management challenges associated with bilateral pathologic fractures in an HIV patient.

**Case Presentation:** A 56 year old black woman with HIV was admitted with bilateral fractures; a left femoral fracture confined her to a wheelchair. She complained of generalized bone pain and weakness with a twelve pound weight loss. She was thought to have osteoporosis and received treatment with alendronate for one month. She denied a history of trauma, falls, steroid or opiate use. An abnormal bone scan and MRI suggested systemic bone pathology. Blood count, calcium, PTH, thyroid profile, 1, 25(OH) D and urinary N-telopeptide were normal; 25OHD was low normal. Total and bone specific alkaline phosphatase were elevated. Normal FGF-23, PTHrp, and PET scan excluded oncogenic osteomalacia. Serum phosphate was low with inappropriate phosphaturia, metabolic acidosis, hypokalemia, and glucosuria was suggestive of Fanconi’s syndrome. Her HAART (Highly Active Antiretroviral Therapy) therapy included Truvada (Emtricitabine-Tenofovir), Ritonavir, and Atazanavir since the diagnosis of HIV, thirteen years ago. A diagnosis of tenofovir-induced Fanconi’s syndrome with hypophosphatemic osteomalacia was made and tenofovir was discontinued. She was treated with phosphorous, calcitriol and surgical fixation of the hips. Bone fragments collected during surgery showed increased osteoid suggestive of osteomalacia. Two months later, she had dramatic clinical improvement with healing fractures and normal ambulation; alkaline phosphatase remained elevated and she continues the phosphorous supplementation.

**Discussion:** Clinically important categories of hypophosphatemic osteomalacia include oncogenic osteomalacia, vitamin D deficiency, familial X-linked hypophosphatemia and antacid-induced osteomalacia. However, tenofovir disoproxil fumarate (TDF) has been associated with isolated hypophosphatemia or the complete Fanconi’s syndrome and may present with osteomalacia and pathologic fractures. The Fanconi’s syndrome may be reversible after stopping tenofovir. TDF is considered a first line agent in the treatment of HIV and is also approved for hepatitis. Recent studies provided evidence of HIV prevention with single-tablet regimen of Truvada (emtricitabine and tenofovir), suggesting that the incidence of tenofovir-induced osteomalacia may increase in the near future.

**Conclusion:** Clinicians should be cognizant of the possibility of acquired hypophosphatemic osteomalacia with pathologic fractures in patients receiving tenofovir. This case also highlights the importance of monitoring not only for renal impairment but also for bone disease in patients receiving this treatment.

Abstract #517

PRIMARY HYPERPARATHYRIDISM PRESENTS DIFFERENTLY IN YOUNG VS OLDER PATIENTS

Jovenel Cherenfant, MD, Nisha Chhabra, BA, Tricia Moo-Young, MD, Shalini Arora, MD, Subhash Patel, MD, Richard A Prinz, MD

**Background:** Primary hyperparathyroidism (pHPT) is typically a disease of postmenopausal women and is rare in young patients. Although rare, we have observed a number of young patients (< 30 years of age) with pHPT. We review our experience to determine if any differences exists between young versus older patients presenting with pHPT.

**Methods:** A retrospective review of 335 consecutive patients undergoing parathyroidectomy for pHPT between 1998 and 2009 was performed. Patients were separated by age into three groups: < 30 years, 30 to 60 years, and >60 years. Those with secondary and tertiary hyperparathyroidism were excluded from the study. Patients completed a questionnaire to evaluate symptoms and family history. Evaluation of serum calcium and parathyroid hormone (PTH) levels was performed pre and post-operatively.

**Results:** There were 40 patients less than age 30, 155 patients between the ages of 30 and 60, and 140 patients over the age of 60. Females represented 63% of our
patient population (n=149). Young patients (age < 30) had significantly higher preoperative calcium and PTH levels when compared with patients > 60 years of age (calcium level 11.7 vs 10.9, p<0.004; PTH 146 vs 123, p=0.002). All patients were cured with postoperative median calcium and iPTH values of 9.35 and 42.1 respectively. Young patients were more likely to have a family history of hyperparathyroidism (12 vs 0%, p=0.0001). At presentation 58% of young patients complained of GERD symptoms versus 26% of those age 30-60, and 23% of those age >60. Kidney stones were reported by 40% of female patients < 30 years of age versus only 11.5% of those >30 years of age. Bone density evaluation showed that 63% of young females had osteopenia versus 43% of patients > 60 years of age. Osteoporosis was most prevalent among older female patients versus young patients (49% vs 9%, p<0.001). When comparing gender alone and controlling for age, females had a higher prevalence of GERD and osteoporosis when compared to their male counterparts. Males of all ages were more likely to present with a history of kidney stones.

**Conclusion:** Primary hyperparathyroidism (pHPT) is not a rare condition among young patients. Seventeen percent of our patient group was less than 30 years of age at the time of diagnosis. Young patients with pHPT present with advanced disease and are more likely to have symptoms of GERD, nephrolithiasis and osteopenia. Since routine calcium screening is not done in younger patients, pHPT should be considered when nephrolithiasis, GERD, symptoms of nephrolithiasis and osteopenia. Since routine calcium screening is not done in younger patients, pHPT should be considered when nephrolithiasis, GERD, and bone disease occur in this age group.

**Abstract #518**

**ONCOGENIC OSTEOMALACIA IN A PATIENT OF CARCINOMA OF PROSTATE**

Sachin Kumar Jain, MD, MBBS, DM, FACE, N. Jain, MD, S. Faizal, MD, Ajay Ajmani, MD, DM

**Objective:** To present a case of oncogenic osteomalacia.

**Case Presentation:** A 50 year old man presented with generalized weakness, bony aches and pains all over the body, anorexia, and weight loss of approximately 8 kg over 6 months. Generalized weakness progressively increased to the extent that patient’s mobility was limited to indoor activities. No history of cough, dyspnoea, urinary or bowel complaints. Patient is a non alcoholic, non smoker. No history of diabetes mellitus or hypertension. Patient had undergone trans-urethral prostatic surgery 2 years back for obstructive urinary symptoms at private clinic (no past records available). Patient was free of any urinary symptoms after surgery. Examination: revealed a lean man with cachexia, pallor & bony tenderness all over. BMI was 15.8 kg/m². He was normotensive. Motor power was grade 4. Rest of the systemic examination was normal. On per rectal examination prostate was enlarged, grade 2, hard in consistency. Investigations: Hb was 5.7gm% (12-17), total leucocyte count was 6400/mm³, DLC P<0.05 E_M1, ESR 53mm 1st hour (up to 20 mm), peripheral smear was dimorphic picture. Serum chemistry revealed corrected S. calcium: 8.4mg/dl (9.0-11.0), S. phosphorus 1.6mg/dl, alkaline phosphate 1099U/L(80-300), fasting blood glucose 95 mg/dl (80-108), kidney function tests were normal (Blood urea35 mg/dl (20-300), S.creatinine1.2mg/dl (0.5-1.4)), S. uric acid 4.3mg/dl(3.1-7.0), S. Na+ 136meq/L (135.0-145.0), S. K+ 4.1meq/L (3.5-5.0), AST 35.0U/L (10-45), ALT 30.0U/L (10-40), S. albumin 3.6g/dl (4.0-5.0), S. globulin 2.7g/dl (1.7-2.8), repeat corrected S. calcium 8.1mg/dl, S. phosphorus 1.5 mg/dl, S. ALP 1290U/L. On two occasions 24 hour urinary calcium was 26 mg & 20mg, 24 hour urinary phosphate was 1214 mg & 1350 mg & 24 hour urinary creatinine was 580mg & 553mg. TmP/GFR was 1.1 mg/dl & 1.3 mg/dl. S. PSA >100 ng/ml on more than two occasions. S. 25(OH) Vit D3 42.1 ng/ml (30-70); 1, 25(OH)2 Vit D2 and Osteomalacia leading to a diagnosis of oncogenic osteomalacia. He was treated with calcitriol (1.5 µg/day), oral phosphorus supplements (3 g/d) and chemotherapy in consultation with urologist. Patient felt improvement in his bony pains, weakness, and appetite improved over next few weeks.

**Discussion:** This patient of carcinoma of prostate had generalized weakness and bony pains along with hypophosphataemia, hyperphosphaturia, Normal 25(OH) Vit D and low 1,25(OH)2 Vit D3 was 5.0 pg/ml (16-45). S FGF-23 could not be done. Prostate biopsy revealed carcinoma prostate. Skeletal survey revealed increased bone density and patchy sclerosis in rib cage, bilateral clavicular heads, humerus, spine and pelvis likely to be metastatic deposits. Diagnosis of tumor induced osteomalacia (oncogenic osteomalacia) was made. He was treated with calcitriol (1.5 µg/day), oral phosphorus supplements (3 g/d) and chemotherapy in consultation with urologist. Patient felt improvement in his bony pains, weakness, and appetite improved over next few weeks.

**Abstract #519**

**ACUTE ONSET LEFT HIP PAIN AFTER ZOLEDRONIC ACID INFUSION-A CASE REPORT**

Ila Khanna, MD, Faryal S. Mirza, MD

**Objective:** To report a case of acute onset left hip pain, joint effusion, soft tissue edema, and greater trochanteric bursitis with calcific tendinitis within 24 hours of the first zoledronic acid infusion.

**Case Presentation:** We present a 69 year old caucasian female with past medical history of primary hyperparathyroidism with surgical resection, hyperlipidemia, hypertension, osteoarthritis, and osteoporosis who had been on oral bisphosphonate therapy...
for a total of six years. She was changed to intravenous zoledronic acid (ZA) due to declining bone density. Within 24 hours of her first ZA infusion into her right arm, patient reported severe and disabling pain in her left hip. She reported weakness initially, followed by a constant pain and difficulty with weight bearing localized to the posterior and lateral aspects of her hip with no known exacerbating or alleviating factors. Pain was refractory to acetaminophen and narcotics. Patient was afebrile. Initial labs revealed leukocytosis with WBC of 14.3x10^3/mm^3, along with elevated erythrocyte sedimentation rate (ESR, 60mm/hr) and C-reactive protein levels (CRP, 239 mg/L). MRI of the left hip revealed greater trochanteric bursitis with calcific tendinitis associated with extensive reactive soft tissue edema. There was also a partial high grade tear of the left hamstrings tendon. No acute fracture or dislocation was present. An unsuccessful attempt was made at aspirating the left hip effusion. Patient was treated conservatively with pain management and non weight bearing initially. She underwent spontaneous resolution of her symptoms over next 2 weeks, with normalization of the leukocytosis, ESR and CRP.

Discussion: Bisphosphonates are currently the first line treatment for osteoporosis. ZA is a nitrogen containing bisphosphonate with the highest affinity for bone mineral. Some common adverse reactions associated with ZA include an acute phase response (APR), characterized by influenza-like symptoms, fatigue, malaise, myalgia, arthralgia, bone pain and fevers. Musculoskeletal pain and swelling has also been reported less commonly with ZA. We report an unusual form of APR with ZA, associated with incapacitating hip pain, joint effusion, soft tissue edema and trochanteric bursitis, which has not been reported previously.

Conclusion: The overall safety and tolerability of bisphosphonate therapy for osteoporosis is good with only rare serious adverse events. This case highlights the need for the astute clinician to be aware of the broad spectrum of severity of acute phase reactions that have been associated with ZA infusion.

Abstract #520

USE OF INJECTABLE PTH 1, 34 FOR POST-SURGICAL HYPOCALCEMIA

Kavya Chitra Mekala, MD, Gary Cushing, MD

Objective: To report a case of post-surgical hypocalcemia successfully treated with PTH 1, 34.

Case Presentation: A 56 year old female with Hashimoto’s thyroiditis underwent total thyroidectomy for progressively enlarging goiter. Post-operative course was complicated by severe stridor secondary to bilateral true vocal cord paralysis. Nasogastric tube was not placed owing to tenuous respiratory status. Immediate post-operative Ionized Calcium (Ca) was 1.09 mmol/L (normal 1.15- 1.35) which trended down despite aggressive IV Ca gluconate administration and Calcitriol 0.25 mcg IV twice daily. Ionized Ca dropped to 0.79 mmol/L on post-operative day 2 and patient developed positive Chvostek’s sign. Intact PTH was low at 2 pg/ml (normal 12- 88). Patient was unable to swallow oral medications until post-operative day 3 when she was started on Ca Carbonate, Vitamin D and Hydrochlorothiazide. Calcitriol dose was doubled. Despite these measures, correction of hypocalcemia remained sub-optimal. We initiated treatment with PTH 1, 34 (Teriparatide) 20 mcg SQ twice daily. Ca levels quickly improved and stabilized between 8-9 mg/dl. Patient was transitioned to once daily dose after 1 week and then taken off Teriparatide at the end of second week with stable Ca levels.

Discussion: Conventional treatment of post-surgical hypocalcemia involves administration of high doses of oral Ca, Vitamin D and 1, 25OH Vitamin D. This case presented a unique challenge where conventional therapy could not be utilized owing to respiratory compromise. PTH 1, 34 is the biologically active amino-terminal portion of PTH molecule. It raises serum Ca levels by 1, 25OH Vitamin D activation increasing intestinal Ca absorption. It also increases renal Ca reabsorption. Advantages over conventional therapy include avoidance of hypercalciuria, nephrocalcinosis and chronic kidney disease. Post-operative hypocalcemia is usually the complication that determines length of hospital stay in total thyroidectomy patients. Treatment with PTH 1, 34 can potentially decrease length of stay by increasing Ca levels quickly. Disadvantages include availability only as injectable form, short half-life and potential risks of osteoporosis and osteosarcoma. Use of PTH 1, 34 for hypocalcemia has been studied extensively by Winer et al, largely for treatment of chronic hypocalcemia. Its specific use in the immediate post-operative setting is the objective of two clinical trials listed on clinicaltrials.gov (one trial terminated due to slow accrual, second trial pending recruitment).

Conclusion: This case report highlights the potential for therapeutic use of PTH 1, 34 in treatment of acute post-surgical hypocalcemia.
VITAMIN D STATUS IN EPILEPTICS ON LONG TERM ANTI EPILEPTIC DRUG THERAPY

Sachin Kumar Jain, MD, MBBS, DM, FACE, N. Jain, MD, S. Faizal, MD, J. Bhattachargee, MD, N. Sharma, MD

Objective: Epilepsy is a common chronic neurological disorder which requires long term treatment with antiepileptic drugs. This treatment with antiepileptic drugs is linked with the variety of biochemical, metabolic and radiological abnormalities, which may go unrecognized, undetected and untreated. Antiepileptic drugs which induce enzymes increase catabolism of Vitamin D causing hypocalcaemia which itself can lead to seizures, even during continued treatment of epilepsy. These patients are often misdiagnosed as uncontrolled and refractory seizures and the antiepileptic drug dosage is either escalated or patient is started on polytherapy. In view of this we conducted this study.

Case Presentation: A comparative, cross-sectional study was conducted at the Department of Medicine, Hardinge Medical College unit at Dr. R.M.L. Hospital, New Delhi. Study was carried out in 60 epilepsy patients in age group of 20-50 years and was on antiepileptic drugs for at least two years and 30 normal age and sex matched healthy individuals. Patients with history of secondary causes of epilepsy and chronic medical conditions were excluded. After an informed consent all selected patients were interviewed and clinically examined. Blood samples were collected and sent for biochemical analysis. Similar procedure was repeated for the control subjects.

Results: Epilepsy subjects- a total of 60 patients, 33 males and 27 females, aged 29.62±9.6 years (Mean ± SD) (range 20-50y) were studied. Duration of epilepsy varied from 2 to 33 years (9.5±7.3y). 11 patients (18.3%) were on one drug, 24 (40%) were on two drugs and 25 (41.7%) were on more than two drugs. The most frequently used anti epileptic drug was phenytoin. Corrected S. Ca: 9.06 ±0.9mg/dl; (Range6.7-10.8). S. phosphorus 3.5 ± 0.6mg/dl (2.4-4.9), S.alkaline phosphatase 230.0 ± 91.9U/L (69.0-440.0) and S. albumin 4.4 ± 0.4g/dl (3.3-5.4). Four (6.6%) patients had severe hypocalcaemia and their corrected S. calcium levels were below 7.20 mg/dl. Definition used to define Vitamin D status was as Vitamin D deficiency: <30 nmol/l; Vitamin D insufficiency: 30-75 nmol/l; Vitamin D sufficiency: >75 nmol/l. 25OH Vitamin D levels were significantly low in patients (71.8 vs 101.2 nmol/l at p-value 0.002). In this study 10 patients (16.72%) had vitamin D deficiency (Vs none in control group), 29 patients (48.3%) had vitamin D insufficiency (Vs. 3 subjects (10%)). Overall 65% of the patients showed low levels (deficiency and insufficiency) of 25(OH) D. However there was no statistically significant difference in Serum calcium, Serum phosphate, and Serum Alkaline Phosphatase and serum Albumin levels between the two groups. 4 (6.6%) patients who had markedly low serum calcium levels were on polytherapy for more than 5 years of anti epileptic treatment.

Discussion: Patients on antiepileptic drugs had significantly low 25(OH) vitamin D levels. Corrected serum calcium levels in both the groups were not different statistically but 4 (6.6%) patients who were severely hypocalcemic were on polytherapy for more than 5 years duration. These patients had breakthrough seizures, but did not undergo any biochemical evaluation for serum vitamin D and serum calcium levels. Instead they were either prescribed escalated doses of antiepileptic or were added on to another antiepileptic, which could further aggravate the situation.

Conclusion: We can conclude that in epilepsy patients with breakthrough seizures vitamin D and calcium should be studied and treated if required before adding on additional drug or escalating the existing drug dosage.
Whole body MRI and CT: mass lesion left sphenoid sinus. Endoscopic sinus surgery: mass lesion in the left sphenoid sinus removed. Histopathology: Mesenchymal tumor. 2 mos. later serum and urine PO4 normalized without any replacement. Follow up FGF23 level returned back normal (78). Patients disability resolved with return to normal life.

Discussion: TIO is a rare disorder of phosphate homeostasis in which rickets or osteomalacia is associated with a tumor. It represents a paraneoplastic syndrome of both renal P04 wasting and abnormal vitamin D metabolism. Most pts are adults who report long-standing, progressive muscle and bone pain, weakness and fatigue. Recurrent fractures usually complicate TIO. Since resection of TIO-causing tumor leads to rapid correction of disorder, existence of a circulating humoral factor designated “phosphatonin”, a 32-kD peptide belonging to the FGF family was postulated & confirmed. Our case is illustrative of the role of a mesenchymal tumor as the source of FGF23 in the causation of TIO. The absence of similar family history, severity of symptoms with the identification of previously normal PO4 level in an adult patient supports the diagnosis of TIO against other hypophosphatemic syndromes such as XLH and ADHR.

Conclusion: The occult nature of TIO and inability to locate the tumor often delays treatment by an average of 5 years. Accurate Dx and resection of underlying tumor leads to a dramatic resolution of disorder.

Abstract #523

HARD BONES, EASY FRACTURE: A RARE SKELETAL DYSPLASTIC SYNDROME

Nitasha Bakhrui, MD, James McCallum, MD

Objective: To describe an aggressive skeletal dysplastic disorder with propensity for bony malignancy.

Case Presentation: A 53 y/o female presented with multiple bilateral fragility fractures of the upper and lower extremities occurring sporadically over the past year. DXA revealed supranormal bone mass and T-score +3.9 at the lumbar spine. Metabolic workup was essentially negative, serum calcium 8.6 mg/dL, PTH 34.5 pg/mL, 25-hydroxyvitamin D 44 ng/mL, urine calcium/creatinine ratio 0.18, alkaline phosphatase 42 U/L, TSH 0.84 uIU/mL, and urine N-telopeptide 57 nM BCE/mM. She had never been on any form of anti-resorptive therapy. Interestingly, family history was significant for similar fragility fractures in a brother beginning at the age of 8. Furthermore, her brother had subsequently developed osteosarcoma prompting a below the knee amputation. Two of his sons had similar histories (the patient’s nephews). A maternal aunt, her daughter, and 4 of 5 of her daughter’s children had experienced a similar history of unexplained fragility fractures and osteosarcoma. Bone biopsy was inconclusive. Genetic testing revealed a diagnosis of diaphyseal medullary stenosis, or Hardcastle Syndrome.

Discussion: Hardcastle Syndrome is a rare familial skeletal dysplastic syndrome having only been described in 7 kindred worldwide. It is believed to be an autosomal dominant disorder with defective osteoclast activity resulting in medullary stenosis limited to the diaphyses of long bones and cortical periosteal thickening. Impaired osteoblast activity is thought to result in malunion of pathologic fractures. Multiple areas of medullar necrosis and infarctions are also characteristic of this disorder. Such changes predispose to malignant transformation to a highly aggressive form of fibrous histiocytoma in the 2nd-5th decades of life. Therapeutic options are limited and recommendations include yearly screening of the proband’s family with radiographs, genetic screening, and technetium bone scans to survey for malignant fibrous histiocytoma.

Conclusion: Diaphyseal medullary stenosis with malignancy (Hardcastle Syndrome) is a rare, aggressive skeletal dysplastic disorder with an autosomal dominant pattern of inheritance. Early recognition of this disorder promotes genetic screening, and surveillance of kindred at risk for the disease.

Abstract #524

THE CHANGING FEATURES OF PARATHYROID CARCINOMA

Sergio Eduardo Chang Figueroa, MD, Liliana Garcia, MD, Uzma Khan, MD

Objective: To report 2 cases of parathyroid carcinoma focusing on the distinct clinical features and recognize that parathyroid carcinoma can present as a mild asymptomatic disease.

Case Presentation: Case 1: A 50 year old man presented with polyuria. His history was significant for idiopathic pancreatitis leading to pancreatectomy, hypertension, recurrent nephrolithiasis, chronic kidney disease stage III, and osteopenia. Physical exam was remarkable for a right neck mass. Laboratory investigations revealed an intact PTH intact (iPTH) of 225pg/ml (10-60 pg/ml) and serum calcium of 12.2 mg/dl (8.4 – 10.2 mg/dl). A parathyroid sestamibi scan revealed a right parathyroid adenoma. Since cancer was suspected, he underwent subtotal thyroidectomy due to a concomitant left hypoechoic nodule with a nondiagnostic FNA. Pathology revealed a left Hurthle Cell Adenoma and a Right Parathyroid 2.1cm carcinoma based on trabeculae, pleomorphic cells, fibrous bands, and vascular invasion. Intraoperative iPTH decreased to 55 pg/ml and serum calcium decreased to 8.4 mg/dl. At 5 months
postoperative follow-up he remains normocalcemic. Case 2: A 50 year old man with depression, on routine laboratory assessment was noted to have serum calcium of 10.4 mg/dl, iPTH of 99 pg/ml, and urine calcium of 370 mg/24h (< 300mg/24h). He had no history of nephrolithiasis and physical exam was unremarkable. A parathyroid sestamibi scan was positive for a left superior adenoma and bone densitometry was normal. After parathyroidectomy the intraoperative iPTH decreased to 32 pg/ml. Pathology unexpectedly revealed a parathyroid carcinoma based on vascular and capsular invasion. He underwent left thyroidectomy and isthmectomy. A positron emission tomography scan was negative and genetic testing was negative for HRPT2 mutation. Jaw X-ray didn’t reveal fibromas and a kidney ultrasound was negative for cysts. At 5 months postoperative follow-up his calcium is 9.6 mg/dl and iPTH is 36 pg/ml.

Discussion: Parathyroid cancer is a rare cause of PTH dependent hypercalcemia. Case 1 highlights a classical presentation recognized by symptomatic hypercalcemia and markedly elevated iPTH, with pathological features including vascular invasion. However, with more widespread laboratory assessment, parathyroid carcinoma can also present as a mild asymptomatic disease as shown by case 2.

Conclusion: A high index of suspicion is needed in order to recognize parathyroid cancer in patients with asymptomatic presentation. Early recognition can provide decreased morbidity and potential cure, as the surgical approach differs from that of resection of a benign parathyroid adenoma.

Abstract #525

INDICES OF PHOSPHORIC METABOLISM IN PRIMARY HYPERPARATHYROIDISM AT THE TIME OF THE DIAGNOSIS

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Objective: Primary hyperparathyroidism (pHPT) deeply affects calcio-phosphoric metabolism. While serum and urinary calcium levels are well established criteria for the diagnosis and the clinical assessment of PHPT patient, serum and urinary phosphorus are of uncertain clinical utility. Moreover the frequencies of abnormalities in indices of phosphoric metabolism have been poorly investigated in PHPT, in particular in mild/ asymptomatic PHPT (now more frequently diagnosed). Aim of the present study was to retrospectively evaluate indices of phosphoric metabolism in our PHPT series.

Methods: In 290 consecutive pHPT patients [F/M= 214/76; Symptomatic / Asymptomatic = 148/142; age (mean ± S.D.): 59.0 ± 13.7 yrs, PTH=198.3 ± 161.0 pg/ml; serum Calcium = 11.2 ± 1.2 mg/dl, eGFR (MDRD) = 91.9±31.9 ml/min] serum phosphorus (P), 24-hour urinary P (uP) and Tubular Phosphate Reabsorption (TPR) were studied/evaluated/investigated.

Results: in the whole group of patients P (mean ± S.D.: 2.5±0.54mg/dl) was below normal (<2.5 mg/dl) in 54.3%. uP (mean ± S.D.: 563.0 ± 355.8 mg/24h) was higher than normal (>1300 mg/24h) in 2.9%. TPR (mean ± S.D.: 80.6 ± 11.9%) was lower than normal (<80 %) in 42.6 %. P, Up, and RTP were not significantly different neither between symptomatic and asymptomatic patients, nor between patients with and without nephrolithiasis. PHPT patients with low levels of 25OH Vitamin D (<30) had significantly reduced levels of phosphorus (p <0.016). TPR and P were inversely related to circulating levels of PTH and calcium; a positive correlation between P and 25OHvitD was also revealed (p <0.04).

Conclusion: In a large series of patients with PHPT, with broad representation of asymptomatic forms, the alterations of indices of phosphoric metabolism were relatively uncommon and of poor clinical utility. Our data therefore seem to confirm the limited clinical relevance of measuring indices of phosphoric acid metabolism in PHPT.

The use of phosphorus as an indirect and unexpensive marker of vitamin D status should be confirmed by prospective and intervention studies, particularly in the forms of PHPT not surgically treated.

Abstract #526

HYPOCALCEMIA IN A CHILD WITH GRAVES’ DISEASE FOLLOWING TREATMENT WITH 131I

Kateryna Komarovskiy, MD, Susan Raghavan, MD,
Stephen J Winters, MD

Objective: Hypocalcemia is a rarely recognized complication of 131I therapy, and has been reported previously in only one child with Graves’ disease treated with radioiodine (RAI).

Case presentation: A 12 y/o girl with asthma taking oral prednisone was treated with 11.1 mCi of 131I for Graves’ disease (GD). Her baseline serum Calcium (Ca) level was normal but within 3 months of RAI treatment she developed brochospasms and paresthesias with a serum Ca level of 6.6 mg/dl (8.9-10.4mg/dl), phosphorus (Phos) 9.0 mg/dl (4.6-5.5 mg/dl), PTH 21 pg/ml (15-65 pg/ml), and 25-OH vitamin D (25(OH)D) 10.4 ng/ml (32-100 ng/ml); her magnesium level and bone mineral density of the hip and spine were normal. After 2 weeks of elemental Ca 1,000 mg/day and calcitriol 0.5 mcg twice/
Discussion: A review of the literature revealed 10 case reports of hypocalcemia in patients with no prior history of parathyroid disease who received RAI, including one 14-year-old boy. In our patient, hypocalcemia may be due to several factors. 1) Direct damage to the parathyroid gland by RAI. Experiments using mice showed that RAI can damage parathyroid tissue and cause hypocalcemia since β particles emitted by 131I can penetrate up to 2.5 mm into surrounding tissues. 2) The hyperthyroid state accelerates bone resorption by osteoclasts with relative osteoblast inhibition occasionally causing hypercalcemia and suppression of PTH secretion. A decrease in the thyroxine level after RAI would lead to resolution of bone resorption and may have contributed to the fall in serum Ca. 3) 9% of US children are vitamin D deficient and 61% are insufficient. The majority are normocalcemic because there is a compensatory rise in PTH synthesis, but if such synthesis is impaired by inflammation from RAI, hypocalcemia may occur. 4) glucocorticoids decrease intestinal Ca absorption by inhibiting vitamin D- mediated transcellular Ca transport, increasing the rate of degradation of 1,25-OH vitamin D, and increasing the urinary excretion of Ca by stimulating the mineralocorticoid receptor in the distal tubule.

Conclusion: In this child with GD, who was initially normocalcemic despite a low vitamin D level and prednisone-treated asthma, RAI compromised the function of the parathyroids sufficiently to produce symptomatic hypocalcemia. We conclude that patients scheduled to receive 131I should be evaluated for risk factors for hypocalcemia in order to minimize the likelihood of this potentially life-threatening complication.

Abstract #527

RAPID TRANSFORMATION OF ASYMPTOMATIC, MILD PRIMARY HYPERPARATHYROIDISM INTO PARATHYROID CRISIS

Brittany Bohinc, MD, John C. Parker, MD, FACE

Objective: To present a rare case of long-standing, benign primary hyperparathyroidism (PHP) that rapidly transformed into acute parathyroid crisis.

Case Presentation: This is a 56-year-old woman with history of non-small cell lung carcinoma (T2N0M0) who at time of diagnosis 3 years prior had a total calcium (Ca) of 15.5 mg/dL (8.4-10.2) with parathyroid hormone (PTH) of 251 pg/mL (10-65). Severe hypercalcemia resolved with intravenous zoledronic acid treatment. The patient underwent surgical lobectomy and adjuvant chemotherapy. Stable, asymptomatic hypercalcemia persisted (Ca ranging from 10.2-11.0), consistent with PHP (PTH 81-202) over 3 years of close follow-up. Despite the previous indolent nature of hypercalcemia, the patient became acutely symptomatic with fatigue, myalgias, constipation, oliguria and polydipsia. Ca measured 18.6, with PTH 1348.7, whereas 3 months earlier, Ca was 10.2 with PTH 202. Her renal function remained stable, although a nonobstructive renal stone was discovered at time of hospitalization. The patient was aggressively hydrated with intravenous saline over the next 96 hours, successfully decreasing Ca to 11.0 mg/dL. Ultrasonography demonstrated a right-sided inferoposterior hypoechogenic parathyroid candidate that had increased in size from previous imaging. Symptomatic and biochemical cure was achieved (Ca 9.1, PTH 36) after parathyroid adenoma removal without evidence for subsequent recurrence.

Discussion: An acute and rapidly fatal course of PHP was first described in 1923, and the term “parathyroid crisis” was coined in 1960. Our patient had features compatible with the criteria of Payne and Fitchett (rapid changes in general condition, rising Ca above 15 mg/dL, and rising urea nitrogen concentration or the onset of oliguria). Of note, hypercalcemia was effectively managed with saline resuscitation, without the use of commonly recommended modalities of furosemide, calcitonin, or bisphosphonate. Also, the preoperative appearance of the parathyroid adenoma by ultrasound is shown, with changes in volume and configuration observed for the parathyroid “in crisis.” As supported by the literature, definitive surgical management is imperative once stabilized.

Conclusion: Mild PHP may rapidly transform to severe hypercalcemia. Predictors of risk for development of this phenomenon are not addressed by current guidelines of management of asymptomatic PHP.

Abstract #528

HYPERCALCEMIA: AN ANTECEDENT OF RECURRENT MALIGNANCY

Shuchi Gulati, MBBS, Gaurav Gulati, MD, Simi Rai, MD

Objective: Hypercalcemia occurs in 10-20% patients with malignancy. We discuss a patient who presented with high serum calcium months after treatment of a localized squamous cell carcinoma of the larynx.

Case Presentation: A 51 year old male with squamous cell carcinoma of the larynx (stage T1N0M0), diagnosed and treated six months ago, presented with swelling in his right arm. Physical exam was otherwise negative. Laboratory evaluation revealed total serum calcium of 12
mg/dL, albumin of 2.3 g/dL and corrected serum calcium of 13.68 mg/dL (nl.8.5-10.5 mg/dL). Serum phosphorus was 2.3 mg/dL, calcitriol normal at 65 pg/mL, PTH suppressed at 1 pg/mL. PTHrP was normal at 1.8 pmol/L. Doppler ultrasound of the right upper extremity revealed deep venous thrombosis of right subclavian vein and he was admitted for anticoagulation. High serum calcium in the setting of the patient’s history of cancer provoked clinicians to work him up for recurrent malignancy. A CT scan of the neck followed by a PET scan was done which revealed hyper metabolic right axillary lymph nodes, which on biopsy tested positive for moderately differentiated metastatic squamous cell carcinoma. During hospital stay, he was treated with IV hydration, furosemide and bisphosphonates. He was started on chemotherapy and palliative radiation therapy. He has had persistently high calcium levels at 11.6 mg/dL at one month follow up.

Discussion: Hypercalcemia of malignancy (HCM) is commonly associated with squamous cell cancers and is most commonly associated with elevated levels of PTHrP. Other mechanisms of HCM which have been recognized so far include increased level of calcitriol (lymphomas), stimulation of osteoclasts by bone metastasis, activation of Receptor Activator of Nuclear Factor-kappaB Ligand (RANKL), produced by either tumor cells or cells of the immune system on stimulation by PTHrP or IL. Since both calcitriol and PTHrP levels were normal and there was no evidence of bone metastasis in our patient, it is not possible to clearly determine the mechanism of hypercalcemia. Nevertheless, this did not exclude the diagnosis of cancer. Early work up in high risk patients presenting with hypercalcemia can lead to early diagnosis of otherwise clinically occult tumors or tumor recurrences. HCM can also help predict survival which is longer in patients whose serum calcium corrects with anti tumor treatment alone compared to those who need to be treated with calcium lowering drugs in addition.

Conclusion: Based on this presentation, we propose that hypercalcemia can help recognize occult tumors and can help predict survival in cancer patients.

Abstract #529

CALCIUM MALABSORPTION ASSOCIATED WITH PROTON PUMP INHIBITOR USE CONTRIBUTING TO REFRACTORY HYPOCALCEMIA POST PARATHYROIDECTOMY

Sol Virginia Guerrero, MD, Jennifer Pedersen-White, DO, FACE

Objective: To report protracted hypocalcemia post parathyroidectomy associated with proton pump inhibitor induced hypochlorhyria.

Case Presentation: A 37 y/o male s/p renal transplant was admitted for subtotal parathyroidectomy. Admission labs were: intact PTH (iPTH) 1713 (11.1-79.5 pg/mL), ionized calcium (ica) 6.7 (4.5-5.3 mg/dL), alkaline phosphatase (alk phos) 461 (45-129 U/L), 1,25-dihydroxyvitamin D3 (1,25D) 82 (18-64 pg/mL), 25-hydroxyvitamin D3 (25D) 14 (25-80 ng/mL), normal magnesium (mag) and phosphorus (phos) with stable creatinine (Cr) at 1.8 (baseline 1.7-2.3 mg/dL). Postoperatively prolonged, symptomatic hypocalcemia developed, requiring 11 days of continuous intravenous (IV) calcium in addition to 4 g elemental calcium (as carbonate) daily, 16.5 mcg calcitriol daily and 3000 iu cholecalciferol daily as well as weekly ergocalciferol 50,000 iu. Inpatient medications included immunosuppressants tacrolimus/mycophenolate and esomeprazole 40 mg daily for chronic gastroesophageal reflux disease. He was discharged on the above oral regimen two weeks after admission. Readmission with severe hypocalcemia occurred two weeks later (ica 2.2 mg/dL, iPTH 4.9 pg/ml, alk phos 283 U/L, 1,25D 148 pg/ml, 25D 28 ng/ml, normal mag/phos/Cr). 14 days of IV calcium and massive doses of calcitriol (42 mcg daily), in addition to previous oral regimen, were required to maintain eucalcemia. Discharge occurred in two weeks. Oral calcitriol was titrated to 1.5 mcg daily within 3 months of discharge.

Discussion: Prolonged hypocalcemia is seen with hungry bone syndrome, surgical hypoparathyroidism and, less commonly, post operative 1,25D resistance. Oral calcitriol directly enhances intestinal calcium absorption. Calcitriol 0.25-4 mcg daily is typically required to treat hypocalcemia in hypoparathyroid patients; our patient received up to 42 mcg daily with no adverse sequellae. We postulate proton pump inhibitor (PPI) induced hypochlorhydria profoundly decreased absorption of intestinal insoluble calcium (calcium carbonate), rendering high doses or calcitriol ineffective. Calcium citrate, which does not require an acid milieu for absorption, should be used as a first line calcium supplement in patients on PPI therapy.

Conclusion: The gastric milieu and its effect on calcium absorption are important to consider when initiating calcium supplementation. Calcium citrate should be used as a first line calcium supplement in patients on PPI therapy.
Abstract #530

DRUG-RELATED OSTEOMYELITIS OF THE JAW (DR-OMJ)

Sunil J. Wimalawansa, MD, PhD, FCCP, FRCP, FACE

Background: Bisphosphonates have been widely used for the past 3 decades for treatment of bone diseases, in particular osteoporosis, Paget’s disease, and complications of skeletal malignancy. An escalating number of cases of bisphosphonate-related osteonecrosis of the jaw (ONJ) have been reported since 2003. In clinical trials, denosumab, a potent anti-osteoporosis agent, also has been implicated in ONJ. Considering overall data, exposure of jaw bones to infection seems to be the primary initiator of ONJ–osteomyelitis (OMJ). Thus, instead of using the terms “bisphosphonate” or “denosumab-associated ONJ,” it is more precise to use the term “drug-associated osteomyelitis of the jaw (DR-OMJ).”

Case Presentation: The estimated incidence of DR-OMJ in patients treated for osteoporosis or Paget’s disease is about 1 in 75,000, but in cancer patients treated with high-dose, higher-frequency bisphosphonates or denosumab, the incidence is between 1% and 4%. No evidence suggests that amino-containing bisphosphonates have a greater likelihood of triggering DR-OMJ. Regardless of the route of administration, oncology patients receive 10 to 15 times higher doses of bisphosphonates at a greater frequency than do patients with osteoporosis or Paget’s disease.

Discussion: OMJ is not a simple avascular event; evidence supports an immune impairment and infectious etiology. OMJ may be precipitated by over-suppression of bone turnover (“the last straw”) secondary to potent anti-resorptive agents, bisphosphonate and denosumab. Albeit exposure of jaw bone to infection is the final common path, the exact mechanisms of developing OMJ are unclear. The higher the dosage and frequency of administration of bisphosphonate or denosumab, the higher the likelihood of OMJ developing. These higher dosages and frequencies of administration are likely to be a key factor in triggering DR-OMJ in cancer patients.

Conclusions: Denosumab and bisphosphonates are very useful therapies, not only in metabolic bone diseases, but also in cancer. Therapy with these agents reduces complications by more than 60% in patients with bone diseases secondary to malignancy, osteoporotic fractures, and Paget’s disease of bone. The risk/benefit ratio and necessity of administration of high doses/frequency of bisphosphonates and denosumab in cancer patients need to be addressed. Clearly, the incidences and risks of OMJ are low when weighed against the benefits of denosumab and bisphosphonate. Although there is a temporal association between bisphosphonate or denosumab and OMJ, no direct causal relation has been established.

Abstract #531

PELVIC FRACTURES ASSOCIATED WITH LONG-TERM BISPHOSPHONATE THERAPY

Vaishali Patel, MD, Barbara Lukert, MD, Leland Graves, MD

Background: Long term bisphosphonate use has been associated with “atypical” subtrochanteric and diaphyseal fractures of the femoral shaft. We wish to report an unusual presentation: pelvic fracture in addition to long bone fractures after long term bisphosphonate use.

Case Presentation: A 58 year old female with a history of osteoporosis was treated with alendronate at age 46. In addition she received estrogen replacement therapy between the years 2000 to 2007. Five years after starting alendronate, in 2003, she suffered a pathologic fracture of the right hip, requiring surgical repair. A year later she experienced fracture of the femur in middle of the hardware following a trivial trauma. Alendronate was discontinued after the first hip surgery. Subsequently she was treated with teriparatide for 2 years. Boniva was started six months after cessation of therapy with Teriparatide. She continued treatment with Boniva until May 2009, when she received an intravenous infusion of zolendronic acid 5 mg. In March of 2010, she experienced pelvic pain while vacuuming and was found to have fractures of both the upper and lower rami of the pelvis on the left side. She has a history of steroid use for a very brief period (less than 3 months) about 8 months prior to the pelvic fracture. The pelvic fracture has not yet completely healed after 8 months. Her bone density has not decreased significantly (by <4%) between 2005 and 2010. In October 2005 her T-score was -1.9 at the spine and -0.7 at the hip and in 2010 the T-score was – 2.0 at the spine and -1.1 at the hip. Bone histomorphometry performed on a biopsy of right iliac crest was negative for malignancy and calcification defects. It showed normal to low/normal bone turnover. These findings correlate well with the NTX level of 12.7[normal is 6.2-19.0 NMBCE/L] in May 2010. We have reviewed post-surgical X-rays from 2003 which reveals cortical thickening and beaking, the classic findings associated with alendronate-related fractures.

Conclusion: Long term bisphosphonate therapy has been associated with “atypical” subtrochanteric and diaphyseal fractures of the femoral shaft, but we are unaware of previous reports of pelvic fractures associated with long term bisphosphonate therapy.
Abstract #532

HIP FRACTURE IN PREGNANCY

Sreevidya Kannoorpatti Subbarayan, MD,
Angelo Licata, PhD, MD

Objective: To describe a case of fracture in the unusual setting of pregnancy and discuss the differential diagnosis.

Case Presentation: A 35-year-old woman (G1P1A0L1) developed severe right-sided hip pain and inability to bear weight immediately postpartum. MRI lumbar spine demonstrated stress fracture of the right femoral neck. Past medical history included clavicular fracture at age 10, acne and thyroid nodule. Menarche was at age 12 with regular menses thereafter. Growth and development were normal. Patient did not smoke, consumed alcohol occasionally and caffeine in moderate amounts. She did not take calcium supplements or consume dairy products. She denied loss of height, back pain or gastrointestinal complaints. She was on no medications except prenatal vitamins. Her mother had a history of osteopenia. Examination was normal except for pain and restricted range of motion at the right hip.

Labs: Calcium 9.5 mg/dl (8.5–10.5), Phosphorus 4.1 mg/dl (2.5–4.5), 25 OH Vitamin D 25.9 ng/ml (31–80), TSH 1.5 (0.27–4.2) PTH 60 pg/ml (10–60). Bone mineral density (BMD) at the spine and total hip were 0.93, 0.86 and 0.73 g/cm² respectively with corresponding Z scores of -2.6 and -2.4. The patient was placed on vitamin D 50,000 units twice weekly and calcium 1200 mg/day. Her hip fracture healed well. A year later, BMD (g/cm²) at the spine was 1.02 (Z score -1.8; 10% increase) and total hip 0.78 (Z score -2.0; 7% increase). The patient continues to do well with no further fractures.

Discussion: Bone mass decreases transiently during normal pregnancy as fetal demand for calcium is met in part by demineralization of maternal skeleton. Bone loss up to 5% in the spine and hip is reported and is completely reversible. While decrease in BMD is normal, pregnancy-associated osteoporosis is a rare condition of unknown cause. It usually manifests in the first pregnancy, presenting as vertebral fracture, hip or ankle fracture, in the late 3rd trimester or early postpartum. Whether pregnancy is the cause or the precipitating factor is debated. Bone loss may be superimposed on preexisting skeletal fragility from other causes. This condition is usually self-resolving. Interestingly, recurrence in subsequent pregnancies is uncommon. Secondary causes for osteoporosis need to be explored before making this diagnosis. In our case, there was a component of osteomalacia with excellent response to calcium and vitamin D, without the need for the use of bisphosphonates in this young woman.

Conclusion: It is very important to recognize the different etiologies for fractures in pregnancy and their interplay because of implications for treatment and prognosis.

Abstract #533

STUDY ON THE ASSOCIATION OF DEGENERATIVE DISEASE OF THE SPINE OF ELDERLY BANGLADESHI WOMEN AND BONE MASS AT THE SPINE

Anisur Rahman, MD, Sultana Amena Ferdoucy, MD

Background: Back pain resulting from degenerative diseases of the spine is one of the most common causes of disability in adults of working age. Between 60% to 80% of adults suffer from low back pain at some time in their lives, especially in their older age. Degenerative joint diseases and decreased bone mass, osteoporosis are two common age related skeletal disorders, responsible for pain and disability. It has been accepted generally that conditions of osteoporosis and osteoarthritis are different diseases, possibly resulting from different pathomechanism. Several investigators have examined the coexistence of osteoporosis and spondylosis in the spine and have reported an inverse relation between decreased bone mineral density (BMD) and intervertebral disc degeneration. Bangladesh, a developing country, has a high incidence of osteoporosis and one important finding that we have come across in most studies is that the incidence of osteoporosis, particularly in women, occurs among a younger age group than in the developed world. However the possible inverse relation between osteoporosis and spondylosis was not evaluated in Bangladeshi population, a population significantly different from Caucasian population where most studies were done. Current study aimed at evaluating correlation between osteoporosis and degenerative changes in lumber spine of elderly women.

Objectives: To observe the bone mineral density of Elderly Bangladeshi women measured by DEXA scan. To evaluate the degree of degenerative changes in lumbar spine radiographs of elderly women using a semi quantitative scoring system. Specific Objectives: To find out the correlation between osteoporosis and degenerative changes in the lumbar spine of elderly Bangladeshi women.

Methods: The study is an open label, cross sectional, single center study carried out on 68 consecutively selected elderly female subjects aged between 50 to 75 years suffering from back pain. An informed consent was obtained from each participant. The subjects were referred to the Department of Radiology and Imaging, BIRDEM...
for Lumbar Spine x-ray (anterior-posterior view and lateral view) After reviewing the clinical history, demographic data – age, height, body weight, body mass index (BMI) of all subjects was collected at the time of x-ray. In addition to the relevant medical records were checked to ensure that selected subjects had no hormone replacement therapy. Interval between X-ray spine and and DEXA scan of more than one year, history of hysterectomy and drop out cases were taken as exclusion criterion so out of initial 80 cases, 68 were finally selected. The radiographs were evaluated by using a semi quantitative scoring system by three separate radiologists separately to eliminate bias. The presence of degenerative changes of each lumbar vertebra was determined by using the Kellgren and Lawrence score. DEXA scan was done on all cases. A sum-score were used to correlate the findings with the BMD. The study was conducted on 63 consecutively selected patients who were having low back pain at their older age. The mean age of the subjects was found to be 56.5 years and ranged from 34 to 75 years. The highest incidence of back pain was found in the age group between 51-60 years. The mean (±SE) BMI was 27.4±0.52kg/m2 ranged from 20.4 to 38.6 kg/m2 and found most 23 (36.5%) patients were obese. The mean weight was 62.9kg with standard error of mean (±SE) ±1.20 kg and the maximum (36.6%) number was found in the age group of 51to 60. The mean height was 151.6 cm with standard error of mean (±SE) ±0.74cm with height range from 140 to 169 cm and nearly a half 31(49.1%) of the patients belonged to 151 to160 age group. For BMD the mean T score was -1.7 with standard error of mean (±SE) ±0.16 with t score ranging from -5 to 2. Most, 30 (47.6%), of the subjects had osteopenia, 18(28.6%) osteoporosis and rest 15 (23.8%) normal T score. Maximum, 47 (74.6%), of the study patients were found grade II, 8 (12.7%) grade III, 6 (9.5%) grade I and 2 (3.2%) grade IV. A significant negative correlation was found between T-score and grade.

Results: Significant negative correlations were found between osteoporosis and degenerative changes in lumbar spine of elderly women. A significant negative correlation (r=-0.531; p<0.05) was found between Bone density(T-score) and degenerative changes (grade).

Discussion: The present study findings were compared with previously published relevant studies. Spinal radiographs and DEXA of spine were done in all 63 cases. Data were categorized according to age, height, weight, Tscore, and Kellgren and Lawrence score for grades of degenerative changes of each lumbar vertebrae. This was first of its kind for Bangladeshi elderly women.

Conclusion: The current study evaluated the relationship between bone mineral density in lumbar spine and severity of spondylitis in elderly females. On the basis of findings of the study it can be concluded that osteoporosis has an inverse relation with spondylitis. However further study can be carried out by taking a larger sample size, and using MRI and bone mineral density of remote site in addition to lumber spine.

Abstract #534

OSTEOMALACIA MYOPATHY

Tariq Abdulrahman Nasser, MD, Abdullah Karawagh, MD

Objective: To report a case of proximal muscle weakness with exaggerated reflexes secondary to vitamin D deficiency.

Case Presentation: A 35-year-old Saudi woman presented with a chief complaints of diffuse bone pain and proximal muscular weakness, mainly in the lower extremities for six months. The pain and weakness progressed to the point that she had difficulties in rising from a chair and walking, and inability to ascend stairs. Neurological examination revealed evidence of bilateral, moderate proximal muscle weakness and hyperactive reflexes with equivocal planter responses in the lower limbs. Muscle tone and sensation were normal. MRI did not show any evidence of myelopathy or vascular malformation. Laboratory workup revealed normal CBC, borderline serum calcium, hypophosphoremia, and raised serum alkaline phosphatase. Vitamin D (25-OH vitD) was very low, and parathyroid hormone was dramatically elevated. Other laboratory investigations were normal, including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), thyroid function tests, liver-function tests, and creatinine kinase. The electromyogram showed mild myopathic changes only. Radiology examination of the pelvis and lower limb showed generalized osteopenia widening of the epiphyseal growth plates around the knees and looser’s zone in proximal femur. A diagnosis of osteomalacia secondary to vitamin D deficiency from lack of exposure to sunlight and to inadequacy of the diet was made. We treated the patient with 6000 IU of vitamin D3 once a day plus 1 g/d of calcium. Three months later, gait disturbances have significantly improved and laboratory findings have all normalized, and she was able to walk pain free.

Discussion: Osteomalacia (OM) is a metabolic bone disorder characterized by an alteration in bone mineralisation, frequently caused by disorders in vitamin D or phosphate metabolism, or by other processes which can also interfere with bone mineralisation. Proximal myopathy has been reported in osteomalacia, however the debate remains that is it the hypovitaminosis D, hypocalcemia, hypophosphatemia, or the hyperparathyroidism is the culprit. Our patient, based on her presentation, was diagnosed by a neurologist as spinal cord lesion and did
not consider vitamin D deficiency and osteomalacia in the differential diagnosis initially. Symptoms can be confused with other conditions; therefore, awareness of this entity and knowledge of the most common findings associated with the different forms of OM are essential. This case is presented to remind colleagues that in case of diffuse musculoskeletal pain and proximal myopathy, do not forget hypovitaminosis D in differential diagnosis.

**Conclusion**: Vitamin D deficiency is an important treatable cause of osteomalacic myopathy in Saudi Arabia.

**Abstract #535**

**HYPERCALCEMIA IN A PATIENT WITH HEMATURIA – ASSOCIATION OF PRIMARY HYPERPARATHYROIDISM WITH TUBEROUS SCLEROSIS**

*Harsha Karanchi, MD, Irum Zaheer, MD, Ruth Wintz, MD*

**Background**: Tuberous sclerosis is a genetic multisystem disorder of variable expression and can cause hamartomas in almost any organ system and has also been associated with adenomas.

**Objective**: To report co-existence of primary hyperparathyroidism due to parathyroid adenoma with tuberous sclerosis.

**Case Presentation**: A 48 year old man with no significant past medical history presented with hematuria and right flank pain ongoing for about a week. There was no family history of any tumors or seizure disorder. On physical exam he had normal vital signs and skin exam showed multiple facial angiofibromas, periungual fibromas on the toes, hypomelanotic macule on the left upper arm, connective tissue nevus on the upper back, and dental pitting. Abdominal exam revealed mild tenderness to palpation in the right costovertebral angle. The remainder of the physical exam, including neck exam, was normal. Laboratory studies were significant for total serum calcium – 11.3 mg/dL (nl 8.6-10.6), PTH – 163 pg/mL (nl 13-65) with normal 25-OH vitamin D level leading to the diagnosis of primary hyperparathyroidism. Tc-99m sestamibi parathyroid scanning showed focal uptake consistent with right inferior parathyroid adenoma and no evidence of ectopic parathyroid tissue. TSH and free T4 were normal. Thyroid ultrasound was normal. Urinalysis showed gross hematuria. Renal ultrasound showed normal sized kidneys with multiple renal masses. CT imaging showed multiple masses bilaterally in the kidneys consistent with angiomylipomas and an aneurysm in the right renal hilum without any renal stones. Several geographic sclerotic foci were seen in multiple areas of the spine and ribs without cortical destruction and suggested osteosclerosis. A PET CT revealed no abnormal uptake.

**Discussion**: Co-existence of tuberous sclerosis (prevalence of 7-12/100,000) and primary hyperparathyroidism (prevalence of 1 in 1000 adults and lower in juveniles) is rare and was unexpected. To our knowledge only two cases of parathyroid adenomas in association with tuberous sclerosis have been reported previously.

**Conclusion**: Parathyroid adenoma might be another adenomatous abnormality associated with tuberous sclerosis and we suggest that plasma calcium should be measured in these patients.

**Abstract #536**

**SERUM TESTOSTERONE, ESTRADIOL, SEX HORMONE-BINDING GLOBULIN IN RELATION TO BONE MINERAL DENSITY, MUSCLE STRENGTH AND BODY COMPOSITION IN ELDERLY MEN**

*Aziza Abdel Moez Hammad, MD, Zeinab Hassan, MD, Fatma Hamad, MD, Dina Abaza, MD, Kalsoum Abdel Hamid, MD, Mervat Elwakeel, MD*

**Objective**: Osteoporosis-related fractures constitute a major health concern not only in women but also in men. Sex steroids play an important role in the maintenance of bone health. However, there is limited information on the association between sex hormones and age-related bone loss in men. Our objective was to study the relationship between sex steroid levels and the changes accompanying aging process, including bone mineral density (BMD), muscle strength and body composition in elderly Egyptian men.

**Methods**: Free Testosterone (FT), Estradiol (E2) and Sex Hormone-Binding globulin (SHBG) were measured in thirty elderly men, age range 60-73 years, and 15 young men (age range 30-36 years), serving as control group. Patients receiving hormonal ablation for prostatic neoplasm and patients with chronic liver, renal disease or receiving corticosteroids were excluded. Sex steroid levels were correlated to BMD measured by DXA, lower limbs muscle strength calculated by isokinetic Biodex dynamometry and body composition assessed by body fat analyzer.
Results: FT and E2 levels were significantly lower in elderly men compared to control group (P<0.01), whereas SHBG significantly increased with age (P<0.01). Peak Torque values of both extensors and flexors were significantly lower in elderly men (P<0.01). Lean mass, water volume and water percentage decreased significantly with age. Low BMD was found in 90% of elderly men; osteopenia (60.5%) and osteoporosis (29.5%). E2 levels were associated positively with BMD at neck of femur in elderly men (P<0.05). FT correlated positively with lean mass and muscle strength (P<0.01), but didn’t correlate with BMD. SHBG showed significant negative correlation with lean mass and muscle strength (r = -0.833, P<0.01).

Conclusion: FT is not associated with BMD in elderly men, however, FT has strong relation with muscle strength and lean mass; so older men with lower FT could be more liable to falls. Elderly men with low E2 are more likely to be osteoporotic as E2 is an important determinant of bone density changes in old age. BMD testing of older men with E2 deficiency may be clinically warranted.

Abstract #537

EFFICACY OF HIGH INTENSITY FOCUSED ULTRASOUND – A NONINVASIVE ABLATIVE METHOD FOR TREATMENT OF PRIMARY HYPERPARATHYROIDISM

Kiran Pal Singh, MD, Avinainder Singh, Rahat Brar, MD

Objective: This pilot study was carried out with the objectives of determining the scope, efficacy and safety of recently developed nonsurgical technique- High Intensity Focused Ultrasound (HIFU) for treating primary hyperparathyroidism.

Methods: 5 patients (4F, 1M) aged 41-66 yr with diagnosis of primary hyperparathyroidism, based on persistent hypercalcemia with elevated PTH were studied for scope of HIFU treatment. Ultrasound neck detected parathyroid tumor only in 4 patients, so 1 was excluded. Two more patients were excluded as one had multinodular goitre and bilateral parathyroid tumor in another. In the fourth patient, the HIFU beam could not reach the tumor due to short neck. The HIFU treatment was performed on one patient in a single session using Thyros One device. Parathyroid functions were monitored by serum iPTH, calcium (ionized and total), phosphorus, and Sestamibi and ultrasound parathyroid up to 11 months. 25(OH) D, thyroid, liver, renal functions, and indirect laryngoscopy were also carried out.

Results: Baseline S.Calcium (Ca) was 10.9mg/dl and PTH 236.4pg/ml. 24 hrs post HIFU treatment Ca was 9.8mg/dl and PTH 134.3pg/ml. At 1 month Ca was 10.1mg/dl and PTH 168pg/ml, 3months Ca was 10.4mg/dl and PTH 206pg/ml. At 10 months Ca was 10.4mg/dl and PTH 180.4pg/ml. Sestamibi scan after 1 month showed subtle tracer retention in the remnant of the parathyroid tissue. During treatment and 11 months after, no adverse event was recorded. Normal S.Ca 8.5-10.5mg/dl and PTH 14-72pg/ml.

Discussion: Surgery is the standard treatment for primary hyperparathyroidism, but many patients are not willing & others have contraindications to surgery. Medical therapy, cinacalcet, is very costly. HIFU causes thermal coagulative necrosis of the target tissue and has been successful in prostatic and thyroid nodules. So far, in a study by Kovatcheva et al AJR 2010; 195; 830, four patients of primary hyperparathyroidism were treated by HIFU and S.Ca normalized in 3/4 patients with reduction in tumor size. In our study S.Ca normalized within 24hrs with reduction of PTH (43.2%) and normal Ca level persisted on follow up. But, PTH levels, though significantly reduced, were not normalized. The reason for persistently elevated PTH may be a explained by single session of HIFU treatment.

Conclusion: A single session HIFU treatment for patients with primary hyperparathyroidism is safe and effective for normalizing serum calcium. However, efficacy of this nonsurgical procedure in terms of normalizing the PTH levels by destruction of diseased parathyroid needs to be observed by larger and longer studies.

Abstract #538

EXPERIENCE IN CLINICAL PRACTICE WITH INTRAVENOUS ZOLEDRONIC ACID TREATMENT IN POSTMENOPAUSAL OSTEOPOORISIS

Corina H. Galesanu, MD, PhD, Alexandru Florescu, MD, Ilinka Grozavu, MD, Andra Iulia Loghin, MD, Veronica Mocanu, MD

Background: It is important to identify clinical conditions that might induce maximum increase to the bone mass by treatment in osteoporosis. We have shown that a normal vitamin D status may affect the increase bone mineral density (BMD). Bisphosphonate therapy is the standard of care in osteoporosis. Zoledronic acid (ZOL) 5 mg, once/yearly infusion is the most recent drug approved for the treatment of postmenopausal osteoporosis.

Objective: We are proposed to evaluate the effect of ZOL treatment on BMD change in a group of postmenopausal osteoporotic women assessed by DXA-BMD using a Hologic bone densitometer. Osteoporosis was defined as a BMD T-score in lumbar spine and/or total hip -2.5 or less.
Methods: Among 520 postmenopausal osteoporotic women registered in the years 2008-2009, 22 women were treated with ZOL iv 5 mg/yearly and 1000 mg calcium/daily. DXA measurement for BMD change was used at baseline and after 12 months. We analyzed also: changes in serum calcium, 25 OHD, PTH and bone alkaline phosphatase (BAP) at baseline and one year post ZOL. The mean age of the patients was 64.5±3.7 years. Time since menopause was 9.6±11 years.

Results: No significant change in serum calcium 9.3±0.3 mg/dl at baseline and 9.2±0.3 mg/dl after a year. No significant difference in serum 25 OHD at the patients after one year ZOL treatment: 35.4±6.3 ng/ml at 37.3±10.2 ng/ml (optimal level). PTH level also rested normal: 45.9±13.2 pg/ml at the beginning and 43.3±14.2 pg/ml at last. BAP varied between 55.5±15.3 UI/L and 59.7±17.4 UI/ml. Lumbar spine mean BMD was: 0.67±0.026 g/cm² and increased at 0.726±0.008 g/cm² (+7.8%). Total hip mean BMD was: 0.77±0.035 g/cm² and increased at 0.809±0.023 g/cm² (+4.6%). Femoral neck mean BMD was: 0.60±0.035 g/cm² and increased at 0.645±0.010 g/cm² (+6.4%). Clinical significantly reduced the hyperalgesia after a mean of 6.7 weeks (6-12 weeks). Adverse events after infusion were flu-like syndrome transient-4 cases (18%), arthromyalgias-2 cases (9%), arterial hypertension-1 case (4.5%). No cardiac arrhythmias, bone necrosis and no fractures.

Conclusion: In our experience iv ZOL has been an effective anti-osteoporotic treatment. BMD lumbar spine, total hip and femoral neck increased and the other biologic parameters remained in normal level. It is now well accepted that increases in bone mass at the women who take bisphosphonate will have a decrease in fracture risk.

Abstract #539

ACUTE PANCREATITIS HERALDING THE DIAGNOSIS OF PRIMARY HYPERPARATHYROIDISM

Kavya Chitra Mekala, MD, Vijay S. Duggirala, MD, Leo Tchong, MD

Objective: To report a case of Acute Pancreatitis (PTS) heralding the diagnosis of Primary Hyperparathyroidism (PHPT) and review literature.

Case Presentation: A 43 year old male presented with epigastric pain, nausea and bilious vomiting for 2 weeks. ROS was positive for leg cramps for several weeks. Past history was significant for tobacco use, diet controlled hypertriglyceridemia (TGL 105 baseline) and GERD. Family history was negative for MEN syndrome, hypercalcemia and renal stones. Physical exam and CT abdomen findings were consistent with Acute PTS. Neck exam revealed no masses. EKG showed sinus bradycardia with possible QT shortening. Labs showed Creatinine 2.2, Ca 16.2, lipase 6507, amylase 294, LDH 255 and normal LFTs. TGL level was 197, WBC 13.8, Magnesium 1.6, Phosphorus 1.8. Intact PTH came back elevated at 136.6 pg/ml (normal: 14-72). 25OH Vitamin D was 16.

Patient was aggressively fluid resuscitated and Corrected Ca down to 11.64. Thyroid Ultrasound revealed a 4.1 x 2.3 x 1.9 cm hypoechoic mass inferior to the left thyroid lobe. This was confirmed on Sestamibi scan. He underwent surgical resection of the parathyroid mass. Intraoperative PTH came down from 160 pg/ml to 45, 32, 23 at 5, 10 and 20 minutes respectively. Pathology showed an adenoma with no capsular invasion with broad fibrous bands seen focally in the central area likely representing degenerative change. Corrected Ca came down to 9.28 on post-operative day 1 and was 9.3 a month later. His abdominal symptoms completely resolved.

Discussion: In 1957, Cope et al documented the first case of PTS and PHPT. Over subsequent years, the causal association between these two disease entities has been widely debated. Prevalence of PTS in PHPT is 1.5 to 13% by different estimates, and a 1980 Mayo Clinic study suggested that it is no more than the general population. Proposed mechanisms include Ca deposition in the pancreatic duct, Ca mediated intra-acinar trypsinogen activation and pancreatic autodigestion and genetic variants. A case series of 40 cases from 1998 reported that cure of PHPT led to healing of acute PTS but did not affect evolution of subacute and chronic PTS. Our patient had no recurrence of PTS after resection of the adenoma and normalization of Ca levels.

Conclusion: Acute PTS is an inflammatory state that is usually associated with hypocalcemia. Per Ranson’s criteria, lower Ca levels indicate a worsening degree of PTS. Suspicion should be high for another disease process if PTS is associated with hypercalcemia as illustrated in this case.

Abstract #540

OSTEOPOROSIS ASSOCIATED WITH FANCONI’S SYNDROME IN A PATIENT ON CHRONIC ADEFOVIR DIPIVOXIL THERAPY

Ayse Bag Ozbek, MD, Michael H. Shanik, MD, FACP

Objective: To report a case of severe osteoporosis due to Fanconi’s syndrome associated with treatment of hepatitis B with Adefovir dipivoxil (ADV).

Case Presentation: A 30-year-old Chinese male patient presented with sudden onset of severe bilateral rib pain. He had chronic hepatitis B and had been treated with ADV at a daily dose of 10 mg for 84 months.
Evaluation revealed multiple bilateral rib fractures. Laboratory and radiologic findings showed urine amino acid levels ranging from 3-90 times higher than normal, elevation of urine phosphorus and calcium (1550mg/24h, 377mg/24h respectively), and lumbar spine T-score -3.8. After discontinuation of ADV and supplementation with calcium carbonate and cholecalciferol, T-score at the lumbar spine was -1.8 after 1 year (32% increase), urine phosphorus and calcium were 775mg/24h and 175mg/24h respectively (>50% decrease), 24 hour urine amino acid levels decreased to 2-4 times higher than normal levels.

**Discussion:** Adefovir dipivoxil (adefovir) is an oral prodrug of 9-(2 phosphonylmethoxethyl) adenine, a nucleoside reverse transcriptase inhibitor that has activity against human immunodeficiency virus-1 and hepatitis B virus. Nephrotoxicity occurs at daily dosages of 60-120 mg with a gradual increase in serum creatinine and decrease in phosphorus. When used at a dose of 10 mg/day, ADV shows an adverse-event profile similar to placebo over the course of 1 year. Fanconi’s syndrome results from dysfunction of the proximal renal tubule leading to impaired reabsorption of amino acids, glucose, urate, bicarbonate, and phosphate with increased excretion of these solutes in the urine. Chronic loss of phosphate and inadequate synthesis of 1,25(OH)2 vitamin D produce phosphate depletion and failure to mineralize bone properly. Despite large clinical trials demonstrating the safety of adefovir dipivoxil 10 mg daily, long-term use may be nephrotoxic and in rare cases, cause Fanconi’s syndrome and severe osteomalacia as seen in this patient.

**Conclusion:** Patients treated with long-term ADV should be monitored for ADV-induced Fanconi’s syndrome and its clinical sequelae.

Abstract #541

**QUS VERSUS DXA IN DIAGNOSING BONE DEMINERALIZATION IN ESRD CASES**

Dana Liana Bucuras, MD

**Objective:** The British Society for Osteoporosis proposed a method for comparing different diagnostic measurements for BMD. It defines the upper and the lower limit for the investigated assay, that will identify osteoporosis with a sensitivity of 90% (the upper limit) and a specificity of 90% (the lower limit), compared with the defined golden standard method, mainly DXA for spine or hip. This rationale generates a small number of false positive or negative results.

**Methods:** 131 cases with ESRD were evaluated by means of DXA and QUS with ISCD validated devices: Hologic Sahara/Hologic Hologic, aparat Delphi W (S/N 70489), lumbar L1-L4, anteroposterior technique, non-dominant hip.

**Results:** We define bone demineralization in cases of T score below –1, confirmed by increased markers of bone turnover. We identified than the limits for each QUS parameter in diagnosis bone demineralization. We also performed ROC diagnostic curves, comparing QUS parameters with DXA results, and we identified the best threshold value for QUI. The best parameter seemed to be QUI. We selected different values for each measured situs. The threshold values were identified by finding the best specificity and sensitivity from the series of number. The most precise interval is that one compared with the femoral neck compartment. When a patient has QUS result between the to limits, there is a very good sensitivity and specificity in diagnosing bone demineralization. QUS can be used as a screening tool, for decreasing the unnecessary DXA measurements, also in these patients. The 90-90 approach seems to be better then the threshold value method, because of the higher NPV and PPV.

**Conclusion:** QUS can be used as a screening method to identify the target population with decreased bone mass, also in patients with ESRD.

Abstract #542

**BONE MINERAL DENSITY ASSOCIATES WITH BSMI VITAMIN D RECEPTOR’S POLYMORPHISM IN CHRONIC USERS OF ANTIEPILEPTIC THERAPY**

Eleni Armeni, MD, George Kaparos, PhD, Andreas Alexandrou, MD, Christos Damaskos, MD, Emanuel Logothetis, MD, Maria Creatsa, MD, Aristidis Antoniou, MD, Evangelia Kouskouni, MD, Nikolaos Triantafyllou, MD, Irene Lambrinoudaki, MD

**Objective:** The BsmI restriction fragment polymorphism of the vitamin D receptor (VDR) has been associated with reduced bone mineral density (BMD) in postmenopausal women, patients with thalassaemia, thyroid disorders, and renal failure. On the other hand, administration of antiepileptic drugs (AEDs) has long been associated with bone deleterious effects. The aim of this study was to examine the association between the VDR’s polymorphism BsmI genotypes and the individual responses of bone metabolism in chronic users of AEDs.

**Methods:** This cross-sectional study evaluated 73 subjects with known epilepsy, chronic users of antiepileptic drug monotherapy. We excluded patients with intake of medications knowing to affect bone metabolism, nutritional deficiency, smoking, daily alcohol intake, thyroid-renal-liver disorders, menopause, hyperparathyroidism, or hypogonadism. Fasting blood samples were obtained to estimate serum levels of calcium, phosphorus, magnesium, 25hydroxyvitamin
D, parathormone, as well as the VDR’s genotype. Bone mineral density at the lumbar spine was measured with Dual Energy X-Ray Absorptiometry.

**Results:** The genotype of VDR was significantly associated with bone mineral density (mean BMD: BB genotype $1.059 \pm 0.113 \text{ g/cm}^2$; Bb genotype $1.056 \pm 0.126 \text{ g/cm}^2$; bb genotype $1.179 \pm 0.120 \text{ g/cm}^2$; P-value < 0.05). Furthermore, the absence of the unfavorable B allele was significantly associated with higher bone mineral density (bb genotype: BMD $= 1.179 \pm 0.119 \text{ g/cm}^2$, BB or Bb genotype: BMD $= 1.057 \pm 0.12 \text{ g/cm}^2$; P-value < 0.01). Bone density below the expected range for age correlated positively with the presence of the BB genotype (P-value $= 0.031$). Finally, patients with at least one B allele had lower serum levels of 25hydroxyvitamin D when compared with bb patients (22.61 ng/ml vs. 33.27 ng/ml, P-value < 0.05), while they tended to have higher levels of parathyroid hormone.

**Discussion:** Vitamin D receptor polymorphism is associated with lower bone mass in patients with epilepsy. Beyond the administration of AEDs, bone loss in the epilepsy population may be related to the disease itself, since it associates with seizure-related injuries, recurrent falls and inactivity. This bone deleterious effect might be mediated through the vitamin D-parathormone pathway.

**Conclusion:** The results of the current study support the routine evaluation of patients with epilepsy for bone loss, as bone pathology can be prevented and treated. The AEDs effects in people with epilepsy may be mediated or calibrated by VDR polymorphisms.
OBESITY

Abstract #600

HEPATIC CIRRHOSIS SECONDARY TO NON-ALCOHOLIC FATTY LIVER DISEASE IN A 12 YEAR OLD GIRL WITH MORBID OBESITY

Animesh Sharma, MD, Seema Kumar, MD, Deborah K. Freese, MD, James M. Swain, MD, Abdalla Zarroug, MD, Suresh Kotagal, MD

Case Presentation: A 12-year-old girl of Middle Eastern origin was seen in the pediatric endocrine clinic for evaluation of excessive weight gain since 4 years of age. Patient had recently been diagnosed with type 2 diabetes, obstructive sleep apnea with central hypoventilation and polycystic ovarian syndrome. Patient was found to be non-dysmorphic with normal stature and severely obese with a BMI of 52 kg/m². Examination revealed acanthosis nigricans and presence of hepatosplenomegaly. Hemoglobin A1C was elevated at 11.2%. AST, ALT, total bilirubin, prothrombin time, and APTT were normal; however, GGT was elevated at 114 Units/L (Normal 6-29 Units/L). CT abdomen revealed fatty infiltration of the liver and splenomegaly. Abdominal laparoscopic examination showed a markedly cirrhotic liver. Esophagogastroduodenoscopy did not reveal varices. Liver biopsy showed minimal macrovesicular steatosis, ballooned hepatocytes, pericellular fibrosis and cirrhosis. Serologies for hepatitis B and C as well as studies for auto-immune hepatitis, alpha 1 antitrypsin deficiency and Wilson disease were unremarkable.

Discussion: Current recommendations for the management of obese children entail an evaluation for NAFLD by measuring serum transaminases. Children with NAFLD are at greater risk of progression to non-alcoholic steatohepatitis (NASH). Even though NASH has historically been a diagnosis of adult obese patients, it is being reported with increasing frequency with the rising incidence of childhood obesity. Progression to hepatic fibrosis and cirrhosis in children is rarely encountered with only a handful of such cases being reported in the past.

Conclusion: With the increasing incidence of obesity worldwide, one should remain cognizant of this rare but serious outcome in all children with obesity and hepatomegaly even in the presence of normal transaminases. Development of other non-invasive surrogate markers of NAFLD would aid in detection and further follow up of this condition in children.

Abstract #601

PATIENT REPORTED “REMISSION” OF TYPE 2 DIABETES MELLITUS AFTER ADJUSTABLE GASTRIC BANDING – 1 YEAR INTERIM RESULTS OF THE LAP-BAND AP® EXPERIENCE (APEX) STUDY

Ted Okerson, MD, John Dixon, MBBS, PhD, Sunil Bhoyrul, MD, Michael G. Oefelein, MD

Objective: Bariatric surgery (malabsorptive vs. restrictive techniques) has been established as an effective treatment to reduce weight in severely obese patients refractory to behavioral and medical therapies. This study reports the 1 year “remission” (elimination of hypoglycemic medication) and/or improvement (reduction in hypoglycemic medication) of type 2 diabetes mellitus (T2D) after laparoscopic placement of the adjustable gastric band (AGB) as documented by T2D medication reduction/discontinuation, and the accompanying change in BMI and co-morbidity benefits.

Methods: The APEX study is an ongoing 5-year, prospective, multi-center, open-label, observational study which will assess weight reduction, co-morbidities and quality of life after implantation of the LAP-BAND AP® gastric band (NCT00501085), a restrictive weight loss technique. This is an interim analysis of subjects who reported daily medical therapy for T2D before AGB and who have completed the 1 year post-operative scheduled visit. Results: At baseline, 94 out of 436 subjects (22%) reported T2D requiring daily medical therapy, with data from 64 containing sufficient information to assess outcome at 48 weeks. Complete “remission” of T2D was reported in 22 patients (34%), with improvement in 33 patients (52%), no change in 8 patients (13%) and worsening in 1 patient (2%). Overall, 86% had “remission” and/or improvement in T2D. Baseline BMI was not significantly different among the 4 responder groups. Mean absolute BMI, change and the percent change in weight was -7.9/-19%, -8.7/-21%, -7.7/-15% and -2.9/-6% in the four groups respectively. Baseline BMI, reductions in BMI and percent change in weight were not statistically different among the groups, although numbers were small. As in patients with T2D, resolution or improvement also occurred in other pre-existing co-morbidities measured: hypertension (78%), hyperlipidemia (57%), depression (71%) obstructive sleep apnea (69%), and GERD (93%). Quality of Life as measured by the Obesity and Weight Loss Quality of Life instrument also improved.

Discussion: These data demonstrate that a minimally invasive restrictive gastric banding procedure in obese patients with T2D resulted in a clinically meaningful reduction in T2D medication requirements, as well
as in multiple obesity-related co-morbidities. These improvements tended to be greater in subjects with a greater change in BMI, but this was not statistically different. Other PRO obesity-related co-morbidities also improved, along with quality of life.

**Conclusion**: Laparoscopic AGB may offer an important adjunctive therapeutic approach to severely obese patients with T2D.

**Abstract #602**

**THE INTERACTION BETWEEN SERUM LEVELS OF SEX HORMONES AND BODY MASS INDEX IN POSTMENOPAUSAL WOMEN RECEIVING LOW-DOSE HORMONE THERAPY**

Eleni Armeni, MD, Demetrios Rizos, PhD, Efthimios Deligeoroglou, MD, Panagiotis Kofinakos, MD, George Kaparas, PhD, Andreas Alexandrou, MD, Maria Creatsa, MD, Emanuel Logothetis, MD, Evangelia Kouskouni, MD, Irene Lambrinoudaki, MD

**Objective**: The adequacy of relief of climacteric symptoms is usually estimated to evaluate the efficacy of postmenopausal hormone therapy (HT). Circulating serum levels of sex steroids in women under HT exhibit a wide fluctuation, depending on the individual or the regimen (active substance, dose, route of administration). The aim of the present study was to evaluate the interaction between body mass index (BMI) and the change in endogenous sex hormone levels in postmenopausal women during six months of oral continuous combined low dose hormone therapy.

**Methods**: This study recruited 50 postmenopausal women who were allocated to receive daily one tablet containing combination of 17β-estradiol (1mg)/norethindrone acetate (0.5mg) for 6 months. Blood samples were obtained to estimate serum levels of follicle-stimulating hormone (FSH), sex hormone binding globulin (SHBG), total testosterone, estradiol, free androgen index (FAI), free estrogen index (FEI), dehydroepiandrosterone sulfate (DHEAS), and Δ4-Androstendione. Mean absolute values at baseline and at the end of 6 months, as well as percent changes from baseline were compared between lean and overweight women.

**Results**: Lean subjects had statistically significant higher increments of FAI and specifically FEI compared to overweight (FAI, lean: 1.94±1.38 increased to 1.53±1.09, Δ=30.7%; overweight: 2.55±1.75 increased to 2.75±2.33, Δ=-13.6%; p (Δ%) between groups=0.010; FEI, lean: 0.14±0.09 increased to 0.29±0.14, Δ=287.1%; overweight: 0.23±0.18 increased to 0.52±0.40, Δ=110.3%; p (Δ%) between groups=0.034). Furthermore, mean levels of FSH decreased significantly in both groups (FSH, lean: 82.3±26.7mIU/ml decreased to 45.0±17.0mIU/ml, Δ=-45.9%, p=0.0001; FSH, overweight: 85.5±22.1mIU/ml decreased to 52.3±23.8mIU/ml, Δ=43%, p=0.003; p (Δ%)between groups=0.661). Finally, mean 17β-estradiol increased significantly in both groups (E2 lean: 23.24±12.55pg/ml increased to 53.62±28.29pg/ml, Δ=194.4%, p=0.006; E2 overweight: 24.17±10.88pg/ml increased to 68.36±53.99pg/ml, Δ=437.4%, p=0.0001; p(Δ%) between groups=0.619).

**Discussion**: Levels of endogenous sex hormones have a wide range of variation in postmenopausal women, being influenced by many factors as well as by BMI. This variation appears to be associated with clinical outcomes such as ischemic heart disease, loss of bone mineral density and breast cancer.

**Conclusion**: BMI does not affect total 17β-estradiol changes in postmenopausal women receiving HT. Overweight women might have a higher absolute FEI than lean women post-treatment, however free sex steroid concentrations increase more steeply in lean compared to overweight women receiving oral low-dose HT.

**Abstract #603**

**NECK CIRCUMFERENCE AS A SCREENING MEASURE FOR ABDOMINAL OBESITY AND ITS ASSOCIATION WITH METABOLIC SYNDROME AMONG HIGH RISK FILIPINO PATIENTS IN MAKATI MEDICAL CENTER**

Nerissa Sia Ang, MD, Josephine Carlos-Raboca, MD, FPCP, FPSEM

**Objective**: This study aims to determine the cut off level of neck circumference as a screening measure for abdominal obesity, with waist circumference as the gold standard; and determine its correlation with metabolic syndrome among High Risk Filipino Patients.

**Methods**: A case control study involving 425 high risk Filipino patients who sought consult at Makati Medical Center for any reason from the period of March to October 2010 were qualified to participate in the study. Excluded were those patients with known major medical conditions, active inflammatory and neoplastic disease; established cardiovascular disease (previous myocardial infarction (MI), stroke or coronary artery disease) or with known thyroid dysfunction, thyroid mass or nodules or any neck mass. Pertinent history, including blood pressure measurement and anthropometric measurements such as height, weight, neck circumference and waist circumference were recorded; after an 8 hour overnight fast, blood samples were sent for fasting plasma glucose, HDL cholesterol and triglyceride levels.
Results: Neck circumference (NC) cut off levels of ≥ 40 cm for males and ≥ 33.8 cm for females is a strong predictor of abdominal obesity with 62.07% sensitivity, 90.09% specificity and 75.77% accuracy for males and 67.59% sensitivity, 85.56% specificity and 75.76% accuracy for females. Similarly, using neck circumference (NC) cut off levels, a strong association exists between obese by neck circumference and the individual risk factors of Metabolic Syndrome (MS). It is also a relatively strong predictor of metabolic syndrome with 69.16% predictive accuracy for males and 69.70% predictive accuracy for females.

Discussion: Waist circumference, a measure of abdominal fat mass, closely correlates with abdominal adipose tissue. Neck circumference (NC), an index of upper body obesity, is a simple screening measure that can be used to identify patients who have central obesity. In the study, neck circumference contributed to more than half of the variability of waist circumference and has a moderately strong positive linear relationship with waist circumference. Patients who are diagnosed to be obese by neck circumference has increased likelihood of elevated fasting plasma glucose, low HDL cholesterol, hypertension, and consequently, metabolic syndrome.

Conclusion: Neck circumference is a simple and reliable screening test for abdominal obesity.

Abstract #604

INSULIN ECONOMY IN POSTMENOPAUSAL WOMEN: IMPACT OF HIGH WAIST CIRCUMFERENCE

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Objective: The purpose of the study was to evaluate the impact of high waist circumference (WC) on parameters of insulin economy in postmenopausal women. This is a cross-sectional study.

Methods: We recruited 420 naturally postmenopausal women without known history of diabetes for the study. The participants were divided into four groups by quartiles of WC. All subjects received a 75-g oral glucose tolerance test for parameters of insulin economy.

Results: The women with high WC (the 4th quartile, Q4) were older in age, heavier in weight, having higher blood pressure, with higher levels of fasting triglycerides and alanine aminotransferase, and with lower high-density lipoprotein cholesterol concentrations than those in the 1st quartile (Q1) group (all p < 0.05). The women in the Q4 also had higher percents of isolated postchallenge hyperglycemia (fasting glucose < 7 mmol/L and 2-h glucose ≥ 11.1) (odds ratio 3.03; 95% CI, 1.45 – 6.34, p = 0.002) as compared with those in the Q1. In univariate analyses of general linear models, the women in the Q4 were less insulin sensitive (indicated by lower value of ISI Matsuda, p < 0.0001 by Bonferroni adjustment) and more insulin resistance (by higher HOMA-IR, p = 0.01) than the women in the Q1, independent of age, physical inactivity and body mass index (BMI). It is noteworthy that the women in the Q4 had higher basal β-cell function than the counterparts based on Log (HOMA-β) from the fasting insulin and glucose (p = 0.02). Early phase of insulin secretion, surrogated by insulinogetic index ΔI30/ΔG30, was also higher in these women (p = 0.005). We used incremental areas under curves of the insulin response (ΔAUCINS) to measure total insulin response after oral glucose challenge. The Q4 group had a higher level of ΔAUCINS compared with the Q1 after adjustments (p < 0.0001). In partial correlation, we identified significant correlations of WC with indices of insulin sensitivity and insulin secretion after controlling age and physical inactivity scores. Furthermore, after additionally controlling BMI, the aforementioned correlations were attenuated, but remained statistically significant.

Conclusion: Our data showed that postmenopausal women with large waist girth were at high risk for isolated postchallenge hyperglycemia and atherogenic dyslipiemia. They were not only associated with insulin resistance but with hyperinsulinemia. It seemed that WC had extra detrimental effects beyond BMI on insulin sensitivity and insulin secretion in these postmenopausal women. (NCT00945217)

Abstract #605

REFRACTORY HYPOTENSION IN A MORBIDLY OBESE MALE FOLLOWING WEIGHT REDUCTION SURGERY

Maha Jawad Abu Kishk, MD, Majdi Hamarshi, MD, Abid Bhat, MD

Objective: To report a rare case of a 39 year old gentleman with refractory hypotension and bradycardia after weight loss from gastric sleeve weight reduction surgery.

Case Presentation: This is a 39-year-old gentleman with type 2 diabetes, hypertension, obstructive sleep apnea, and morbid obesity with BMI of 50 kg/m². He underwent gastric sleeve weight reduction surgery with resultant 60% weight loss over six months. He was referred to our ER by his surgeon for acute renal failure (ARF) and complaints of nausea, vomiting, and oliguria. Physical exam revealed hypotension 78/42 mmHg and bradycardia 58. Blood pressure (BP) continued to be low after 3 L IVF boluses, patient was then started on dopamine drip and admitted to...
the ICU. ARF resolved with IVF within a week. Patient continued to be hypotensive and bradycardic with positive orthostasis requiring dopamine that was switched to phenylephrine drip for a better BP response. Meanwhile, the following conditions were ruled out: dehydration, sepsis, adrenal insufficiency, hypothyroidism, diabetes insipidus, and hypogonadism. Electrocardiogram and echocardiography showed normal rhythm and systolic function, respectively. Hypotension and orthostasis were managed with the following stepwise approach: positive fluid balance, liberal salt intake, compression stockings, physical therapy, midodrine up to 10 mg every 8 hours, fludrocortisone up to 0.5 mg daily, darbepoetin 40 mcg weekly, and finally octreotide up to 100 mcg subcutaneous every 8 hours. This approach was successful after six weeks to discontinue phenylephrine drip, BP ranged between 81/24 and 113/58 with no orthostasis and patient was transferred to a regular medical floor. Four weeks later patient was discharged home on octreotide, fludrocortisone and midodrine.

**Discussion:** Weight loss induced hypotension is rarely reported in the literature and has been linked to significant weight loss following weight reduction surgery. The exact mechanism is still unknown; autonomic function and vascular tone might be affected with changes in weight but no pathologic data are available to support this theory. Most cases were reported in diabetic patients with more than 50% weight loss over several months after surgery. To our knowledge there are three reported cases of similar presentation.

**Conclusion:** High blood pressure might not only normalize after weight loss, but it might get seriously low with orthostatic changes if patients experienced significant weight loss. Orthostatic hypotension from weight loss can be refractory and may require a combination of therapies.

**Abstract #606**

HEPATOCELLULAR CARCINOMA MASQUERADING AS EXENATIDE INDUCED WEIGHT LOSS

_Castro Bali, MBBS, Sartaj Sandhu, MBBS, Maria Farooqi, MBBS, Ajay Varanasi, MD, Ajay Chaudhuri, MD_

**Objective:** Exenatide, a GLP-1 agonist, used to treat Type 2 Diabetes (T2D) induces weight loss by reducing energy intake and increasing energy expenditure. The following case emphasizes the need for high index of clinical suspicion for a coexisting medical illness, if patient experiences more than the expected weight loss on Exenatide.

**Case Presentation:** A 53-year-old Hispanic male was diagnosed with T2D when he underwent liver transplantation for Hepatitis C and Hepatocellular carcinoma (HCC). He was started on steroids as part of immunosuppressive regimen for liver transplantation. At his initial presentation he weighed 86 kg (189.5 lbs) with a BMI of 31.6 kg/m². Despite the fact that his glucose was well controlled with insulin he continued to gain weight. Five years after his liver transplant his weight had increased to 107.2 kg (236 lbs) with BMI of 41.8 kg/m². The patient was started on Exenatide and following its initiation, he started losing weight. Patient lost 13 kg (30 lbs) over the next 6 months. To investigate this rapid and more than expected weight loss, an ultrasound of the abdomen was obtained which revealed a large suprarenal mass. MRI of abdomen confirmed a large heterogeneous mass measuring 70 x 80 x 75 mm in close contact with posterior margin of liver. Suspicion for HCC was high considering his prior history of HCC and Hepatitis C infection. Liver biopsy was done which did confirm the presence of HCC. The patient had a curative surgical resection of the recurrent HCC.

**Discussion:** Along with diet, exercise and behavior modification, drug therapy is an important component of treatment of T2D. Drugs like Exenatide that improve glycemic control and induce weight loss are recommended as add on therapy in subjects with T2D, as a majority of them are overweight. Mean weight loss with Exenatide is 4.5 kg with 25% of the subjects losing up to 12 kg over a period of 2.5 years without any additional diet or exercise recommendations. While voluntary or drug induced weight loss is desirable, if it is more than what is expected, it should be considered suspicious and investigated. Our patient lost significant amount of weight which was initially attributed to Exenatide. However, on investigating further it became clear that HCC was responsible for the weight loss.

**Conclusion:** The above case emphasizes the importance of being vigilant for coexisting conditions when patient experiences weight loss that is more than expected while being treated with drugs like Exenatide.

**Abstract #607**

ABDOMINAL ADIPOSITY AMONG TYPE 2 DIABETES PATIENTS IN CALABAR, SOUTH EAST NIGERIA

_Ofem Egbe Enang, MBCh_

**Objective:** To report the prevalence of abdominal adiposity among Type 2 diabetes patients attending a tertiary health facility in Calabar, Nigeria.
Methods: This was a cross-sectional study using an opportunity sample of 100 adult Nigerians with Type 2 diabetes attending the diabetes clinic at a tertiary health facility in Calabar, and 100 controls matched for age and sex. Height, weight, and waist circumference (WC) for each subject was determined using standard techniques. Nutriture was based on Body Mass Index (BMI) and WC while socio demographic data was obtained using modified WHO STEPS questionnaire. WC above 102cm for men and 88 cm for women was regarded as high risk for likely CV event.

Results: Overall mean waist circumference for males was 93.9 ±11cm and 93.9 ±9cm for females. The prevalence of abdominal obesity among male and female diabetes patients was 22% and 75% respectively, while for controls it was 20% and 63.3% respectively. Males had higher mean WC than females (P=0.09). The difference between diabetes patients and controls was not statistically significant (P=0.09).

Discussion: There is an increasing prevalence of obesity, including abdominal obesity among the general population. However, abdominal obesity and type 2 diabetes often coexist, promoting insulin resistance and a host of cardiovascular risk (CV) events. Patients with type 2 diabetes are well known to be at elevated risk for first or repeated CV events, compared with non diabetics.

Conclusion: Waist circumference is a simple way of routinely identifying obese Type 2 diabetes patients at risk for cardiovascular events and the prevalence of abdominal adiposity is higher among females than males.

Abstract #608

KNOWLEDGE, ATTITUDE AND PRACTICE ON OBESITY OF TYPE 2 DIABETES SUBJECTS: A STUDY IN TERTIARY CARE HOSPITAL IN BANGLADESH

Fazlarabi Khan, MBBS, Anisur Rahman, MD, Nazrul Islam, MD

Objective: Obesity is becoming an epidemic problem in developing countries as well as developed countries. Prevention depends on patient education and motivation. These, in turn, can be greatly facilitated by adequate baseline data on the knowledge, attitude, and practice (KAP) of patients. Very few studies have been performed on these issues particularly in developing countries and such data is almost nonexistent in Bangladeshi population.

The aim of this study was to assess KAP scores on obesity and to identify deficient areas of obesity management related knowledge among hospital based type 2 DM subjects.

Methods: Under an analytical cross-sectional design, a total of 160 type 2 diabetic subjects {age 45 (35-55) yrs, median (range); M 45%, F 55%}) were collected purposively from the out-patient department of BIRDEM (the tertiary hospital of Diabetic Association of Bangladesh). The level of knowledge was measured by an interviewer-administered questionnaire. Likert scale was used to assess attitude on various items and practice was measured by assessing patient’s management outcome in terms of fasting glucose, total cholesterol, triglyceride, and BMI. The data was expressed as the M±SD or median (range). Statistical methods include Pearson’s correlation coefficient and multivariate analyses were done.

Results: In this study, BMI (kg/m², M±SD) of the study subjects were 25.6 ±4. Among them 25% belongs to normal weight, 50% from overweight, and 25% from obese. The mean (±SD) KAP score of the study subject was (%, 60.03±13.82, 79.30±8.27 and 55.50±19.21 respectively). Majority of the subjects (99%) did not have idea about obesity. More than half of the subjects did not give the correct answer about the normal fasting blood glucose level, duration between weight measurement, and rules for measuring weight. About 88% did not know their own energy requirement and 64% had no idea about their own ideal body weight. Half of the subjects did not have any idea about good and bad lipids. Almost 80% of subjects were told that fast foods and soft drinks were not harmful for weight management. Most of the study subjects (90%) gave correct answer about fiber rich food, beef, egg yolk, butter, ghee and dalda. A significant relationship was found between knowledge and attitude (p<0.0001), knowledge and practice (p<0.006) and attitude and practice (p<0.004). Age, sex, year of education, monthly income, total knowledge score, total attitude score, duration of exercise, and attending education class on obesity were tested in a multiple regression model with the BMI as the dependent variable. Sex (β= 0.259, p=0.001) showed a significant positive association with BMI. Duration of exercise (β= -0.192, p=0.008) and attending education class on obesity (β= -0.392, p=0.001) showed a significant negative association with BMI.

Conclusion: Half of the subjects (50%) are overweight including 25% of them being obese. Overall knowledge scores were not significantly related to BMI or other management outcome variables. There is a huge possibility to increase their knowledge on their present condition.
OTHER

Abstract #700

OPTIMAL SURGICAL MANAGEMENT OF WELL DIFFERENTIATED THYROID CANCER (WDTC) ARISING IN STRUMA OVARI

Jennifer Lynn Marti, MD, Victoria Clark, BA, Holly Harper, MD, David Chhieng, MD, Julie Ann Sosa, MD, Sanziana Roman, MD

Objective: Struma ovarii (SO) is a monodermal variant of ovarian teratoma, representing <1% of all ovarian tumors. Treatment for SO involves surgical resection due to the risk of malignant degeneration and hyperthyroidism. WDTC arising in SO is rare. There is limited literature on the optimal management of WDTC in SO. Surgical management and post-operative treatment are not standardized. Unilateral cystectomy, unilateral salpingo-oophorectomy (USO), or hysterectomy with bilateral salpingo-oophorectomy (TAH/BSO), in addition to total thyroidectomy and radioactive iodine (RAI) has been employed. We review a series of four patients from a single institution, compare the extent of treatment and outcomes, and present an algorithm for evaluation and management.

Case Presentation: Four patients with WDTC arising within SO were treated between 1998-2010. Median age was 44 (range 43-57). WDTC histologies included papillary (n=3) and follicular thyroid carcinoma (n=1). Two patients underwent TAH/BSO, one patient had a prior history of TAH for endometrial sarcoma and underwent BSO, and one patient underwent left USO and right ovarian cystectomy. One patient underwent prophylactic total thyroidectomy in anticipation of RAI, and was found to have a synchronous 5 mm papillary thyroid carcinoma with extrathyroidal extension and central lymph node metastasis (T3N1a), negative for BRAF V600E. One patient had a prior thyroid lobectomy for benign disease, and is being followed with interval sonograms. The two other patients did not have thyroidectomy and are being followed clinically. All patients are clinically NED, at a median followup of 56 months (range 5-106).

Discussion: WDTC arising in SO, with synchronous cancer in the thyroid gland, is rare. There are limited data to suggest an optimal treatment strategy from the gynecologic and endocrinologic perspectives. Controversy exists regarding the extent of pelvic resection and evaluation of the thyroid gland. In our series of four patients, all patients are well, despite a variety of approaches to surgical resection and adjuvant treatment.

Conclusion: Extensive pelvic surgery (TAH/BSO) and prophylactic total thyroidectomy with RAI may not be necessary in all patients. In addition to our single institution case series, we present a systematic review of the literature, and present an algorithm for evaluation and management.

Abstract #701

NONFUNCTIONING INTRATHYROIDAL RECURRENT PARATHYROID CARCINOMA

Mohammed Ahmed, MD, FACP, FACE, Alyaa Elhazmi, MD, Ali Al-Jubran, MD, Bader Al-Ajlan, MD, Hindi Al-Hindi, MD, Mohammed Khalid, MD, Ashour Mahmoud, MD

Objective: Nonfunctioning parathyroid carcinoma (NPTC) is one of the rarest malignant tumors. A paucity of information mandates reporting of all available cases to provide a better understanding of this disease.

Case Presentation: A 61-year-old woman presented to her local hospital with anterior neck mass, stridor & dyspnea. CT scan; right thyroid lobe mass. She had normal Ca++, PTH was not done then. Thyroidectomy performed at local hospital revealed 8 cm hard right neck mass adherent to strap muscles, trachea and carotid sheath. Our review of histopathology: intrathyroidal 8 cm, invasive parathyroid carcinoma, multiple vascular emboli, and perithyroid extension, Ki67 index 5%. Immunostains: chromogranin+, synaptophysin and PTH weak +, thyroglobulin-, TTF1-, p53-. follow up US Neck 19 mos post-op: interval development of 4 hypoechoic nodules, largest measuring 2.5 cm. FNA: Cellular neuroendocrine neoplasm consistent with recurrent parathyroid carcinoma. Repeated serum Ca++, PO4-, PTH, ALKptase, albumin for the next 30 mos. were normal. For last 6 wks. dyspnea and stride got worse and recent US neck: multiple locally invasive soft tissue masses, largest measuring 3.4 cm. Bone scan: negative. CT scan of the neck and chest: Mass lesion infiltrating right half of tracheal wall and exophytic tumor growth into the lumen of trachea. Rx Palliative: Endoscopic laser-fulguration of large intratracheal tumor, followed by stent insertion and XRT. CT: Lytic vertebral metastases of C4 and C6 impinging on spinal cord and confirmed on PET-CT that shows avid uptake of FDG in these & peri/intratracheal tumor. XRT to spinal metastases under steroids. Tumor genetic analysis for potential deletion/mutation of Pro-PTH gene are underway.

Discussion: Parathyroid carcinoma is an uncommon tumor accounting for 0.5% to 5% of parathyroid tumors. Majority are functional producing very high PTH and severe hypercalcemia. Experience with NPTC is limited to less than 30 cases. Their clinical course is more aggressive as described in our case. She developed recurrence with extensive tracheal wall and intratracheal...
obstructive lesions and evidence of spinal metastases. Surgical resection of her recurrent tumor and tracheal invasion is deemed high risk and management is mainly palliative. ChemoRx is restricted to a single case report with a dramatic & complete resolution of mediastinal mass & malignant pleural effusion.

**Conclusion:** NPTC are difficult to diagnose and treat. The failure of the tumor to produce PTH allows it to be diagnosed at an advanced stage. Detection of these tumors is based on presence of expanding neck mass. Accordingly, parathyroid cancer should be considered in the presence of neck mass regardless of serum Ca++ and PTH values.

**Abstract #702**

**EVEROLIMUS: AN EMERGING TREATMENT OPTION IN THE MANAGEMENT OF MALIGNANT GLUCAGONOMA**

Ayoola Olukunmi Oladejo, MBBS, M Pavel, MD, TJ Kroencke, MD, C Bartel, MD, T Denecke, MD, B Wiedenmann, MD

**Objective:** To report a case of partial remission after 3 years of treatment with everolimus in a female patient with malignant glucagonoma.

**Case Presentation:** A 78-year-old female was referred to our center on account of a suspected gastroenteropancreatic neuroendocrine tumour. The diagnosis of glucagonoma was confirmed by immunohistochemistry after pancreatectomy. There was a positive staining for glucagon by immunohistochemistry and Ki67 proliferation index of 20%. The tumor also had a positive staining for chromogranin A, synaptophysin and CD56. She had a relapse two years after surgery as evidenced by metastatic lesions in the liver and regional lymph node after which she had a session of peptide receptor radionuclide therapy and 2 cycles of streptozotocin and 5-fluoro-uracil (5-FU), but the chemotherapy was discontinued on account of nephrotoxicity. The patient was commenced on everolimus with consequent reduction in the hepatic mass and she has remained stable over 3 years of treatment with no evidence of new lesions. The initial glucagon level was 333pg/dl (50-150) but later plummeted to 57.02pg/dl after 3 years of treatment with everolimus.

**Discussion:** Glucagonomas are rare neuroendocrine tumors which originate from the alpha-2 cells of the pancreas producing clinical syndrome of necrolytic migratory erythema (NME), cheilitis, diabetes mellitus, anemia, weight loss, venous thrombosis, and neuropsychiatric symptoms. The therapeutic armamentarium available for the treatment of glucagonoma includes both curative and palliative surgeries, loco-regional ablative treatments, peptide receptor radionuclide therapy, and several medical treatments (hormonal/biotherapy, chemotherapy and most recently molecular targeted therapy). A better understanding of the molecular pathways that characterize tumor growth and the observation that gastroenteropancreatic neuroendocrine tumor over-express several pro-angiogenic molecules which include vascular endothelial growth factor (VEGF), epidermal growth factor (EGFR) and the PI3K-AKT-m TOR pathway have formed the basis for the use of inhibitors of these important pathways of which everolimus is a notable example.

**Conclusion:** Everolimus is a novel therapy that shows promising efficacy in the management of malignant glucagonoma.

**Abstract #703**

**PREVALENCE OF IODINE-INSUFFICIENCY INDUCED GOITER IN WOMEN OF NEW JERSEY**

Amy Chow, MD, Xiangbing Wang, MD, PhD, FACE, Richard Ro, MD, Sarika Sanghvi, DO, Aaron Rockoff, MD

**Objective:** Since the introduction of iodized salt in the 1920s, iodine deficiency is rare in the US. However, sporadic cases of euthyroid goiter related to iodine deficiency have been reported in NJ, an iodine-replete state. This retrospective study is to investigate the prevalence of goiter induced by iodine deficiency among women in NJ, which we refer to as iodine-insufficiency-induced goiter (IIIG).

**Methods:** 792 charts of female patients between June 2006 and January 2010 with diagnosis of nontoxic multinodular, uninodular or simple goiter from an endocrine clinic in a major university hospital were reviewed. Patients’ lab data, including 24-hour urinary iodine (UI) levels, were collected. The diagnosis of IIIG was made if the following criteria were met: a 24-hour UI <100 μg AND goiter size reduction was noted after iodine replacement.

**Results:** Among 792 patients, 7 patients (1%) were diagnosed with IIIG. The characteristics of the patients include: all belong to minority groups; all patients had normal thyroid function; 4 patients had family history of thyroid disease; 6 patients had a BMI ≥ 27; the duration of goiter ranged from 1 to 11 years and 6 patients had high I123-uptake scan results. When compared with 10 caucasian women matched for age, BMI, and iodized-salt avoidance dietary patterns, the minority patients had a much lower 24-hour UI level (≤ 28.9±27.6 μg vs. 248.1±189.7μg with P< 0.05).
Discussion: Our study showed that iodine insufficiency can still be a cause of goiter among women in NJ. Compared to iodine-deficiency-induced goiter, IIIG occurred in an iodine-abundant environment with the following special characteristics: 1) patients were minority women; 2) patients had mild to moderate sized goiter as opposed to large goiter; 3) patients had strong family history of thyroid disease; 4) most patients were overweight or obese. The exact mechanism of iodine insufficiency induced goiter is unknown. Dietary avoidance of iodized salt due to seafood allergy, hypertension or personal preferences, and over-dependence on food high in goitrogens such as cassava/yucca, sweet potatoes and cabbage, etc may be contributors, and further study is needed.

Conclusion: This study highlighted the importance of obtaining specific dietary information related to the intake of iodized salt and seafood when evaluating patients with a goiter, and measuring 24 hour urinary iodine excretion in suspicious cases. Treatment should include iodized salt and iodine containing prenatal multivitamins especially in the setting of pregnancy and lactation or in patients with hypertension who are inclined to limit or refrain from added salt in their diet.

Abstract #704

A CASE OF FAMILIAL PARTIAL LIPODYSTROPHY AND IMPACT OF LEPTIN THERAPY

Ila Khanna, MD, Subramanian Kannan, MD, Manmeet Kaur, MD, Michael Radin, MD

Objective: To report a patient with familial partial lipodystrophy (FPLD)-Dunnigan variety who was treated with leptin resulting in significant improvement of physical and metabolic features.

Case Presentation: 28-year-old caucasian female presented to the endocrine clinic for evaluation of “Cushing Syndrome” because of moon facies and hypertension. The patient noted worsening fatigue, 40 pound weight gain, hirsutism, and abnormal skin pigmentation. She had noticed an abnormal muscle distribution since puberty. Review of systems was positive for polydipsia, nocturia, irregular menses, episodes of flushing and hot flashes. Past medical history was positive only for hypertension. Family history was significant for father and paternal aunt with abnormal body habitus with prominent musculature. On physical exam she was noted to have moon facies, dorsocervical fat pad, acanthosis nigricans, and hypertrrophic muscles of the gluteal, thigh, calf and arms. No abnormal striae, bruising or proximal myopathy were noted. Labs were significant for diabetes with elevated insulin levels. Triglycerides were elevated with low HDL. Work up for Cushing’s syndrome, pheochromocytoma, and Carcinoid syndrome was all negative. Ultrasound of the liver was consistent with hepatic steatosis. Genetic testing for lipodystrophy was consistent with familial partial lipodystrophy of the Dunnigan variety with mutations in the gene encoding Lamin A/C located on chromosome 1q21-22. She was initially treated with oral hypoglycemics, fenofibrates, diet and exercise. Ultimately, she was enrolled in Long Term Efficacy of Leptin Replacement and Treatment of Lipodystrophy trial at the NIH. Follow up in 1 year showed remarkable improvement in her physical phenotype and her metabolic profile with cessation of medications for diabetes and dyslipidemia.

Discussion: The Familial Partial Lipodystrophy syndrome- Dunnigan variety is a rare autosomal dominant genetic disorder. Clinical appearance may mimic Cushingoid features but instead of the proximal myopathy there is muscular hypertrophy. Leptin, a hormone secreted by the adipocytes, is found to be deficient in lipodystrophic disorders. This condition of hypoleptinemia is associated with insulin resistance, hyperglycemia and hypertriglyceridemia. Exogenous leptin treatment has been shown to be superior to conventional therapy in controlling dyslipidemia and hepatic steatosis.

Conclusion: This case illustrates how leptin replacement therapy resulted in phenotypic and biochemical resolution of features associated with Familial Partial Lipodystrophy of the Dunnigan variety.

Abstract #705

A CASE OF METASTATIC MALIGNANT GIANT INSULINOMA IN PREVIOUSLY DIAGNOSED TYPE 2 DIABETES MELLITUS: CONTROLLED WITH MEDICAL THERAPY WITHOUT SURGERY

Nalurporn Chokrungvaranon, MD, Allison Peckumn, DO, B. Sylvia Vela, MD

Objective: To report an unusual case of coexisting type 2 diabetes mellitus (T2DM) and metastatic insulinoma in a patient whose disease is controlled by somatostatin analogs without surgery.

Case Presentation: An 80-year-old male patient with a history of T2DM presented with recurrent episodes of hypoglycemia. The patient was confirmed to have metastatic malignant insulinoma by having high levels of insulin, proinsulin, and c-peptide during a hypoglycemic episode, as well as the presence of a 9.6x8.0x7.6 cm heterogeneously enhancing lobular soft tissue mass within the body and tail of the pancreas seen on abdominal CT. Fine needle aspiration of the mass was consistent with
ASSOCIATION BETWEEN METABOLIC SYNDROME AND THE EXTENT OF SEVERE PERIODONTITIS IN GULLAH POPULATION

Nicoleta Sora, MD, Nicole Marlow, MSPH, Dipankar Bandyopadhyay, PhD, Renata Leite, DDS, Elizabeth Slate, PhD, Jyotika Fernandes, MD

Objective: To analyze the effect of Metabolic Syndrome (MetS) and its individual components on the extent of severe periodontitis in a Gullah African-American (AA) population with type 2 diabetes mellitus (T2DM). The Gullah is a distinctive, essentially genetically homogenous, and largely underserved AA population from coastal Georgia and South Carolina.

Methods: Extracting data from a cross-sectional study of Gullah AAs with T2DM (N=313), we included those subjects with non-missing data for our variables of interest (N=285). We assessed the extent of severe periodontitis as total diseased tooth-sites/person (evaluated as separate outcomes: 6+mm clinical attachment level [CAL], 5+mm probing depth [PD]). Primary independent variables assessed in separate models included MetS status (yes/no) and each MetS component (low HDL, hypertension, high triglycerides, large waist circumference) exhibited in addition to T2DM. We fitted negative binomial regression models appropriate for clustered count data with overdispersion, controlling for glycemic control (HbA1c), age, CRP, albumin, BMI, smoking, gender and interaction effects of MetS status by HbA1c.

Results: Prevalence of MetS and HbA1c ≥7% was 85.61% and 61.89%, respectively. Prevalence for MetS components included 49.47% for low HDL, 84.91% for hypertension, 14.74% for high triglycerides, and 84.21% for large waist circumference. CAL- (5.31±11.65%) and PD-outcomes (5.31±10.93%) each ranged 0-79.17% tooth-sites/person.

Discussion: We observed a significant interaction for MetS status by HbA1c in CAL models; stratified results showed significantly increased rates for those with MetS when HbA1c ≥7% (rate ratio [RR]=11.95, 95% CI=3.23-44.15, p<0.05), but not when HbA1c <7% (RR 1.64, 95% CI=0.47-5.75, p=0.44). Also, separate CAL models showed marginally increased rates among those with large waist circumference (RR=3.11, 95% CI=0.99-9.74, p=0.05). However, PD models did not show significant associations for our primary independent variables, nor did these models show a significant interaction for MetS status by HbA1c.

Conclusion: Metabolic Syndrome is associated with the extent of severe periodontitis in this Gullah population, particularly among those with poor glycemic control. These findings further support the clinical relevance of evaluating patients with T2DM and additional metabolic risk factors for the extent of periodontitis.

Abstract #707

ENOUGH TO MAKE YOU BLUSH: AN UNUSUAL CASE OF FLUSHING

Jessica Megan Triay, MBBS, Parag Singal, MBBS

Objective: To raise awareness of an unusual and likely under-reported condition presenting with flushing.

Case Presentation: A 70-year-old man suffered intense nocturnal flushing and erythema causing waking 4 times nightly. Symptoms originated around the genitalia and spread across the body, palms and soles.
with simultaneous painful erections, all lasting up to 20 minutes. Problems began 13 months prior to assessment and erectile function at other times remained normal. Simvastatin, bisoprolol and aspirin were all started after symptom onset. During admission for observation, these problems were corroborated and medical examination was consistent with known mitral valve prolapse, but was otherwise normal. Screening blood tests for flushing, sex hormone axis and baseline EKG were normal. Autonomic studies showed mild dysfunction in postural blood pressure and cardiac responses, but were consistent with age. CT chest and abdomen showed gallstones only. A diagnostic polysomnography was arranged and showed marked Rapid Eye Movement (REM) sleep fragmentation with frequent arousals when symptomatic, compatible with a diagnosis of REM Sleep Related Painful Erections. He was given coping strategies and Clonazepam 500mcg, titrating up to 1.5mg 4 nights weekly, to reduce drug tolerance. Symptoms improved, but only on treatment days.

Discussion: This condition is likely to be under-reported and under-recognized according to sleep clinic data. There are no known predisposing factors, but it affects men over 40 and progresses gradually. For diagnosis the International Classification of Sleep Disorders recommends polysomnography and the following features should be present: 1. painful erections during sleep, 2. non-painful erections during wakefulness, 3. increase penile girth (tumunescence) associated with awakenings from REM sleep on polysomnography, 4. absence of other associated medical or mental disorders, 5. not accounted for by other sleep disorder. Possible explanations for the condition are few and varied. There is evidence for autonomic nervous system involvement, but whether the disruption is sympathetic or parasympathetic is unclear. There is no evidence to suggest progressive autonomic dysfunction. The possibility of central neurotransmission disturbance has also been suggested.

Conclusion: Sleep Related Painful Erections syndrome causes individuals significant distress and sleep disruption affecting quality of life. Treatment options are currently suboptimal but offer sufferers a degree of relief provided the condition is adequately recognized.

Abstract #708

CASE OF INCIDENTAL MEDULLARY THYROID CARCINOMA AND SUBSEQUENT DIAGNOSIS OF MEN 2A

Ria Madeliene Lim, MD, David Sionit, MD, Teresa McInnis, RN, Latha Dulipsingh, MD

Objectives: 1. To describe a case of incidental medullary thyroid carcinoma, later noted to have multiple endocrine neoplasia type 2A. 2. To outline the clinical features and management of MEN2A

Case Presentation: 45 y/o female, with history of DM2 and hypertension well controlled on two medications, underwent screening for a clinical study and was incidentally noted to have elevated calcitonin (390 pg/ml). She was asymptomatic except for mild episodic night sweats. Physical exam was unremarkable. She denied any family history of thyroid cancer or multiple endocrine neoplasia. Ultrasound of the thyroid showed a multinodular goiter with the largest nodule measuring 1.8x1.3x1.4cm. Fine needle aspiration biopsy of the left and right thyroid nodules was consistent with medullary thyroid carcinoma. Because of concern for MEN2, she was worked-up for pheochromocytoma. Plasma metanephrine and 24 hour urine metanephrine were elevated at 210 pg/ml and 1688 mcg/24hr, respectively. MRI of the abdomen showed bilateral adrenal masses. I-123 MIBG showed increased tracer uptake in left adrenal gland and low grade tracer uptake in right adrenal gland. RET oncogene testing revealed heterozygous mutation at p.C620R. She had normal calcium and parathyroid hormone levels. After starting phenoxybenzamine preoperatively, she underwent laparoscopic bilateral adrenalectomy. Pathology was consistent with pheochromocytoma. Few weeks later, she underwent total thyroidectomy and central compartment lymph node dissection which showed medullary carcinomas on both right and left thyroid lobes and benign lymph nodes. Post-operative course was unremarkable. Screening of family members for RET gene mutation is ongoing.

Discussion: Multiple endocrine neoplasia type 2A (MEN2A) is characterized by medullary thyroid carcinoma in combination with pheochromocytoma and/or parathyroid hyperplasia. The frequency of medullary thyroid carcinoma approaches 100%, while pheochromocytoma and parathyroid hyperplasia has a frequency of 40-50% and 10-20%, respectively. MEN2A is caused by mutations affecting cysteine residues in codons 609, 611, 618 and 620 within exon 10 and codon 634 in exon 11 of RET. When medullary thyroid carcinoma is suspected, pheochromocytoma screening and RET gene testing should be done preoperatively. Pheochromocytoma surgery precedes total thyroidectomy. RET gene testing is offered to index patients and their families since this may suggest predilection towards a particular phenotype and clinical course.

Conclusion: Patients suspected to have medullary thyroid carcinoma should have pheochromocytoma workup and RET gene testing prior to thyroidectomy.
Abstract #709

CAPECITABINE/OXALIPLATIN (CAPOX), A NOVEL TREATMENT OPTION IN THE MANAGEMENT OF REFRACTORY HYPOGLYCEMIA IN MALIGNANT PRO-INSULINOMA

Ayoola Olukunmi Oladejo, MBBS, M Pavel, MD, TJ Kroencke, MD, C Bartel, MD, T Denecke, MD, B Wiedenmann, MD

Objective: To report a case of clinical, biochemical and radiological response to Capecitabine/Oxaliplatin therapy after failure of several conventional therapies in a patient with malignant pro-insulinoma.

Case Presentation: A 38-year-old man was referred to our center on account of a suspected pancreatic neuroendocrine tumor. Ultrasonography, endoscopic ultrasound and abdominal CT confirmed a tumor mass in the head of pancreas, multiple hepatic metastases and lymph node metastases seen between the head of pancreas and the hepatic hilus. Neuron specific enolase was significantly elevated, 26.61 (< 12.5), but chromogranin A done on three separate occasions were all within normal reference range. Pro-insulin level done were 54 and 63pmol/L (<11) while the insulin level, C-peptide, and insulin like growth factor (IGF-1) were all within normal reference range. The diagnosis of pro-insulinoma was confirmed by immunohistochemistry with a Ki67 proliferation index of 15%. Patient had treatment with octreotide, diazoxide, temozolamide, streptozocin and 5-fluorouracil, all of which failed to achieve symptomatic, biochemical or radiological response. This necessitated the introduction of CapOx, which resulted in the control of hypoglycemia and a significant reduction in the level of tumor marker (neurone specific enolase) and partial reduction of the hepatic and pancreatic masses. However, the treatment was stopped after 8 cycles on account of severe polyneuropathy.

Discussion: Insulinomas are the most common functioning endocrine tumors of the pancreas. Pro-insulinoma is much rarer than insulinomas, the exact incidence and prevalence is not exactly known. The most common clinical manifestation is a fasting hypoglycemia, with discrete episodes of neuroglycopenic symptoms that may or may not be preceded by sympathoadrenal symptoms. The management of hypoglycemia may be challenging, especially when conventional agents fail to achieve adequate response. Medical treatment is generally restricted to patients with unresectable metastatic disease, high risk candidates for surgery, or patients who have undergone an unsuccessful operation with persistent symptoms. The use of novel therapies with everolimus, radionuclide therapy and combination chemotherapy with CapOx are already gaining acceptability and may be quite useful in the near future.

Conclusion: CapOx may be a viable option in malignant insulinoma/pro-insulinoma in the setting of refractory hypoglycemia.

Abstract #710

ECTOPIc ACTH PRODUCTION IN A RAPIDLY GROWING SARCOMA

Sarika Chopra, DO, Shalini Dabbadi Lakshmipathi, MD, Manmeet Kaur, MD

Objective: To demonstrate a rare case of an ectopic adrenocorticotropic hormone (ACTH) producing sarcoma.

Case Presentation: A 55-year-old male presented with a rapidly growing epigastric mass. Biopsies of the mass favored a neuroendocrine tumor. He underwent chemotherapy treatment to which he was clinically unresponsive. A repeat needle biopsy favored a poorly differentiated sarcomatoid carcinoma. After 2 months of chemotherapy, while waiting for the final diagnosis of the tissue sample, the patient presented with DM and a hemoglobin A1C of 9%, lower extremity swelling and hypokalemia refractory to spironolactone. Given these new findings he was extensively worked up for possible paraneoplastic syndrome. His ACTH levels were elevated at 123pg/ml and 164pg/ml. A twenty-four hour urine collection of 1800ml found a creatinine of 1.2g/24 hours and an elevated cortisol level of 7,518 mcg/24 hours. A serum cortisol level was 57 mcg/dl and, after a 2 mg dexamethasone suppression test, was found to be unsuppressed at 79 mcg/dl. CT of the chest was negative for masses. MRI of the brain showed no evidence of pituitary enlargement. CT of the abdomen revealed a 23.5x17 cm anterior abdominal mass with extension into the left lobe of the liver, with normal appearing adrenal glands. Metyropone therapy was initiated. The patient later developed lower extremity and scrotal edema from a thrombus in the IVC. Enoxaparin therapy was initiated. The microassay later confirmed that the tumor was a sarcoma. The patient then received one cycle of Adriamycin, however became septic. He was placed on comfort measures only and died.

Discussion: Here we present a rare case of ectopic adrenocorticotropic hormone (ACTH) producing sarcoma. Ectopic ACTH is most often expressed from neuroendocrine tumors, most commonly small cell lung cancer, thymic, islet cell and bronchial carcinoid tumors. The ensuing paraneoplastic syndrome is characterized by fluid retention, hypertension, metabolic alkalosis, glucose intolerance and hypokalemia. In this unique case, the patient developed
Objective: To describe a case of escitalopram causing hyponatremia. Hyponatremia is a well known side effect of selective serotonin reuptake inhibitors (SSRIs) and has been reported with fluoxetine, sertraline, paroxetine, citalopram and fluvoxamine. However there are only four reported cases of escitalopram causing hyponatremia.

Case Presentation: We report a case of a 68-year-old male who presented with symptoms of headache, fatigue, sleepiness and dizziness. His past medical history was significant for longstanding depression. Physical examination was significant for orthostasis and vitiligo. The patient was assessed to be clinically euolemic. Initial laboratory studies revealed hyponatremia with sodium of 126 mmol/L. The patient underwent an extensive workup for hyponatremia. Serum osmolality was 292 mOsmol/kg, and urine osmolality was 524 mOsmol/kg. Urine sodium was 73 mmol/L. Adrenal insufficiency and hypothyroidism were excluded after obtaining normal cortisol and TSH values. At this point we considered SIADH in our differential diagnoses. We conducted an extensive review of the patient’s chart in an attempt to determine the etiology of the patient’s hyponatremia. We found that the patient had been on escitalopram for over ten years and laboratory studies obtained within this period revealed hyponatremia. No lab data prior to the patient’s commencement of escitalopram were available. On a presumptive basis we tapered the escitalopram from 10 mg daily to 5 mg every other day and eventually it was discontinued. The patient reported complete resolution of his headaches, fatigue and dizziness. Repeat laboratory studies after this intervention revealed a sodium value of 137 mmol/L. Given the normalization of the patient’s sodium after discontinuing escitalopram, we concluded that the drug was responsible for his hyponatremia.

Discussion: Hyponatremia caused by SSRIs is attributable to a syndrome of inappropriate antidiuretic hormone secretion induced by a nonosmotic release of antidiuretic hormone. Our literature search revealed 4 other cases of escitalopram-induced hyponatremia. In this case we systematically excluded other etiologies that could have caused hyponatremia. This is the fifth reported case of escitalopram causing hyponatremia.

Conclusion: We predict that there will be increasing reports of cases espousing a causative association between escitalopram and hyponatremia as more physicians are prescribing this newer SSRI and are also more cognizant of this potential side-effect. We propose that hyponatremia caused by SIADH may well be a class effect of the SSRIs and this should inform monitoring protocols for patients on these medications.

Abstract #712

ECTOPIC PARATHYROID HORMONE SECRETING NEUROENDOCRINE TUMOR

Ajaz Ahamad Banka, MBBS, Mohamed Abdel Khalek, MD, Nicholas Avitabile, MD, Shamsa Ali, MD, Tina Thethi, MD, Emad Kandil, MD

Objective: The current approach to the treatment of primary hyperparathyroidism is based on the concept that hypercalcemia associated with increased levels of intact PTH is limited to primary parathyroid lesions, rather than production by an ectopic source. This case report adds to this concept by describing a hypercalcemic patient whose increased PTH secretion was due to an ectopic neuroendocrine tumor in the neck.

Case Presentation: A 73-year-old female with history of recurrent primary hyperparathyroidism presented with nephrolithiasis, depression, osteopenia, and recent onset of fatigue. She previously had left thyroid lobectomy and parathyroid surgery at age 31. Workup revealed elevated levels of intact PTH (126 pg/ml) and calcium (10.6 mg/dl). There was no evidence of bone metastasis or increased PTHrP. Preoperative sestamibi scan and comprehensive neck ultrasonography failed to localize a source of the disease. Patient underwent bilateral neck exploration and completion thyroidectomy - dissection of the right central compartment identified a 1.5 cm lesion in the thyrothymic ligament behind the right sternoclavicular joint that was resected. The lesion weighed 520 mg. PTH levels dropped to 12 pg/ml (from baseline of 93 pg/ml) ten minutes after removal of the lesion. Frozen section analysis revealed evidence of a multicystic neuroendocrine tumor, with no parathyroid tissue. Pathological examination confirmed the presence of unencapsulated multicystic endocrine tissue mixed with fat. Foci of normal parathyroid tissue...
were identified within the lesion which exhibited diffuse cytoplasmic staining for parathyroid hormone and diffuse strong immunohistochemical cytoplasmic staining for chromogranin A. Postoperative course was uneventful. At six months follow up, patient continued to be eucalceemic with serum calcium levels of 8.0 mg/dl.

Discussion: Although they are rare, few cases of hypercalceemia due to ectopic intact PTH production have been reported. Strewler and colleagues described the first patient with hypercalceemia and elevated levels of intact PTH which originated from a neuroectodermal tumor in the neck. The remaining lesions which caused hypercalceemia associated with elevated levels of intact PTH were malignancies from solid organs.

Conclusion: These cases support the ectopic production of intact PTH by a neuroendocrine tumor and indicate the importance of being mindful of neoplastic cause of hyperparathyroidism.

Abstract #713
UNCOVERING THE BIZAARE: INSULINOMA PRESENTING AS BEHAVIORAL CHANGES
Zarah Lucas, MD, Aileen Cielo, MD,
Gayatri Jaiswal, MD

Objective: To present a rare but potentially reversible cause of neuropsychiatric symptoms.

Case Presentation: A 45-year-old Hispanic male with HIV, Hepatitis C, and personality disorder with history of polysubstance abuse presented with behavioral changes. In the past month, the patient had irritability and difficulty concentrating but denied any illicit drug use in the past 4 months. He also has been off his highly active antiretroviral therapy in the last month including lopinavir/ritonavir. On the day of admission, he woke up agitated, restless and combative requiring lorazepam and olanzapine at the emergency department. He was found to be hypoglycemic but no other episode of hypoglycemia was documented during his first admission. The patient continued to have hypoglycemic episodes at home, ranging from 20-50 mg/dL, which occurred both pre- and postprandial. He was readmitted for a 72-hour fast where his insulin and C-peptide levels were both elevated at 11.5 uIU/mL and 2.7 ng/mL, respectively, while his serum glucose was 25 mg/dL. Sulfonylurea intake was ruled out. Subsequently, the patient underwent an abdominal CT, which revealed a 1.9 cm vascular mass in the body of the pancreas. While awaiting surgery, the patient was given diazoxide, which prevented frequent hypoglycemic symptoms for the patient. Enucleation of the mass was initially attempted but the mass was very vascular, hence, a splenic-preserving distal pancreatectomy was done. Pathology confirmed that the mass was an insulinoma with no lymph node metastasis. Blood glucose monitoring postoperatively revealed no episodes of hypoglycemia and the patient had no recurrence of irritability and anxiety.

Discussion: Insulinoma is a rare neuroendocrine tumor with an incidence of 1-4 per 1,000,000 yearly. Patients can manifest in a variety of symptoms of hypoglycemia including erratic behavior. Among 42 insulinoma patients in one center (Ding et al. 2010), 25 patients with neuropsychiatric symptoms were initially misdiagnosed as having a neurological or psychiatric disorder. Despite the availability of reliable diagnostic tests such as the 72-hour fast, the diagnosis is often delayed. The patient’s intake of lopinavir could have contributed to the delay in diagnosis by attenuation of hypoglycemic symptoms, as lopinavir is known to produce insulin resistance. Fortunately for our patient, his insulinoma was localized easily and resected promptly.

Conclusion: A search for a metabolic cause of neurologic and psychiatric disorders should always be performed to prevent missing an important and potentially curable diagnosis such as insulinoma.

Abstract #714
“BAD MEDICINE”: IMPROPER PRESCRIBING PATTERNS AMONG WOMEN OF CHILDBEARING AGE IN THE MEDICINE & DIABETES CLINICS
Taral Mahendra Jobanputra, MD, Michael Carson, MD,
Sunil Asnani, MD

Objective: Evidence supports a reduction in neural tube defects when women take pre-natal (PNV) vitamins containing folic acid prior to conception. Additionally, first trimester exposure to angiotensin converting enzyme inhibitors (ACEI) has been associated with congenital anomalies. Angiotensin receptor blockers (ARB) are best avoided because of their similarity to ACEIs, and statins are pregnancy category X. Since 50% of pregnancies in the U.S. are unplanned, the PNV should be administered and high risk medications avoided in all young women, including diabetics and hypertensives, unless they use birth control or have received counseling about avoiding pregnancy. We hypothesized that these recommendations might not routinely be followed and conducted a chart review to assess the degree of adherence. We chose patients with diabetes (DM) and hypertension (HTN), expecting that many would be prescribed either an ACEI, ARB, or statin.

Methods: Retrospective chart review of women aged 18-45 with DM or HTN seen in our medicine or diabetic clinics in 2007-2008. Those with hysterectomy and/or
tubal ligation were excluded. Primary outcome ("Failure Rate") was the percentage of women treated with an ACEI, ARB, or statin or who did not receive a PNV, who also were a) not on adequate contraception or b) had not been counseled about avoiding pregnancy.

**Results:** 77 charts were reviewed. 17 from diabetes clinic and 36 from medical clinic were not excluded. Results: PNV Use: Medical 2/36 (6%) vs. Diabetes 4/17 (26%). ACEI Use: Medical 15/36 (42%) vs. Diabetic 6/17 (35%). ARB Use: Medical 2/36 (6%) vs. Diabetic 1/17 (6%). Statin Use: Medical 12/36 (33%) vs. Diabetic 6/17 (35%). Failure Rate: Medical 25/36 (69%) vs. Diabetic 8/17 (47%). The respective rates in medical vs. diabetes clinic were as follows: documentation of pregnancy counseling 7/36 patients vs. 6/17; oral contraceptive/IUD use 7/36 patients vs. 5/17. There were 214 medical and 39 diabetic clinic visits where physicians did not document a discussion regarding the medications and pregnancy.

**Conclusion:** Clinics managing young women at risk should liberally prescribe PNVs with folic acid to decrease the risk of neural tube defects, and we found that our clinics can improve in this regard. We found a huge opportunity to improve care in terms of counseling regarding pregnancy, contraception, and medication use in our clinic; and this may exist in other clinics as well. We will develop an educational program to improve prescribing practices in our clinic and reassess our performance.

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**Abstract #715**

**IGF-BP3 IS A GOOD PREDICTOR OF RESPONSE TO GH AND INCRELEX IN NON-GHD PATIENTS WITH LOW IGF1**

Oksana Lazareva, MD, Iuliana Predescu, MD, Shahid Malik, MD, Amrit Bhangoo, MD, Svetlana Ten, MD

**Objective:** To study relationship of baseline IGF-BP3 and IGF-1 levels and response to GH and IGF-1 therapy in patients with normal GH secretion and low IGF-1 level (-2 SDS).

**Methods:** 43 children age 9.07±2.75 years with Ht (-2.72) ± 0.7 SD and baseline IGF-1 level (-2.76) ±0.58 SD, who passed GHRH stimulation test (>15ng/ml) were included in the study. They were treated with GH (0.46±0.1 mg/kg/week). IGF-1 and IGF-BP3 levels were done at baseline, 3 and 6 months after GH initiation. Patients with poor response to GH, (growth velocity (GV) <-1 SD for 6 months, cut off point for the group <7 cm/year), were switched to IGF-1 therapy 0.24 mg/kg/day. GV onIncrelex after 6 months was analyzed. According to GV all patients were divided in three groups: Mild GHI - responders to GH (n=23, boys=14), Moderate GHI - non-responders to GH, responders to IGF-1 (n=14, boys=10), Severe GHI- non-responders to either GH/IGF-1. (n=6, boys=5)

**Results:** There were no difference in age, BW, Ht SDS and IGF-1 SD at baseline, delta IGFBP-3 after 6 months of GH treatment and GH peaks after GHRH between 3 groups. IGF-1 was lower in severe compared to mild group with borderline significance (p=0.05). IGF-1 SD on GH therapy was lower in severe group with borderline significance (p=0.07). Mild GHI group had higher IGBP3, Δ IGF-1, IGF-1 after GH treatment, Δ Ht SD compared to moderate and severe GHI. There was no difference between moderate and severe groups in IGF-1 SD on GH treatment and Δ IGF-1 after 6 months of GH treatment, while IGBP3 and Δ Ht SD were higher in moderate than in severe group. IGFBP-3 correlated with GV (r=0.47, p< 0.01), and inversely correlated with GH peak (r=-0.45, p=0.02). GV correlated with Δ IGF-1 SD (r=0.37, p=0.02).

**Conclusion:** This pilot data revealed in GHI patients with IGF-1 less than – 2 SD, IGBP3 is a good predictor of response to GH and Increlex therapy. Δ IGF-1 after GH treatment can differentiate between groups who can benefit from GH or Increlex treatment. In case of low IGFBP-3 and low Δ IGF-1 response on either therapy was poor.

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**Abstract #716**

**BODY FAT MASS, CIRCULATING 25 (OH) VITAMIN D CONCENTRATION, AND TESTOSTERONE LEVEL IN HEALTHY MEN: ARE THE ASSOCIATIONS REAL OR CASUAL?**

Donna Lawson, DO, Barbara Dunn, PA, Ali Iranmanesh, MD

**Objective:** A role of vit D in testosterone homeostasis has been recently reported. This assumption has been primarily based on association, rather than cause and effect. The present study was intended to explore a potential effect of vit D on circulating testosterone levels in healthy men across a wide range of age and body fat mass.

**Methods:** 59 healthy men in the age range 19-78 yrs and BMI 19-39 kg/m² were studied after an overnight fast. Blood was collected for measurement of 25 (OH) vit D (ng/mL), total and free testosterone (ng/dL), LH (µIU/mL), SHBG (nmol/L), and albumin (g/dL). Free (cFTe) and bioavailable (cBioTe) testosterone were calculated using the values for total testosterone, SHBG and albumin. Body fat was assessed by DXA. Fat mass index (FMI) was
calculated by dividing fat mass in kg by height in meter squared. Student’s t-test, simple and multiple regression statistics were used for data analysis.

**Results:** Of 59 men, 3 (5.1%), 7 (11.9%), and 26 (44%) had 25 (OH) vit D levels of =<10, =<20, and =<30, respectively. Subjects were stratified into 2 groups according to vit D levels, with a cut-off value of 30 ng/mL. While comparable in age, the group with 25 (OH) vit D of <30 had higher FMI (7±0.5 v 4.8±0.4; P=0.001), with decreased total testosterone (439±32 v 519±25; P=0.055) and SHBG (26.4±2.0 v 36.5±2.4; P=0.003). Serum concentrations of free testosterone by equilibrium dialysis, calculated free and bioavailable testosterone and LH were not significantly different in the 2 groups. Serum 25 (OH) vit D concentration was negatively correlated with FMI (R/P:-0.29/0.025) and positively associated with total testosterone (R/P:0.30/0.02) and SHBG (R/P:0.33/0.02). There was no correlation between vit D levels and either measured or calculated free testosterone.

**Discussion/Conclusion:** The results indicate: (1) high prevalence of vit D deficiency in healthy men, which does not appear to be age-dependent; (2) increased fat mass with decreased 25 (OH) vit D. While low levels of vit D could be postulated as the mechanism for higher fat mass, the latter may as well promote low vit D levels via enhancing its adipose tissue storage; (3) decreased total but not free testosterone associated with decreased vit D levels. These results along with decreased SHBG argue against a role of vit D in testosterone homeostasis. The association of lower total testosterone and vit D is most probably due to higher fat mass and related decrements in SHBG.

**Abstract #717**

**PANCYTOPENIA DUE TO BONE MARROW INFILTRATION FROM NEUROENDOCRINE TUMORS: BLEEDING DIATHESIS AT PRESENTATION**

Mohammed Ahmed, MD, FACP, FACE, M Al-Muqhim, MD, R. Al-Nounou, MD

**Objective:** To draw attention that bleeding diathesis and bone marrow infiltration causing pancytopenia can be a presenting feature of Neuroendocrine tumors. Both patients had NET metastatic to bone marrow, liver, and bones. Patient A had sporadic medullary thyroid cancer. Patient B had malignant pheochromocytoma. Patient A was a 35 year old female who presented with persistent vaginal bleeding, epistaxis, hemoptysis, and diffuse ecchymosis of 3 weeks duration. CBC: WBC 3.35x10^9/L (Ref.Range: 4-11 X10^9/L), RBC 3.14x10^12/L (Ref.Range: 4-5.20 X10^12/L), Hb 79 g/L (RR: 118-148g/L), platelets 3x10^9 to 36x10^9/L (RR: 140-350 X10^9/L), She had a 2x4 cm hard nodule in the left thyroid lobe that had been present for 5 months, and hepatomegaly. Also, she had slow disseminated intravascular coagulopathy, and abnormal PT, possibly related to liver involvement and/or nutritional deficiency of vitamin K. FNA Bx thyroid nodule: Clusters of pleomorphic cells, serum calcitonin 13,436 pg/ml (RR: <8 pg/ml), CEA 1416 ug/L (RR: up to 3.4 ug/L). Bone Marrow Bx: Diffuse and heavy infiltration by metastatic cells, positive for Calcitonin, CEA, cytokeratin, synaptophysin, and chromogranin but negative for thyroglobulin. PET Scan: Wide spread bone marrow involvement, infiltrative hepatomegaly, focal uptake left lobe thyroid. Patient B was a 72-year-old lady who had undergone removal of a left sided pheochromocytoma 10 years earlier. Two months prior to the presentation she underwent hemicolectomy for colonic metastases of the pheochromocytoma and developed generalized ecchymosis. CBC: WBC 3.7x10^9/L, Hb 70 g, platelets 36x10^9/L. Bone Marrow Bx: Heavy and diffuse infiltration by a malignant tumor. Immunostains were positive for synaptophysin, chromogranin, and PGP 9.5 and negative for cytokeratin, S100 & calcitonin, consistent with pheochromocytoma involving the bone marrow.

**Discussion:** Both patients had NET metastatic to bone marrow, liver, and bones. In addition, patient A. had bilateral pulmonary and mediastinal involvement. Patient B. had colonic metastases. Bone marrow infiltration by NET causing pancytopenia with bleeding diathesis secondary to severe thrombocytopenia is distinctly unusual and to our knowledge has not been reported previously.

**Conclusion:** These cases unfold unusual and heretofore unrecognized features in the natural history of disseminated NET. Diagnosis of bone marrow infiltration by NET emphasizes early and effective recognition, surveillance and therapeutic intervention to prevent devastating complications and improvement of quality of life.
Abstract #718

SHORT-TERM BALNEOTHERAPY IS ASSOCIATED WITH CHANGES IN SALIVARY CORTISOL LEVELS

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Objective: Since ancient times, physicians have speculated that balneotherapy (therapeutic bathing in medicinal and thermal springs) has a stress-relieving effect. While bathers usually experience a sense of well-being and relaxation during balneotherapy, the stress-relieving effects of balneotherapy have not yet been scientifically established. Therefore, the aim of this study was to evaluate the stress-relieving effects of a short term (twenty-five minutes) balneotherapy in a controlled trial. To evaluate the stress-relieving effects of balneotherapy by measuring salivary cortisol as a sensitive stress marker. Additionally we assessed two control groups; one which employed a well established technique for stress relief (muscle relaxation), and one which was simply asked to rest.

Methods: 49 healthy probands were randomized into three intervention groups. The interventions were balneotherapy, resting, or progressive muscle relaxation (PMR). Group one performed bathing in a thermal spring (Bad Loipersdorf, Styria Thermal Region, Province of Styria, Austria), group two (control group 1) relaxed in deckchairs in order to rest, and group three (control group 2) performed PMR. In each group the intervention lasted for 25 minutes. Saliva samples were collected immediately after getting up in the morning, before and after intervention, and participants rated their subjective relaxation level on a quantitative scale. Salivary cortisol was determined by enzyme-linked immunosorbent assay. Additionally, the following psychological tests were employed: Perceived Stress Scale, Recovery-Stress Questionnaire, Symptom list. One-way ANOVAs for repeated measures were performed to detect changes in salivary cortisol and subjective stress ratings between groups.

Results: In all three groups, saliva cortisol decreased (F=23.532, p<0.001) and subjective relaxation ratings increased (F=132.178, p<0.001) after intervention. Interestingly, the increase of the study participants subjective level of relaxation was significantly higher in the balneotherapy group as compared to control groups (F=5.216, p=0.009).

Conclusion: These findings suggest both an objective and subjective stress-relieving effect associated with short-term balneotherapy, with respect to changes in saliva cortisol levels other stress reduction interventions seem to produce similar effects but may not be experienced as similar beneficial as balneotherapy.

Abstract #719

A CASE OF MULTIPLE ENDOCRINE NEOPLASIA TYPE 1 (MEN1) WITH A NOVEL MUTATION

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Objective: To present a case of MEN1 with a novel mutation.

Case Presentation: A 54-year-old caucasian male presents with a clinical history of MEN1 status post pituitary adenoma resection, bilateral inferior parathyroid gland resections, and multifocal gastrinoma with Zollinger-Ellison syndrome, inoperable due to metastases to celiac lymph nodes. He presented to the emergency room following a period of noncompliance with nausea, vomiting, diarrhea, abdominal pain, sore throat, and cough. Ionized calcium = 1.44 mmol/L and intact PTH =220 pg/mL. Parathyroid scan showed bilateral superior parathyroid adenomas. MRI revealed a small residual non-functional tumor in the right paramedian aspect of the sella not threatening optic chiasm or invading cavernous sinus. Endoscopic ultrasound showed pancreatic multifocal gastrinoma with metastasis to a celiac node with marked gastrin elevations. He was prescribed high dose proton pump inhibitors and octreotide and was discharged in stable condition. His genetic testing revealed a unique splice site mutation in the MEN1 gene. Subsequently he had removal of his remaining two parathyroid glands with autotransplantation. His estranged brother has had recurrent parathyroid hyperplasia and has subsequently tested positive for this same mutation. The proband’s daughter is planned for genetic testing.

Discussion: MEN I, with a prevalence of 2 per 100,000, is clinically defined as the presence of two of three main MEN1 tumor types.1 Primary hyperparathyroidism (> 90%), pituitary tumors (10-20%), and enteropancreatic tumors (60-70%). The MEN1 gene, on the long arm of chromosome 11 (11 q13), is inherited autosomal dominantly. Our patient’s mutation is, to our knowledge, a novel mutation, resulting from a nucleotide substitution at the 3 position of Intron No. 3. (IVS3+3 A>T or c654+3 A>G). A distinct mutation at the same nucleotide (IVS3+3 A>T) has been reported previously in association with MEN12 in a Japanese kindred.

Conclusion: This case illustrates a severe clinical presentation associated with a novel mutation of the autosomal dominant MEN1 gene. Genetic counseling and screening has helped identify family members at risk prior to the clinical development of inoperable gastrinomas.
Abstract #720

RESOLUTION OF HYPERINSULINEMIC HYPOGLYCEMIA AFTER SURGICAL CORRECTION OF LONG STANDING GASTRIC OUTLET OBSTRUCTION

Liviu G Danescu, MD, Gayathri Sathiyamoorthy, MD, Barbara Mols-Kowalczevski, MD

**Objective**: To describe the first case of nesidioblastosis in a male with longstanding gastric outlet obstruction that resolved after gastrojejunostomy.

**Case Presentation**: A 65-year-old male with severe gastric outlet obstruction for 14 years, requiring pureed diet at home, was found unconscious with a glucose level of 23 mg/dl. He did not have diabetes and was not taking hypoglycemic agents (negative results for sulfonylurea drugs and exogenous insulin). His history included peptic ulcer disease, schizophrenia, chronic pain syndrome, and gout. Liver and kidney function were normal. He had persistent hypoglycemia in the hospital despite receiving continuous intravenous D10 and a pureed diet. Normoglycemia was achieved with diazoxide and 24 hour continuous total parental nutrition (TPN). A 72 hour fast and glucagon stimulation test confirmed hyperinsulinemic hypoglycemia (glucose 41 mg/dl, insulin 6.8 uU/ml, c-peptide 3.4 nmol/l, proinsulin 4.5 pmol/l, beta-hydroxybutyrate 0.4 mmol/l). CT scan, MRI, and endoscopic ultrasound failed to identify a pancreatic mass. Mesenteric angiogram delineated a possible mass in the head of the pancreas but results from a selective calcium stimulation test suggested a diffuse process, with a 4 to 10 fold hyperinsulinemic response [increase to 98.5, 48.8 and 71.7 uU/ml] in the superior mesenteric, gastroduodenal and splenic arteries, respectively. Retrocolic gastrojejunostomy was performed, and a 1.3 x 1 cm nodule in the body of the pancreas was resected with pathology consistent with nesidioblastosis. Post surgery, TPN and diazoxide were discontinued and hypoglycemia did not recur. He was normoglycemic at 2 month follow-up.

**Discussion**: Endocrinologists have become increasingly aware of reports of hyperinsulinemic hypoglycemia after bariatric surgery. To our knowledge, this is the first report of a patient with long-standing gastric outlet obstruction who developed hyperinsulinemic hypoglycemia with pathologically confirmed nesidioblastosis. We theorize that our patient’s long-standing peptic stricture led to chronic stimulation of L cells and the development of islet hyperplasia. Although we cannot exclude the possibility that resection of the nodule played a role, surgical correction of the obstruction may have reversed hormonal abnormalities that caused pancreatic hyperplasia and hypoglycemia.

**Conclusion**: We describe hyperinsulinemic hypoglycemia in a patient with chronic gastric outlet obstruction. His hypoglycemia resolved after surgical reversal. Better understanding of the pathophysiology of this condition may provide further insights into the rare development of hypoglycemia after gastric bypass.

Abstract #721

REFRACTORY HYPOKALEMIA AS A MANIFESTATION OF ECTOPIC ACTH SYNDROME

Sandra Barrow, MD, Harsha Karanshi, MD, Dale Hamilton, MD, Marietta Clewing, MD

**Background/Objective**: A 75-year-old woman with past medical history of hypertension and diabetes was admitted for bilateral lower extremity edema, muscle weakness and right leg cellulitis for 2 weeks. On physical exam, B.P. of 170/100 mm Hg, 4+ bilateral lower extremity pitting edema and right leg cellulitis were noted with the remainder of the exam being normal.

**Case Presentation**: Laboratory investigations showed serum potassium -3.2 mEq/L, serum bicarbonate-31 mEq/L and plasma glucose -411 mg/dL. Urine biochemistry showed urinary potassium-70 mEq/L and transtubular potassium gradient-11.9. On review of records we found that the patient’s blood pressure and diabetes were well controlled in the past. Uncontrolled hypertension, persistent hypokalemia despite daily replacement, renal potassium wasting and metabolic alkalosis lead to the suspicion of mineralocorticoid excess. Plasma renin and aldosterone levels were low. Due to worsening glycemic control and the above metabolic abnormalities, we tested for ACTH – 216 pg/mL (nl. 6-58), cortisol – 190 µg/dL (nl. 10-25) and 24 hr urinary free cortisol - 7410 µg/d (nl. <=45), all of which were very elevated and consistent with ACTH dependent Cushing’s syndrome. We were unable to obtain an MRI due to previous coiling of cerebral aneurysm. A CT scan of the chest obtained due to suspected lung nodule on chest X-ray showed a 1.6 x 2.2 cm nodule in the right lower lobe in association with extensive mediastinum lymphadenopathy. On PET scan these areas showed significant uptake and were highly suspicious for malignancy. Mediastinoscopy and lymph node biopsy were performed showing metastatic small cell carcinoma with positive immunostaining for ACTH. A diagnosis of ectopic ACTH syndrome associated with small cell lung cancer was made. Ketoconazole was used for control of hypercortisolism. Hypokalemia was adequately controlled by spironolactone in addition to potassium supplementation. Chemotherapy with etoposide and carboplatin was started. Stable potassium...
levels, improving blood pressure and glycemic control necessitated discontinuation of spironolactone, ketoconazole and potassium after the first round of chemotherapy.

**Conclusion:** In this case, workup for persistent hypokalemia led to the diagnosis of lung cancer. Hypokalemia is due to the state of functional mineralocorticoid excess from hypercortisolemia causing saturation of the 11-β hydroxysteroid-dehydrogenase enzyme (inactivates cortisol at the renal tubule) thereby allowing access of the excess intact cortisol to the mineralocorticoid receptor. Physicians should be aware of ectopic ACTH syndrome causing hypokalemia in lung cancer patients.

**Abstract #722**

**GABAPENTIN INDUCED HYPOGLYCEMIA IN A HEMODIALYSIS PATIENT**

Sruti Chandrasekaran, MBBS, William Valente, MD

**Objective:** Hypoglycemia is common in end stage renal disease (ESRD) patients due to defective gluconeogenesis and decreased clearance of insulin. We report a case of drug induced hypoglycemia in an ESRD patient on hemodialysis (HD) due to gabapentin.

**Case Presentation:** 42-year-old African American male was transferred to our center due to persistently low blood glucose requiring dextrose 10% water (D10) drip. He presented to a local hospital 3 days prior to the transfer due to acute onset of shortness of breath and had emergent HD for acute pulmonary edema. Incidentally his blood glucose was (BG) of 36 mg/dl. He was given two ampoules of D50 and was started on D10. His capillary blood glucose (CBG) ranged 60-70 mg/dl on a D10 drip for three days. A CT scan done in the local hospital was negative for insulinoma. His past medical history included ESRD on HD, hypertension, secondary hyperparathyroidism, hepatitis C, peripheral neuropathy, dilated cardiomyopathy and status post two failed renal transplants. His medications included cinacalcet, sevelamer, renal vitamin, lisinopril, gabapentin and carvedilol. He was taking 3000mg of gabapentin for the past two months for itching. His physical examination was unremarkable. His laboratory findings showed Na 133 mmol/L (nl 136-145), K 4-6 (nl 3.5-5.1), BUN 85mg/dl (nl 6-20), creatinine 11.5 (nl:0.6-1.25), AST 38U/L (nl 10-41) ALT 27 U/L (nl 17-63), albumin 3.8g/dl (nl 3.5-5.2). Insulin levels were 10 uU/mL (nl 0-24.9) and C peptide 15.8ng/ml (nl 1.1-4.1) with a BG of 82mg/dl. Upon his transfer, the D10 drip was stopped, gabapentin was discontinued and he was fasted to induce hypoglycemia. Insulin levels were 1.2-2.0, C peptide 3-4.4, proinsulin 3.2-4.1pmol/L (nl 0-10), AM cortisol 10.4 mcg/dL (nl 4.2-38.4). After 54 hour of fasting the patient requested to discontinue the fast. He did not have symptomatic hypoglycemia and his CBGs ranged between 70-80mg/dl. He was discharged home in a stable condition. He did not have any hypoglycemic episodes following discharge.

**Discussion:** Drug induced hypoglycemia is the most common cause of hypoglycemia in ESRD patient. The other causes include sepsis, chronic malnutrition, alcohol abuse and other endocrine disorders like adrenal insufficiency. Gabapentin as an inciting agent has been described in a previous case report. In animal studies gabapentin has shown to cause proliferation of pancreatic acinar cells.

**Conclusion:** A detailed review of medication history is very important in hypoglycemic patients as the withdrawal of medication can dramatically improve hypoglycemia.

**Abstract #723**

**ESTROGEN-DEPENDENT INHIBITION OF HYPERGLYCEMIA-INDUCED ENDOPLASMIC RETICULUM STRESS AND SUPEROXIDE GENERATION IN ENDOTHELIAL CELLS**

Rosalyn Alcalde, MD, Emad Naem, MD, Prafull Raheja, MD, Mae Sheikh-Ali, MD, Arshag D. Mooradian, MD, Michael J. Haas, PhD

**Objective:** Increased oxidative stress and endoplasmic reticulum stress (ER stress) have been implicated in atherosclerosis. Estrogens have potent antioxidant activity but their effect on ER stress has not been well studied. Therefore, we studied the effects of estradiol and related sex steroids on dextrose-induced ER stress and superoxide (SO) generation in human umbilical vein endothelial cells (HUVEC).

**Methods:** Superoxide levels and ER stress were measured by hydroethidine binding and endoplasmic reticulum stress-sensitive temperature resistant alkaline phosphatase (ES-TRAP) assay, respectively. JNK activity and GRP75 expression were measured by Western blot.

**Results:** In HUVEC treated with physiological (5.5 mM) or supra-physiological (27.5 mM) dextrose concentrations, supra-physiological dextrose concentrations increased ER stress and SO generation. However in the presence of estrogen (E) or testosterone (T), ER stress and SO generation were significantly reduced. In contrast to T-treated cells, dihydrotestosterone (DHT) and 5-methyltestosterone (5-meT) were ineffective at alleviating ER stress or SO generation. When HUVEC were treated with T and the aromatase inhibitor 4-hydroxy-4-androstene-3, 17-dione (F), T was no longer effective at
suppressing ER stress or inhibiting SO generation. Similar results were obtained in HepG2 liver cells. Western blot analyses of the changes in GRP75 expression and JNK activity, markers for ER stress, support the results obtained in the ES-TRAP assay.

**Discussion:** Oxidative stress and endoplasmic reticulum stress are implicated in the pathophysiology of endothelial dysfunction in cardiovascular disease. To determine the mechanism by which this happens, further studies are needed to measure estrogen-dependent changes in cell signaling and gene expression that give rise to the phenotypes we observed.

**Conclusion:** These results indicate that hyperglycemia-induced ER stress and SO generation are reversed by E and T; however the latter requires aromatase-dependent conversion to E.

**Abstract #724**

**A RARE TRIAD OF LATE ONSET TYPE 1 DIABETES MELLITUS, CEREBELLAR ATAXIA, AND POSITIVE GAD ANTIBODIES**

Netee Papneja, MB, BCH, BAO (HONS), Derek Haaland, MD, Ally Prebani, MD, Michael Francis Mazurek, MD, Judah A. Denburg, MD

**Objective:** To describe the triad of progressive cerebellar ataxia, late onset Type 1 Diabetes Mellitus (DM 1) and positive anti-glutamic acid decarboxylase (GAD) antibodies and recognize that timely diagnosis and treatment of the triad is important.

**Case Presentation:** A 58-year-old man was presented in 2008 with progressive dysarthria, dysphagia, and ataxia over six years. Neurological examination revealed diplopia, dysmetria, dysdiadochokinesis, poor heel to shin testing, and an ataxic gait. Of note, eight months after neurologic symptom onset, he was diagnosed with late onset DM I at age 53. Extensive investigations at initial presentation revealed no underlying etiology. Further testing in 2008 with magnetic resonance imaging showed cerebellar atrophy and immunological screening was positive for anti glutamic acid decarboxylase antibodies (GAD-Ab), elevated at 170.4 U/ml (normal <1), and thyroperoxidase antibodies high at 90 KIU/L (normal <35). Features were consistent with the syndrome of autoimmune progressive cerebellar ataxia in association with late-onset DM1 and positive anti-GAD antibodies. Our patient was treated with intravenous immunoglobulin (IVIG) 2 g/kg monthly for six months which resulted in minimal improvement likely due to delay in diagnosis of his condition (approximately seven years) that led to significant cerebellar atrophy.

**Discussion:** The pathogenic role of autoimmunity and GAD-Ab in cerebellar ataxia remains unclear but there are a few theories published that have attempted to explain why the GAD-Ab is not merely a reflection of the presence of DM 1 or polyendocrine autoimmunity observed in these patients. We have documented all English-language studies of cerebellar ataxia associated with GAD-Ab that have reported various modalities of pharmacological treatment effect for the condition. Unfortunately, there have not been any controlled studies so far and they are definitely warranted in these patients. Based on the current evidence, patients with GAD-Ab positive cerebellar ataxia should be treated either with high-dose corticosteroids and immunosuppressants or IVIg depending upon patients’ preferences and co morbidities.

**Conclusion:** Autoimmune cerebellar ataxia with GAD-Ab is a rare condition that endocrinologists should be aware as it typically affects individuals with late onset DM1 or other autoimmune polyendocrinopathies given possibility of therapeutic benefit with immunotherapy or immunosuppressants, before irreversible Purkinje cell injury occurs.

**Abstract #725**

**PERSONAL HEALTH RECORD: AN EFFECTIVE TOOL IN DIABETES MANAGEMENT FOR MINORITY POPULATIONS**

Abdelwahab Alamin Suliman, MD, Gail Nunlee-Bland, MD, Wolali Odonkor, MD, Vijaya Ganta, MD, Rabia Cherqaoui, MD, Tadele Desalew, MD, Theresa Fynn, MD, Samuel Mortoti, MD, John Kwagyan, PhD

**Objective:** Today in the USA, diabetes is an epidemic in minority populations. Subsequent to the number of clinicians required to effectively treat patients with diabetes; health records are often fragmented and incomplete. This is especially true in underserved communities. The objective of this study is to determine if use of personal health record (PHR) in a predominantly African American population, attending an urban diabetes clinic, will result in lowering of their hemoglobin A1c (HbA1c).

**Methods:** Electronic medical records of 134 patients (18-80 years of age ), between July 2008 to October 2010, from the Diabetes Treatment Center at Howard University Hospital were reviewed. Patients who agreed to be followed with their PHR and had at least one HbA1c were included in this review. These patients were compared to a group who elected not to enroll in the PHR program over the same time period. The two groups received progressive treatment in an attempt to reach target A1c < 7%. Comparisons of their HbA1c before and after use
of PHR, computer use, internet access and body mass index (BMI) were reviewed. Baseline characteristics were compared between the PHR group and the non-PHR group using the chi-square test for categorical variables and independent sample t-test for continuous variables.

**Results:** Of the 134 patients included in this review, seventy seven patients (51 females/26 males) agreed to be followed with their PHR and 57 patients (36 females/21 males) did not. The average age for the PHR group was 50.8 +/- 17.1 years and 58.7 +/- 14.3 years in the non-PHR group (P = 0.0005). The BMI was similar for both groups with a BMI of 32.3 +/- 8.1 for the PHR group and 33.1 +/- 9.5 for the non-PHR group (P=0.6). The PHR group demonstrated a significant decrement in HBA1c (-0.73%) as compared to the non-PHR group which showed a worsening of diabetes control over the follow up period with mean increment in HBA1c of 0.26% (p=0.009). There was a statistically significant difference between the PHR and non-PHR groups with regard to computer access (76.3% and 40.4% respectively, p<0.001) and internet access (78.9% and 35.1% respectively, p<0.001).

**Conclusion:** PHR and other technologies need to be explored to empower patients to improve self-care and personal health management. This review suggests the benefit of PHR as a useful adjunct tool to improve diabetes outcomes in an urban minority population with diabetes.

**Abstract #726**

**PREVALENCE AND CHARACTERISTICS OF METABOLIC SYNDROME IN PATIENTS ADMITTED TO AN INPATIENT PSYCHIATRY UNIT**

Yanal Masannat, MBBS, Tamer Hassan, MD, Samia Kanooz, MD, TW Gress, MD, MPH, Abid Yaqub, MD, FACE, FACP

**Objective:** To identify the prevalence of metabolic syndrome (MS) in patients admitted to an inpatient psychiatry unit and to study the relationship between MS and various clinical, socioeconomic and life style variables in these patients.

**Methods:** We retrospectively collected data from 200 charts of patients admitted consecutively to psychiatry unit at St Mary Medical Center at Huntington, West Virginia between July-October 2009 with DSM IV defined psychiatry disorders. Patients were considered to have MS if they met any three of the five ATP III defined criteria. We used BMI criteria of >30 to diagnose obesity in the place of waist circumference used in ATP-III criteria as the latter was not available for most of patients. We excluded patients with incomplete medical records. The total number of evaluable patients was 114.

**Results:** Mean age was 46 years. 60% were females. Of the 114 evaluable patients, 50 patients (43.86%) met the ATP III criteria for MS. Of those with MS 43 (86%) were obese. Of the MS group at least 58% had low HDL, 56% has high triglyceride and 54% had high fasting blood sugar. We found that patients with MS were more likely to be on benzo diazepines (p=0.033) and 1st generation antipsychotic medications (p=0.01) as compared to those without MS. We did not find any significant correlation between prevalence of MS and patients socioeconomic status and life style variables.

**Discussion:** We found that prevalence of MS in our patient group was 43.86% as compared to 34.5% of general US adult population as reported in NHANES 1999-2002 database utilizing the ATP-III criteria. Our finding of higher prevalence of MS in the inpatients in a psychiatry unit is in line with previously published studies. The higher prevalence of MS in psychiatry patients could be related to multiple physiological factors or pharmacological effects of medications. Our observation shows an association between benzodiazepines and first generation antipsychotics with MS.

**Conclusion:** We found a high prevalence of MS in patients admitted to our psychiatric inpatient unit. We also found a significant correlation between MS and use of benzodiazepines and 1st generation antipsychotic medications. While second generation antipsychotic medications, typically clozapine, have been implicated with MS, Benzodiazepines and first generation antipsychotic medications have not been previously reported to be associated with MS. Further larger studies are needed to study this association carefully.

**Abstract #727**

**PET SCANS – NOT ALWAYS WHAT THEY SEEM**

Megan Krause, MD, Diana Dean, MD

**Objective:** To describe a rare cause of positive PET scan findings, cosmetic hyaluronate injections, to broaden the differential diagnosis of FDG uptake.

**Case Presentation:** A 50-year-old woman presented for a second opinion for chronic symptoms of fatigue and night sweats. As part of her local evaluation, she was found to have an elevated CA125. Her past medical history was significant for transverse myelitis two years earlier. For evaluation of transverse myelitis, she underwent MRI imaging of the cervical spine which revealed an incidental thyroid nodule, 1.5 cm in diameter. Family history included a sister with Hashimoto’s thyroiditis but no history of thyroid cancer. Her father had multiple myeloma and cousin had non Hodgkin’s lymphoma. On examination, the thyroid nodule was difficult to palpate...
with the overall gland 15 g in size. Further, her cardiac, pulmonary, abdominal, and skin examination were normal. There was no evidence of lymphadenopathy. She had mild hyperreflexia in the knees bilaterally. For evaluation of the thyroid nodule, she had normal TSH and no TPO antibodies. Since this nodule had not previously been biopsied, she underwent fine needle aspiration which was consistent with benign pathology. Due to her constellation of constitutional symptoms and elevated CA125, she underwent a positron emission tomography (PET) scan. This revealed evidence of dense calcifications in the subcutaneous tissues of the bilateral face anterolateral to the maxillary teeth with associated likely inflammatory FDG uptake. Based on these findings, sarcoidosis as an explanation was considered. However, this was in the setting of normal calcium and angiotensin converting enzyme (ACE) level. Further, she had no radiologic support for a diagnosis of sarcoidosis. On further review with the patient, she described Restalyne® injections, hyaluronate derivatives intended as a mid to deep intradermal injection for wrinkles, in this location three months earlier.

Discussion: PET scans are an extremely helpful tool for evaluating patients, but the clinical context must also be kept in mind to interpret results successfully. There are limited reports of hyaluronate derivative injections leading to positive PET results. This case serves as an example of, at times, the difficulty interpreting PET results. The variety of conditions leading to positive PET scans is vast and range from granulomatous, infectious, inflammatory, and malignant.

Conclusion: While PET scans serve as an invaluable resource for occult malignancy, interpretation of PET scan findings must be taken in the context of the clinical condition.

Abstract #728

MULTIPLE GASTRIC CARCINOIDS AND PRIMARY HYPERPARATHYROIDISM: MORE EVIDENCE FOR A DISTINCT ASSOCIATION

Rafael Gonzalez-Rosario, MD, Meliza Martinez, MD, Myriam Allende, MD, Margarita Ramirez, MD, Marielba Agosto, MD

Objective: To report a case of a woman with primary hyperparathyroidism and multiple gastric carcinoid tumors.

Case Presentation: A 60-year-old woman with history of pernicious anemia (PA) was referred to our endocrinology clinics after being found with hypercalcemia and inappropriately elevated Parathyroid Hormone (PTH) levels. She presented with abdominal pain, nausea, and constipation, without vomiting or diarrhea. There was no history of bone fracture, nephrolithiasis, or renal insufficiency. A parathyroid scan showed a left parathyroid adenoma. She underwent left parathyroid adenoma resection. Pathology was consistent with parathyroid adenoma. Patient continued having epigastric discomfort, heart burn, and increased bloating for which an upper endoscopy was performed and three sessile polyps (0.6-0.8 cm) were found on lesser and greater curvatures of the stomach, on a background of non-erosive gastritis. No peptic ulcers were found. Pathologic evaluation was consistent with chronic gastritis (CG) and special stain was positive for Helicobacter pylori. Examination of gastric polyps was consistent with gastric carcinoid (GC).

Upper endoscopy was repeated and the three gastric polyps were completely removed. All three biopsies showed well differentiated endocrine GCs. Laboratory work up showed stable calcium, phosphate, urea and creatinine, normal prolactin levels, and mild hypergastrinemia. Abdominal computed tomography showed no pancreatic or duodenal lesions. A pituitary MRI was negative for pituitary pathology. Patient has no family history of MEN 1, hypercalcemia or pituitary tumor.

Discussion: The increasing number or reports of GCs coexisting with primary hyperparathyroidism (PHPT) has raised the question if such cases might represent a new association. In the past, these cases were characterized as “atypical” or “incomplete” MEN 1. However, there are many cases in which the diagnosis of MEN 1 can not be substantiated. There are many theories about possible pathologic mechanisms, including the actions of gastrin, β-catenin, H. pylori, and histamine. However, the etiology is not clear yet. Our patient’s history of GC, PHPT, and PA is consistent with this syndrome which is seen mostly, but not exclusively, in the clinical setting of CG and PA. This patient had no clinical evidence of MEN 1.

Conclusion: Gastric carcinoids can occur in association with primary hyperparathyroidism as part of a distinct syndrome. This emphasizes the need for awareness on part of the treating physician to recognize the possibility of this syndrome and screen accordingly.

Abstract #729

A CASE OF METASTATIC SMALL BOWEL CARCINOID TUMOR

Abdelwahab Alamin Suliman, MD, Rabia Cherqaoui, MD, Gail Nunlee-Bland, MD, Wolali Odonkor, MD, Vijaya Ganta, MD

Background/Objective: Carcinoid tumors are relatively rare tumors which have been thought to be mostly benign. However, it has been shown that these...
neoplasms often exhibit a malignant clinical course. The size of the small bowel carcinoids is an unreliable predictor of metastatic potential. The aim of this presentation is to highlight this relatively rare disease and the potential of inducing typical carcinoid syndrome without liver metastasis.

**Case Presentation:** A 51-year-old African American man was evaluated for chronic diarrhea and weight loss. He described his diarrhea as non-bloody watery, occurring about five to six times a day associated with generalized abdominal discomfort and a 31-lbs weight loss over 6 months. He also admitted to frequent episodes of facial flushing exacerbated by emotions over the same period. Physical examination was unremarkable except for bi-temporal muscle wasting. Stool osmolar gap was consistent with a secretory diarrhea. TSH, serum VIP, and gastrin were normal. 24-hour urine 5-Hydroxyindoleacetic acid (5-HIAA) was 15.8 mg/24h (0-14.9). Plasma chromogranin A was 23 nmol/L (0-5 nmol/L). Abdominal CT scan showed two mesenteric spiculated masses as well as extensive retroperitoneal and mesenteric lymphadenopathy but without evidence of liver metastasis. Indium 111–labeled octreotide scintigraphy was positive for lymph node metastases. Attempt at tumor debulking was unsuccessful due to the intense desmoplastic reaction. Pathological examination was consistent with metastatic neuroendocrine tumor. Staining was positive for synaptophysin and chromogranin. Patient started on octreotide monthly depot injections for symptomatic relief.

**Discussion:** Typically, carcinoid syndrome occurs when hepatic spread results in hormonally active tumor products exceeding the hepatic capacity for degradation. Extensive retroperitoneal carcinoid lymph node metastases can result in carcinoid syndrome via thoracic duct and retroperitoneal venous collaterals drainage bypassing the liver. Treatment of patients with disseminated midgut carcinoid tumors is primarily palliative and aimed at ameliorating symptoms. Treatment with long-acting somatostatin analogues has increased quality of life and life expectancy in patients with metastatic disease. 5 year survival rate is 44.1% for patients with disseminated midgut carcinoid tumors.

**Conclusion:** Functional neuroendocrine neoplasms are a rare cause of chronic diarrhea. Patient with metastatic disease and significant tumor burden can develop carcinoid syndrome even without liver metastasis.

### Abstract #730

**AUTOIMMUNE POLYGLANDULAR SYNDROME TYPE I IN A PATIENT WITH LONG-STANDING HYPOPARATHYROIDISM**

Soo Shin Rhee, MD

**Objective:** To report a case of Autoimmune Polyglandular Syndrome (APS) Type I diagnosed after presentation for new onset type 1 diabetes mellitus (Type 1DM) and primary adrenal insufficiency.

**Case Presentation:** A 29-year-old man with history of hypoparathyroidism and cutaneous fungal disease since infancy presented with several months of generalized weakness and fatigue, salt craving, polydypsia, sexual dysfunction, and unintentional weight loss. Physical examination was notable for hypotension, onychomycosis, and hyperpigmentation of palmar creases and oral mucosa. Initial laboratory data revealed significant hyponatremia and hyperglycemia. Diagnosis of autoimmune primary adrenal insufficiency was made with low a.m. serum cortisol, elevated a.m. serum ACTH, failure to stimulate appropriately after cosyntropin administration, and positive anti-adrenal antibodies. Diagnosis of Type 1DM was confirmed with positive glutamic acid decarboxylase antibodies and islet cell antibodies. History of sexual dysfunction led to the diagnosis of primary hypogonadism. Additional testing revealed positive antithyroid peroxidase antibodies and TSH 4.99 uIU/mL. This constellation of endocrine disorders led to the diagnosis of APS Type I with associated Type 1DM, primary hypogonadism, and autoimmune thyroid disease.

**Discussion:** APS Type I is a monogenic disorder caused by a variety of mutations in the autoimmune regulator gene (AIRE), most of which are inherited in an autosomal recessive manner. APS Type I is defined by the presence of at least 2 of the following: hypoparathyroidism, chronic mucocutaneous candidiasis, and/or autoimmune primary adrenal insufficiency. Associated autoimmune disorders include primary hypogonadism, primary hypothyroidism, Type 1DM, celiac disease, and pernicious anemia. A high clinical suspicion for the development of autoimmune disease needs to be maintained in patients with APS Type I and their first-degree relatives. Recommendations are to screen for autoantibodies in these patients, and to conduct functional testing if autoantibodies are present without associated clinical disease. In this patient, the presence of hypoparathyroidism and cutaneous fungal disease since infancy were suggestive of APS Type I. Screening and functional testing could have led to earlier detection and treatment of adrenal insufficiency, Type 1DM, and hypogonadism.
Conclusion: Early detection and treatment of autoimmune disorders associated with APS Type 1 results in less morbidity and in some cases, mortality. If APS Type 1 is suspected and confirmed, then screening and treatment for other autoimmune disorders should be conducted.

Abstract #731

THE EFFICACY OF ORAL VERSUS INJECTABLE ESTRADIOL IN MALE TO FEMALE TRANSGENDER PATIENTS

Jaya Reddy Kothapally, MD, Emily Knezevich, PharmD, BCPS, CDE, Andjela Drincic, MD

Objective: To report a case series of male to female (MTF) transgender patients who showed significant improvement in achieving therapeutic goals with injectable estradiol therapy.

Case Presentation: Case 1: A 22-year-old MTF transgender patient on Estradiol 4mg and Spironolactone 200mg orally daily had a Total Testosterone (TT) of 869 ng/dl, Free Testosterone (FT) of 106.9 pg/ml and an estradiol of 64 pg/ml. After changing to im Estradiol 10mg q2 weeks, the TT and FT decreased to 135 ng/dl and 10.4pg/ml respectively, and estradiol increased to 176pg/ml (five days post injection). Case 2: A 40-year-old MTF transgender patient on Estradiol 3mg and Spironolactone 300mg orally daily had a TT of 43 ng/dl, FT of 4 pg/ml and estradiol of 80 pg/ml. Two months after changing to im Estradiol 10mg q weekly, the TT and FT decreased to 5 ng/dl and 0.4pg/ml respectively, and estradiol increased to 123 pg/ml (mid injections). Case 3: A 20-year-old MTF transgender patient on Estradiol 2 mg and Spironolactone 100mg orally daily, had a TT of 728 ng/dl and FT of 166 pg/ml. One month after increasing estradiol to 4mg, the TT was 546 ng/dl, FT was 100 pg/ml and Estradiol was 36 pg/ml. One month after taking im Estradiol 10mg q 2 weeks, the TT and FT decreased to 137 ng/dl and 19 pg/ml respectively and estradiol increased to 305 pg/ml (mid injections).

Discussion: The hormone regimen for MTF transsexual individuals typically consists of an antiandrogen in conjunction with an estrogen. Estrogen can be given orally as 17β estradiol, 2.0–6.0 mg/day, transdermal estradiol patch, 0.1–0.4 mg twice weekly, or injectable estradiol valerate or cypionate 5–20 mg im every 2 wk or 2–10 mg im every week. While the equipotent dose of oral versus injectable estrogen have not been adequately studied, it is generally accepted that the preparation potencies fall into categories low, medium and high. Measurement of serum estradiol levels can be used to monitor the efficacy of therapy. The goal serum estradiol level is 125-200 pg/ml (about one-third to one-half the normal female mid-cycle peak) and the goal serum testosterone level is < 55 ng/dl. Some patients on high dose oral preparations do not achieve estradiol goals, presumably due to the first pass hepatic metabolism of estrogen. Our cases illustrate that in patients who do not respond to oral preparations, one can successfully use corresponding doses of injectable preparations.

Conclusion: Injectable estradiol therapy may be useful in the treatment of male to female transgender patients who do not reach goal levels on oral therapy.

Abstract #732

PUBERTAL GROWTH AUGMENTATION AFTER LIVER TRANSPLANT IN A 23 YEAR OLD PATIENT WITH GLYCOCEN STORAGE DISEASE TYPE I

Rajib Bhattacharya, MD, Bhavika Bhan, MD

Objective: Glycogen storage disease type I (GSD1a) is one of the few genetic-biochemical causes of hypoglycemia in newborns. The homeostatic mechanism cannot halt the rapid drop in blood glucose levels that normally occurs during the first several hours after birth. Seizures, cyanosis, and apnea may ensue. In older children, repeated episodes of hypoglycemia may result in brain damage.

Case Presentation: A 23-year-old male with a history of Glycogen storage disease type 1 a diagnosed at age 2 by liver biopsy. He was found to be a compound heterozygote for the mutations R83H and Q347X. The disease process led to hyperlipidemia, short stature with growth hormone deficiency, lactic acidosis, hypogonadism, hypothyroidism, osteoporosis, and hepatic adenomas. He was non adherent to dietary restriction. Patient underwent hepatic transplant after due evaluation at age 21. A year after his transplant he was noted to have significant improvement in his height (5 inches in six months), weight and normal growth hormone stimulation test. He also had resolution of his hypogonadism. A repeat DXA scan showed improvement in his bone mineral density by 64% at the hip and 60% at the spine.

Discussion: GSD1a is due to deficiency in G6PD hydrolase activity and comprises 80% of cases. GSD I is an autosomal recessive disorder. It is characterized by hepatomegaly, short stature, hyperuricemia, anemia, hypercholesterolemia, increased serum triglycerides, hepatic adenomas, proteinuria or microalbuminuria, renal calcifications, osteopenia or fractures.

Conclusion: Liver transplantation not only resulted in reversing the glycogen storage disease in this patient
but also induced a delayed puberty normalizing his GH deficiency causing a growth spurt as well as clinical virilization. Interestingly, a significant improvement in bone density was also noted, although typically liver transplantation has not been associated with improvement in bone density. This is unusual and calls for further research to determine the pathophysiologic and clinical implication of this relationship.

Abstract #733

A CASE OF MEN TYPE 1, THE DIAGNOSTIC CHALLENGES OF INSULINOMA, AND A LITERATURE REVIEW

Takako Araki, MD, Fumiko Dekio, MD, Takanori Ushiba, Vanessa Sy, MD, Barnett Zumoff, MD

Objective: To describe a case of MEN type 1, the diagnostic challenges of insulinoma, and a literature review.

Case Presentation: A 34-year-old female presented with oligomenorrhea and galactorrhea for 3 years. She was found to have an elevated prolactin level (107 ng/ml) and a pituitary microadenoma; she was also found to have primary hyperparathyroidism (calcium 10.5 mg/dL, intact PTH 165 pg/ml). She reported occasional dizzy spells, fasting and post-prandial. One of her post-prandial spells was observed during a clinic visit (plasma glucose 46 mg/dl). CT of the abdomen showed a 2 cm mass in the tail of the pancreas. She underwent a 72 hour fast. Plasma glucose, insulin, proinsulin, and C-peptide were measured serially. After 62 hours of fasting, test results were as follows: glucose 30 mg/dl, insulin 2.6 μIU/ml, proinsulin 11.8 pmol/L, C-peptide 1.3 ng/ml, β-hydroxybutyrate 15.2 mmol/L. DNA analysis revealed a mutation in exon 2 on MEN1 gene. She is scheduled for pancreatectomy and parathyroidectomy. One of her relatives was also found to have an elevated prolactin level (107 ng/ml) and a pituitary microadenoma; she was also found to have primary hyperparathyroidism (calcium 10.5 mg/dL, intact PTH 165 pg/ml). She reported occasional dizzy spells, fasting and post-prandial. One of her post-prandial spells was observed during a clinic visit (plasma glucose 46 mg/dl). CT of the abdomen showed a 2 cm mass in the tail of the pancreas. She underwent a 72 hour fast. Plasma glucose, insulin, proinsulin, and C-peptide were measured serially. After 62 hours of fasting, test results were as follows: glucose 30 mg/dl, insulin 2.6 μIU/ml, proinsulin 11.8 pmol/L, C-peptide 1.3 ng/ml, β-hydroxybutyrate 15.2 mmol/L. DNA analysis revealed a mutation in exon 2 on MEN1 gene. She is scheduled for pancreatectomy and parathyroidectomy. One of her relatives was also found to have a pancreatic mass, and familial genetic screening is in process.

Discussion: MEN type 1 is an autosomal dominant with a prevalence of 1 in 30,000. Enteropancreatic tumors occur in 60%, with insulinoma accounting for 25%. Insulinoma can be suspected by clinical symptoms. Fasting hypoglycemia is confirmatory but the gold standard diagnostic test is the 72-hour fasting test which has high sensitivity and specificity. Our case had several interesting features: 1) the clinical findings included both fasting and post-prandial hypoglycemia, the latter of which is a relatively unusual finding (6%). 2) The marked hypoglycemia during the fasting test was asymptomatic. 3) In severe hypoglycemia not due to insulin hypersecretion, the insulin level should be suppressed to ≤ 3.0 μIU/ml, the proinsulin level ≤ 0.6 ng/ml, and β-hydroxybutyrate level should be elevated to ≥ 2.7 mmol/L. In our case, the normal suppression of insulin itself and the development of ketosis pointed away from insulin hypersecretion, but the failure of suppression of proinsulin and C-peptide indicated abnormally high secretion of insulin despite the low levels of insulin itself. Perhaps the tumor may have retained some glucose-sensing ability and therefore underwent only partial suppression of insulin secretion during the hypoglycemia.

Conclusion: Hypoglycemia in insulinoma can be fasting, postprandial. Our results with a 72-hour fast were suggestive, but not diagnostic of insulinoma. The presence of a pancreatic tumor made the diagnosis more likely, and the positive genetic findings of MEN-1 made it virtually certain.

Abstract #734

DEMENTIA BY DEFAULT

Jonathan Andrew Stringer, MD, Debra Simmons, MD, Brendon Colaco, MD

Objective: To describe an elderly patient diagnosed with dementia eventually found to have hypoglycemia from an insulinoma.

Case Presentation: An 87-year-old caucasian lady with a presumed diagnosis of Alzheimer’s disease was transferred for recurrent hypoglycemia and worsening mental status. She had decreasing mentation over the preceding months along with episodes of hypoglycemia related to poor nutritional status. She resided in an assisted living facility and was hospitalized for more prolonged episodes, and at that time had a CT that did not detect an insulinoma. On arrival to our hospital, she was responsive but not oriented, with a Mini Mental Status Examination (MMSE) score of 14, thought to be her baseline. She had frequent hypoglycemia resulting in obtundation that would respond to ampules of Dextrose 50 consistent with Whipple’s Triad. Remarkably, correcting her hypoglycemia using diazoxide and maintaining normoglycemia for approximately one week improved her mental status dramatically to a normal MMSE score of 24.

Discussion: Hypoglycemia is suspected when a patient presents with confusion and altered mental status corresponding with a low blood sugar level. In elderly patients, hypoglycemia-induced confusion and slowed mentation can be masked by dementia. Our patient’s work-up and ultimately her diagnosis of an insulinoma was delayed due to her prior diagnosis of dementia. After sustained euglycemia, her MMSE score improved to normal. Hence, although she satisfied MMSE criteria for dementia on initial presentation, the diagnosis of dementia is questionable, as her mental status improved...
with sustained euglycemia. She changed from a demented person relying on family for her entire care to an individual completely aware of her surroundings and able to make decisions independently.

**Conclusion**: Recurrent hypoglycemic episodes can contribute to deteriorating mental status and should be included in the differential diagnosis for altered mentation/dementia. Elderly patients are particularly vulnerable to neurological sequelae from frequent hypoglycemic episodes. Metabolic derangements must be considered in the work-up of suspected dementia. Further, the clinical features of hypoglycemia in the elderly may be masked by senile dementia and superimposed delirium. In any patient with altered cognition, hypoglycemia should be considered and evaluated with re-assessment after prolonged periods of euglycemia.

Abstract #735

**THE CHALLENGE OF CLINICAL ENDOCRINOLOGY AND DIABETOLOGY IN EMERGING COUNTRIES**

*Karim Ait Aissa, MD*

**Objective**: Endocrinology and diabetology was fully recognized as an independent specialty in Algeria in the late 1970’s. Since then, there have been many developments, both in knowledge and in practice. Our practice is primarily diabetes mellitus and thyroid disorders. However, we face two major challenges.

**Case Presentation**: First, we do not have easy access to new technologies, including modern laboratory testing and sophisticated medical imaging such as nuclear medicine. Often we must limit and adapt the studies we order. This could have negative consequences on the relevance and the promptness of diagnosis in one hand, the quality and safety of therapies in other hand. Furthermore, there is a problem of communication including between patients and practitioner and between endocrinologist and colleagues in other specialties. This is often due to lack of awareness of endocrinology. Actually, endocrinology is still not a famous medical specialty even in medical people. We believe that solutions to these problems must be adapted to the social and economic considerations of the country. Endocrinologists should be more present in the media. They should be involved in lobbying the government to influence political and public health decisions. Endocrinologists should build efficient scientific and multidisciplinary networks with colleagues. Finally endocrinologists should master specific endocrine procedures including neck ultrasonography and ultrasound-guided fine needle aspiration.

**Conclusion**: The American Association of Clinical Endocrinologists can be a precious and effective partner in achieving such goals, by establishing partnership with divisions of endocrinology around the world, by promoting AACE’s guidelines and by supporting global medical and prevention educational programs in endocrinology and diabetology.

Abstract #736

**THE ROLE OF HIGH CLINICAL SKILLS IN MANAGEMENT OF AN UNUSUAL CASE IN METABOLISM AND PEDIATRIC ENDOCRINOLOGY**

*Ali Hasan Dhari Al-Jumaili, MD*

**Objective**: To discuss the role of clinical experience and skills in management of case of Smith Lemili Optiz Syndrome (SLOS). When there is a discrepancy between clinical findings, and medical imaging results.

**Case Presentation**: A 14-year-old boy evaluated in our clinic for a concern about his gender, delivered with multiple malformations. At 30 months old, the patient underwent right inguinal hernia repair and the parents were informed that an ovary had been discovered during surgery. Ultrasound studies at that time and later showed vagina, endometrium with absent testes. Until his referring to our clinic there were no further investigations nor treatment. On physical examination: unattractive, mentally retarded, narrow frontal area (trigonacephaly), bilateral simian crease, bilateral ptosis, syndactyly of second and third toes of the right foot, micropenis, hypospadius, bilateral undescended testes, no cardiac abnormality. Investigations: XY karyotype, pelvic U/S studies: vagina, endometrium and absent tests, bone age 14-15 years, echocardiography study normal. Laboratory tests: FSH-0.3 mlu/ml normal for male (1.7-12), LH less than 0.1 mlu/ml for (male1.1-7), prolactin 6.8 ng/ml for male (1.5-19), progesterone 1.2 ng/ml for male (0.11-0.6). Testosterone 0.13 ng/ml for male (3.0-10.6), estradiol less than 9.9 pg/ml normal for female folic -18-147 for male less than 62. T3-0.49 nmol/l (normal1.23—3.23.), T4-58.8nmol/l (normal (60-120), TSH 0.8 MIU/ml (normal 0.25-5.0). Lipid profile fasting: cholesterol 5.3mmol/L (3.9-6.50), triglycerides 0.7 mmol/l (0.9-2.4), HDL 1.05 mmol/L (0.9-4.3), LDL 4.1 mmol/l (1.8-4.3) the other tests were unremarkable.

**Discussion**: The clinical findings, investigations, especially the 46 XY karyotype pattern, and multiple malformations collectively are with suspicion of Smith Lemili Optiz Syndrome (SLOS) diagnosis rather than intersex and the results of U/S studies and the supposed ovary discovered in the previous inguinal repair require
revision. For that, pelvic U/S studies were repeated that showed: left sided inguinal testis with vas deferens, without any female internal organs confirmed by MRI and histopathology after orchoectomy. This supports our diagnosis. The previous U/S studies were misleading and finding ovary in the previous inguinal repair was unlikely, and was likely abdominal testis that removed. Smith-Lemili-Opitz syndrome (SLOS) is a congenital multiple anomaly syndrome caused by an abnormality in cholesterol metabolism resulting from deficiency of the enzyme 7-dehydrocholesterol (7-DHC) reductase. Characterized by prenatal and postnatal growth retardation. The malformations include distinctive facial features, cleft palate, cardiac defects, underdeveloped external genitalia in males, second and third syndactyly of the toes. Mental retardation. The diagnosis of SLOS relies on clinical suspicion and detection of elevated serum concentration of 7-DHC.

Conclusion: Many medical situations require clinical experience and skill with high suspicion for diagnosis especially if there is discrepancy between the clinical findings and results of investigations with lack of advanced specific tests as in our case. In developing countries or underdeveloped countries the need for highly skilled, well-trained personnel in specialized centers who are capable of handling patients with metabolic and pediatric endocrine disorders, such as SLOS exists. In this direction, we had submitted a project to Iraqi Minister of Health to establish a center of excellence for the specialty of the pediatric endocrinology with metabolic disorders in Central Teaching Hospital for Pediatrics-Baghdad. We gained the agreement for that which the first one in Iraq.
PITUITARY DISORDERS

Abstract #800

EFFECTIVENESS AND SAFETY OF AN OCTREOTIDE HYDROGEL IMPLANT IN PATIENTS WITH ACROMEGALY

Carla Chieffo, PhD, Lawrence A. Frohman, MD, Harry Quandt, BS, Stefanie Decker, MS, Mônica R. Gadelha, MD, PhD

Objective: Current formulations of octreotide effectively suppress growth hormone (GH) and insulin-like growth factor 1 (IGF-1) and have adequate tolerability, but only provide control for <2 months. This open-label phase II study evaluated the effectiveness and safety of a subcutaneous 52-mg octreotide hydrogel implant designed to deliver a continuous therapeutic dose for ~6 months.

Methods: Adults with a GH-secreting tumor (postglucose GH ≥1 ng/mL; IGF-1 ≥30% above upper limit of age-adjusted normal value) ≥3-mm from the optic chiasm and demonstrated response to octreotide were randomized to have 1 or 2 implants inserted subcutaneously in the upper arm. Monthly visits occurred over 7 months (implant removal at mo 6). Primary endpoints were suppression of serum IGF-1 to normal age-adjusted ranges at each visit and GH to <1.0 ng/mL after an oral glucose tolerance test (OGTT) at month 6. A post hoc analysis compared IGF-1 and GH suppression with the implant vs prestudy octreotide long-acting release (OLAR) for 3–6 months. Secondary endpoints included signs/symptoms, tumor size, and quality of life. Safety was assessed by adverse events (AEs), physical exam, laboratory chemistry, and gallbladder ultrasonography.

Results: In groups with 1 (n=5) and 2 (n=6) implants, mean ± SD age was 50.8±15.6 and 43.8±9.3 years. IGF-1 suppression to normal age-adjusted ranges occurred in 3 patients (n=1, 1 implant; n=2, 2 implants); for all patients, mean percent IGF-1 reductions were 54% (mo 1) and 49% (mo 6). GH suppression to <1.0 ng/mL occurred in 4 patients (n=1, 1 implant; n=3, 2 implants); for all patients, mean percent reductions were 82% (mo 1 and 6). Compared to historical OLAR, there were similar or greater mean reductions in IGF-1 (implant, 53% vs OLAR, 39%) and GH (84% vs 80%). At month 6, tumor size was reduced by 38% (2 implants) and 23% (1 implant). Patients reported fewer acromegaly signs/symptoms vs baseline. Mean ratings (1–10 scale) were high for treatment effectiveness (9.8) and satisfaction (9.6); 2 patients at month 6 vs 4 at baseline reported thinking about treatment daily. The most common AEs were fatigue, diarrhea, hyperhidrosis, arthralgia, and headache. There were no new occurrences of gallstones and no clinically significant findings for other safety parameters.

Discussion: The octreotide hydrogel implant provided consistent suppression of IGF-1 and GH over 6 months and reduced tumor size and acromegaly signs/symptoms. Post hoc analysis suggested comparable effectiveness to previous OLAR therapy.

Conclusion: The octreotide hydrogel implant is an effective and safe delivery system for treating patients with acromegaly.

Abstract #801

OMENTECTOMY ADDED TO ROUX-EN-Y GASTRIC BYPASS IMPROVES GLUCOSE AND ADIPOKINES AT 90 DAYS: A RANDOMIZED, CONTROLLED TRIAL

Troy Dillard, MD, Jonathan Purnell, MD, Mark Smith, MD, J Laut, BA, M. Ed W Raum, MD, D Hong, MD, E Patterson, MD

Background: Visceral adipose tissue (VAT) predicts incipient diabetes mellitus and cardiovascular disease (CVD). Human data is mixed regarding the potential benefits of selective VAT reduction.

Objective: To investigate the effect of adding sub-total omentectomy to laparoscopic Roux-en-Y gastric bypass (LRYGB) on glucose homeostasis and levels of lipids, inflammatory markers and adipokines after 90-days in non-diabetic patients.

Methods: We conducted a single-blinded, randomized study of LRYGB plus sub-total omentectomy vs. LRYGB alone in 28 subjects (7 male, 21 female). Groups were closely matched at baseline for gender, age, and body mass index (BMI). Eligibility included age ≥ 18 years old, a body mass index (BMI) ≥ 40 and < 50 kg/m2 without co-morbid conditions or BMI ≥ 35 and < 50 kg/m2 with co-morbid conditions. The primary outcome measures were changes in fasting plasma glucose, insulin and HOMA-IR. Secondary measures were BMI and levels of hs-CRP, TNF-α, interleukins, total and HMW adiponectin, fibrinogen, and PAI-1.

Results: After surgery, BMI decreased significantly in both groups and were not different at follow-up. While many outcome parameters improved with weight loss in both groups post-operatively, only the omentectomy group experienced statistically significant decreases in fasting glucose (p<0.05), total (p=0.004) and VLDL (p=0.001) cholesterol, and an increase in the HMW:total adiponectin ratio (p=0.013).

Discussion: Selective reduction in VAT by omentectomy in non-diabetics resulted in statistically significant reductions in fasting glucose, total and VLDL cholesterol at 90 days, while no statistically significant reductions were noted in these parameters in a closely
matched control group. Furthermore, the omentectomy group alone showed a favorable change in the ratio of high-molecular weight adiponectin to total adiponectin. Neither of these findings can be explained by changes in BMI or inflammatory markers since the groups showed no meaningful differences in changes in these parameters. The only complications were two patients in the omentectomy group who developed gastroenterostomy stenosis, treated with outpatient endoscopic balloon dilatation, and one patient in the control group who developed urinary retention.

**Conclusion**: We conclude that omentectomy added to a LRYGB results in favorable changes in glucose homeostasis, lipid levels, and adipokine profile at 90 days. These data support the hypothesis that selective ablation of VAT conveys metabolic benefit in non-diabetic humans.

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**Abstract #802**

**PLASMA PHARMACOKINETICS OF THE OCTREOTIDE HYDROGEL IMPLANT IN PATIENTS WITH ACROMEGALY**

*Carla Chieffo, PhD, Lawrence A. Frohman, MD, Harry Quandt, BS, Stefanie Decker, MS, Mônica R. Gadelha, MD, PhD*

**Objective**: Somatostatin analogs (SSAs) are the gold standard medical therapy for acromegaly. Octreotide, the primary SSA, achieves biochemical control and tumor shrinkage in ~60% and ~40% of patients, respectively, and has an overall good safety profile, but requires monthly injections. To minimize fluctuation in drug levels and reduce the administration frequency, an implant has been developed that contains octreotide in a pelletized form within a hydrogel capsule that controls the rate of diffusion into the aqueous environment. We report pharmacokinetic (PK) data from a phase II open-label, dose-response study of a subcutaneous 52-mg octreotide hydrogel implant designed to continuously deliver a therapeutic octreotide dose for 6 months.

**Methods**: Adult patients with diagnosis of acromegaly, a growth hormone-secreting tumor ≥3-mm distant from the optic chiasm, and response to octreotide (previous use) were randomly assigned to have 1 or 2 implants inserted subcutaneously in the upper arm. Implants were removed after 6 months, and blood samples were collected monthly through 7 months. Serum octreotide levels were determined by validated radioimmunoassay, and maximum serum concentration (Cmax), time to Cmax (Tmax), and area under the serum drug concentration-time curve (time 0 to the last measurable concentration, AUC0–t) were derived and analyzed using descriptive statistics.

**Results**: 5 patients received 1 implant and 6 patients received 2 implants; in these groups, mean ± SD age was 50.8±15.6 and 43.8±9.3 years and 100% and 33% were women, respectively. In the group receiving 2 implants vs those receiving 1 implant, mean ± SD Cmax was ~2.5-fold higher (4182±2288 pg/mL, range 2527–8684 vs 1705±589 pg/mL, 1181–2570, respectively) and mean ± SD AUC0–t was ~2-fold higher (14,427±6189 pg/mL, range 8763–25,657 vs 6702±1944 pg/mL, 4841–9103). After reaching Tmax in month 1, octreotide levels changed more slowly from months 2 to 6. Percent change in mean octreotide concentrations from month 2 was +24% (mo 2 vs 3), −2% (mo 2 vs 4), −9% (mo 2 vs 5) and −35% (mo 2 vs 6) for 2 implants and −28% (mo 2 vs 3), −37% (mo 2 vs 4), −27% (mo 2 vs 5), and −45% (mo 2 vs 6) for a single implant. At month 6, mean serum octreotide remained at therapeutic levels (2 implants, 1514 pg/mL; 1 implant, 805 pg/mL).

**Discussion**: Drug concentrations were ~2-fold higher in patients receiving 2 vs 1 implant.

**Conclusion**: The 52-mg octreotide hydrogel implant provided consistent and durable drug delivery over 6 months.

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**Abstract #803**

**DIAGNOSIS OF CUSHING’S DISEASE IN A PATIENT WITH CONSISTENTLY NORMAL URINARY FREE CORTISOL LEVELS: A CASE REPORT**

*William Henry Ludlam, MD, Kelley J. Moloney, Jennifer U. Mercado, Marc R. Mayberg, MD*

**Objective**: To illustrate the potential for failure to diagnose Cushing’s disease (CD) correctly, we present the case of a patient with repeatedly normal 24-hour urinary free cortisol (UFC) levels. However, this patient exhibited other elevated biochemical markers of hypercortisolemia and post-surgical adrenocorticotropic hormone (ACTH) staining of a pituitary adenoma.

**Case Presentation**: A 31-year-old female suspected of Cushing’s syndrome underwent a total of 13 24-hour UFC tests at multiple testing sites using high-performance liquid chromatography-tandem mass spectrometry. All of the patient’s urine cortisol levels fell within normal limits and ranged between 7.2 and 19 μg/24 hours (normal <50). However, the patient exhibited features typical of CD including: precipitous central weight gain, hirsutism, acne, bruising, violaceous skin striae and hypertension. Despite the negative UFCs, other biochemical markers for hypercortisolemia were positive including a positive overnight 1-mg dexamethasone suppression test (morning serum cortisol 14.1 μg/dL) and a positive dexamethasone/corticotropin-releasing hormone (Dex/CRH) test (serum
cortisol 7.14 µg/dL 15 minutes after CRH stimulation). The patient’s serum ACTH concentration was not suppressed (37 pg/mL). Pituitary head MRI revealed a small hypo-enhancement on the left side of the gland. Inferior petrosal sinus sampling confirmed a central source of ACTH that lateralized to the left side of the pituitary gland. The patient was referred to surgery and a white milky semisolid adenoma was removed, which stained positively for ACTH. Following surgery, the patient’s serum cortisol decreased to 0.58 µg/dL, which was consistent with a complete removal of the tumor. The patient is currently in remission.

Discussion: Correctly identifying Cushing’s syndrome in patients suspected of hypercortisolemia can be complicated by the nonspecific symptoms of steroid excess that overlap with more common conditions. Although the UFC test is a common screening method for the diagnosis of CD, which is Cushing’s syndrome due to an ACTH-secreting pituitary tumor, recent clinical practice guidelines confirm that normal initial UFC test results should not be cause to dismiss the diagnosis of Cushing’s syndrome in patients if the clinical suspicion is high (Nieman et al. JCEM 2008; 93:1526–1540). These patients should be monitored by an endocrinologist and undergo additional serial testing.

Conclusion: Physicians must be aware that the UFC may occasionally be negative in patients with Cushing’s syndrome and that the utilization of complementary tests (other than UFC analysis) may be necessary to make the diagnosis in some cases.

Abstract #804

SAFETY OF A PROTOCOL FOR POST-OPERATIVE HYPOTHALAMIC-PITUITARY-ADRENAL (HPA) AXIS TESTING AFTER PITUITARY SURGERY

John Lambeth, MD, Julie Sharpless, MD

Objective: Assessment of the HPA axis is critical for patient safety in the immediate post-operative period after pituitary surgery. The use of a care bundle checklist has been shown to reduce medical errors among hospitalized patients in a number of other clinical contexts. The best approach to steroid administration following pituitary surgery is controversial. Morning serum cortisol levels are often used to guide glucocorticoid prescription at hospital discharge, but have not been specifically evaluated in the context of perioperative dexamethasone administration. The authors examine the safety and efficacy of using a multidisciplinary care protocol to guide glucocorticoid replacement after pituitary surgery.

Methods: 261 cases of pituitary surgery performed at UNC Hospitals between 2004-2010 were reviewed. Of these, 151 had followed a specified post-operative protocol for cortisol testing, and met additional inclusion criteria. Patients with biochemically proven Cushing’s disease were excluded. All patients received empiric perioperative steroid replacement with dexamethasone, had morning serum cortisol testing on post-op day 2, and were discharged with glucocorticoid replacement based on cortisol levels. The post-op day 2 results were compared with the biochemical and clinical requirement for glucocorticoid replacement at 6-month follow-up in our Multidisciplinary Pituitary Clinic. Potential confounding factors were also examined, including timing of cortisol measurement and tumor staining for ACTH.

Results: In the setting of perioperative dexamethasone, a post-op morning cortisol of >10 µg/dL has a PPV of 92.2% (sensitivity 39.5%, specificity 87.5%) for predicting adrenal sufficiency, as defined by absence of clinical requirement for steroids at 6-month follow-up. Lowering this cutoff to >8 µg/dL would not have misclassified any additional patients with adrenal insufficiency (PPV 93.3%, sensitivity 47.1%, specificity 87.5%). Exclusion of patients with cortisol measurements obtained before 06:00 or after 09:00 increased the PPV (for cortisol >8 µg/dL) to 97.1% (sensitivity 55.7%, specificity 94.4%). In addition, this protocol appropriately classified patients with ACTH+ staining adenomas but no clinical or biochemical evidence of Cushing’s disease.

Discussion/Conclusion: Morning serum cortisol values of >8 µg/dL safely predict normal HPA axis function in patients who have undergone pituitary surgery. Although many patients with normal adrenal function may be covered with steroids for a short period of time after surgery, this protocol is very reliable in preventing untreated adrenal insufficiency.

Abstract #805

PROLACTINOMAS AT THE SAN JUAN DE DIOS HOSPITAL IN COSTA RICA: A SINGLE CENTER EXPERIENCE

Paula Wang-Zúñiga, MD, Chih Chen-Ku, MD

Objective: To describe for the first time a case series of prolactinomas in Costa Rica.

Methods: All patients with prolactinomas in control at the Endocrinology Unit at San Juan de Dios Hospital were collected and their charts were reviewed. Variables were analyzed with SPSS 18.0.

Results: A total of 114 patients were reviewed. 91.2% females. Mean age at diagnosis was 32.73 years (44 years in males and 31.72 years in females, p <0.001).
Prolactin levels were higher in men (1229.5 ± 2059.28 vs 270.88 ± 701.16 ng/ml, p=0.004). 69.3% of patients had galactorrhea, 44.7% had headaches. 60% of men had erectile dysfunction and 50% had decreased libido. 57.6% of women had amenorrhea. At presentation, 29.16% had macroadenomas (60% males vs 25.6% females, p=0.109). Microadenomas had an initial mean prolactin level of 169.64 ± 321.35 ng/ml compared to macroadenomas (1653.31 ± 2031.95 ng/ml, p=0.001). 4.3% patients did not receive treatment and 89.5% began treatment with bromocriptine. 29.8% received treatment with cabergoline (94% due to bromocriptine side effects). 7.9% underwent hypophysectomy (89% because of tumoral size). Overall, 8.7% had visual impairment and 9.7% had extrasellar invasion. 9.6% of patients are currently cured; these patients were older at presentation (39.6 vs 32.2 years, p=0.027). Comparing cured patients with not cured, there were no significant differences in initial prolactin levels, tumor size, treatment with bromocriptine, cabergoline, surgery nor duration of treatment. Average follow up is 8.8 years. Currently, 80% of males have a prolactin level of less than 20 ng/ml. 46.2% of women have prolactin levels of less than 25 ng/ml. No patients had worsening of visual symptoms during follow up.  

Discussion: The San Juan de Dios hospital in Costa Rica attends a population of around 1 million persons. With 114 cases, we have a prevalence similar to that reported in other series. As expected, men have larger tumors and higher prolactin levels at diagnosis. Contrary to other series, less than ten percent of our patients achieved long term normal prolactin levels without treatment. 

Conclusion: Most of our prolactinoma patients are females. Women are diagnosed at a younger age and usually have microadenomas and lower prolactin levels. However, on follow up they achieve lower control rates despite similar treatments compared to males. Most of our patients are treated medically and only a few patients undergo surgery due to visual impairment or tumor size mainly. A minority of patients achieve cure either by medical or surgical treatment. 

Abstract #806

CENTRAL HYPOTHYROIDISM WITH AN ELEVATED TSH

Gregory Dodell, MD, Nancy A. Rihana, MD, Joseph Ghassibi, MD, Lynn R. Allen, MD

Objective: Hypothyroidism can have a wide range of signs and symptoms and differentiating between primary and secondary disease is crucial for both initial and long-term management. An elevated TSH is a common finding in the setting of primary hypothyroidism; however it can also occur in central hypothyroidism. An index of suspicion for central hypothyroidism can unmask additional hormone deficiencies, and most importantly prevent the serious complication of adrenal crisis.

Case Presentation: A 66-year-old male with a history of hypothyroidism was admitted with cough, dyspnea and progressive weakness. Hypothyroidism was diagnosed in the 1970’s, unknown primary or secondary cause, and the patient took thyroid replacement in the 1980’s but had not taken it since. At admission the TSH was 8.43mU/l (0.55-4.78) and the free T4 was 0.2 ng/dl (0.7-1.7). At initial evaluation the patient appeared cognitively slow and he was only oriented to place. Pertinent positives were cold intolerability, progressing weakness and fatigue. Remarkable physical exam findings included bibasilar crackles, minimal body hair, and delayed relaxation of tendon reflexes. Given weakness, anemia (hemoglobin 10.8 g/dL, ferritin 287 ng/mL) and clinical signs of heart failure with an elevated TSH it seemed like a straightforward case of primary hypothyroidism. However, with an extremely low free T4 level a higher TSH was expected so an AM serum cortisol level was checked which was 1µg/dl. A subsequent cosyntropin stimulation test demonstrated adrenal insufficiency (baseline-1, 30 minutes-6, 60 minutes-4). Additional studies included: ACTH level-19pg/ml (7-69), LH<0.1mIU/mL (2-12), FSH<0.5mU/L (1-12), IGF-1<17µg/L (71-290), Prolactin 5 ng/ml (2.1-17.7), Testosterone free <3 pg/mL. Prednisone 10 mg daily was started and followed by 50 mcg of levothyroxine. An MRI of the brain demonstrated an empty sella with no discrete intrasellar lesion. His weakness and confusion began to improve over the first few days of treatment. He was discharged home on 20 mg of hydrocortisone in the AM and 50 mcg of levothyroxine. The patient was seen in clinic the following week and noted continued improvement. 

Discussion: Central hypothyroidism is a rare disease with an incidence of 50 cases/million that results from a variety of conditions affecting the hypothalamus and the pituitary gland. It is usually associated with a normal TSH, but TSH can be low or elevated.

Conclusion: Diagnosis of central hypothyroidism is essential to avoid adrenal crisis, to uncover any other pituitary deficiencies, and to prevent ongoing management of thyroid disease based on TSH alone.
Abstract #807
FULLY SUPPRESSED POSTOPERATIVE SERUM CORTISOL LEVEL IN A CUSHING’S DISEASE PATIENT DESPITE INCOMPLETE SURGICAL REMOVAL OF A PITUITARY MACROADENOMA
William Henry Ludlam, MD, Jennifer U. Mercado, Kelley J. Moloney, Marc R. Mayberg, MD

Background/Objective: We present a patient with Cushing’s disease (CD) who, despite incomplete surgical removal of an adrenocorticotropic hormone (ACTH)-secreting macroadenoma, had fully suppressed postoperative serum cortisol. This result erroneously suggested biochemical cure and delayed further needed treatment.

Case Presentation: A 46-year-old female, diagnosed with CD in 2001, exhibited elevated urinary free cortisol (UFC) [264 mcg/dL, normal <34], plasma ACTH (145 pg/ml), and overnight 1-mg dexamethasone suppression test (morning serum cortisol 15.6 μg/dL). The patient underwent transsphenoidal adenectomy (TSA) to remove a 1.2-cm pituitary tumor confirmed as a corticotroph adenoma. Postoperative serum cortisol levels decreased to 1 mcg/dL, suggesting complete tumor removal. However, postoperative MRI revealed a 3×5×6-mm region of hypo-enhancing tissue. The patient showed improvement initially (50 lbs weight loss), but relapsed over the next year (60 lbs weight gain). In 2007, UFC (73 mcg/dL, normal <50) and ACTH (103 pg/mL) were mildly elevated and a dexamethasone/corticotropin-releasing hormone (Dex/CRH) test was positive (serum cortisol 7.6 μg/dL 15 min after CRH). Pituitary MRI revealed no change in the hypo-enhancing tissue noted six years earlier. The tumor was removed via TSA and pathology confirmed it was residual corticotroph adenoma.

Discussion: A fully suppressed postoperative serum cortisol level following corticotroph adenoma resection in patients with CD is thought to represent complete removal of the pituitary tumor. Similarly, the recurrence of CD is presumed to be due to the regrowth of the pituitary tumor from undetectable amounts left behind after surgery. However, the data presented here indicates that postoperative serum cortisol can be fully suppressed despite the presence of a substantial amount of residual corticotroph adenoma (5% of original tumor volume). Furthermore, a relapse of CD can occur without substantial regrowth of the remaining tumor. This demonstrates the potential to erroneously assume that a patient has been cured of CD after TSA and therefore delay further treatment. In patients with CD that do not achieve remission in this setting, there are medical treatment options (cabergoline and ketoconazole); however, none are indicated for CD. Medical therapies such as the pituitary-targeted somatostatin analogue pasireotide or the glucocorticoid receptor antagonist mifepristone may soon be available as a treatment for Cushing’s disease.

Conclusion: Despite the presence of residual corticotroph after TSA, postoperative serum cortisol level may fully suppress erroneously suggesting complete tumor removal.

Abstract #808
CENTRAL DIABETES INSIPIDUS AS THE HARBINGER OF ACUTE MYELOID LEUKEMIA RELAPSE
Pearl Dy, MD, Jennifer Kelly, DO

Objective: Central diabetes insipidus (DI) is commonly idiopathic or secondary to tumors, infections, trauma or infiltration. It is rarely observed in hematologic malignancies such as myelodysplastic syndrome and acute myeloid leukemia (AML). We present a patient with AML who reported polyuria and polydipsia in the months preceding her AML relapse.

Case Presentation: A 44 year-old female, diagnosed in 2009 with normal cytogenetic AML, was in complete remission after autologous peripheral blood stem cell transplant. She presented with 2 months history of increasing fatigue and decreased ability to perform daily activities. She was re-admitted and diagnosed with relapse of AML. Approximately 6 months prior to her admission, she noted polydipsia and polyuria. A few days prior to admission, she also had watery diarrhea and diagnosed with c. diff colitis. Her sodium level went up to 151 mmol/L and her fluid losses both from polyuria and diarrhea were not adequately compensated by her oral intake. She had elevated serum osmolality of 301 mOsm/Kg and low urine osmolality of 146 mOsm/Kg. Central DI was suspected and she was started on desmopressin (DDAVP) orally with improvement in sodium levels, urine osmolality and clinical symptoms. Anterior pituitary hormones were evaluated with normal morning cortisol level, thyroid function tests, LH and slightly elevated FSH. Her ADH level was low at 1.2pg/mL (1.0 – 13.3). MRI of the brain revealed borderline thickening of the pituitary stalk and adjacent hypothalamus but the posterior pituitary gland had normal signal and size.

Discussion: It has been postulated that the mechanism of the development of central DI in AML is probably secondary to infiltration of leukemic cells of the posterior pituitary gland and/or thrombosis of the small vessels in the hypothalamic nuclei and posterior pituitary causing impaired secretion of ADH. It has been
associated particularly between AML with monosomy 7 and is an indicator of poor prognosis. In our case, she had normal cytogenetic AML with DI. There have been reports implicating central DI as the initial presentation of diagnosis or relapse of AML. Rare cases subside after chemotherapy while several reports showed failure of antileukemic therapy to alleviate symptoms of DI. In our case, DDAVP facilitated the improvement and stabilization of symptoms and laboratory results.

**Conclusion:** Central DI is a rare but possible harbinger or complication of underlying hematologic malignancy, particularly AML. It has to be considered in the evaluation of these patients to facilitate faster diagnosis with prompt treatment to achieve better outcome for both underlying malignancy and diabetes insipidus.

Abstract #809

RISK OF STROKE IN PITUITARY DISEASE: ASSESSMENT BY A BRAIN SPECT INDEX OF CEREBRAL FLOW RESERVE

Harold Thomas Pretorius, MD, PhD, Nichole M. Richards, CNMT, Jerome J. Kelly, MD, Shelley Haste, PsyD, John Idoine PhysD, Luis F. Pagani, MD

**Objective:** Use a brain SPECT cerebral flow reserve index (FRi) to assess stroke risk in pituitary patients with or without hypothalamic deficits (HD) vs. others with increased or near normal stroke risk.

**Methods:** Outpatients (n = 580) age (56±14) years, 60% women, 40% men, 23% minorities, with neurologic complaints had basal and perfusion-stimulated brain SPECT using Tc-99m-ECD or Tc-99m-HMPAO IV. Cortical metabolic (CMi), perfusion (CPi), flow reserve (FRi) indices and multicompartmental analysis (MCA) of brain, renal, and hepatic tracer concentration were computed for patients with pituitary disease (PD), diabetes mellitus (DM), hypertension (BP), renal failure (RF), liver failure (LF), traumatic brain injury (BI), clinical depression (CD), and near normals (NN). Neurocognitive testing included MMSE, TYM (Test Your Memory), Millon, SASSI, Beck, and selected psychiatric evaluation.

**Results:** NN patients (n = 25), age (54±15) yrs, had CMi (60±10)%; CPi (63±10)%; FRi (5±2)% and HD in < 2% vs. 70% (43/61) of PD, only 9.8% (6/61) of whom had macroadenomas. FRi = CPi − CMi was < 3% in 78% (46/59) of PD, similar to DM 61% (51/84) or BP 79% (64/81), but not uncomplicated RF 36% (18/50) or LF 25% (1/4). Initial MCA predicted that 50% decrease in renal or hepatic activity would cause > 15% increase in brain tracer activity, 1 to 5% increase in CMi and CPi, and 3% increase in FRi. Over 5 years, stroke or TIA occurred in 31% (19/61) of PD, 23% (16/70) of RF and 18% (15/84) of DM. FRi, HD, and neurocognitive measures trended to improve with > 6 months of incretin or other effective therapy for DM or PD. Correlation of abnormal orbitofrontal SPECT and CD occurred in > 50% of strokes and was also noted in 39% (29/61) of PD.

**Discussion:** Pituitary macroadenoma increases major stroke risk (pituitary apoplexy); however, stroke risk with more prevalent but more subtle PD such as microadenoma, trauma or opiate-induced PD (> 90% of this series) is uncertain. Frequent hypothalamic deficits on brain SPECT suggest a neuroendocrine basis of pituitary effects on brain perfusion. Conditions such as RF or LF, that decrease tracer blood clearance may result in increased brain concentration predicted by MCA, but do not necessarily decrease stroke risk.

**Conclusion:** Brain SPECT derived FRi is typically decreased in untreated PD and indicates an increased risk of stroke similar to patients with DM or RF. Hypothalamic SPECT deficits are also a nonspecific marker of PD and risk of stroke.

Abstract #810

ERDHEIM-CHESTER DISEASE: A CASE REPORT

Aqiba Sarfraz, MBBS, FCPS, Qamar Masood, MD

**Objective:** To describe the case of diabetes insipidus secondary to Erdheim-Chester disease.

**Case Presentation:** This report describes the case of a 55 year old female presented to us with history of prolonged fever and headache sometimes associated with nausea and vomiting. She was amenorrheic for last 15 yrs and had 8-year history of central diabetes insipidus, primary empty sella syndrome and hypertension for which she was on oral desmopressin and ramipril. Physical examination revealed normal vital signs with temperature 37°C. There was no postural drop. No neurological, cardiovascular and pulmonary abnormalities were found. Routine work up showed increased level of CRP and ESR. Hormonal profile showed low FreeT4, FSH, LH and high Prolactin levels. Her short synecthin test was normal. She was started on levothyroxine 50µg QD. Because of the history of diabetes insipidus and hypopituitarism with increased levels Prolactin, MRI head and brain was done and it revealed multiple extra-axial masses along the bilateral cerebral convexities, intraventricular region involving occipital horn of left lateral ventricle and en plaque meningioma. Findings are consistent with meningiomatosis and primary empty sella. Neurosurgical opinion was sought and Craniotomy with microsurgical excision was done in July 2009. She was recovered and discharged. Later on the histopathology showed Xanthogranulomatous lesion morphological,
clinical and radiological features favor Erdheim-Chester disease. Her CT abdomen and bone scan was also done and showed typical abnormalities of Erdheim-Chester disease. She was referred to oncologist for chemotherapy.

Discussion: Erdheim-Chester disease is a rare, non-Langerhans' cell histiocytosis of unknown etiology. There are typical radiographical and pathological features, which can lead to the diagnosis, but the clinical spectrum shows a broad variation, ranging from asymptomatic tissue infiltration to fulminant multisystem organ failure. The patient we report was a diagnosed case of diabetes insipidus which is the most common endocrine manifestation of Erdheim-Chester disease. Anterior pituitary hormonal deficiencies have also been reported in ECD patients. On the other hand, alterations of the anterior pituitary function have been described in up to 30% of patients with primary empty sella, where as the involvement of the posterior pituitary function in the empty sella syndrome is a rare occurrence. Presently, less than 20 instances of diabetes insipidus in patients with empty sella have been reported in literature. The majority of these patients also had coexistence of anterior pituitary dysfunction, particularly deficient gonadotropin secretion. Very few cases with primary empty sella, diabetes insipidus, and ECD have been reported so far. In our patient we see the association of ECD syndrome and empty sella with both anterior and posterior pituitary function deficiencies. Unfortunately, a casual relationship b/w the two syndromes cannot be excluded and needs to be addressed.

Conclusion: Erdheim-Chester disease is a rare non-Langerhans' cell histiocytosis with characteristic radiological and histological features. About half of those affected have extra skeletal manifestations, including involvement of the hypothalamus–pituitary axis, lung, heart, retro peritoneum, skin, liver, kidneys, spleen, and orbit. Though it is a rare disease but should be considered as differential diagnosis of brain masses especially when the patients present with diabetes insipidus and empty sella with both anterior and posterior pituitary function deficiencies.

Abstract #811

CURE OR RESISTANCE – WHAT IS THE FINAL OUTCOME OF MACROPRLACTINOMAS ON DOPAMINE AGONISTS

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Mihail Coculescu, MD, PhD, FACE

Background: Dopamine agonists (DA) are the treatment of choice in macroprolactinomas. Due to low cure rate and high recurrence rate after DA withdrawal, long life therapy could be necessary in the majority of “responsive” patients.

Methods: 211 patients with macroprolactinomas (87 M/124F), treated with DA for 5 years median period. 29 patients (13.7%) fulfilled the criteria for DA withdrawal after at least 18 months therapy: normal prolactin on DA treatment, tumor maximum diameter ≤ 10 mm and had a minimum 6 months follow-up period after DA withdrawal. PRL was measured by fluoroimunoassay or chemiluminescence. CT scan and/or MRI with contrast agents were used for imaging, maximum diameter evolution was reported.

Results: Median duration of treatment in 29 patients (7 M/22 F, median age 28 years) fulfilling the criteria for DA withdrawal was 4 years. 13 patients received bromocriptine, 11 patients received both bromocriptine and cabergoline, and 5 patients received only cabergoline. The overall cure rate in selected patients without significant residual tumor was 65.5% (19 out of 29 patients). However, from the whole series, cure rate remains low (9%, 19 out of 211 patients). Cured patients remained free of recurrence at a median of 27 months of follow-up after DA withdrawal. Cure of macroprolactinomas after DA therapy occurred in 11 cases (4M/7F). Normal prolactin levels were noticed at a median of 27 months after DA withdrawal. After combined therapies, including radiotherapy (4 high voltage radiotherapy, 3 normal voltage radiotherapy, 1 -198Au implant), 8 additional women were cured. Normal prolactin levels were noticed at a median of 24 months after DA withdrawal. The overall recurrence rate was 34.5% (10 out of 29 patients). Among these "pseudo-cured" patients, the median time to recurrence was 4.5 months after DA withdrawal (range: 3-12 months). All recurrences occurred within one year after dopamine agonists' withdrawal and 80% occurred within 6 months of DA discontinuation. Tumor re-growth was noticed on CT/MRI in 7 patients (70%); in all cases but two, tumor size was less than 1 cm. There were no significant differences between cured and "pseudo-cured" patients regarding gender, age, PRL and maximum diameter at diagnosis, PRL and tumor diameter at DA withdrawal, DA treatment duration, pregnancies.

Conclusion: Cure rate in this large series of macroprolactinomas remains low, even after radical therapies and in selected patients with residual tumor less than 10 mm. Both in so-called “responsive” and “resistant” prolactinomas, some cells could not be destroyed by therapy, generating the resistance to cure.
Abstract #812

PRIMARY HYPOTHYROIDISM ASSOCIATED WITH HYPERPROLACTINEMIA AND PITUITARY MACROADENOMA

Dragana Jokic, MD, Xiangbing Wang, MD, PhD, FACE

Objective: To report a case of primary hypothyroidism associated with hyperprolactinemia and pituitary macroadenoma.

Case Presentation: A 28 year old female presented with 7-months of amenorrhea with occasional dizziness in 2009 with no headache, visual disturbances nor galactorrhea. Initial laboratory work done by gynecologist was negative for pregnancy, but showed prolactin of 139 ng/ml and thyroid studies were ordered but patient did not follow up. MRI of the brain showed a 1.7 cm pituitary macroadenoma extending into the suprasellar region with indentation of the optic chiasm. The gynecologist started patient on Cabergoline 0.25 mg twice weekly. After 6 months, prolactin level decreased to 11.7 ng/ml and repeated MRI of the brain showed no change in size of pituitary adenoma. Patient was referred to an endocrinologist for possible surgery because of failure of the adenoma to shrink. Although no symptoms suggested hypothyroidism except her feeling cold all the time, blood tests showed TSH of 562.5 µU/ml and FT4 0.18 ng/dL with normal IGF-1 level. Cabergoline was discontinued and patient was started on levothyroxine. The dosage was titrated to 112 mcg daily. 6 months later, the repeated prolactin was 23.2 ng/ml with regular periods; repeated TSH was 0.237 µU/ml, T3 total 127 ng/dL, FT4 1.63 ng/dL. Repeated MRI one year after starting levothyroxine showed complete resolution of pituitary adenoma.

Discussion: TRH is a potent prolactin releasing factor and also causes thyrotroph hyperplasia. The high level of TRH in severe primary hypothyroidism might cause proliferation and hypertrophy of both thyrotrophs and lactotrophs in pituitary gland mimicking pituitary adenoma. Regression of the pituitary macroadenoma after treatment of levothyroxine confirmed the hypothesis of pituitary hyperplasia secondary to primary hypothyroidism. Cabergoline decreased prolactin levels but did not have any effect on adenoma size which also supports the diagnosis of pituitary macroadenoma likely secondary to hypothyroidism.

Conclusion: This case illustrates that primary hypothyroidism can present with amenorrhea and pituitary mass. Our case suggests the importance of thyroid function testing during the investigation of hyperprolactinemia and pituitary adenoma.

Abstract #813

DIABETES INSIPIDUS AS SOLE PRESENTING SYMPTOM OF METASTASIS TO THE PITUITARY: CASE REPORT AND REVIEW OF THE LITERATURE

Sapna Shah, MD, Paula Silverman, MD

Objective: To describe a case of pituitary metastasis presenting with diabetes insipidus (DI) with preserved anterior pituitary function and review the literature regarding pituitary hormonal deficiency in similar cases.

Case Presentation: An 84-year-old woman with breast cancer status post lumpectomy and radiation developed presyncope, weight loss, increased thirst and increased urination over a period of 7 months. Extensive inpatient workup revealed diffuse osseous and pulmonary metastatic disease consistent with adenocarcinoma of the breast proven by bone marrow biopsy. Her serum sodium was 137 mmol/L and her urinalysis revealed dilute urine (specific gravity 1.004). Given daily urine output of more than 5 liters, a water deprivation test was performed and confirmed partial central DI. Testing of the hypothalamic-anterior pituitary axis was without abnormality: free thyroxine 1.04 ng/dL, thyroid stimulating hormone 0.66 uIU/mL, prolactin 15.1 ng/mL, luteinizing hormone 8.9 mIU/mL, follicle stimulating hormone 22.2 mIU/mL estradiol <10 pg/mL, and random cortisol 11.5ug/dL. MRI of the brain and sella turcica revealed a small mass in the pineal gland, thickening of the pituitary stalk with hypothalamic involvement and a 4 mm lesion in the right aspect of the pituitary gland. Intranasal desmopressin was initiated with marked improvement of her symptoms and normalization of serum osmolality and sodium. No other hormone replacement therapy was required.

Discussion: DI is an uncommon presentation of pituitary insufficiency, especially as an isolated finding. Although pituitary adenomas are the most common lesions of the pituitary gland, other diagnoses include hypophysitis, Rathke’s cysts and metastasis to the pituitary. The overall reported incidence of pituitary metastasis in patients with cancer is 1 to 3.6%, breast and lung being the most common primary origin. The diagnosis of metastasis to the pituitary is usually made by clinical history and radiographic findings (dumbbell shaped mass with a clear margin at the diaphragm level, sclerotic changes around the sella, and the presence of concomitant brain mass). While most metastases are asymptomatic, those with symptoms most commonly present as DI, reported in 29-71% of cases. In our review of the literature, 77 case reports of metastasis to the pituitary were found. DI was part of the initial presentation in 55 cases (71.4%) and of these 42 (76.4%) presented with isolated DI. This is in
contrast to pituitary adenoma where isolated DI occurs in less than 2% of patients.

**Conclusion:** Isolated DI, especially in patients with prior history of malignancy, should raise the consideration of pituitary metastasis.

**Abstract #814**

**DIABETES INSIPIDUS (DI) COMPLICATED BY ADRENAL INSUFFICIENCY**

*Tulsi Sharma, MBBS, Pearl Dy, MD, Arnold M. Moses, MD*

**Background:** Hyponatremia is a common medical problem but can be challenging in the presence of an associated endocrine disorder.

**Case Presentation:** A 21-year-old female with DI well controlled on DDAVP presented to an outside facility with nausea, vomiting and serum sodium of 127meq/L. The sodium level normalized with normal saline (NS) and her outpatient DDAVP dose. Her symptoms recurred a week later and she returned to the ER with sodium level of 130meq/L. The sodium however decreased to 119 in 3 days despite NS! DDAVP was discontinued and hypertonic saline was initiated. Why did the sodium go down despite therapy? Adrenal insufficiency was suspected and treated with intravenous hydrocortisone. Serum sodium rose to 132 in 10 hours. She became increasingly lethargic, nonverbal and developed a blank affect. She was transferred to Upstate University Hospital. Her sodium at arrival was up to 157, a rise of 38meq/L in 18 hours. During this period, there was no record of urine volume or osmolality and she had not received any DDAVP. She had multiple episodes of seizures and had to be intubated. MRI suggested extrapontine osmotic demyelination. Endocrine consult was obtained. Considering the hypernatremia with hypotonic urine (osmolality 80mosm/kg) DDAVP was restarted. Serum sodium, urine volume and osmolality were closely monitored. She was treated with hydrocortisone, antiepileptics and NS. Urine osmolality normalized, serum sodium was slowly brought down to 140 in 48 hours. Her clinical status however failed to improve despite the correction of hyponatremia. She was then given intravenous immunoglobulin (IVIG) for 5 days and her motor functions improved dramatically, followed by speech and cognition. Even though she had tremendous clinical improvement, repeat MRI showed worsening of the brain lesions.

**Discussion:** This is a very interesting and challenging case which highlights multiple teaching points: 1. Adrenal insufficiency should be strongly considered when hyponatremia develops in a patient with DI who was previously in good control. Repletion with corticosteroids should be done cautiously as it can lead to diuresis of hypotonic urine. This can cause a rapid rise in serum sodium concentration predisposing the patient to risk of myelinolysis. 2. Prognosis of ODS is not uniformly bad. IVIG therapy may accelerate recovery of ODS based on data from a few case reports. Effect is possibly caused by the reduction of myelinoxic substances, antimyelin antibodies, and the promotion of remyelination. 3. MRI changes in ODS may be delayed and MRI severity is not prognostic of clinical outcome.

**Abstract #815**

**A CASE OF A PITUITARY MASS AND MEDIALSTINAL LYMPHADENOPATHY: ‘HICKAM’S DICTUM OR OCCAM’S RAZOR’**

*Dorothy Kodzwa, MD, Bruce Frankel, MD, Marc Judson, MD, Joseph Jenrette, MD, Pierre Giglio, MD, Jyotika Fernandes, MD*

**Objective:** When patients with pituitary mass present with hilar and mediastinal lymphadenopathy, a unifying diagnosis is limited to sarcoidosis, tuberculosis or lymphoma. However, we present a patient had dual diagnoses at presentation to explain the thoracic and central nervous system findings.

**Case Presentation:** A 22 y/o caucasian woman, presented to an outside hospital with fatigue, night sweats, weight loss, polyuria, and polydyspia for the past several months. More recently she complained of amenorrhea, galactorrhea, blurred vision, nausea, emesis and syncopal episodes. Her visual fields were reportedly normal. An MRI scan had suggested a pituitary macro adenoma vs. inflammatory and a serum Prolactin was mildly elevated at 65ng/ml. Bromocriptine was initiated for a presumed diagnosis of prolactinoma, but she tolerated it poorly. A few weeks later, she was readmitted for worsening nausea and vomiting and was found to have hypercalcaemia (with suppressed PTH), diabetes insipidus, hypothyroidism, hyperprolactinemia and hypogonadism. A chest X-ray and CT chest showed high FDG metabolism in the mediastinal and...
hilar lymph nodes. Hence she underwent another EBUS-TBNA to obtain more tissue for diagnosis. The pathology from this specimen was consistent with granulomatous inflammation consistent with sarcoidosis. She is currently receiving pituitary hormone replacement and radiation therapy for the pituitary germinoma. She was not started on corticosteroids for sarcoidosis as she has no pulmonary symptoms and her hypercalcemia, and other endocrinologic abnormalities are controlled.

**Conclusion:** Most cases of metastatic germinomas with mediastinal lymphadenopathy have been described in patients with ventricular shunts. There have been a few case reports of patients with germ cell tumors who have subsequently developed granulomatous disease. The mediastinal lymph node granulomas in this case are unlikely a reaction to the germinoma in that they are in typical locations for sarcoidosis, are distant from the primary tumor, and would not explain the hypercalcemia. This is the first known case of the pituitary germinoma and lung sarcoidosis lesions manifesting together at presentation, which caused initial diagnostic confusion.

**Abstract #816**

**OLIVER-MCFARLANE SYNDROME: AN ENDOCRINE PERSPECTIVE ON A RARE DISORDER**

Matthew Crowley, MD, Jennifer Perkins, MD

**Objective:** To present a new case of Oliver-McFarlane syndrome (OMS), review the 13 previously reported cases, and characterize the Endocrine manifestations of this disorder.

**Case Presentation:** Our patient is a 50 year-old woman with a history of multiple endocrine, neurologic, and morphologic abnormalities detected early in life. Detailed childhood records establish diagnoses of growth hormone deficiency by insulin tolerance testing, hypogonadotropic hypogonadism, central hypothyroidism, and prolactin deficiency. Her adrenal axis remained intact by metyrapone testing. Other abnormalities included retinitis pigmentosa (RP), cerebellar degeneration with severe ataxia, peripheral neuropathy, and morphologic abnormalities including prominent eyebrows and alopecia. Magnetic resonance imaging revealed pituitary hypoplasia. Treatment with growth hormone during adolescence led to linear growth, and treatment with estradiol and medroxyprogesterone produced menarche and secondary sexual development. The patient’s syndromic presentation remained undiagnosed until she reestablished Endocrine care at age 50, at which time her pituitary function abnormalities were confirmed.

**Discussion:** OMS is an extremely rare disorder. Required clinical manifestations appear to include deficiencies of growth hormone and gonadotropins, RP, and trichomegaly. Other abnormalities appear variably, and include thyroid stimulating hormone deficiency, prolactin deficiency, cerebellar degeneration, peripheral neuropathy, alopecia, and mental retardation. Deficiencies of adrenocorticotropic hormone and posterior pituitary hormones have not been noted in OMS. The genetic basis of this disorder is not understood, but pituitary morphologic abnormalities and hormone deficiencies suggest possible involvement of known gene pathways, and several manifestations of OMS have been independently associated with inactivating mutations in G-protein-coupled receptors. Therapeutic measures should include early treatment with growth hormone to achieve appropriate height and treatment of hypogonadism to achieve secondary sex characteristics and maintain bone health. Ours is the fourteenth reported patient with OMS, and is the oldest documented new case.

**Conclusions:** OMS is a rare genetic disorder, with only 13 cases reported previously. No prior report has examined the Endocrine abnormalities associated with OMS in detail. The extensive records available in our case, the duration of follow-up, and the completeness of our patient’s Endocrine evaluation provide significant insight into the presentation and natural history of this disorder.

**Abstract #817**

**RECURRENT CUSHING’S SYNDROME**

Devendra Wadwekar, MD, Robert E Jones, MD

**Objective:** To discuss an unusual case of recurrent Cushing’s syndrome.

**Case Presentation:** A 44 year old female was diagnosed with Cushing’s disease in March 2000 with unequivocal biochemical work up and MRI of her pituitary revealing a 4 mm microadenoma. She was treated with trans-sphenoidal adenomectomy. Two years later she had a recurrence with symptoms and increased urinary free cortisol and underwent a second trans-sphenoidal surgery. She had persistent disease with elevated urinary free cortisol values and declined pituitary radiation therapy. She underwent bilateral laparoscopic adrenalectomy in 2003 and pathology showed the left adrenal gland to have focal areas of nodular cortical hyperplasia. The right adrenal gland had a focal cortical adenoma and nodular cortical hyperplasia. She was started on glucocorticoid and mineralocorticoid replacement therapy. She had several follow up pituitary MRI’s which showed small residual pituitary tissue without any tumor recurrence. Her ACTH
levels remained stable in the range of 100-200 and she did not develop any skin hyperpigmentation. In November of 2009, she was noted to have darkening of the skin and fullness of her face. She was placed on dexamethasone 0.5 mg per day and a 24 hr urine-free cortisol returned within the normal range at 16.7 µg/L. She had an MRI of her pituitary that showed no evidence of tumor recurrence. In 2010 she underwent 1 mg dexamethasone suppression test and 8 AM ACTH was 383 pg/ml with a cortisol of 17.8 µg/dL. She had a CT of her abdomen which demonstrated a 1.8 cm by 0.8 cm soft tissue mass adjacent to the left adrenal surgical clips. Both pelvic CT and an ultrasound were negative for ovarian rests. She underwent a laparoscopic removal of this mass and pathology showed adrenal cortical tissue consistent with recurrent cortical adenoma, size measuring 0.6 cm and 0.5 cm.

**Discussion:** This is a very unusual case of recurrent Cushing’s disease. Extensive review of the literature reveals isolated case reports of recurrent Cushing’s syndrome in patients who have had pituitary surgery as well as bilateral adrenalectomy. Although extensive adrenalectomy was performed initially, it is likely that small microscopic tissue was left behind which was stimulated by ACTH. The other possibility is that she had accessory adrenal tissue around the left kidney which enlarged with time and ACTH stimulation.

**Conclusion:** Cushing’s syndrome can recur in spite of pituitary and adrenal surgeries and lifelong careful monitoring and follow up is indicated.

Abstract #818

**HYPERGLYCAEMIA AMELIORATED BY PITUITARY SURGERY**

Arinola Ipadeola, MBBS, Augustine Adeolu, FWACS, Jokotade Adeleye, FWACP

**Objective:** To report the case of a patient with a recurrent pituitary tumor who developed steroid induced hyperglycaemia which improved following surgery despite steroid replacement therapy.

**Case Presentation:** A 29 year old lady presented with progressive visual impairment and headaches of 2 months duration, 2 years after she had surgical excision of a giant pituitary tumor. She had no history of menstrual irregularities and was observed to have coarse facial features with deranged hormonal profile while being worked up for surgery. Her 8am Cortisol was 7.95(54.94-287.56ng/ml), FT3- 1.66pmol/l(4.8-3.3) FT4-6.38pmol/l(9-20), TSH-0.698iu/l(0.27-4.7), Estradiol 9.79pg/ml(18-147)pg/ml, FT3- 1.66pmol/l(4-8.3) FT4-6.38pmol/l(9-20), TSH-0.698iu/l(0.27-4.7), Estradiol 9.79pg/ml(18-147)pg/ml, Growth Hormone – 19.10 µg/L (<5.4 µg/L) and mildly elevated Prolactin. Serum electrolytes, urea and creatinine were within normal limits. Fasting Plasma Glucose was 66mg/dl and 2 hours post prandial glucose was 106mg/dl. She was subsequently commenced on Dexamethasone for correction of secondary hypoadrenalism and reduction of intracranial pressure. Two weeks later, she was commenced on Levothyroxine 100micrograms daily. Fasting blood glucose was subsequently found to be 215mg/dl and she was commenced on insulin for management of steroid induced Diabetes Mellitus. She required 140 iu of insulin and 2grams of metformin for optimal glycaemic control prior to surgery. Following excision of the tumor, she did not require insulin as random blood glucose values remained within normal limits. Metformin was prescribed for persistently impaired fasting glucose while she continued hormonal replacement.

**Discussion:** Insulin resistance is well known in cases of excess growth hormone production. This may be responsible for the high insulin requirement in this patient apart from the steroid therapy. Hyperglycaemia resolved following tumor excision despite the continued use of steroids for treatment of hypoadrenalism.

**Conclusion:** Steroid induced diabetes mellitus is common in patients being managed for neurosurgical tumors on dexamethasone for treatment of vasogenic cerebral oedema. It appeared that in this patient the primary tumor had a role to play in the worsening of hyperglycaemia prior to surgery and improvement in glycaemic control following its excision supports this.

Abstract #819

**43 YEAR OLD FEMALE WITH NON-HEALING PATHOLOGIC PELVIC FRACTURE**

Kasra Navabi, MD, Saka Kazeem, MD, Shireen Zindani, MD, Viplov Mehta, MD

**Objective:** Clinical decision making for patients with Cushing’s syndrome involves a complicated diagnostic assessment and one of the most challenging endocrine pathologies. Systematic approach even in complicated or atypical clinical features leads to early diagnosis and treatment.

**Case Presentation:** We present an unusual presentation of Cushing’s disease due to adrenocorticotropic hormone (ACTH) secreting pituitary adenoma. A 43-year-old woman was seen because of new onset diabetes, pathologic non-healing hip fracture, weight gain, swelling of the face, hypertension; until approximately two years ago she was relatively healthy without diagnosis of diabetes or hypertension or obesity. It was found that patient had non-healing hip fracture and was sent for endocrinology evaluation for metabolic bone disease. Physical examination revealed the features suggesting of Cushing’s syndrome. Urinary free cortisol levels were
significantly elevated. After overnight (1 mg), low dose (2 mg) dexametasone tests serum cortisol levels were not suppressed and adrenocorticotropin hormone (ACTH) levels were high. An 8-mm mass lesion suggesting a microadenoma was shown on the magnetic resonance imaging of the pituitary gland. Endoscopic transnasal transsphenoidal resection of the adenoma was done in another institution and adrenocorticotropin hormone (ACTH) positive adenoma with no positive markers for any other hormone was described on pathology report. After resection of the adenoma the levels of adrenocorticotropin hormone (ACTH) and cortisol immediately returned to normal and fracture healed. The patient lost 90 pounds, blood glucose level and blood pressure are now in control. 

Discussion: Most of the studies in the literature on Cushing’s syndrome with pathologic fracture refer to exogenous over-exposure to cortisone and its synthetic derivatives which is caused by the use of synthetic glucocorticoids to treat an inflammatory condition. Only a small number of works concern endogenous hypercortisolism. Endogenous Cushing’s syndrome has an incidence of 1 to 2.5 cases per 1 million persons per year in the United States. It occurs five times more frequently in women than in men, with the peak incidence occurring between 20 to 50 years of age. Excess ACTH secretion by pituitary tumor is the cause of endogenous Cushing syndrome in 70% of patients. Although Cushing’s syndrome is not common, the clinical features of hypercortisolism are common and are associated with increased morbidity and death. The diagnosis of Cushing’s syndrome still represents a challenge for the endocrinologist. Correct implementation and interpretation of diagnostic procedures require expertise and a high degree of clinical knowledge. 

Conclusion: This is an instructive case that reminds us to consider Cushing’s syndrome including Cushing’s disease with overlapping clinical features with those of common diseases found in the general population or in some patients have an atypical clinical presentation with only isolated symptoms.

Abstract #820

A RARE CASE OF SECONDARY ADRENAL INSUFFICIENCY IN HEREDITARY HEMOCROMATOSIS

Himara Davila Arroyo, MD, Sreedevi Guttikonda, MD

Objective: To report a rare case of secondary adrenal insufficiency in a patient with hereditary hemochromatosis (HH).

Case Presentation: Here we describe a 41-year-old Caucasian male who presented with fatigue, abdominal pain, nausea, vomiting, dyspnea, and lower extremity edema. On examination, his signs and symptoms were consistent with fluid overload, and bronze pigmentation of the skin was also noticed. Congestive heart failure was suspected for which an echocardiogram was performed showing biventricular failure with an ejection fraction of 15% and subsequent cardiac catheterization was suggestive of restrictive cardiomyopathy. An infiltrative disease was then suspected and further workup revealed elevated percent iron saturation at 88% and elevated ferritin at 1910 ng/mL. HH was confirmed with PCR for HFE gene that showed C282Y homozygous polymorphism for the hemochromatosis mutation. With the additional symptoms of abdominal pain, fatigue and nausea; hypocortisolism was also suspected and an 8 am cortisol level was obtained which was low at 3.99 µg/dL. Cosyntropin stimulation test with 250 mcg of cosyntropin IV was performed and measured peak cortisol levels at 30 and 60 minutes after the infusion were < 18 µg/dL which confirmed adrenal insufficiency. A simultaneous 8 am ACTH level was 10 pg/mL which was suggestive of secondary adrenal insufficiency. Other hormonal tests showed a FSH of 1.60 mIU/mL, LH 1.83 mIU/mL, testosterone 13.3 ng/dL, prolactin 13.7 ng/mL, TSH 11 mIU/mL, and Free T4 of 1.24 ng/dL. With the abnormal ACTH stimulation test, low normal ACTH level, absence of electrolyte abnormalities, and unremarkable CT and MRI of the adrenal glands; the diagnosis of pituitary dysfunction was suggested in this patient with HH.

Discussion: The two most frequent endocrine complications of HH are diabetes mellitus and hypogonadotropic hypogonadism. Other endocrine disorders related to this disease are very rare. The consensus view has been that iron predominantly deposits in the gonadotrophs, but there is evidence of iron deposition in other secretory cells. From a literature review, gonadotropic insufficiency was observed in 46%, growth hormone axis insufficiency in 15%, lactotroph insufficiency in 8%, thyroid axis dysfunction in 4%, and adrenocortical axis dysfunction in 1.5% or less of patients with HH.

Conclusion: Here we report a rare case of pituitary dysfunction manifesting as secondary adrenal insufficiency in a patient with HH. Physicians must be aware of the most common, as well as, the rare endocrine manifestations of hemochromatosis because clinical suspicion will be the key for a rapid diagnosis and treatment.
Abstract #821

CHLORPROPAMIDE TREATMENT FOR DDAVP-RESISTANT DIABETES INSIPIDUS AFTER TRANSSPHENOIDAL SURGERY FOR GIANT PITUITARY ADENOMA

Elkin Armando Nunez, MD, Maya Raghuwanshi, MD, Jean Anderson Eloy, MD, James K. Liu, MD

Objective: Diabetes insipidus (DI) following transsphenoidal pituitary surgery is a well-recognized entity and readily controlled with DDAVP. We describe a rare case of DDAVP-resistant DI that improved after chlorpropamide therapy.

Case Presentation: A 51-year-old male presented with bitemporal hemianopsia, erectile dysfunction and chronic headache secondary to a giant non-functioning pituitary adenoma that extended into the top of the third ventricle with optic compression. Endonasal endoscopic extended transsphenoidal resection of the tumor was performed to decompress the optic chiasm. Post-operatively, the patient developed DI, which was readily controlled with small doses of DDAVP. On post-operative day 12, the patient developed recurrent DI with minimal to no response to DDAVP. The urinary output increased from 705 to 2454ml/hr. Sodium levels increased to as high as 155 with a urine S.G. of < 1.004, and a serum osm of 315. Intravenous hydration was increased since the patient was unable to keep up with such high fluid demands. Oral chlorpropamide was initiated at 125 mg bid and the patient began to respond to a desmopressin drip resulting in decreased urine outputs. Chlorpropamide was discontinued after four days and the patient remained normonatremic on a steady dose of oral DDAVP.

Conclusion: DDAVP-resistant DI is a rare condition following transsphenoidal pituitary surgery and should be recognized early during the postoperative period so that appropriate therapy can be initiated. Chlorpropamide appears to be a favorable treatment for DDAVP-resistance. To our knowledge, this is the first case report using chlorpropamide in severe DDAVP-resistant DI after transsphenoidal pituitary surgery.

Abstract #822

METASTATIC RENAL CELL CARCINOMA MIMICKING A PITUITARY MACROADENOMA

Anuritha Reddy Marumganti, MD, Antoine Makdissi, MD, Varuna Nargunan, MD, Kruti Shah, MD, Ajay Chaudhuri, MD, Jody Leonardo, MD

Objective: To report a rare case of renal cell carcinoma metastasing to the sella turcica.

Case Presentation: A 63-year-old woman presented with headaches and diplopia. Eighteen months prior, she had left radical nephrectomy for renal cell carcinoma with bony metastases followed by chemotherapy. On ophthalmologic examination, there was left lateral rectus palsy with no visual field deficits. Magnetic resonance imaging demonstrated a 20 x 29 x 30 mm enhancing sellar mass with cavernous extension bilaterally and erosion of the floor of the sella. Superiorly, it was causing displacement of the optic chiasm. The initial radiological impression was that of a pituitary macroadenoma. Biochemical evaluation revealed, morning serum cortisol value of 6.3 mcg/dL [reference range: 5-25], serum ACTH 12 pg/mL [6-46], FSH 1.8 milliUnit/ml [post menopausal range: 22-120] and LH 0.4 milliUnit/ml [post menopausal range: 10-50]. Prolactin concentration was marginally increased at 29.4 ng/mL [2-20] with no change with dilution, IGF-1: 239 ng/mL [47-264] and alpha subunit level <0.3 ng/ml [0, 9-3.3] were normal. She was on thyroid replacement s/p total thyroidectomy with free T4: 1 ng/dL [0.8-1.8] and TSH: 0.021 mcUnit/ml [0.4-5]. Serum sodium and potassium were 138 mmol/L and 4.4 mmol/L, respectively. Hormone replacement was started with hydrocortisone due to low normal morning basal cortisol, and levothyroxine dose was adjusted. The patient underwent endoscopic trans-nasal trans-sphenoidal biopsy of the tumor. Histological examination of the tumor revealed metastatic renal cell carcinoma. With subsequent gamma knife stereotactic radiotherapy, patient exhibited marked improvement in headaches and visual symptoms.

Discussion: Renal cell carcinoma has a complex and variable natural history. Symptomatic metastases to the pituitary from renal cell carcinoma are rare. Data in literature are mostly case reports. Carcinomas of the breast or lung are most frequently involved. Anterior pituitary dysfunction and visual disturbances are more common initial features with renal carcinoma metastases, compared to those from other primaries, whereas diabetes insipidus is less common. Clinically in practice, it is also rare to have pituitary macroadenomas present with diplopia, unless apoplexy is involved. Magnetic resonance
imaging shows strong enhancement of the tumor. Sellar bony destruction is another characteristic feature.

Conclusion: This case illustrates that metastatic pituitary lesions from renal cell carcinoma can mimic typical symptoms and signs of pituitary macroadenoma.

Abstract #823

TUBERCULOUS HYPOPHYSITIS IN A CASE OF TUBERCULOUS MENINGITIS

Sachin Kumar Jain, MD, MBBS, DM, FACE, N. Jain, MD, R. Ekka, MD, T. Akhtar, MD, D. Rath, MD, H. Gupta, MD

Objective: Present a case of tubercular meningitis with recurrent hyponatremia which also turned out to be panhypopituitarism, secondary to tubercular hypophysitis.

Case Presentation: A 45-year-old male who was earlier presented with complaints of generalized weakness, loss of appetite, urinary incontinence, low grade fever, and headache for 14 days. Clinically patient was diagnosed to be a case of meningitis following which, a lumbar puncture was done, which revealed tubercular meningitis. His NCCT head was normal. He was started on category I anti-tubercular therapy with steroids. Steroid was given for 1 ½ month and was gradually tapered and stopped. On many occasions, it was found that he was having persistent hyponatremia for which a possibility of SIADH in a case of tubercular meningitis was made. His salt intake was increased and water intake was restricted but of no avail. Patient was administered 3% NaCl. Subsequently his serum Na⁺ returned to normal, he improved symptomatically and was discharged. He was readmitted after 4 months with complaints of headache and altered sensorium for 2 days. His complaints of weakness and decreased appetite persisted even after earlier discharge. There was no fever, vomiting, loose motions, or blurring of vision. There were no complaints suggestive of focal neurological deficit. His urine output was adequate. On routine investigation, he was found to have hyponatremia, with serum Na⁺ level hovering around 110-115. During second admission his general physical examination was normal. His nutritional status had improved (BMI 22Kg/m2). There were no signs of vitamin deficiencies and no skin pigmentation. His blood pressure was 100/70 mm Hg. Systemic examination did not reveal any abnormality. During second admission: Hb: 12.7 g/dl (12-16); TLC: 4800 (4000-11000); DLC: P³ L⁴ E₂; Platelet: 2.10 lakh; Blood glucose: 64 mg% (70-110); Na⁺ 110 meq/l (135-145); K⁺ 3.8 meq/L (3.5-5.5); Ca²⁺: 8.6 mg/dl (8.5-10.5); Kidney function and liver function tests revealed no abnormality. Total Cholesterol: 166 mg/dl (150-200); Triglyceride: 117 mg/dl (130-230), Chest X-ray: normal; USG abdomen: normal study; NCCT head: Normal study; CSF protein: 84 mg/dl (40-70), CSF Sugar: 53 mg/dl (60-100); CSF cytology: 5 cells, all lymphocytes. ZN stain and India ink stain: negative; Culture: revealed no growth. HIV I & II: negative. Urinary Na⁺: 136 mmol/L. Inspite of clinical and biochemical improvement, patient continued to have persistent hyponatremia. So we decided to work up further. fT₃: 2.15 pg/ml (2-4.4), fT₄: 0.24 ng/dl (0.6-2.2), TSH: 6.2 mIU/L (0.5-5.5); Total Testosterone: 0.283 nmol/L (4.56-28.2 males 20-50 years); FSH: 3.98 mIU/ml (1.55-9.74 in males), LH 1.23 mIU/ml (1.8-7.8 males); Lactrogen: 37.7 ng/ml (3-18.6); Cortisol: 3.29 nmol/L (123-626); ACTH: 10 pg/ml (7.20-63.30). The above finding clearly shows that the patient has secondary hypothyroidism, secondary hypogonadism, and possibly hypocortisolism. (Patient had received steroids for 2 months, 4 months earlier.) His MRI report revealed an empty sella. IGF -1 and growth hormone stimulation studies could not be done. Detailed work up revealed that patient also had secondary hypothyroidism and secondary hypogonadism and hypocortisolism, so a diagnosis of panhypopituitarism was made, possible etiology being tubercular hypophysitis in this case of tubercular meningitis.

Discussion: The patient was started on steroid, thyroxine and testosterone replacement therapy and anti-tubercular therapy was continued. The patient started showing significant improvement and feeling of well-being and appetite. His serum Na⁺ remained within normal range even on normal salt diet.

Abstract #824

PITUITARY APOPLEXY IN A YOUNG WOMAN WITHOUT ANY IDENTIFIED PRECIPITATING FACTOR

Amanjot Singh Lehil, MBBS, Kaartik Soota, MS4, Vaishali Patel, MD, Rajib Bhattacharya, MD

Objective: “Pituitary apoplexy” refers to a clinical syndrome caused by rapid enlargement of a pituitary adenoma usually due to hemorrhage or infarction. Several precipitating factors have been reported, most frequently hypotension, advanced age, closed head trauma, hypertension, cardiac surgery, anticoagulant therapy, dopamine agonists, and dynamic testing of pituitary function. In this case no such factor was identified.

Case Presentation: A 24 year old female came to ER with severe throbbing headache, nausea, vomiting, and diplopia that started several hours ago. She also had amenorrhea for past 4 months, and hirsutism and central obesity since childhood. Past medical and surgical history was unremarkable. Vital signs were stable. Physical examination was remarkable for right sided 3rd nerve
palsy, moon facies, marked obesity, hirsutism over face, acanthosis nigricans and coarse skin. She was started on i.v. hydrocortisone q8h, and underwent transsphenoidal resection of adenoma the following day. Workup of anterior pituitary hormones revealed low level of TSH, high IGF-1. ACTH, FSH, LH, prolactin were within normal limits. After 3 days on i.v. steroids she was switched to a tapering course of oral hydrocortisone. Diplopia improved, but not resolved, by the time of discharge.

Discussion: Sudden hemorrhage or infarction in the pituitary adenoma leads to increase in intrasellar pressure due to rigid walls of sella. Most common symptoms include headache, nausea, and visual abnormalities. Altered sensorium, hemiplegia, SAH and meningeal irritation can also occur. Compression of normal pituitary tissue and vasculature can result in hypopituitarism, most concerning of which is acute adrenal insufficiency. MRI is the imaging modality of choice. Management includes supraphysiological doses of glucocorticoids. Prompt transsphenoidal surgery is recommended for patients with associated visual acuity or visual field defect, because if performed within 8 days of presentation, it results in significantly greater improvement in vision abnormalities as compared to delayed surgery. Long term hormone replacement is required in many patients, and in some patients partial or complete recovery of pituitary function can occur. Close follow up is recommended for all patients on a long term basis.

Conclusion: Pituitary apoplexy is a life threatening endocrine emergency that may occur in individuals with few or no risk factor or precipitating events.

Abstract #825

CUSHING’S DISEASE, AN IMPORTANT DIFFERENTIAL DIAGNOSIS OF POLYCYSTIC OVARY SYNDROME

Rachel Baerga Duperoy, MD, Marjan Vahedi, MD

Objectives: To emphasize that Polycystic Ovary Syndrome (PCOS) is a diagnosis of exclusion.

Methods: A 25 year old female presented to our endocrinology clinic with 70 pounds of weight gain, depression and amenorrhea for one year. Her boyfriend had died one year before. She attributed the weight gain to the depression and lack of activity. There was history of polyuria, polydipsia and acne. The patient was told that she had PCOS, she was on no medications. On physical examination, blood pressure was 160/90 mm Hg, pulse rate was 70/min and weight was 244 lbs. She had oily skin, generalized obesity, moon facies, facial acne and wide pinkish striae on her abdomen. There was no hirsutism. The following lab values were normal: Electreoytes, BUN, creatinine, thyroid function tests and also testosterone and gonadotropins. The abnormal tests included: LDL 276 mg/dL, HDL 25 mg/dL, slightly high LFTs, HBA1C 12 %, prolactin 45 ng/mL (high), 24 hour urine free cortisol were in 480 mg and 360 mg in two consecutive collections (normal up to 50 mg/ 24 hour). ACTH at midnight was 43 pg/mL (high). Pituitary MRI showed a 1.5 cm macroadenoma, with slight deviation of the stalk. Patient underwent transsphenoidal resection of the tumor. Pathology stained positive for ACTH. During 3 months post-op, the patient lost about 40 pounds, her moon facies improved significantly and her acne resolved. Before the surgery, she required Lisniopril 40 mg daily, Norvasc 10 mg daily, insulin 100 units/day and Metformin 1000 mg twice daily. Shortly after the surgery, Norvasc was stopped; blood pressure is now well controlled on Lisinopril 20 mg daily. Her need for insulin decreased from 100 units/d to 35-40 units/d. Initially, she was started on Lipitor 80 mg/d, which was then gradually decreased to 10 mg/d. Last HB1C was 6.3%, last LDL was 75 mg/dL. Post-op, she was started on Hydrocortisone 20 mg in the am, and 10 mg in the pm. On this dose, she experienced steroid withdrawal symptoms. With the increase in the dose of Hydrocortisone, these symptoms resolved. Her pituitary adrenal axis has now recovered; we are gradually decreasing her Hydrocortisone dose. Repeat MRI did not show any tumor residue.

Discussion: The diagnostic criteria for PCOS are as following: 1-Oligo- or anovulation 2- Clinical and/ or biochemical signs of hyperandogenism 3- Polycystic ovaries and exclusion of other etiologies (Congenital adrenal hyperplasia, androgen-secreting tumors, Cushing’s syndrome). The key point is to remember that PCOS is a diagnosis of exclusion.

Abstract #826

VIABLE PREGNANCY IN ACROMEGALY AFTER TRANSPHENOIDAL RESECTION OF A GROWTH HORMONE SECRETING MACROADENOMA

Rachanon Murathamun, MD, Mais Trabolsi, MD, Tahira Yasmeen, MD, FACE, Farah Hasan, MD, FRCP, FACE

Objective: To report a case of pregnancy in an acromegalic woman following transphenoidal resection of a growth hormone-secreting pituitary macroadenoma.

Case Presentation: A 25 year-old female presented with a 15 month history of amenorrhea. Patient reported
were as follow: IGF-I was consistent with her symptoms. The laboratory results hairs, oily skin, and deepening of voice. Physical exam increase in body and facial features. She also noticed increase in size of her hands, feet and change of her an increase in the size of her hands, feet and change of her facial features. She also noticed increase in body and facial hairs, oily skin, and deepening of voice. Physical exam was consistent with her symptoms. The laboratory results were as follow: IGF-I 827 ng/mL (normal, 89-397); normal prolactin, FT4 and TSH; low estrogen with normal LH and FSH levels. A 75-g glucose tolerance test demonstrated no suppression of GH. MRI of the pituitary gland revealed a 2.2 cm pituitary macroadenoma and displacement of optic chiasm with no extension to cavernous sinuses. Patient underwent a transphenoidal resection of the pituitary macroadenoma. One month postoperatively IGF-I level was still elevated at 440 ng/mL (normal, 89-397) and GH remained non-suppressed with glucose tolerance test. Two months following surgery and before initiation of pharmacological therapy, patient became pregnant. This was confirmed with a positive β-HCG and a viable intrauterine pregnancy demonstrated by ultrasonography. Patient was advised to follow up closely. During pregnancy she reported no visual changes or headaches. No visual field defects, gestational diabetes or hypertension was revealed. IGF-I level was 225 ng/mL (normal, 89-397) in the second trimester. Patient had an uneventful vaginal delivery of a healthy, full term infant. Four months after delivery the pituitary MRI demonstrated minimal residual tissue present in the anterior sella with more bulky normal appearing pituitary gland posteriorly. Postpartum IGF-I level and glucose tolerance were normal.

Discussion: Our patient was diagnosed with acromegaly and secondary hypogonadism. Several mechanisms have been described in the literature to explain the infertility of acromegalic patients. These mechanisms include hypopituitarism and decreased gonadotropin reserve due to destruction or compression of gonadotroph cells; hyperprolactinemia; and excessive GH/IGF-I secretion leading to sensitization of the ovaries to gonadotropin stimulation. Transphenoidal resection of GH secreting pituitary macroadenoma might be adequate to restore fertility, as in our case. During pregnancy patients are at increased risk of tumor enlargement, visual loss, glucose intolerance, gestational diabetes and hypertension. Changes in serum GH and IGF-1 concentration are variable during pregnancy. Pituitary MRI is indicated before conception and should be repeated after 4 months gestation only if there is presence of headache or visual field loss. In absence of clinical evidence of tumor expansion, pituitary MRI can be repeated postpartum.

Conclusion: Pregnancy is rare in women with acromegaly and secondary hypogonadism. Several mechanisms have been described in the literature to explain the infertility of acromegalic patients. These mechanisms include hypopituitarism and decreased gonadotropin reserve due to destruction or compression of gonadotroph cells; hyperprolactinemia; and excessive GH/IGF-I secretion leading to sensitization of the ovaries to gonadotropin stimulation. Transphenoidal resection of GH secreting pituitary macroadenoma might be adequate to restore fertility, as in our case. During pregnancy patients are at increased risk of tumor enlargement, visual loss, glucose intolerance, gestational diabetes and hypertension. Changes in serum GH and IGF-1 concentration are variable during pregnancy. Pituitary MRI is indicated before conception and should be repeated after 4 months gestation only if there is presence of headache or visual field loss. In absence of clinical evidence of tumor expansion, pituitary MRI can be repeated postpartum.

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Discussion: Most patients with acromegaly during PG do not have an increase in tumor size, metabolic complications are uncommon, and neonatal outcome is largely unaffected. IGF-1 tends to decrease during PG in such patients possibly due to high estrogen levels causing GH resistance. Dopamine agonists, somatostatin analogues, and GH receptor antagonist (single case) have been reported to be safe during PG. Patients with visual field defects should be considered for surgery, but in most

Abstract #827

A RARE CASE OF ACROMEGALY DIAGNOSED DURING PREGNANCY

Vicky Cheng, MD, Fadi Khoury, MD, Laurence Kennedy, MD, Charles Faiman, MD, Betul Hatipoglu, MD, Robert Weil, MD, Amir Hamrahian, MD

Background: Fertility in women with acromegaly is decreased due to altered gonadotropin secretion resulting from a pituitary mass effect and/or hyperprolactinemia. Evaluation of acromegaly may be difficult during pregnancy (PG) due to placental GH secretion and the physiological elevation of IGF-1 in PG.

Objective: To report a case of acromegaly diagnosed and treated with a somatostatin analogue during PG.

Case Presentation: A 30-year-old woman, G2P1, 13 weeks’ gestation, was referred because of elevated IGF-1 805 ng/mL (117-329) at six weeks’ gestation and clinical features suggestive of acromegaly. She had noticed worsening headache, acne, increase in jaw line, and larger hands and feet for two years. A PG two years prior was uneventful. On exam, she had coarse facial features, broad hands and normal visual fields. Labs: prolactin 99 ng/mL (2.0-17.4), IGF-1 816 and 1085 ng/mL, basal and nadir GH during OGTT 13.9 and 12.8 ng/mL, respectively. Glucose levels and blood pressure were normal. Pituitary MRI without contrast revealed a 1.5 cm macroadenoma with no impingement of the optic chiasm. She was unable to tolerate bromocriptine and was started on octreotide at 19 weeks’ gestation. She reported relief of the headache and improvement in clinical features. IGF-1 increased to 1078 ng/mL one week postpartum while on octreotide. MRI was stable four weeks postpartum following which she underwent transsphenoidal resection of the pituitary adenoma which stained positively for GH. Post-operatively, GH and IGF-1 were 7.5 and 892 ng/mL, respectively, and she was treated with a long-acting somatostatin analogue during PG.

Discussion: Most patients with acromegaly during PG do not have an increase in tumor size, metabolic complications are uncommon, and neonatal outcome is largely unaffected. IGF-1 tends to decrease during PG in such patients possibly due to high estrogen levels causing GH resistance. Dopamine agonists, somatostatin analogues, and GH receptor antagonist (single case) have been reported to be safe during PG. Patients with visual field defects should be considered for surgery, but in most
cases this can be safely postponed until after delivery.

**Conclusion:** Overall, pregnancy has a favorable effect on acromegaly. The majority of pregnancies are uneventful and newborns unaffected. Somatostatin analogues have not been associated with major adverse effects to the fetus; however, more data are needed to validate their safety during pregnancy.

**Abstract #828**

**BRASS CANCER METASTASIS PRESENTING AS A SELLA MASS**

Ashita Gupta, MD, MPH, Harmeet Narula, MD

**Objective:** To recognize manifestations of pituitary metastasis and differentiate from primary pituitary tumors.

**Case Presentation:** A 43-year-old caucasian female was admitted for headache, vision changes, nausea, vomiting and confusion since 3 months that had worsened over last few weeks. Her past medical history was significant for Stage IV breast cancer with bone metastases. The patient’s presenting symptoms had been initially worked up 3 months prior by her oncologist. An MRI Brain at that time had revealed a 9mm infundibular lesion. A follow up MRI Brain done a few weeks prior to this admission showed significant increase in the size of the mass, seen as a 25mm sella/suprasellar mass with thickened stalk. On physical exam, our patient was morbidly obese with stable vital signs and waxing and waning consciousness. Lab work up showed that she had panhypopituitarism (TSH 6.5mcUnits/ml, T4 5.2mcg/dL, FTI 4.7, FSH 2mcUnits/ml, LH < 0.7mcUnits/ml, AM Cortisol 1.5mcg/dL). Prolactin was high: 86ng/ml with normal dilution study. She had a urine output of approximately 250cc/hr overnight with a high serum osmolarity of 302 mOsm/kg and a low urine osmolarity of 95 mOsm/kg. The patient was admitted to the MICU stepdown for close monitoring and her diabetes insipidus was treated with DDA VP with good response. The patient’s pituitary lesion was treated with dexamethasone and a course of radiation therapy. This case underscores the important distinguishing characters between primary and metastatic pituitary lesions.

**Abstract #829**

**CUSHING’S DISEASE OR CUSHING’S CONUNDRUM: A VIEW FROM ENDOCRINE FELLOW’S CONTINUITY CLINIC**

Sergio Eduardo Chang Figueroa, MD, Uzma Khan, MD, Lilamani Kurukulasuriya, MD, Stephen Brietzke, MD

**Objective:** To examine the course of four cases of Cushing’s disease (CD) persistent after transsphenoidal adenomectomy.

**Case Presentation:** Case 1: 46-year-old man presented with multiple vertebral fractures associated with low bone mineral density (T-score -3.5) in the L-spine. Serum cortisol failed to suppress after dexamethasone 0.5 mg (LDDST); 24-hr urine free cortisol was 201ug/24hr, and plasma ACTH was not suppressed, establishing a clinical diagnosis of ACTH-dependent Cushing syndrome. Pituitary MRI was normal, but inferior petrosal ACTH sampling (IPSS) demonstrated > 3:1 IPS:peripheral venous ACTH. Left hypophysectomy confirmed a 2-mm corticotroph adenoma (CA) but was not curative. Subsequent treatment has included gamma knife radiotherapy and ketoconazole 1200mg daily. Case 2: 46 year old woman presented with DM, hypertension, morbid obesity, severe osteoporosis and muscle wasting. Two of three midnight salivary cortisol samples were significantly elevated and serum cortisol failed to suppress on a LDDST and plasma ACTH was elevated, consistent with ACTH-dependent Cushing syndrome. Sellar MRI was normal, but IPSS localized an IPS: peripheral venous ACTH. Left hypophysectomy confirmed a 2-mm CA but serum cortisol remained elevated postoperatively, and ketoconazole was initiated pending repeat sellar surgery. Case 3: 41 year old woman with new onset hypertension and DM, failed LDDST cortisol.
and had slightly elevated midnight salivary cortisol. Pituitary MRI and IPSS localized to the left, and left hemi-hypophysectomy demonstrated CA. At six months’ follow-up, hypercortisolism appears resolved. Case 4: A 27-year-old woman underwent urgent sellar decompression for hemorrhagic pituitary apoplexy. At 1 and 3 months postoperatively, serum pituitary hormones appeared normal; however, she developed avascular necrosis of both hips, and at that time, she failed LDDST and had elevated plasma ACTH. Pituitary MR 1 showed recurrent mass lesion, identified as CA on repeat transsphenoidal resection. Persistent postoperative hypercortisolism is being treated with ketoconazole and radiotherapy.

Discussion/Conclusion: Residual hypercortisolism following transsphenoidal surgical treatment of Cushing’s disease is common and requires diligent reassessment and interdisciplinary management. An individualized approach and close cooperation between the patient, endocrinologist, neurosurgeon, and radiotherapist is essential.

Abstract #830

CENTRAL DIABETES INSIPIDUS POSSIBLY SECONDARY TO ROAD TRAFFIC ACCIDENT

Sachin Kumar Jain, MD, MBBS, DM, FACE, N. Jain, MD, D. Rath, MD, A. Mantri, MD, H. Gupta, MD

Objective: To present a case of diabetes insipidus.

Case Presentation: A 27-year-old man presented with increased urination and thirst of 4 months duration. Patient was fine 4 months back, when he suddenly developed increased frequency of urination (8-10 times during the daytime and 6-8 times during the night). No history of dysuria or haematuria. Frequency and volume of urine increased over next 15 days to a urinary output of 8-9 liters/day associated with markedly increased thirst leading to 8-10 liters of fluid intake per day. Patient also felt dizzy at times. No history of headache, vomiting, fever, change of appetite, disturbed sleep rhythm, visual disturbances, any psychiatric illness or any drug treatment. There was a history of motor bike accident 6 year back. There was history of fall (patient was not wearing helmet at the time of accident) but no history of vomiting or loss of consciousness at that time and there was nothing to suggest for any brain injury. There was history of use of anabolic steroid for body building 4 years back. Pulse 84/min, BP 110/70 mmHg, no postural drop and rest of general and systemic examination was normal. Hb14.1 gm% (12-16), TLC 9300/mm³ (4000-11000), PCV 46.8%, rest of blood counts are within normal limits. Fasting blood glucose 91 mg/dl (60-110), serum urea 23 mg/dl, creatinine 0.8 mg/dl, uric acid 6.8 mg/dl, total bilirubin 0.6 mg/dl (direct 0.2 mg/dl, indirect 0.4 mg/dl), AST 37 U/L, ALT 22 U/L, ALP 128 U/L, serum total protein 7.6 g/dl, albumin 3.8 g/dl, globulin 3.8 g/dl, serum Na⁺ 148 meq/l, serum K⁺ 3.9 meq/l, serum Ca++ 8.9 mg/dl, serum PO₄⁻³ 4.2 mg/dl, 24 hour urine volume 8.4 liter (117 ml/kg ), Serum osmolality 313 mosm/kg of water (282-303), Urine Na⁺ 35meq/L (40-220), Urine osmolality 134mosm/kg of water (200-1192), Urine specific gravity 1.005 (1.015-1.025). Water deprivation test reveals that he had neuro-hypophyseal diabetes insipidus. MRI brain for hypothalamic pituitary region was normal. Diagnosis of central diabetes insipidus was made. Tab desmopressin 0.1 mg/day started, with which urine volume decreased to 4-5 lt./day and then dose was increased to 0.2 mg/day with which urine volume came down to 1.5 to 2 lt./day. We plan to have a follow up MRI brain after 1-2 years.

Discussion: Interesting point in this patient of central diabetes insipidus is whether it is related to possible head injury sustained during bike accident or due to any other etiology for which we will repeat MRI of Hypothalamic Pituitary area.

Abstract #831

SIDE EFFECTS OF STEREOTACTIC THERAPY IN PATIENT WITH ACROMEGALY

Mariela Nieves-Rodriguez, MD, Margarita Ramirez, MD, Myriam Allende-Vigo, MD, MBA, FACP, FACE, Marielba Agosto, MD, Meliza Martinez, MD

Objective: To report a patient with acromegaly who two years after Stereotactic Radiosurgery developed radio necrosis.

Case Presentation: A 28-year-old female patient diagnosed with Acromegaly in 2006 after complaints of headaches, arthralgias, engorgement of lips, tongue and fingers. Elevated levels of IGF-1 and no suppression of Growth Hormone after glucola were documented at the time of diagnosis; MRI was done revealing a pituitary mass of 1.4 cm without any other cerebral parenchyma lesion. Patient had Trans Sphenoidal Surgery in 2007 without resolution of her Acromegaly. She was started on Octreotide after surgery and one year later, patient underwent Stereotactic Radiosurgery. She lost follow up and came to our clinics in January 2010 without therapy for her Acromegaly and presenting severe headaches, described as pressure and throbbing pain. New MRI was ordered and showed a left temporal lobe solitary ring enhancing mass of 1cm x 1cm with associated edema; pituitary in this study did not showed any lesion, and when compared with previous imaging studies, this lesion was completely new. Patient was started on corticosteroids for the edema and due to no resolution of.
Abstract #832

NEUROSARCOIDOSIS AND DIABETES INSIPIDUS: A TWIST IN THE TALE

Adedayo David Adegite, MBBS, Dinky Levitt, MD

Objective: To describe a dramatic case of Neurosarcoidosis and diabetes insipidus.

Case Presentation: A 29-year-old lady was diagnosed with Bell’s palsy by a private GP and commenced on a course of corticosteroid. The following week she developed weakness of the left leg and arm with dysphagia and dysarthria. She was thereafter referred for further investigation. She had leucocytosis and ESR of 52mm in 1 hour (0-15), abnormal LFT with ALT 64U/L (5-40), AST 33U/L (5-40), GGT 106U/L (0-35) ALP73U/L (40-120). Screening for VDRL, HIV, SLE and vascular collagen disease were all negative. CSF analysis showed: protein 0.96g/L (0.15-0.45), glucose 2.7mmol/L (2.2-3.90) Lymphocyte 32, PMN 0, RBC 0.

Discussion: Post radiation reactions in the CNS are well described and catalogued as acute, subacute and late CNS reactions. Acute reactions occur as a transient swelling phenomenon that occurs 12-48 h after therapy and is due to disruption to blood brain barrier, usually is reversible without late problems. Subacute reactions occur 3-10 months after therapy; it may present with edema in the surrounding normal brain and may be partially or completely reversible, or progress to permanent sequelae. Both acute and subacute complications are steroid responsive. Persistent neurological signs and MRI changes beyond 2 years indicate late reaction. It usually represents scarring or coagulative necrosis without mass effect, but if there is a low signal area with mass effect and considerable surrounding edema, liquefactive necrosis has occurred and surgical decompression is occasionally needed.

Conclusion: Stereotactic radiosurgery of pituitary adenoma may cause radiation necrosis and if neurologic symptoms and changes in brain imaging do not improve may require surgical intervention.

Abstract #833

PET SCAN: A PROMISING NEW DIAGNOSTIC MODALITY FOR DETECTION OF PITUITARY ADENOMAS

Mais Trabolsi, MD, Rachanun Murathanun, MD, Tahira Yasmeen, MD, FACE, Farah Hasan, MD, FACE, FRCP

Objective: MRI has always been considered the imaging diagnostic modality of choice for detection of pituitary lesions. PET scan has been a topic of great interest in the recent years and its diagnostic use has been expanding to recently include pituitary lesions. We describe a rare case of incidental pituitary adenoma complicated by hypogonadism detected by PET scan during the work up of pleural effusion to rule out malignancy.

Case Presentation: A 67-year-old male with known hypertension presented to the ED with left-sided shoulder and pleuritic chest pain for 4 weeks’ duration. He denied any other complaints. Physical examination revealed normal vital signs, diminished breathing sounds and dullness to percussion over the left chest. Cardiovascular, abdominal and neurological exam including the visual field were otherwise normal. Incidental left sided pleural effusion was demonstrated on the shoulder-x-ray. Chest-
x-ray and CT scan revealed similar findings in addition to scattered calcified appearing nodules. Thoracentesis and bronchoscopy were subsequently done showing exudative fluids with significant protein and leukocytes but negative for malignancy. Lung cancer was suspected, $^{18}$F-fluorodeoxyglucose (FDG)-PET/CT was done revealing intense increased uptake within the sella turcica with 24SUV suggestive of pituitary macroadenoma. Subsequent brain MRI showed lobulated large sellar and suprasellar mass 4.2 cm x 2.8 cm suggestive of pituitary macroadenoma with the displacement of optic chiasm. Further evaluation of the functionality of the tumor revealed significant hypogonadism with total Testosterone of 25.9ng/dL, normal FSH 1.7mIU/mL and LH 0.8mIU/mL, prolactin, IGF-1, TSH, Ft4 and cortisol were normal. The patient was diagnosed with pituitary macroadenoma complicated by hypogonadism. The patient refused the surgery and was treated for his hypogonadism as an outpatient.

**Discussion:** Pituitary adenoma is the most common cause of suprasellar mass. Non-functioning pituitary macroadenomas are usually large at the time of diagnosis, therefore they can manifest by compression symptoms or hypopituitarism. Most non-functional pituitary tumors tend to have gonadotrophic origin, secrete gonadotropins or their subunits. That explains the inappropriate normal levels of FSH and LH in our patient. The normal pituitary gland doesn't accumulate FDG and therefore it is not usually detected on PET scan. However, PET scan was found in recent studies to be complementary to the MRI and a very sensitive method to detect pituitary abnormalities whether it is a macro or microadenoma even for lesions that cannot be visualized on MRI. Increased uptake was found to be highest among non-functional and believed to be related to tumor growth potentials, cellular proliferation and overexpression of hexokinase enzyme responsible for utilization of FDG.

**Conclusion:** We report a rare finding of pituitary incidentaloma discovered by PET scan. Our case underscores the evolving significance of PET scan as a promising new diagnostic modality for pituitary adenomas.

**Abstract #834**

SPONTANEOUS REGRESSION OF PITUITARY MACROADENOMA AFTER PITUITARY APOPLEXY

Hussein A Rajab, MD, Jeremy Soule, MD

**Objective:** To report a case of spontaneous regression of pituitary macroadenoma in a patient presenting with a clinical syndrome suggestive of pituitary apoplexy.

**Case Presentation:** A 73-year-old female with history of DM2, HTN, came to ER with 1 day H/O severe headache of sudden onset, left eye pain, nausea and photophobia. Exam was WNL except BP 155/78. CTA of the head was initially reported as negative. The patient signed AMA, refusing a lumbar puncture to R/O meningitis and subarachnoid hemorrhage. A week later, she was admitted with the same symptoms. BP was 97/52 but the remainder of exam was normal. By now, the CT from her prior ER visit had been reinterpreted as showing a 1.9 cm pituitary mass. She had low TSH 0.27 mIU/L (0.55-4.78), low FT4 0.61 ng/dL (0.8-1.9), low 5:30 am cortisol 0.57 mcg/dL (4.3-22.4), mildly elevated IGF 240 ng/mL (55-188), normal prolactin 2.6 ng/ml (1.8-20.3), normal Na (136). Head MRI w/o contrast showed a 1.5 X 1.6 X 2.1 mass with heterogeneous T2-W signal and iso-to hyperintense T1-W signal. The patient was started on synthroid but not steroids and she was not offered surgery at that time. Two weeks later, she was evaluated in our clinic; she reported some polydepsia but no polyuria. Na was elevated (147), serum osm (311), IGF-1 normalized (92), cortisol (3.2), prolactin (7.7), LH 0.8 mIU/mL (15.9-54), FSH 3.1 mIU/mL (23-116), FT4 0.9, TSH 0.02 on 50 mcg of synthroid daily. Prednisone 5 mg daily was started. One mcg stim test showed low cortisol response (5.5 at baseline at 9:45 am, and 14.9 after 90 min). Contrasted MRI showed significant decrease in the size of the pituitary mass which now measured 8 mm x 4 mm. Findings were interpreted as likely due to pituitary apoplexy.

**Discussion:** Pituitary apoplexy is a clinical syndrome consisting of severe headache, visual deficit, and AMS. PA is due to acute hemorrhage or bland infarction of an adenoma. Although early surgery to prevent permanent visual damage has been advocated, conservative treatment has been reported in several studies for less symptomatic patients. Post apoplexy hormone deficiency has been reported as well. Our patient had no symptoms or signs of acromegaly but she was found to have an unexplained elevation of her IGF-1 which returned to normal level in about 4 weeks.

**Conclusion:** In this interesting case, failure to identify a pituitary adenoma on an initial CT scan, and refusal of the patient of timely testing led to unintentional lack of therapy and spontaneous resolution of mass on serial MRI. Earlier endocrine consultation during her admission may have allowed earlier recognition and treatment.
Abstract #835

LATE PRESENTATION OF TRIPHASIC PATTERN OF POSTOPERATIVE DIABETES INSIPIDUS

Soamsiri Niwattisaiwong, MD, Adrienne Edgren, MD, Wilsania Rodriguez, MD, Jennifer B Bernard, MD

Objective: The triphasic pattern of postoperative diabetes insipidus (DI) is uncommon. It can be a diagnostic challenge if presenting late or is masked by other conditions causing polyuria.

Case Presentation: A 52-year-old diabetic woman presents with altered mental status (AMS) for 2 months. She had a pituitary macroadenoma treated 1 year ago by transphenoidal hypophysectomy (TSH). The patient developed polyuria and hypernatremia after surgery, followed by a short period of hyponatremia. Serum sodium (Na) ranged from 139-144 mmol/L during follow-up visits. Laboratory studies upon admission revealed serum Na of 168 mmol/L and glucose of 300 mg/dL. The patient was given intravenous (IV) normal saline, resulting in serum Na of 177 mmol/L the next day. Glucose was 300-400 mg/dL. Urine output (UOP) was 325 mL/hr. IV fluids were changed to 5% dextrose and IV insulin was started to control hyperglycemia. Despite serum glucose under 200 mg/dL, UOP was still 250 mL/hr. The next day serum Na was 161 mg/dL, with urine osmolality of 218 mOsm/kg. Central DI was suspected. With 1 µg of subcutaneous desmopressin (DDAVP), UOP decreased to 120 mL/hr and serum Na decreased to 149 mmol/L in the next 10 hours. Without DDAVP, UOP increased to 180 mL/hr and serum Na gradually increased to 152 mmol/L. The diagnosis of central DI was made. DDAVP was resumed, resulting in gradual normalization of serum Na along with improving mental status. The patient was discharged on 0.1 mg of oral DDAVP every 12 hours.

Discussion: The triphasic pattern of DI occurs in 3.4% of patients who undergo TSH. The first phase of DI typically lasts 5-7 days, followed by a second phase of SIADH, lasting 2-14 days. The first phase is caused by temporary dysfunction of arginine vasopressin (AVP) neurons, while the second phase is caused by the release of stored AVP from degenerating neurons. After AVP stores are depleted, the third phase may ensue. In this phase, there are insufficient remaining AVP neurons, resulting in permanent DI. Intraoperative CSF leakage is a risk factor for permanent DI. Our patient maintained normal serum Na for many months after TSH. Only in the setting of AMS coupled with reduced fluid intake, did the patient develop hypernatremia, and the third phase of DI was revealed. The diagnosis of DI should be suspected in a patient with history of TSH and polyuria. Hyperglycemia should be controlled to eliminate osmotic diuresis as a cause of polyuria.

Conclusion: This case illustrates the triphasic pattern of postoperative DI and the value of a detailed history. A history of TSH is a clue for DI. Other causes of polyuria should be treated before making the diagnosis.
THECA LUTEIN CYSTS WITH MATERNAL VIRILIZATION AND MARKEDLY ELEVATED SERUM TESTOSTERONE IN PREGNANCY

Poonam Khadka, MD, Chandana Konduru, MD, Maria Davila, MD, Irene Weiss, MD

Background: Maternal virilization in pregnancy is rare and causes include theca-lutein cysts, luteoma, ovarian and adrenal tumors. Theca-lutein cysts are usually associated with multiple gestations, polycystic ovarian syndrome or molar pregnancy. We present a case of maternal virilization associated with theca lutein cysts.

Case Presentation: A 26-year-old female gravida 4 para 0 was consulted for maternal virilization at 24 weeks of gestation. Patient reported fatigue, acne, excessive hair growth and deepening of voice since the first trimester. Physical exam was significant for coarse facial features, acne, hirsutism of the face, lower abdomen and clitoromegaly. Endocrine work up revealed elevated total testosterone (2952ng/dl), free testosterone (262.7pg/ml), sex hormone binding globulin (181nmol/L) and 17 hydroxyprogesterone (4740ng/dl). Quantitative HCG, progesterone, FSH, LH, TSH and free thyroxine index were appropriate for pregnancy. Pelvic ultra sonogram (USG) showed an enlarged right ovary with multiple follicles. MRI confirmed bilateral enlarged ovaries with multiple cysts. No pituitary abnormality was seen on MRI of the brain without contrast. A diagnosis of theca lutein cyst in pregnancy was made and the mother and fetus were monitored closely. Patient delivered a preterm female baby at 30 weeks of gestation with no signs of virilization. Evaluation of cord blood showed normal total and free testosterone. There was no evidence of trophoblastic disease on placental histology. Maternal total and free testosterone decreased to 77ng/dl and 6.9pg/ml respectively two weeks after delivery. Repeat USG showed normal ovaries without cysts. There was gradual improvement in patient’s acne, voice and hirsutism but clitoromegaly persisted. Theca lutein cyst in pregnancy is a benign condition associated with maternal virilization. There is increased intrinsic sensitivity to gonadotropins with hypertrophy and luteinization of the theca interna. They are often bilateral and associated with mild maternal hyperandrogenism in 30% of the patients, versus 70% to 100% in malignant cases. The natural course of the disease is postpartum regression. However, a complete workup is mandatory to exclude other causes of virilization. The high levels of testosterone observed in our patient is rare in theca lutein cysts, and is usually indicative of luteoma or malignancies like Sertoli-Leydig tumor and Krukenberg tumor.

Conclusion: Clinicians should be able to recognize the unusual presentations of this rare but benign condition and differentiate it from the malignant causes of maternal virilization.
fibrinolysis. Treatment with testosterone has been reported to improve the ulcers by reducing PAI-1 levels.

**Conclusion:** Our case emphasizes that Klinefelter syndrome should be considered in the differential diagnosis of nonhealing venous ulcers in male patients with erectile dysfunction in whom the cause of the ulcers cannot be otherwise explained. Androgen replacement therapy promotes better healing of ulcers in these patients.

**Abstract #902**

PARTIAL ANDROGEN INSENSITIVITY SYNDROME- A SOCIAL DILEMMA FOR GENDER ASSIGNMENT

Khurshid Ahmad Khan, MD, FACE, Javed Akram, MD, MRCP

**Objective:** To describe a case of partial androgen insensitivity syndrome where because of the late age of diagnosis and for social and cultural beliefs assignment of future gender was a major dilemma.

**Case Presentation:** A 16-year-old female presented to the endocrinology clinic with complaints of primary amenorrhea. On exam she had female habitus, hirsutism, and scant pubic and axillary hair. Breast development was at Tanner stage III. Genital exam revealed incomplete vaginal pouch, posterior labial fusion, significant enlargement of clitoris and small undescended testes in both inguinal canals. On pelvic ultrasound she had absent ovaries and no uterus. Her lab values were: Testosterone 23 ng/dl (5 to 20 ng/dl), FSH 8 mU/ml (1-10 mU/ml), LH 12 mU/ml (1-10 mU/ml). Sex chromosome karyotyping was XY. A diagnosis of partial resistance to the effects of androgen hormone was made. Bilateral orchiectomy was done for undescended testes. Detailed sessions were held with the patient and family regarding gender of rearing for this patient. Patient wanted to stay as female but family wanted her to be a male. Psychotherapist was involved in conflict resolution. Ultimately final decision was made to change her phenotype to male in line with her genotype based on her and family’s preference and especially in lieu of the fact that she was partially resistant to androgens and did have some facial hair. She was started on testosterone injections and in collaboration with plastic surgeon and urologist her external genitalia was improvised for male phenotype. Currently patient is studying in college enrolled as boy and is doing fine.

**Discussion:** Androgen insensitivity syndrome is characterized by defects in androgen receptor function that cause a disorder of sexual development in which 46, XY males do not virilize normally, despite the presence of bilateral testes. Less severe impairments of androgen receptor (AR) function cause a spectrum of defects in virilization and most of these patients have an overall female phenotype with female breast development and predominantly female external genitalia except for posterior labial fusion and/or clitoromegaly. At all ages, the major differential diagnosis can be extensive, including the following: Mixed gonadal dysgenesis, 46,XY individuals with disorders in androgen synthesis, 46,XY individuals with steroid 5-alpha-reductase type 2 deficiency.

**Conclusion:** Early diagnosis in partial androgen resistance syndrome or in any other condition with ambiguous genitalia is of utmost importance for psychological and physical well being of the patient.

**Abstract #903**

PARTIAL ANDROGEN INSENSITIVITY SYNDROME

Ankit Shrivastav, MD, Anirban Sinha, MD, DM, Satinath Mukhopadhyay, MD, DM, Subhankar Chowdhury, MD, DM, MRCP

**Objective:** To report a case of Partial Androgen Insensitivity syndrome presenting at puberty, highlighting the complexities of gender assignment and psychosocial issues involved in a developing country.

**Case Presentation:** A 16-year-old girl, born of consanguineous marriage, presented with poor development of breast and delayed menstruation. On examination, her breast was tanner stage B1 and pubic hair was tanner stage P4, interestingly in male pattern. There was rugosity and pigmentation of labioscrotal tissue (External masculinization score of 1) with perineal urethral opening and poorly formed vaginal introitus. Her clitoris was prominent with presence of erectile tissue & well formed glans. There were no palpable gonads in labioscrotal tissue or inguinal canal. On ultrasonography, the uterus or ovary could not be visualized. An Intra abdominal testis like structure was seen along with well developed prostate measuring 25 × 19 × 19 mm. Hormonal evaluation revealed FT4: 1.43 ng/ml, TSH: 1.08, Prolactin: 13.96 ng/ml, Cortisol (8 am): 14.26 µg/dl, FSH: 37.12 mIU/ml, LH: 13.13 mIU/ml, Estradiol: 30.2 pg/ml, Testosterone (T): 453 ng/dl, DHEAS: 147 (35 – 430), DHT: 464 pg/ml (0.46 ng/ml) and Androstenedione of 1 ng/ml. Karyotyping revealed XY pattern. Possibility of Partial Androgen Insensitivity syndrome was considered and a Mutation analysis of the androgen receptor gene was done which confirmed the diagnosis of PAIS. The diagnosis was discussed with the patient and his parents informing them of the treatment options available. The parents, after learning that child was genetically male, wanted male gender assignment while the girl wanted to continue with female gender. The
parents were counseled regarding choice of child and difficulty in male genitalia reconstruction with EMS score of 1. Family elders were involved and ultimately they agreed for female gender assignment. A clitoroplasty along with neovaginal construction and gonadectomy was done and she was started on hormone replacement therapy.

**Discussion:** Androgen insensitivity syndrome (AIS) results in failure of normal masculinization of the external genitalia in chromosomally male individuals. This failure of virilization can be either complete androgen insensitivity syndrome (CAIS) or partial androgen insensitivity syndrome (PAIS), depending on the amount of residual androgen receptor function. PAIS is rarer than CAIS. PAIS is more complicated problem for gender identity with highly varied genitalia depending on degree of virilization.

**Conclusion:** PAIS should be identified early in childhood, though it is often difficult due to highly variable genital appearance. Gender assignment may be troublesome in adolescence especially in developing countries.

**Abstract #904**

**A CASE OF TURNERS SYNDROME**

Ignatius U Ezeani, MD, A Eregie, MBBS, FMCP, Andrew Edo, MBBS, FMCP; Aesanya Adewole, MBBS, Oluwatosin Ohenhen, MBBS

**Objective:** To report a case of Turner's syndrome and to highlight the importance of early diagnosis and management.

**Case Presentation:** We present a 15-year-old female senior secondary school student who was brought by her mother due to absence of secondary sexual characteristics since 2 years. She is yet to attain menarche and there is history of poor growth as the younger siblings are all taller than her. At birth she was noticed to have unsightly skin folds on both sides of the neck. She had normal developmental milestones, pregnancy and delivery were uneventful. She had cosmetic surgery 8 years ago for removal of neck folds. Her academic performance at school has been good. Examination revealed hyperpigmented nodules over her back, sparse axillary and pubic hair with a scar on both sides of the neck. Height = 135cm, upper segment = 65cm, Lower segment = 70cm, Arm span = 147.5cm. Musculoskeletal system revealed bilaterally short metacarpals and metatarsals of the 4th digit with cubitus valgus. Clinical diagnosis of Turner’s syndrome was made. Buccal smear revealed absence of Barr bodies. X-ray of hand revealed osteopenia of the carpometacarpal bones, bilateral shortening of the 4th metatarsal bones while x-ray of the feet showed osteopenia and shortening of the 4th metatarsal and phalangeal bones bilaterally. Abdominal ultrasound showed infantile uterus, while the ovaries were not visualized. Fertility profile test showed: FSH = 10.1u/L, LH = 8.5u/L, PRL = 5.4ng/ml, Progesterone = 0.3ng/ml, Estradiol = 2.8ng/ml, Testosterone = 0.1ng/ml (all been within normal range). She was also reviewed by pediatricians, surgeons and the gynecologists. She was commenced on Tabs Progenova 4mg BD, Tabs Norethisterone 5mg daily.

**Discussion:** Turner’s syndrome encompasses several clinical conditions of which monosomy X is the most common. All or part of the X chromosome is missing. Presence of 45X cell line or deletion of short arm of chromosome. Cause is unknown though genetic causes or non-disjunction has been implicated. They can present with short stature, lymphedema, webbed neck, low set ears, broad chest, long posterior hair line, poor breast development, short 4th metacarpal, and small finger nails. Associated features include coarctation of the aorta associated with hypertension, horse shoe kidneys, hypothyroidism, osteoporosis, learning disorders.

**Conclusion:** The importance of early detection and management cannot be overemphasized in a case of Turner’s syndrome. It is imperative that the endocrinologist has a high index of suspicion.

**Abstract #905**

**WEIGHT LOSS IMPACT ON HYPERANDROGENIA IN FEMALES WITH PCOS**

Dana Liana Bucuras, MD, Anasasiu Doru, MD, PhD

**Objective:** To see the impact of weight loss on the clinical and biochemical problems in PCOS patients.

**Methods:** From the total of 250 females, evaluated for overweight, in our endocrinological department, 48 cases had the Rotterdam 2003 diagnostic criteria for PCOS. Hipothyroidism, hypercorticism and 21 hydroxilaza deficiency were excluded. The patients had a low glicemic index diet and a special physical activity plan. Clinical exam, ultrasound, biochemical and hormonal assays were performed at the beginig and after 1, 6 and 12 months of follow-up.

**Results:** After 6 months, a medium weight loss of 13.2 ± 4.7 kg, 5 to 16.8% of initial weight (p < 0.02). We observed a decrease in menstrual disturbances. Tegumentar hyperadrogenism decreased, but Ferriman Gallwey score did not change significantly (11.824 ± 3.022 versus 12.035 ± 3.088).

**Conclusion:** Significant and sustained weight loss decreased the androgenic excess, at all levels.
Abstract #906

**MALE WITH TURNER-SYNDROME 45, X/46, XY MOSAICISM: A CASE REPORT OF PRIMARY HYPOGONADISM IN AN ELDERLY MALE CAUSED BY TURNER-SYNDROME MOSAICISM**

Monika Elizabeth Olchawa, MD, Boby Theckedath, MD, Sant P. Singh, MD

**Objective:** To recognize and diagnose Turner’s syndrome mosaicism, a rare congenital cause of primary male hypogonadism and to discuss an interesting case of an elderly man with Turner syndrome and normal male phenotype.

**Case Presentation:** We report a case of a 60-year-old male with past medical history of hypertension, hyperlipidemia, who presented for evaluation of low testosterone levels. Patient had low libido, difficulty sustaining erections, and episodic hot flashes. He had no children. Physical exam demonstrated a tall, (6 feet 2 inches, 270 lbs) normal appearing male with normal external genitalia, no loss of secondary sexual characteristics. Patient did not exhibit any clinical features consistent with Turner’s syndrome. Laboratory evaluation revealed low morning total testosterone 187 ng/dl, free testosterone 28.6 pg/ml, % free testosterone 1.53; elevated LH 16 mIU/ml and FSH 30 mIU/ml; normal SHBG 28 nmol/L, prolactin 6 ng/ml, PSA 0.51 ng/ml, and TSH 1.42 uIU/ml. Patient also had normal liver and kidney function tests. Ultrasound of the scrotum showed normal testes. Further investigation of chromosomal karyotype uncovered Turner’s syndrome 45,X-55%/ 46,XY-45% mosaicism.

**Discussion:** Primary male hypogonadism also known as primary testicular failure refers to either decrease sperm or testosterone production in the testes. Most common chromosomal abnormalities are Klinefelter’s syndrome (defect in the presence of an extra X chromosome 47,XXY) and Turner’s syndrome 45, X/46,XY karyotype (mosaic for loss of Y chromosome). Reported cases of Turner’s mosaicism vary in clinical characteristics and phenotypes, ranging from phenotypic females with or without virilization, mixed gonadal dysgenesis, male pseudohermaphroditism to normal males.

**Conclusion:** Turner’s syndrome is characterized by structural abnormalities of one from the two X chromosomes. Sex chromosome monosomy (45,XO) is present in 50-75% of the cases with female phenotype, the rest are mosaic karyotypes. 45,X/46,XY mosaicism accounts for 2-6% of the cases. Diagnosis is often prenatal from amniotic fluid sampling, or found incidentally based on characteristic Turner’s syndrome stigmata such as short stature, gonadal dysgenesis, cardiac or renal anomalies.

45,X/46,XY mosaicism have been linked with increased risk of gonadoblastoma. Our patient was diagnosed at the age of 60 with 45,X/46,XY mosaicism, normal male phenotype without abnormal clinical features, laboratory tests consistent with primary hypogonadism, low testosterone, elevated gonadotropin levels.

Abstract #907

**MULTIPLE ENDOCRINE NEOPLASIA TYPE II WITH TURNER SYNDROME: FIRST REPORT OF A CASE**

Laure Sayyed Kassem, MD, Jawad Al-Khafaji Armand Krikorian, MD

**Objective:** To present a case of Turner Syndrome with Multiple Endocrine Neoplasia Type 2a (MEN 2a).

**Case Presentation:** We present the case of a 21-year-old Nepalese female who was referred for evaluation of profound hypothyroidism confirmed to be autoimmune (Hashimoto’s) thyroiditis. History and physical examination revealed primary amenorrhea, Tanner II pubertal stage and short stature. Pelvic ultrasound showed uterine and ovarian agenesis, and chromosome analysis confirmed TS with a mosaic pattern 45,X[25]/46,X,i(X)(q10)[5]. Bone age was markedly delayed at 13 years. She was initiated on thyroid hormone as well as estrogen replacement after declining growth hormone therapy. Incidentally, she was also noted to have mild hypercalcemia in the setting of elevated PTH at 100-119 pg/ml and normal urinary calcium excretion, consistent with primary hyperparathyroidism (PHPT). Surgical resection of a hyperplastic parathyroid gland resulted in normalization of calcium and PTH levels. RET-oncogene testing was positive for MEN 2A mutation. Calcitonin levels and plasma metanephrines were normal. Prophylactic thyroidectomy, as well as genetic screening of her family members for RET-oncogene mutations, is planned.

**Discussion:** To our knowledge, this is the first reported case of MEN in a patient with TS. TS is associated with several endocrinopathies such as gonadal failure, growth failure and low bone mineral density which are related to specific sex chromosomes abnormalities. Less common associations such as autoimmune thyroiditis and Diabetes Mellitus occur in 10-25% of cases but do not have a clear causal relationship with sex chromosome abnormalities. Less common associations such as autoimmune thyroiditis and Diabetes Mellitus occur in 10-25% of cases but do not have a clear causal relationship with sex chromosome abnormalities. Although several neoplasms are associated with Turner Syndrome, MEN in the setting of TS has not yet been reported. Several of the individual disorders that comprise MEN have been separately described with TS. Our review yielded at least 7 reported cases of PHPT due to hyperplasia and adenocarcinoma, both in pediatric and
adult subjects. Pituitary adenomas have also been reported in at least 15 cases. Two reports of pheochromocytoma as well as 10 reports of ganglioneuroma of the adrenals were identified. Whether these disorders are more prevalent in TS than in the general population is unknown.

**Conclusion:** Should there be a true association between TS and MEN, several implications need to be entertained, foremost being the decision to screen patients with TS for RET-oncogene and for pheochromocytoma as almost half the adult population of TS has hypertension. Given the significant morbidity associated with MEN, larger cohort studies to assess for a true association with TS would be of great significance.

**Abstract #908**

“INCREASED FACIAL HAIR” IN A POST-MENOPAUSAL WOMAN: A COMMON COMPLAINT THAT WARRANTS INVESTIGATION?

Pooja Sherchan, MD, Cynthia Sites, MD, Kamal Shoukri, MD

**Objective:** To describe a case of hirsuitism secondary to ovarian hyperthecosis in a post-menopausal woman.

**Case Presentation:** A 67 year-old caucasian female, postmenopausal for 15 years, presented with complaints of increasing facial hair for two years. O/E She had generalized obesity with BMI of 42. Hirsuitism was limited to few terminal hair growth in her upper lip, chin and sideburn area with no other signs of virilization. She had been diagnosed with type 2 DM for 5 years. Laboratory test revealed testosterone: 233 ng/dL (6-18), free testosterone: 4.52 ng/dL (0.1-1.1), SHBG: 33.4 nmol/L (38-111), DHEAS: 37 ugm/dL (60-230), 17OH Progesterone: 111 ng/ml (30-100, follicular phase), FSH: 35 mIU/ml, LH 27 mIU/ml, Prolactin: 8.7 ng/ml, TSH: 1.92, FT4: 1.1, 24 hour urinary free cortisol: 2 ugm/ml. CT Abdomen showed normal adrenals. Transvaginal U/S revealed ovarian volumes that measured 5 ml on the left and 6 ml on the right side (upper limit of normal for age) with no masses. Bilateral oopherectomy was performed laproscopically. Pathology revealed stromal hyperthecosis in both ovaries. One month after sugery, the total testosterone and free testosterone levels decreased to 30 ng/dL and 0.66 ng/dL respectively.

**Discussion:** Hirsutism is a common complaint of post-menopausal women. Recent onset, rapidly progressing hirsutism warrants workup for ovarian or adrenal neoplasm. Transvaginal U/S lacks the sensitivity to detect two ovarian conditions that can lead to hyperandrogenism: hilar cell tumor and hyperthecosis. Hyperthecosis is an ovarian condition in which the stromal cells become hyperplastic, leutinized and steroidogenically active. Its pathophysiology is not entirely known; hyperinsulinism due to insulin resistance has been implicated and the entity has been frequently reported as part of HAIR-AN syndrome (hyperandrogenism, insulin resistance and acanthosis nigricans). It has also been recognized as a severe variant of PCOS. Unlike PCOS which mainly occurs in reproductive age, hyperthecosis can occur in postmenopausal years as well, although less commonly. Hirsutism occurring in hyperthecosis is usually severe, often progressing to virilization. The accompanying high androgen levels often simulate the presence of neoplasm. Our case had a rather mild degree of hirsuitism albeit high androgen levels.

**Conclusion:** This case report illustrates hyperthecosis and high androgen levels despite mild hirsuitism in a post-menopausal woman.

**Abstract #909**

MACROPROLACTINOMA COEXISTING WITH POLYCYSTIC OVARIAN SYNDROME: A DILEMMA IN MANAGEMENT

Adedayo David Adegite, MBBS, Ian Ross, MD, Dinky Levitt, MD

**Objective:** To present two cases of macroprolactinoma co-existing with polycystic ovarian syndrome.

**Case Presentation:** CASE 1: A 34-year-old lady with primary infertility was referred for further endocrine workup. She was previously diagnosed with macroprolactinoma in 2004, and was initially started on bromocriptine at a baseline Prolactin of 1,315µg/L (4.8-23.3) but later switched over to dostinex. She had been amenorrheic for 9 months prior to presentation. She has a strong family history of hirsutism and complained of mild headache, blurring of vision but no galactorrhea. On examination she was obese with a BMI of 31.6. She was hirsute with significant hair on the face and the chest. Her BP was 130/90 and visual field was normal. Repeat MRI suggested that there was no interval change in the tumor size. Basal (8am) blood showed FBS of 4.6mmol/L(4.1-5.9), Fasting insulin 53.9uIU/L(2.6-24.9), plasma Cortisol 314nmol/L(171-536), Testosterone 3.3nmol/L(0.2-2.9), DHEAS 7.5nmol/L(2.7-9.2), 17(OH) progesterone 9.8nmol/L(0.6-5.5), LH 6.4IU/L, FSH 3.2IU/L, Prolactin 40.2µg/L, fT4 14.2pmol/L(12-22), TSH 1.74mIU/L, Human growth hormone <0.1µg/L(0.0-8.0). Thirty minutes after 250µg Synacthen test plasma Cortisol was 825nmol/L, but DHEAS, testosterone and 17(OH) progesterone levels were unchanged. Plasma Cortisol level suppressed to 11nmol/, nine hours after
overnight 1mg dexamethasone test. Pelvic ultrasound showed ovarian morphology consistent with polycystic ovaries (PCO). She continued to have worsening of hirsutism and infertility despite a reasonable Prolactin levels.

CASE 2: A 32-year-old lady had wedge resection of an enlarged right ovary in 1998 but presented to the endocrine clinic in 2000 with a 7 month history of amenorrhea, severe acne and headache. There were no symptoms of Cushings, hypothyroidism, galactorrhea or visual disturbances. Her baseline blood revealed Proactin of 111µg/L, LH 9.9IU/L, FSH 6.2IU/L, Estradiol 249, TSH 2.23mIU/L, 24 hr urinary Cortisol 469nmol/L(150-700), Fasting insulin 13.5mU/L, FBS 4.5mmol/L. Pelvic USS showed features consistent with PCO morphology. She was initially commenced on androcur, diane and bromocriptine. During follow up, Prolactin level had raised to 284 and MRI brain showed a pituitary macroadenoma. Prolactin levels remained persistently >100 despite high dose of bromocriptine while she was on diane. There was a marked decline in serum Prolactin following discontinuation of diane and switch from bromocriptine to dostinex, although this was accompanied by worsening of acne and amenorrhea.

Discussion: About 35% of PCOS patients have slightly high prolactin. This is believed to be due to inappropriately enhanced chronic stimulation of the lactotroph by estrogen feedback. Coexistence of prolactinoma with PCOS is very rare. The increased risk of prolactinoma may be related to the potential mitotic activity of oestrogen on the abundant estrogen receptors in the pituitary lactotrophs. In the same vein, use of estrogen containing pills like diane can potentially counteract the effect of Prolactin lowering medication.

Abstract #910

PRECOCIOUS PUBERTY PRESENTING WITH UNILATERAL GYNAECOMASTIA

John Adi Ashindoitiang, MBBCCh

Objective: To report a case of idiopathic precocious puberty which occurs unusually early (18-month-old girl) and also with only one component, which again is confine to one breast.

Background: Precocious puberty is defined as the development of secondary sexual characteristic before the age of 8 years in girls and 9 years in boys. Precocious puberty is more common in girls. Normal puberty is comprised of 4 pubertal changes viz: 1)Thelarche-breast development 2) adrenache –axillary and pubic hair 3) growth sprout 4) menarche. The classification of precocious puberty is either complete in which all the four changes are seen or incomplete if only one component is encountered. We report a case of 18 months old girl with isolated unilateral gynaecomastia.

Case Presentation: Miss O. D. an 18-month-old female child presents with 13 months history of progressive left breast enlargement notice by the mother. Mother feels the enlargement has increased about 10 times since the onset. No associated axillary and pubic hair and history of bleeding per vaginam. No prior history of trauma or ingestion of any steroid containing medication. Past medical history was eventful. Pregnancy and neonatal history were unremarkable except for neonatal jaundice. Patient has completed her immunization. Diet history and developmental history were both normal. Physical examination reveals no abnormality. She was evaluated with U/E/C. Urinalysis, hormonal profile (pituitary ovary axis and pituitary adrenal axis), ultrasonography and CT scan of abdomen and pelvis. All investigations were normal except for markedly elevated estradiol( 48ng/ml normal value less than 10mls)

Discussion: Precocious puberty could be divided into two types namely 1 incomplete in which one of the components of puberty manifest is that either thelarche, adrenache or menarche. In our patient it is only thelarche that manifest. What is interesting is that only unilateral breast enlargement occurs. Further more patients have elevated Estradiol without the possible cause as there was no source of this hormone dictated by the investigations carried out. Since incomplete isosexual precocious puberty is usually due to transient rise in estrogen or unusual sensitivity to estrogen, it will be logical to say our patient case is case of incomplete isosexual precocious puberty with the affected breast showing increased sensitivity to pre pubertal elevated estrogen. Again, precocious puberty may be gonadotropic dependent or not, FSH/LH was normal implying not dependent cause which principally are mccune Albright syndrome or granulosa tumor of the ovary. Both conditions were ruled out by a normal abdominal/pelvic CT SCAN.

Conclusion: 80% of precocious puberty is constitutional, hence after hormonal profile and abdominal ultrasound, if no cause is found patient should be managed conservatively.
Abstract #911

EXCEPTIONAL CAUSE OF HYPERPROLACTINEMIA: LEYO-MYO-SARCOMA OF THE UTERUS

Catalina I. Poiana, MD, PhD, FACE, Mara Carsote, MD, Dana Terzea, MD, Cristina Dumitrescu, MD, PhD, Corina Chirita, MD, Adriana Gruia, MD, Dan Hortopan, MD, PhD

Objective: We report a female patient case diagnosed with uterine leyo-myo-sarcoma, with an atypical endocrine profile.

Case Presentation: A 53-year-old female patient is known with a uterine fibroma for several years, as revealed by ultrasound. For the last 3 months she was under sequential progestive therapy 10 days/month in order to control a severe uterine bleeding. On admission, the endocrine profile showed high serum prolactine - 292 ng/mL (the normal ranges are 5 up to 19.5 ng/mL) and high levels after PEG were presented, too. The pituitary CT was normal, making the diagnosis of prolactinoma less likely. Despite the therapy, the tumor rapidly grew so that an emergency hysterectomy with anexectomy was performed.

Discussion: There are many extrapituitary causes of high serum prolactine. Among them, the gonads diseases are often involved, as well as breast pathology. The leyo-myo-sarcoma is a malign tumor which may be associated with hyperestrogenemia. The pathological report in our case showed a tumor of 10 by 9 cm, a leyo-myo-sarcoma with areas of necrosis. Multiple giant multinucleated cells are described with frequent mitosis (> 5 mitosis/10HP) and intravascular tumor embolus. The immunohistochemistry was positive for VIM, ACT, DESM, SMA, CALDESMON, CD10, CD44, CD34 (into the vessels and negative into the tumor), and negative for CD117, PRL. The hormonal potential was revealed by ER positive of 40-45% and PGR positive of 70-75%, explaining the rapid growth after progestative therapy. The proliferation index was marked by P53 (of 50-55%), and Ki-67 (of 35-40%). Whole body PET CT was negative. After surgery the prolactine went rapidly back to normal, proving that the uterine tumor was actually the cause. Close follow up is indicated.

Conclusion: The practitioners should take into consideration even unusual causes of hyperprolactinemia as malign uterine sarcoma.

Abstract #912

GYNECOMASTIA IN YOUNG NIGERIAN HIV SEROPositIVE PATIENT

Olufunmilayo Olubusola Adeleye, MD, AO Ogbera, MBBS, FACE, FACP, FMCP, O Abatan

Objective: To describe the presentation of a young Nigerian HIV positive patient with bilateral gynecomastia.

Case Presentation: A 22-year-old man presented to the endocrine clinic with a 6 month history of painless enlargement of both breasts. He had no history of nipple discharge. He was diagnosed to be HIV seropositive at 20 years of age and attained puberty at 16 years of age. He has been on HAART for about two years and noticed the gynecomastia 18 months after commencement of HAART. There was no history suggestive of hepatic or renal dysfunction. He denied use of alcohol or recreational drugs and has no family history of cancer of the breast. His HAART regimen comprises of Efavirenz, Lamivudine, and tenofovir. Clinical examination revealed a young man with BMI of 20 kg/m², eunuchoid body habitus, bilateral symmetrical non tender breast enlargement with no expressible galactorrhoea. No other clinical features of hypogonadism. No thyroid symptoms/signs CD4 count 250 cells/µl, normal Liver function tests, Hormonal profile-Estradiol-18pg/ml, (nl<40pg/ml), FSH 5mIU/ml(nl 0-15mIU/ml), LH 6.4(nl 2.5-16mIU/ml), Prolactin38(nl 4-18ng/ml), Testosterone 5.6(nl 3-10ng/ml). Breast ultrasound scan revealed subareolar hypoechoic mass.

Discussion: There is scanty report in literature on HIV related gynecomastia (GM) in Africans. The possible causes of GM in HIV positive individuals is reported to include hypogonadism arising from the presence of HIV infection and the use of antiretroviral drugs especially efavirenz. Prolactin is elevated in this patient confirming earlier reports of elevated prolactin in absence of other hormonal abnormalities in HIV seropositive individuals.

Conclusion: Physiological cause of GM is not likely in this patient and the possible causes of gynaecomastia in this case report is namely those of immune reconstitution disease and possibly antiretroviral therapy.
OBJECTIVE: To describe rare case of thyroid hormone malabsorption.

CASE PRESENTATION: We present a 31-year-old woman who presented to our clinic for hypothyroidism. She reported weight loss, generalized weakness, nausea, vomiting, and diarrhea. She had past medical history of chronic diarrhea and Graves’ disease, received radioactive iodine treatment 10 years prior to presentation and had been on replacement since. Several combinations of high dose oral thyroid hormones (levothyroxine and liothyronine) were attempted but she remained severely hypothyroid. She denied using antacids and adherence was repeatedly verified. She had used intravenous levothyroxine for several months via peripherally inserted central catheters (PICC), but was discontinued due to line infection on two occasions. Physical examination showed mild bradycardia and paraumbilical tenderness. Laboratory studies revealed TSH of 178 µIU/ml, Free T4 of 0.3 ng/dl and Free T3 of 1.16 pg/dl, as well as normal hemoglobin, albumin and pre-albumin levels. We started Intramuscular levothyroxine twice weekly and performed oral absorption test with 1 mg levothyroxine when she became euthyroid. Free T4 levels rose from a baseline of 0.3ng/dl to 0.5, 0.9 and 0.9 ng/dl, and Free T3 from 0.74 pg/ml to 0.74, 1.16 and 1.09 pg/ml, respectively at 1, 2 and 4 hours after oral loading, which was deemed inadequate. Celiac panel, CT scan of the abdomen, and upper gastrointestinal endoscopy with biopsies were unremarkable. TSH improved with intramuscular levothyroxine but she developed pain and swelling at the injection sites. We switched to intravenous levothyroxine via port at 700 mcg once weekly, but it became infected and was removed. We tried to determine whether the i-port device (Patton Medical Devices, Austin, TX), indicated for insulin self-administration, could be used in this situation. 100 mcg of levothyroxine was given subcutaneously through i-port. Free T4 raised only by 0.1 ng/dl from baseline at 2, 4 and 6 hours. She was subsequently switched back to intravenous administration.

DISCUSSION/CONCLUSION: This patient, with severe idiopathic levothyroxine malabsorption, only responded to parenteral levothyroxine. The i-port device, typically used to administer insulin, was tested without success. Levothyroxine malabsorption is not uncommon. Once celiac disease and other malabsorption syndromes are ruled out, and adherence verified, the only option is parenteral levothyroxine, which has the potential for complications. Future directions should look into alternative ways of administering levothyroxine to such patients.

ABSTRACT #1001

BRANCHIAL POUCH TUMOR MIMICKING PAPILLARY THYROID CARCINOMA

Maricel Ridella, MD, Matthew Levine, MD

OBJECTIVE: Soft tissue tumors arising from branchial pouches are extremely rare. We present a case of one arising from the thyroid of a young female patient.

CASE PRESENTATION: 34-year-old female incidentally found a nodule in her neck. Thyroid ultrasound revealed a 1.4 x1.2x0.9 cm nodule on the left lobe of the thyroid gland. Ultrasound-guided FNAB of the thyroid suggested papillary thyroid carcinoma lacking certain typical characteristics. The patient was referred for total thyroidectomy. Surgical pathology demonstrated a 1.5 cm low grade malignant tumor possibly arising from a branchial pouch. Incidentally found in the left and right lobes were foci of papillary microcarcinoma. Immunohistochemically this tumor showed staining features similar to the ones found in papillary thyroid cancer but negative for thyroglobulin as well as calcitonin. Chromogranin A and Cytokeratine 5/6. Because of the unusual appearance of this tumor it was sent for consult to Dr. Juan Rosai who authored a paper classifying and characterizing these tumors. The consultative letter reports a unique tumor arising from branchial pouch derivatives with the caveat that it does not fit into any of the described four categories. We recommended no further therapy with radioactive iodine considering the very small foci of papillary microcarcinoma and the main tumor not originating from thyroid follicular tissue. We plan to follow this patient clinically on thyroid hormone replacement and with serial ultrasound images. The patient was evaluated by Radiation Oncology and Hematology Oncology Specialists who recommended no further treatment.

DISCUSSION: Neck tumors arising from branchial pouch tissue show similar histologic characteristics to thymus tissue, from fetal to mature stage or even thymomas, and behavior ranges from benign to malignant. They probably arise from ectopic thymus, vestiges of the thymopharyngeal duct, or branchial pouch remnants in the soft tissues of the neck or inside the thyroid gland. The classification includes four categories on the basis of morphologic features: ectopic hamartomatous thymoma, ectopic cervical thymoma, spindle epithelial tumor with thymus-like differentiation, and carcinoma showing thymus-like differentiation. This particular tumor derives...
from the branchial pouches but does not completely fit any of these characteristics.

**Conclusion:** Tumors arising from branchial pouches are very rare. We present a case of one with characteristics never described in the literature before to our knowledge, arising inside the thyroid gland. We consider this presentation as a way to make our colleagues aware.

**Abstract #1002**

**VERTEBRAL METASTASES OF THYROID CANCER CAUSING SPINAL CORD COMPRESSION**

Mohammed Ahmed, MD, FACP, FACE, Ali Al Enazy, MD

**Objective:** To draw attention to a serious complication of spinal cord compression (SCC) in thyroid cancer (TC) patients and how best to manage it.

**Case Presentation:** Between 1975 and 2008, we have treated 4200 cases of TC and have encountered 126 cases of skeletal metastases (SM). 29 (23%) of these had vertebral metastases (VM). 13 (45%) patients with VM developed varying degrees of SCC: 7 were females and 6 males, ages ranged 32-78 yrs. Primary tumor: follicular ca in 6, Papillary in 6 and Hurthle cell Ca in 1. Primary tumor was 2-7 cm. Symptoms: Bone pains in all, Palpable paravertebral masses in 3, Pathological fractures in 3. Neurological deficits were evident in all. It consisted of paraplegia/paraparesis in 9, nerve root compressive symptoms in 3, loss of sphincter control in 2, Conus medullaris syndrome in 1. For primary tumor: Thyroid US, FNA Bx thyroidal lesion, I 123 whole body scan following near total thyroid (NTT), Serum Thyroglobulin (ranged 290->5000 µg/L), TSH, FT4, thyroid antibodies. For detection of metastases: 123 iodine scan/whole body bone scan/FDG PET-CT/CT/MRI as warranted. Metastases were functional in 6 patients, vertebral Bx (n=8) revealed metastatic tumor to be FTC in 4, PTC in 3 and HCC in 1, myelogram done in 4. Wu revealed: complete thoracic cord compression in 6, lumbar cord compression in 3, cervical cord compression: 3, and one had combined cervical and thoracic cord compression. Large Paraspinal masses in 8. Estimated goiter sizes ranged from 30 to 130 grams. Ultrasonographic findings included heterogeneous parenchyma and diffusely enlarged thyroid. CT findings included diffusely enlarged lipid like thyroid. All had thyroid dysfunction: 2 hypothyroidism, 2 thyrotoxicosis, and 1 with progressively elevated TSH, now in a sick euthyroid state. The 2 patients who underwent thyroidectomy had technically difficult year survival is only 20%. In the context of SM of TC, VM is an unusual yet a specially challenging encounter. However, a rare and a dramatic consequence of VM in our observation is the finding of SCC. Timely DL, whenever possible is mandatory. Adjuvant Rx consisting of 1 131 administration and XRT are also important. Despite these modalities of Rx the prognosis for life and QOL remains guarded. Hence the need for a coordinated multidisciplinary approach

**Conclusion:** Spinal cord compression in TC patients is an unusual albeit a serious complication attended with poor prognosis. It is associated with a spectrum of neurological deficits. It requires multidisciplinary team management including emergency decompression laminectomy whenever feasible.

**Abstract #1003**

**AMYLOID GOITER: REPORT OF 5 CASES SEEN IN 23 YEARS**

Jennie Law, MD, Diana Dean, MD, Bernd Scheithauer, MD, Franklin Earnest, MD, Vahab Fatourechi, MD

**Objective:** While microscopic amyloid deposits in the thyroid is common, massive amyloid deposition to the point of goiter formation is rare. Amyloid goiters may occur as an uncommon manifestation of primary or secondary systemic amyloidosis. Here, we present a case series of five patients, illustrating the presentation, radiographic findings, tissue specimen, thyroid function, and clinical outcomes associated with this rare disease entity.

**Methods:** Five patients with tissue confirmation of thyroid enlarged by amyloid deposits (1 surgical specimen and 4 fine needle aspiration specimens with Congo red staining and 2 confirmed by mass spectrometry) identified between 1987-2010 were studied.

**Results:** All five patients presented with compressive symptoms consisting of dysphagia and local pressure. Three cases had history of persistent hoarseness, suggesting a significant delay in diagnosis of several years. One case involved primary amyloidosis (AL), 3 involved secondary amyloidosis (AA), and 1 involved amyloidosis of uncertain origin. Estimated goiter sizes ranged from 30 to 130 grams. Ultrasonographic findings included heterogeneous parenchyma and diffusely enlarged thyroid. CT findings included diffusely enlarged lipid like thyroid. All had thyroid dysfunction: 2 hypothyroidism, 2 thyrotoxicosis, and 1 with progressively elevated TSH, now in a sick euthyroid state. The 2 patients who underwent thyroidectomy had technically difficult

**Discussion:** It is generally agreed that SM of TC are associated with a poor prognosis such that a 10-
surgical procedures. One patient experienced significant goiter shrinkage following dexamethasone therapy and stem cell transplant for amyloidosis. Follow-up ranged from 5 months to 13 years.

**Discussion:** Clinically recognized cases of amyloidosis resulting in thyromegaly are rare. The growth of amyloid goiters may not always be rapid. Compressive symptoms and thyroid dysfunction is fairly common. It may occur in both primary and secondary amyloidosis. CT imaging and ultrasound images are characteristic. Diagnosis is made by FNA with Congo red staining and if needed, spectrophotometry. Surgical intervention may occasionally be needed and can be technically difficult. In some cases partial regression can occur with therapy of amyloidosis.

**Conclusion:** Our clinical observations suggest a slower goiter progression and a higher prevalence of thyroid dysfunction than previously thought.

**Abstract #1004**

**PREVALENCE OF BREAST CANCER IN WOMEN WITH NON-TOXIC GOITER**

Sarika Patel Sanghvi, DO, Amy Chow, MD, Xiangbing Wang, MD, PhD, FACE, Richard Ro, MD, Aaron Rockoff, MD

**Objective:** Associations have been found between breast cancer and a variety of thyroid abnormalities such as goiter, hypo- and hyperthyroidism, thyroiditis, and increased thyroid autoimmunity. The relationship between benign thyroid disorders and breast cancer has long been a subject of debate. The aim of this retrospective chart review study was to determine the prevalence of breast cancer in patients with uninodular, multinodular or diffuse non-toxic goiter as compared with that of the general female population of New Jersey.

**Methods:** Data was obtained from a retrospective chart review of 789 female patients with a diagnosis of nontoxic multinodular, uninnodular goiter or simple goiter (ICD9 code 241.1, 241.0 or 240.0 respectively), attending the endocrine clinic at Robert Wood Johnson University Hospital from June 2006 to January 2010. The prevalence of breast cancer in females living in New Jersey was obtained from a survey performed by the Cancer Epidemiology Services of the New Jersey Department of Health and Senior Services in 2003.

**Results:** Twenty eight patients (3.55%) were noted to have a history of breast cancer, with average age of 58.6±11.3 and BMI of 29.8±8.9. The prevalence of breast cancer in non-toxic goiter patients was significantly higher compared to the prevalence of breast cancer in New Jersey women (3.55% vs 1.6 % respectively, p< 0.001).

**Discussion:** In this study, we found the prevalence of breast cancer in patients with goiter to be higher than the prevalence of breast cancer in the general female population of New Jersey. As this was a retrospective chart review, there was no standard past medical history questionnaire for the patients. Hence, many of the patients may not have had detailed medical histories taken, so the prevalence rate may be higher than stated above. Proposed mechanisms regarding the relationship between breast cancer and goiter include the increased prevalence of both in postmenopausal women, and the finding of elevated thyroid peroxidase antibodies levels in breast cancer patients. Iodine has also been theorized as being a causative factor because it is utilized by both tissues, and animal studies have demonstrated suppression of the development of mammary tumors by iodine supplementation. Whether there is an association between breast cancer and benign thyroid disease remains a matter of conjecture.

**Conclusion:** This study indicates that non-toxic goiter patients may have a 2.2 fold increased risk of breast cancer, emphasizing the importance of breast cancer screening in patients with benign thyroid disease.

**Abstract #1005**

**PTU-INDUCED MIGRATORY ARTHRITIS MASQUERADING AS SEPTIC ARTHRITIS**

Soe Naing, MD, MRCP, Swapna Busa, MD, Tushar Acharya, MD, Jaynesh Patel, MD, Jagrati Mathur, MD

**Objective:** To describe a rare presentation of PTU-induced arthritis.

**Case Presentation:** A 41-year-old male was diagnosed with Graves’ hyperthyroidism and initiated on methimazole (MTZ). He was admitted 1 month later with 1 day history of headache, vomiting and fever associated with severe muscle weakness of several days duration. He was given Rocephin for suspected meningitis but the workup for meningitis was negative. His muscle weakness was attributed to thyrotoxic myopathy. He had normal WBC (7.2), normal ESR (12 mm) and slightly high CRP (9.2 mg/l) on admission. MTZ was switched to PTU on 2nd day of hospitalization as he was intolerant of MTZ. One day later, he developed severe right knee pain and swelling, associated with sudden rise in ESR (83 mm) and CRP (166). He was started on vancomycin and underwent knee joint irrigation for suspected septic arthritis. However, he continued to have fever and further increase in inflammatory markers and developed severe migratory polyarthritis affecting large joints over next 5 to 7 days. There was no growth at cultures from blood, knee aspirate
and fluid from knee irrigation. Work-ups for rheumatic fever, Lyme’s disease and connective tissue disorders were all negative. ANA and ANCAs were negative and there was no skin rash. At that point, PTU was discontinued for suspected PTU-induced polyarthritis. There was a dramatic improvement in joint pain and swelling and fever within 1 day. ESR, CRP and WBC also decreased from 113, 205 and 14.9 to 88, 106 and 4.4, respectively, within 2 days. He received RAI therapy 7 days later. At 3 months follow-up, he was euthyroid and had no further polyarthritis and muscle weakness. ESR and CRP also returned to the baseline.

Discussion: Migratory polyarthritis is the very rare manifestation of hypersensitivity to PTU and severe joint pain and swelling are thought to be unusual. It may occur without any skin lesion as observed in this case. The cases previously reported took PTU from a few days to several months before the onset of arthritis. Our patient developed severe knee joint pain and swelling followed by migratory polyarthritis 1 day after the drug exposure. He failed to improve with the antibiotic and joint washout; however, there was a dramatic clinical and laboratory improvement within 1-2 days after PTU withdrawal.

Conclusion: This case demonstrated that acute onset of severe pain and swelling in a large joint may be a rheumatologic manifestation of hypersensitivity to PTU. Prompt recognition, early diagnosis and withdrawal of PTU may result in rapid improvement of the arthritis.

Abstract #1006

MICROSCOPIC PAPILLARY THYROID CARCINOMA PRESENTING AS A MEDIASTINAL MASS

Melissa Roether Piech, MD, Gary Cushing, MD

Objective: Microscopic papillary thyroid carcinoma (PTC) rarely presents as a distant metastasis. A case of microscopic PTC presenting as a mediastinal mass is described.

Case Presentation: A 53-year-old female presented with a persistent non-productive cough and retrosternal chest discomfort. CT scan and MRI of the chest demonstrated a 3.0 x 2.6 cm cystic paraseophageal mass in the posterior thorax. There was no FDG uptake on PET scan. The suspected diagnosis was benign bronchogenic cyst. Video-assisted thoracoscopic was performed and the frozen pathology result was consistent with a benign epithelial cyst. Final pathology revealed cystic PTC involving lymph node and surrounding perinodal tissue. No nodules were palpated on thyroid exam. Thyroid ultrasound (US) showed diffuse microcalcifications throughout the right lobe without a discrete nodule. CT scan of the neck demonstrated a heterogeneous thyroid gland with calcifications and non-specific lymph nodes on multiple levels. In view of the mediastinal metastasis and diffuse thyroid microcalcifications without a discrete nodule for FNA biopsy, a total thyroidectomy with central, right, and selective left lymph node dissection was performed. Pathology revealed bilateral, multifocal microscopic PTC with the largest focus being 2 mm. Extrathyroidal extension was present as well as positive lymph nodes in the central and right compartments. The patient received 150 mCi of I-131. Post-therapy whole body scan showed two foci of increased uptake in the thyroid bed without activity at distant sites. Stimulated thyroglobulin level pre-ablation was 1.0 ng/ml. Her identical twin was subsequently diagnosed with PTC following US guided FNA biopsy of a 0.5 cm left thyroid nodule.

Discussion: Microscopic PTC is defined as a primary lesion measuring 1 cm or less. The incidence of microscopic disease has risen, largely due to increased use of neck ultrasound and FNA. Many microscopic tumors are found incidentally at surgery done for an otherwise benign pathology. Series of microscopic PTC report 8-20% incidence of extrathyroidal extension, 10-50% cervical metastasis, 0-3% distant metastasis, and a 1.5-11% rate of recurrence. Therefore, a small group of microscopic PTC can behave aggressively. These tumors may represent a different mutational subset.

Conclusion: The incidence of microscopic PTC is on the rise and several studies show aggressive behavior, though infrequent, is possible. However, a distant metastasis is rarely the initial presentation. We report a case of microscopic PTC presenting as a mediastinal mass.
tachycardia at a rate of 138 and blood pressure of 140/90. Thyroid tests showed a suppressed TSH of <0.03mU/L (normal 0.55-4.78mU/L), Free thyroxine of 3.9ng/dL (normal 0.7-1.7ng/dL), and a high free triiodothyronine of 10.6 pg/ml (normal 2.3-4.2 pg/mL). CT abdomen showed a high grade small bowel obstruction around the tubing of the lap band reservoir. The surgical team placed a nasogastric tube to suction and kept the patient NPO. Intravenous or rectal methimazole could have been given to control her hyperthyroidism. As our pharmacy did not have equipment to prepare IV methimazole or methimazole rectal suppositories, a suspension of methimazole 10milligrams per 1cc of normal saline was administered as an enema twice a day. She received 20 milligrams twice a day and stayed in the lateral decubitus position for 15 minutes after each administration. The patient also received intravenous beta blockade for heart rate control. Free T3 levels normalized in 4 days and Free T4 became normal in 12 days. By day 7 of hospitalization, the patient’s bowel obstruction resolved and thereafter was started on oral methimazole 20 milligrams daily.

**Discussion:** This case illustrates the possibility of using methimazole via an alternate route when the oral route is not an option. Intravenous methimazole preparations need to be prepared using aseptic precautions and should be filtered through a 0.22micro meter filter. Suppositories are made using special equipment. We did not have such equipment and thus used methimazole per rectum via a suspension enema with a timely and effective reduction in T4 and T3 levels. Oral and rectal methimazole have been shown to have comparable pharmacokinetics in terms of absorption rate and time to peak level. For patients who are allergic to methimazole Propylthiouracil can also be administered as a suppository or suspension enema with similar therapeutic effects.

**Conclusion:** For patients who cannot take medications orally and need antithyroid medication, rectal methimazole is an effective, practical and feasible alternative form of therapy.

**Abstract #1008**

SAFETY AND TOLERABILITY OF INSULIN TOLERANCE TESTS

**Olubukola Ajala, MBBS,**
**Gina Twine Daniel Flanagan, MD**

**Objective:** We reviewed the depth and length of hypoglycaemia in a cohort of patients undergoing Insulin Tolerance Tests (ITTs). We evaluated the safety of the test, its reproducibility and using multiple regression analysis, explored factors that might predict the optimal dose of insulin.

**Methods:** 220 ITTs were performed at Teaching hospital in the south west of England between 2005 and 2010. An experienced endocrine specialist nurse in cooperation with a physician performed all the ITTs. At 0 min, i.v. insulin was administered. The insulin dose was 0.15 IU/kg in the majority of patients (187/220), 0.3IU/kg if insulin resistant (26/220), and 0.1IU/kg if insulin sensitive (7/220). Blood samples were taken at 0, 30, 60, 90 and 120 min for Growth Hormone, cortisol, and plasma glucose analyses. Verbal ands written consent is obtained in all patients.

**Results:** The major indication for ITT was non-functioning pituitary macro adenomas. 76% of the cohort was hypoglycaemic (<2.0mmol/l) for 60 minutes or more. The nadir plasma glucose (NBG) ranged from 0.1-4.6mmol/l and correlated significantly with Basal Plasma Glucose (BPG) (r. 0:56; P <0.0005), Insulin dose (r 0.27 P <0.0005), and weight (r 0.21 P 0.004). 24 patients received an insulin dose exceeding 0.15 IU/kg body weight. These patients were characterized by higher weight (mean 93 vs. 86 kg) and BPG (mean 103 vs. 88 mg/dl) compared with the rest of the population. Using multiple regression analysis, the independent factors determining nadir blood glucose were venous plasma glucose (b 0.56, p<0.0005 20% contribution) and weight (b 0.14 p0.05 2% contribution). The within subject variability of nadir glucose ranged from 6.9%- 124% (p=0.2). Only one patient had an adverse effect during the test. He developed unstable angina and needed coronary artery by-pass surgery following a finding of 3 vessel coronary artery disease. The mean NPG and insulin dose in this patient was comparable with those of the total population.

**Discussion:** The ITT has been the gold standard for the assessment of the pituitary-adrenal axis and GH reserve for about 40 years. The limitations of the test include the perceived risks and unpleasant effects of prolonged hypoglycaemia. Our data shows that the resultant hypoglycaemia can be prolonged and unpredictable in a significant proportion of patients. We have also shown that baseline plasma glucose and the patient’s weight predict the nadir plasma glucose.

**Conclusion:** The ITT is relatively safe; however we propose that a better way to avoid unnecessarily prolonged hypoglycaemia is the use of an insulin and glucose infusion with bed-side plasma glucose analysis.
PREVALENCE OF OVERT AND SUBCLINICAL HYPOTHYROIDISM AMONG PREGNANT WOMEN ATTENDING TWO REFERRAL HOSPITALS IN SAUDI ARABIA AND ITS ASSOCIATED MATERNAL AND FETAL COMPLICATIONS

Inass M Taha, MD, PhD, Jihan Alhazmi, MD

Background: Thyroid disorders are among the common endocrine problems in pregnant women. Overt and subclinical hypothyroidism has been shown to be associated with an adverse outcome for both the mother and the offspring. There are no sufficient published data from Saudi Arabia about the prevalence of hypothyroidism in pregnancy and its associated adverse outcomes.

Objectives: This study is aimed to find out the prevalence of overt and subclinical hypothyroidism, and their pregnancy outcomes among Saudi pregnant women at AlMadinah region.

Methods: A hospital-based cohort study performed at Madina Maternity and Children hospital (MMCH) and Ohud hospital, where 936 Saudi pregnant women at 12 to 30 weeks of gestation enrolled between July 2009 and June 2010. All women received routine antenatal care. TSH level estimation was done and if TSH level was deranged, free T4 and free T3 levels were then requested. Patients were managed accordingly.

Results: Overt hypothyroidism was found in 9.3%, and subclinical hypothyroidism in 14.9% of women studied, with a significantly higher maternal age (p=0.02). In both hypothyroid groups there was a significant increased risk of pregnancy induced hypertension (16.1%, OR 2.4 (95% CI 1.3-4.5) & 9.4%, OR 7.7 (95% CI 4.1-1.5), gestational diabetes (23%, OR 1.9 (95% CI 1.1-3.3) & 34.5%, OR 0.30 (95% CI 0.20-0.45)), abortion (11.5%, OR 5.28 (95% CI 2.3-11.9) & 16.5%, OR 0.12 (95% CI 0.06-0.24)), CS deliveries (35.6%, OR 1.9 (95% CI 1.17-3.1) & 30.2%, OR 0.63 (95% CI 0.42-0.97)) and low APGAR score (16.1%, OR 1.97 (95% CI 1.05-3.68) & 10.1%, OR 0.87 (95% CI 0.47-1.60)).

Conclusion: Pregnancy is associated with a high prevalence of subclinical and overt hypothyroidism among Saudi women living in Al-Madinah region, with increased risk of both maternal and fetal poor outcomes. Awaiting further studies, screening all Saudi pregnant women at first antenatal visit by serum TSH is highly recommended.

DETERMINANTS OF EXTRA-OCULAR MUSCLE VOLUME IN PATIENTS WITH GRAVES’ DISEASE

Samer El-Kaissi, MD, Jack R Wall, MD

Objectives: To examine factors contributing to extraocular muscle (EOM) volume increase in patients with recently-diagnosed Graves’ hyperthyroidism.

Methods: Orbital magnetic resonance imaging for the purpose of measuring EOM volume was performed on 39 patients with recently-diagnosed Graves’ disease. Receiver-Operating-Characteristic analysis was used to determine cut-off values of MRI-measured volumes by comparing patient volumes to those of 13 normal volunteers.

Results: Of the 39 patients recruited, 31 were found to have at least one enlarged EOM, of whom only 2 patients had clinically evident EOM dysfunction. Active ophthalmopathy was detected in 18/39 patients using the abbreviated clinical activity score (CAS). Compared to patients without EOM enlargement, the mean serum thyrotropin (TSH) was significantly higher in patients with EOM volume increase (0.020 ± 0.005 vs. 0.007 ±0.002 mU/L; P-value 0.012), as were the serum free-T4 (52.9 ± 3.3 vs. 41.2 ± 1.7 pmol/L; P-value 0.003) and Technetium uptake on thyroid scintigraphy (13.51 ± 1.7% vs. 8.55 ± 1.6%; P-value 0.045). There were no differences between the 2 groups in the proportion of males, tobacco smokers, those with active ophthalmopathy (CAS ≥ 4), elevated serum free T3, or TSH-receptor (TSH-R) antibody levels. Moreover, there was no association between TSH-R antibody positivity and EOMV enlargement.

Discussion: This study shows that patients with newly-diagnosed Graves’ disease and EOM enlargement have higher serum TSH and more severe hyperthyroidism, as suggested by the higher serum free-T4 and greater uptake on thyroid scintigraphy, than patients without EOM enlargement. The paradoxically higher mean serum TSH in patients with EOM enlargement despite greater free T4 and feres T3 levels raises questions about the relationship between TSH levels and thyroid hormone levels in hyperthyroid patients with suppressed serum TSH. The lack of an association between TSH-R antibody positivity and EOMV enlargement should be interpreted with caution given the small sample size and the positive correlation in previous studies between TSH-R antibody levels and the prevalence of TAO in untreated Graves’ disease.

Conclusions: Patients with Graves’ disease and EOM enlargement have higher serum TSH and more severe hyperthyroidism at baseline than patients without
Abstract #1011

HYPOTHYROIDISM AND HYponATREMIA, ARE YOU A BELIEVER?

Arpeta Gupta, MD, Noreen Nazir, MD, Sameera Daud, MD, James Bena, MS, Christian Nasr, MD, FACE

Background: Hypothyroidism as a cause for hyponatremia has been repeatedly described in the literature and has remained a traditional part of teaching. The pathogenesis of this relationship remains uncertain. Fluid retention and impaired cardiac or renal functions that may accompany hypothyroidism are some of the proposed hypotheses. A role for antidiuretic hormone has been suggested. On the other hand, some literature has disputed the association between hypothyroidism and hyponatremia, the latter being attributed to co-existing morbidities that patients may have.

Objective: To revisit the association between hyponatremia and hypothyroidism.

Methods: We retrospectively reviewed sodium and thyrotropin (TSH) values on 143,720 patients whose serum samples were collected at outpatient clinics or during hospitalization. Only measurements taken within one week of one another were considered. One pair of measurements (the first) per patient was used.

Results: Spearman correlation estimates were developed given non-normality in the sodium and TSH distribution. A statistically significant correlation was found (rho -0.01, p<0.001). Ninety-seven percent of sodium measures were in the normal range and 88% of patients were euthyroid. Of the 10,424 (7.2%) patients with hypothyroidism, 2,863 (1.9%) had hyponatremia including 320 euthyroid and 2,543 hypothyroid patients with sodium <115 mEq/L as compared to 13 euthyroid and 4 hypothyroid patients with sodium <115 mEq/L. There were no patients with severe hypothyroidism (TSH >50 mIU/L) and severe hyponatremia (Na<115 mEq/L). Three hundred sixty-one patients with severe hypothyroidism had normal sodium (Na 133-145 mEq/L), 14 had mild hyponatremia (Na 125-132 mEq/L) and one had moderate hyponatremia (Na 115-124 mEq/L). Sodium and TSH values were dichotomized and Pearson’s chi square test was applied. Patients with hyponatremia had 1.8 times higher odds of hypothyroidism than patients without hyponatremia (p<0.001).

Conclusion: There seems to be a statistically significant relationship between the presence of hyponatremia and hypothyroidism. However, the correlation estimate being extremely small indicates little association between the measures. In this case, the statistical significance seems to be an artifact of the large sample size. Again, a correlation between the severities of hypothyroidism and hyponatremia is difficult to establish given the small number of subjects in these groups. Given the finding of this weak association, one needs to always consider the presence of co-morbidities or non-thyroidal illnesses.

Abstract #1012

FALSE POSITIVE 131 I WHOLE BODY SCAN IN PUERTORRICAN MALE WITH PAPILLARY THYROID CARCINOMA

Nixzaliz Rodriguez, MD, Marielba Agosto, MD, Margarita Ramirez, MD, Meliza Martinez, MD, Miriam Allende, MD

Objective: To describe a case of a false positive 131 I whole body scan in an adult male patient in Puerto Rico.

Case Presentation: A 55 year old male with past medical history of arterial hypertension, rheumatoid arthritis, systemic lupus erythematosus, G6PD deficiency on antihypertensive medications, chronic prednisone use and hydroxychloroquine, that presented with right large thyroid mass in neck CTScan measuring 5 x 6 x 8 cm. He underwent a total thyroidectomy with a pathologic report of papillary thyroid carcinoma, follicular variant of 9 cm in greatest dimension, surgical margins free of tumor, negative for lymphovascular space invasion, negative for extra thyroid extension. An oral dose of 105.6 mCi of 131 I (RAI) was given as ablation therapy. Whole body radiiodine scan post-therapy findings were: Functional thyroid tissue in the neck as expected after radioiodine therapy. Two additional foci of increase activity are observed in left axillary region and right hemipelvis highly suggestive of metastatic disease. Also considerable deposition of the radiopharmaceutical in the following joints: shoulders, elbows, wrists, metacarpophalangeal and interphalangeal joints,hips and knees probably due to active inflammation secondary to arthritis. Axillary mass FNA showed lymphoid hyperplasia with no evidence of metastasis.Thyroglobulin Antibodies < 20 IU/mL. Thyroglobulin < 0.2 IU/mL...Post thyroidectomy ultrasound: No distintic mass is identified. Pelvic MRI: Bilateral femoral heads avascular necrosis.

Discussion: Radioiodine whole-body scanning is the imaging modality of the highest accuracy in diagnosing metastases from differentiated thyroid cancer. However, unrelated pathology in one of several nonthyroidal tissues...
that normally take-up/secrete radioiodine may result in a false positive scan. False positive scans are usually the result of four general causes: body secretions, pathological transudates and exudates, infection or inflammation, and non-thyroid tumors.

**Conclusion:** Nonthyroidal pathology should be excluded before exposing patients with apparent thyroid cancer metastases that have atypical characteristics on radiiodine whole body imaging.

**Abstract #1013**

**TYPE 2 DIABETES MELLITUS AND PRIMARY HYPOTHYROIDISM- SHOULD TSH BE TESTED IN ALL PATIENTS WITH DIABETES?**

Hector Eloy Tamez Perez, MD, Alejandra Tamez, MD, Esteban Martinez, MD, Jose Barquet, MD, Mayra Hernandez, MD, Dania Quintanilla, MD

**Objective:** To identify the prevalence of patients with diabetes treated for hypothyroidism and compare this prevalence with that found in a control group of patients without diagnosis of type 2 diabetes.

**Methods:** We developed a retrospective cross-sectional study in a private outpatient clinic in Monterrey, Nuevo Leon in 2009. We reviewed the computerized clinical records of patients attending to the clinic as a search strategy. During this period we identified patients with a diagnosis of T2DM who were treated with levothyroxine. The control group was identified as those patients in treatment with levothyroxine who did not have a diagnosis of T2DM. T2DM was defined as those patients that met the diagnostic criteria recommended by current guidelines. PH was defined in all patients with thyroid hormone therapy. We excluded patients with a thyroid neoplasia, panhypopituitarism, or surgical complications of multinodular goiter or a thyroid nodule.

**Results:** We included 1,848 adult patients with T2DM in the study group, 1071 (58%) women and 777 (42%) men. For the control group, we took a convenience sample (N = 3,313) from the non-diabetic population, 1822 (55%) women and 1491 (45%) men. The mean age in the study group was 52 ± 7 years, and 47 ± 4 in the control group (P ≤ .0001; OR 3.45, 95% CI 2.51-4.79)

**Discussion:** The prevalence of thyroid dysfunction in patients with type 2 diabetes mellitus (T2DM) figures in the 10-31% range. The most common form of thyroid dysfunction in T2DM is subclinical hypothyroidism but there is evidence that subclinical hypothyroidism only progresses to clinical hypothyroidism at a low rate (<1% over five years). Current clinical guideline recommendations are inconsistent in the detection of PH in patients with T2DM. Both primary hypothyroidism and T2DM are independent risk factors for atherosclerotic cardiovascular disease. The benefit of early identification of both diseases has a significant impact on improving cardiovascular function, blood pressure, and lipid profile, thereby reducing long-term cardiovascular risk and improving quality of life for persons with diabetes.

**Conclusions:** A strong association between type 2 diabetes and hypothyroidism was found. These results are consistent with an increased cardiovascular risk. A thyroid profile should be a diagnostic test in all patients with type 2 diabetes; similar to what occurs in type 1 diabetes mellitus.

**Abstract #1014**

**STUDY OF FREQUENCY OF GOITER IN OAXACA (MEXICO): ANALYSIS OF ETIOLOGIC FACTORS**

Estanislao Ramirez Vargas, MD, PhD, Rosalino Vasquez-Cruz, MD

**Objective:** This study was planned to investigate goiter prevalence in the Valley of Oaxaca (Mexico), to analyze the etiologic factors and to study the correlation between goiter prevalence and the etiologic factors studied.

**Methods:** 1400 subjects (717 men and 683 women) of 10 to 18 years old were studied and engaged in clinical and laboratory tests. Physical examinations were: weight, size, BMI, palpation of neck for diagnosis of goiter by two experts' endocrinologist; the goiter was classified according to the criteria of the WHO. Biological examinations were: Collect salt of various origins (gem, sailor, iodized) and collect water (taps and mineral water). Collect urines for determination of urinary iodine concentration (µg iodine/mg of creatinine). Two recall of food consumption of 24 hours was administered with questionnaires.

**Results:** The goiter prevalence in the population studied of Oaxaca was of 9.6%, and the value of urinary iodine concentration was 79.8 µg I/mg of creatinine (S.D. = 10.89). We found an important correlation between the prevalence of the goiter and the family history of goiter (O.R. = 2.4) and tobacco (O.R. = 2.2).

**Discussion and Conclusion:** The goiter prevalence in the population studied of Oaxaca was 9.6%, near of the top threshold of endemia (according to I.C.C.I.D.D.). The value of the found average of urinary iodine was 79.8 µg I/mg of creatinine (the recommendation of WHO is 150-200 µg per day). We found an important correlation between the prevalence of the goiter and the family history of goiter and Tobacco addiction. No correlation was found between the presence of goiter and type of consumed salt, drunk water, the caloric consumption daily and the BMI.
Abstract #1015

COURSE OF UNTREATED ENDOGENOUS SUBCLINICAL HYPERTHYROIDISM – IN AN ACADEMIC OUTPATIENT CLINIC

Saleh A. Aldasouqi, MD, FACE, ECNU, Bhavini Bhavsar, MD, Ved Gossain, MD, FACE, FACP

Objective: Subclinical hyperthyroidism (SCH) is defined as low TSH (<0.35 uIU/mL) with a normal free T4 and free T3 levels. The course of untreated SCH is variable. Some patients may progress to overt hyperthyroidism, some may revert to normal and others may remain persistently subclinically hyperthyroid. Therefore, the treatment of SCH remains controversial and practice variations exist. The objective of this study was to report the course of untreated SCH in an academic outpatient clinic.

Methods: Consecutive patients with a new diagnosis of endogenous SCH were identified in an academic multispecialty clinic. Follow-up data were obtained in those patients who were not treated.

Results: A total of 59 patients (mean age ± SD, 56.8 ± 16.3 years) with endogenous SCH were identified, of which, 19 were men and 40 were women. Mean follow up was 28.5 months (± SD 23.0 months). Forty-six patients (78%) were not treated. Thirteen patients were treated and were excluded from further analysis. Out of 46 patients, who were not treated, SCH resolved spontaneously in 23 patients (50%). Mean resolution period ± SD was 11.7 ±11.16 months. Twenty-two patients (48%) had persistent SCH and 1 patient (2%) developed overt hyperthyroidism. Three patients (6.5%) with untreated SCH had atrial fibrillation at the time of diagnosis. One patient was not treated because of old age (89 years) and multiple comorbidities. In the other 2 patients, it was unclear from review of their medical records, why they were not started on treatment for SCH, but one was lost to follow up and in the other patient SCH resolved spontaneously.

Discussion: Our study showed that only 1 out of 46 untreated patients with SCH became overtly hyperthyroid, while the rest either reverted to normal (50%) or remained in persistent SCH without serious consequences. These findings are somewhat discrepant to a recent large study where 65-80% patients remained persistently subclinically hyperthyroid for a period of 2-5 years. However, our study findings are limited by a small sample size. The aim of our study was to observe the course of SCH in a routine clinical setting. Given the controversies in treatment guidelines, we wished to study the trend of whether our specialists opt to treat or not to treat these patients. We showed that the majority opted not to treat. From our study, we cannot recommend either way, because the follow up time is not long enough to conclude complete absence of occurrence of arrhythmia upon longer follow up in untreated patients.

Conclusion: Our findings showed that most patients with SCH either remain subclinically hyperthyroid without serious consequences or revert to normal (Odds: 50%).

Abstract #1016

SUPRAGLOTTIC MYXEDEMA

Ajaz Ahamad Banka, MBBS, Andleeb Afzal, MBBS, Shamsa Ali, MD, Nicholas Avitable, MD, Donald Beahm, MD, Amna Khan, MD

Objective: Primary myxedema of the supraglottis is a rare cause of upper airway obstruction. Deposition of mucopolysaccharides into the tissues of the hypopharynx results in edema of the supraglottic structures. This case report emphasizes rare but important presentation of hypothyroidism.

Case Presentation: Herein we present a case of a 44-year-old Moroccan female who presented with shortness of breath while awaiting radioactive iodine ablation with I-131 after removal of recurrent papillary thyroid cancer. At her first endocrine visit, patient informed us that she had thyroid surgery at age 8 (no details available) in her home country. She denied any prior radioactive iodine ablation or any radiation therapy. She had been treated to the ENT clinic with a neck mass. Biopsy of this mass revealed papillary thyroid cancer. Subsequently, she underwent total thyroidectomy with bilateral neck dissection. Pathology was consistent with multifocal papillary thyroid cancer with peritracheal invasion but no lymph nodes were positive for malignancy. She was then referred to us for further therapy. In lieu of radioactive iodine ablation (RAIA), she had not been started on any thyroid replacement. At the time of presentation, her TSH was greater than 100 IU/ml (0.50-5.00 IU/ml) with free T4 less than 0.25 ng/dl (0.60-1.15 ng/dl). She was clinically hypothyroid. Her radioactive iodine ablation was scheduled for 2 weeks later (first available). A week later, she presented in respiratory distress with stridor indicating upper airway obstruction. Fiberoptic laryngoscopic evaluation by ENT demonstrated supraglottic edema. Except for periorbital puffiness, she did not have any other signs of myxedema. There was no change in her neck. Her RAIA was postponed till she was clinically more stable and had secure airway. Levothyroxine replacement was started. She reported dramatic improvement in her symptoms especially shortness of breath. She was able to speak full sentences.

Discussion: Although hoarseness of voice, tracheal compression secondary to goiter, sleep apnea or respiratory depression in severe hypothyroidism are known associations, it is uncommon for hypothyroidism...
to result in airway obstruction at the level of the supraglottis or glottis. Supraglottic edema secondary to overt hypothyroidism is a very rare presentation. Only 2 cases have been reported so far.

**Conclusion:** Overt hypothyroidism rarely may manifest as supraglottic edema causing upper airway obstruction which dramatically improves with levothyroxine therapy.

**Abstract #1017**

**IODINE SUPPLEMENTATION TO REDUCE IODINE DEFICIENCY IN PREGNANCY**

Rachel Pessah Pollack, MD, Deirdre Cocks Eschler, MD, Helen Looker, MD, PhD, Zhenya Pozharny, MD, Terry Davies, MD, FRCP, FACE

**Background:** Iodine is essential for the synthesis of thyroid hormones by mother and fetus. Pregnancy is a time of increased thyroid hormone synthesis, when even mild thyroid deficiency states are revealed.

**Objective:** To determine if iodine supplementation reduces the risk for iodine deficiency.

**Methods:** Cross-sectional study to assess iodine levels in random urine specimens (UI) during pregnancy in New York City. One hundred and eighty two women were from a clinic where iodine supplementation was offered (Group A) (complementary Foltab prenatal multivitamins, containing 150 mcg of potassium iodide), and one hundred and eighty three women were from a practice where no supplementation was offered (Group B).

**Results:** Overall, nearly one out of two pregnant women in New York City were iodine deficient with a spot UI level less than 150 mcg/dL. The median urine iodine concentration for the entire group was 152.5 mcg/dl but there was considerable variation from 10.9 to 1210 mcg/dl. When urine iodine measurements were expressed in quartiles, 60% of pregnant women in New York City had a urine iodine level of below 150 mcg/dl and could be defined as iodine deficient in pregnancy.

**Discussion and Conclusion:** New York, inner-city pregnant women were significantly less prone to iodine deficiency when provided with iodine supplementation. Nevertheless, more than 20% of such women remained iodine deficient according to WHO guidelines suggesting that current supplementation remains insufficient.

**Abstract #1018**

**RELATIONSHIP BETWEEN SERUM THYROTROPIN AND MICROALBUMIN EXCRETION IN EUTHYROID PATIENTS WITH DIABETES**

Gautam Das, MD, Onyebuchi Okosiehme, MD, MRCP

**Objective:** Our aims were to analyse the relationship between serum thyrotropin concentration and microalbumin excretion in euthyroid diabetic patients.

**Methods:** We studied 420 euthyroid diabetic patients attending our diabetes clinic for annual reviews (mean age 60.1 ± 15.7 yrs; males 63.6%, females 36.4%; type 1 diabetes 12.4%, type 2 diabetes 87.6%). For each patient we measured anthropometric indices, thyroid hormones (FT4 and TSH), glycosylated haemoglobin (HbA1c), and albumin creatinine ratio (ACR) in spot urine samples. Patients were categorised according to their serum TSH as (1) TSH < 2.0 mU/L or (2) TSH ≥ 2.0 mU/L.

**Results:** Patients with TSH ≥ 2.0 mU/L were older than those with TSH < 2.0 mU/L (68.9 ± 15.3 vs 58.6 ± 15.7 yrs; p=0.03) and had higher ACR (10.3 ± 29.0 vs 5.8 ± 12.5 mg/mmol; p=0.03). Glycaemic control (8.7 ± 2.0 vs 9.2 ± 5.2 %; P=0.22) was not much different, but serum TSH strongly correlated individually with HbA1c (p=0.00) in the two subgroups. Body mass index (33.2 ± 5.7 vs 32.5 ± 5.1 kg/m²; P=0.29), total cholesterol (4.0 ± 1.0 vs 4.0 ± 1.1 mmol/L; P=0.84) and triglycerides (2.5 ±1.9 vs 2.6 ±1.6 mmol/L; P=0.68) did not differ between the groups but HDL cholesterol was significantly higher in patients with TSH ≥ 2.0 mU/L compared to those with TSH < 2.0 mU/L (0.95 ± 0.2 vs 0.91 ± 0.2 mmol/L; P=0.03). People with type 2 diabetes had a positive correlation in age category (p=0.05) only in the two TSH subgroups.

**Discussion:** Thyroid dysfunction is associated with increased cardiovascular disease risk. Although serum thyrotropin (TSH) has been shown to correlate with various cardiovascular risk factors such as blood pressure, lipid profile, and indices of insulin resistance, the relationship between serum thyrotropin and microalbumin excretion has so far received scant attention. Microalbuminuria is now an established cardiovascular disease risk factor in diabetic patients and its relationship with serum TSH is quite interesting in stratifying cardiovascular disease risk in these patients. A familial component influences both UAE (urinary albumin excretion) in diabetic patients and development of thyroid disease and the same genes may underlie both conditions. A dysthyroid status (hypo or hyper) can influence renal blood flow and GFR thereby influencing microalbumin excretion, but our study
demonstrates that variation in microalbumin excretion exists in people even with normal thyroid function but with different levels of TSH. These parameters should be routinely estimated along with other metabolic indices during routine review of diabetic subjects for reductions in future cardiovascular events.

**Conclusion:** Our findings suggest that high normal serum TSH is associated with older age and greater albumin excretion in euthyroid patients with diabetes. Further prospective studies, which control for the interactions of co-morbidities and concurrent use of cardiovascular disease modifying medications in this population, are needed to clarify these preliminary findings.

### Abstract #1019

**FOLLICULAR THYROID CANCER WITH DIRECT TUMORAL EXTENSION INTO GREAT CERVICAL, MEDIASTINAL VEINS AND RIGHT ATRIUM**

Mohammed Ahmed, MD, FACP, FACE, Nora Al-kahtani, MD, Maha Al-Fehaily, MD, Fawaz Skaff, MD, Faisal Al Malki, MD

**Objective:** We report a case of locally advanced recurrent follicular thyroid cancer (FTC) with residual neck and mediastinal tumor that invaded major cervical and mediastinal veins & developed intracavitary right atrial tumor thrombus.

**Case Presentation:** The dx of tumoral thrombus (TT) in a 58-year-old lady was made at Doppler US study showing thrombus initially in the right internal jugular vein (RIJV) only. It was confirmed at her second neck exploration for recurrence, upon CT scan and FNA Bx of TT. Eight mos later, PET-CT revealed extension of the TT into rt. brachiocephalic vein & SVC. Five mos. later CT chest and MRI showed TT had extended into right atrium. She remained on anticoagulation Rx and had no evidence of involvement of the tricuspid valve, right ventricle or pulmonary embolism. She had residual disease in neck and mediastinum. A multidisciplinary team of Endocrinologists, a team of thyroid/Vascular/Cardiac surgeons, soon planned for resection of residual tumor, open heart/vascular surgery for evacuation of the TT. Pt had no evidence of pulmonary or skeletal metastases. Her initial tumor was multifocal, an aggregate tumor size of 7.7x 6.5cm with capsular/angio/lymph node invasion. She underwent 2 surgeries, received 2 sessions of I 131 Rx (cumulative dose 345 mCi), last I 131 Rx was given for Tg positive and scan negative findings with no detectable lesions on post ablation scan. Her suppressed and unsuppressed thyroglobulin remained at > 5000 ug/l, during 22 mos. Follow-up regardless of Rx given.

**Discussion:** In our experience of 4200 cases of thyroid cancer (TC) over a period of 30 yrs we have encountered this single case of intracardiac tumoral invasion. We have provided data of sequential development over a 2-yr period of TT into RIJV, followed by right brachiocephalic vein; thence downstream into SVC and eventual direct intracavitary extension into right atrium. Imaging modalities have provided evidence for direct contiguous extension invasion into the major veins. We are aware of 12 other reported thyroid cases with tumoral extension into great cervical veins and right atrium. A case of right ventricular outflow tract obstructing mass from FTC was also reported. Some of these cases have benefited from resection of the obstructing intracardiac tumor, underscoring the importance of early and active intervention.

**Conclusion:** TC invasion into great veins of neck and mediastinum is a distinctly rare event that deserves awareness in dealing with advance/aggressive cases. Adverse hemodynamic consequences including fatal pulmonary embolism and cardiac tamponade can ensue if the lesion is left unresected. The need for a multidisciplinary team management is obvious.

### Abstract #1020

**HYPOTHYROIDISM IN PATIENTS TREATED WITH LENALIDOMIDE FOR HEMATOLOGICAL MALIGNANCIES**

M. Kathleen Figaro, MD, Warren Clayton, MD, Chineny Usoh, BS, Kara Brown, BS, Adetola Kassim, MD, Vipul Lakhani, MD, Shubhada Jagasia, MD

**Objective:** Lenalidomide, a thalidomide-derived antiangiogenic drug associated with hypothyroidism, is now routinely used for hematological diagnoses. We describe a case-series of lenalidomide use in hematological cancers and the prevalence of thyroid abnormalities. We reviewed electronic records of patients treated with lenalidomide for hematological malignancies at a single center from 2005 to 2010.

**Case Presentation:** One hundred and seventy patients on lenalidomide were included in our analysis. From each patient’s chart, information about demographics, thyroid function tests (TFTs), previous thyroid disease, and risk factors for thyroid disease was gathered. The follow-up of any abnormal TFTs was also examined. Of the 170 patients with confirmed lenalidomide use, 6%
had thyroid abnormalities that were attributable only to lenalidomide. In addition, 12% had preexisting thyroid disease with changes while on lenalidomide therapy. Most of these patients had a diagnosis of hypothyroidism treated with levothyroxine. The median age was 64.9 years (Interquartile Range (IQR) 15). Previous use of thalidomide and prior stem cell transplantation were not related to thyroid abnormalities. Lenalidomide was associated with increased thyroid dysfunction in patients with prior thyroid disease (18%) compared with no previous thyroid dysfunction (6%) (P=0.0001). New TFT abnormalities occurred at a median of 5.0 months (IQR 6.25) post start of treatment. Of 20 patients who did not undergo any thyroid function evaluation before or while on lenalidomide, 35% developed new symptoms of hypothyroidism such as fatigue, cold intolerance and constipation after a median of 9.4 months (IQR 6.5) of treatment.

**Discussion**: The cause of lenalidomide-induced thyroid dysfunction is unknown, possible causes include a direct injury to thyrocytes, an immune response against the thyroid, an inhibition of iodine uptake, or a decrease in thyroid secretory capacity. Because symptoms of hypothyroidism overlap with side effects of lenalidomide. Because the symptoms of hypothyroidism could be alleviated with addition of levothyroxine or adjusting dosage of levothyroxine, evaluation of TFTs is important and should not be overlooked.

**Conclusion**: Thyroid function is not often evaluated while patients are taking lenalidomide for cancer. In this setting, we recommend frequent biochemical evaluation, especially early in treatment and based on suggestive symptoms, to monitor for hypothyroidism and potentially improve patients’ quality of life while on lenalidomide.

**Abstract #1021**

**HURTHLE CELL ADENOMA OF THE THYROID IN A CHILD: A RARE PRESENTATION**

*Jennifer N Osipoff, MD, Thomas A. Wilson, MD*

**Objective**: To describe an 8-year-old male with a thyroid nodule that was determined to be a Hurthle cell adenoma. To our knowledge, he is the youngest individual diagnosed with this lesion.

**Case Presentation**: Patient is an 8.25-year-old previously healthy male referred for a thyroid mass. Patient reported constipation and an “intermittent choking sensation.” No history of radiation, iodine deficiency, or family history of endocrine neoplasias. Exam revealed a 1.5 x 2 cm firm, well circumscribed, non-tender, mobile mass in the mid-lower left thyroid lobe. There were no overlying skin changes, enlargement of the gland itself, or lymphadenopathy. Remainder of exam was normal. Ultrasound obtained prior to visit showed a 2.3 x 1.9 x 1.9 cm complex cystic/solid mid pole left thyroid nodule and a normal right lobe. Ultrasound guided FNA revealed atypical follicles with variable degrees of nuclear overlap and enlargement. Patient underwent a left sided thyroidectomy and isthmusectomy. Surgical pathology was consistent with a Hurthle cell adenoma with an incidental microscopic focus of papillary carcinoma. The tumor was confined to the thyroid with clear margins. Post operative labs showed TSH 5.89 mIU/L, T4 9.0 mcg/dL, calcium 10.3 mg/dL and negative thyroid antibodies. Levothyroxine 50 mcg a day was started and patient has done well clinically.

**Discussion**: Thyroid nodules are found in < 2% of the pediatric population and < 2% of such nodules occur prior to adolescence. Hurthle cell cancers are infrequent in adults, accounting for ~5% of all differentiated thyroid neoplasms, and are exceedingly rare in pediatrics. Prior to our patient, the youngest person with a Hurthle cell adenoma was a 12 year old girl (Bremer et al, Thyroid, 2007). Compared to adults, thyroid nodules in children, particularly those younger than 10 years old, have an increased risk of malignancy. As our patient is the first child less than ten years old with a Hurthle cell adenoma, further complicated by a microscopic focus of papillary carcinoma, guidelines do not exist outlining his optimal treatment plan. Management of thyroid nodules, particularly in pre-pubertal children, remains a controversial topic in pediatric endocrinology.

**Conclusion**: Although extremely uncommon, Hurthle cell neoplasms do occur in pediatric aged patients. Clinicians need to be aware of this possibility as FNA cannot distinguish Hurthle cell adenomas from carcinomas. Surgery is required to determine if vascular and/or capsular invasion has occurred, which by definition, is diagnostic of a Hurthle cell carcinoma.

**Abstract #1022**

**CASE SERIES OF 4 ADULTS WITH WORSENING HYPOTHYROIDISM SECONDARY TO NEPHROTIC SYNDROME**

*Nicola Gathaiya, MBBS*

**Background/Objective**: Rising thyroid stimulating hormone (TSH) levels in patients being treated for primary hypothyroidism usually indicate poor compliance with thyroxine therapy. Drugs or diseases affecting GI absorption of thyroxine or drugs that accelerate T4 metabolism can manifest in a similar fashion. Nephrotic
syndrome is a rare and unrecognized cause of such a presentation. We report 4 patients with worsening hypothyroidism secondary to nephrotic syndrome.

**Case Presentation:** Case 1: 62-year-old male, with worsening fatigue, laboratory evaluation showed an elevated TSH of 71.3 mIU/l, free T4-0.7 ng/dl. 24hr protein collection showed urinary protein of 10,000mg/24hrs. Kidney biopsy confirmed Nephrotic syndrome secondary to minimal change disease and he was started on high dose steroids. Initial Synthroid dose of 125mcg was increased to 150mcg. Repeat thyroid function testing 2 months later showed a TSH of 0.9 mIU/l. Case 2: 75-year-old female with worsening lower extremity edema, shortness of breathe and weight gain. Laboratory evaluation showed a TSH of 97.4 mIU/l, free T4 of 0.7 mg/dl 24hr urinary protein collection showed urinary protein of 14,020mg/24hr. Kidney biopsy confirmed Nephrotic Syndrome secondary to Amyloidosis. She was treated with Melphalan and dexamethasone. Initial Synthroid dose of 125mcg was increased to 200mcg. Follow-up TSH was 0.3 mIU/l. Case 3: 65 yo female with worsening peripheral edema and shortness of breathe and laboratory evaluation showed an elevated TSH of 41.78 mIU/l. Further evaluation showed 24hr urinary protein of 8,759 mg/24hrs. Kidney biopsy confirmed Nephrotic syndrome secondary to Amyloidosis. She was treated with Lenolidomide. Initial Synthroid dose of 125mcg was increased to 225mcg. Repeat TSH 2 months later was within normal range at 2.2. Case 4: 48 yo with worsening bilateral lower extremity edema, abdominal distention and shortness of breath. TSH was elevated at 178 mIU/l, Free T4-0.6 ng/dl. 24 hr urinary protein was elevated at 7,022 mg/24 hr. Kidney biopsy showed IgA nephropathy and minimal changes disease. He was treated with high dose steroids, cyclosporin, and cyclophosphamide. Initial Synthroid dose of 125mcg was increased to 175mcg. After over 3 yrs, of treatment his Nephropathy was in complete remission and laboratory values showed a TSH of 0.05 indicating over replacement and his levothyroxine dose was decreased.

**Conclusion:** Nephrotic syndrome is a rare and unrecognized cause of rising TSH. Thyroid function abnormalities, comprising urorinary loss of thyroid binding globulin (TBG), free T4 and free tri-iodothyronine (T3), with consequent falls in serum T4, T3 and TBG levels is well documented in children with untreated nephrotic syndrome. Examination of the urine should form part of the investigation strategy in all compliant patients with rising thyroxine requirements in primary hypothyroidism.

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### Abstract #1023

**CALCITONIN-NEGATIVE MEDULLARY THYROID CANCER**

**Zinnia San Juan, MD, Susana Dipp, MD**

**Background/Objective:** Medullary thyroid carcinomas (MTC) comprise about 4% of thyroid cancers. They arise from parafollicular C cells that secrete calcitonin, a marker for biochemical activity. We report a rare case of calcitonin-negative MTC.

**Case Presentation:** This is a 61-year-old male with a 5-year history of an enlarging neck mass. Three years ago imaging identified an 18-cm substernal goiter but he refused further evaluation. In the past 7 months there has been rapid growth of the mass associated with hoarseness, dysphagia and 20-lb weight loss. He denies history of radiation exposure or family history of thyroid cancer. Examination revealed a well-nourished man with a grossly visible goiter that spans the left side of the neck extending to the posterior triangle and up to the angle of the mandible with some fullness on the right side and no lymphadenopathy. There was left vocal cord involvement and tracheal compression on laryngoscopy. Although a biopsy was negative for malignancy, surgery was advised for both symptoms and suspicion of malignancy given his clinical course. He had a total thyroidectomy with radical neck and mediastinal dissection. Pathology showed two foci of MTC (15-cm primary tumor) with extensive lymphovascular invasion and metastasis to 4/23 nodes. Two distinct histological patterns were seen: a classical round cell pattern that stained positive for calcitonin and negative for chromogranin, CEA, and thyroglobulin and a higher grade spindle cell pattern that was negative for all three stains. Postoperative evaluation revealed undetectable calcitonin (<5 pg/mL, normal 0-15.9) and CEA (<1 ng/mL, normal 0-5) despite multiple foci of metastases later identified in both lung fields and C7 vertebra. Radiation and chemotherapy were given but he had poor subsequent course and expired within a few months of surgery.

**Discussion:** Calcitonin is the main biomarker used in detection, monitoring and prognosis of MTC where it is elevated in nearly 100% of cases. Biochemical cure is seen only in 10% of node-positive cases and not if the primary tumor is >40 mm. Serum levels typically require several months to reach a nadir. Our patient had widely metastatic disease even after thyroidectomy and yet calcitonin level immediately after surgery was undetectable. To date, there have been few other cases reported of this calcitonin-
negative MTC. Some tumors, as in this case, report positive immunohistochemical staining while others do not. Defective synthesis or secretion of calcitonin has been the postulated mechanism. More aggressive course has also been suggested and whether this is due to a more aggressive histology or to difficult monitoring is unclear.

Abstract #1024

PARALYSIS AND THE IMPORTANCE OF FURTHER ANALYSIS

Mais Trabolsi, MD, Luay Rifai, MD, Mohammad Kawji, MD, Roshani Sanghani, MD

Background: Thyrotoxic periodic paralysis (TPP) is a rare disorder. The estimated prevalence is 0.2% in Caucasians and 2% in Asians. It is characterized by episodic, potentially reversible weakness and hypokalemia. Diagnosis is often delayed due to overlap with more common types of paralysis. We are reporting a case of TPP as the initial presentation of Graves’ disease (GD).

Case Presentation: A 28-year-old Filipino healthy man presented with sudden onset bilateral lower extremity weakness. He reported eating baked potato and rice, then playing video games for three hours. He was then unable to get up and dragged himself to bed. Symptoms continued to progress and required assistance to be brought to the ED. He also reported palpitations and tremors. He denied headache, vomiting, laxatives or diuretic use. No family history of similar illness. Physical examination revealed regular pulse of 114 beat/min, fine tremors, diffusely enlarged symmetric thyroid gland. Motor strength was 4/5 and 2/5 in bilateral upper and lower extremities respectively with normal reflexes and sensation. Initial I123 uptake scan at that time showed a low TSH and a high free T4. A radioactive I123 uptake scan at that time was read as showing minimal uptake in the thyroid. She was diagnosed with thyroiditis when she presented with symptoms of weight loss, tachycardia, and heat intolerance. Evaluation at that time showed a low TSH and a high free T4. A radioactive I123 uptake scan at that time was read as showing minimal uptake in the thyroid. She was diagnosed with thyroiditis when she presented with symptoms of weight loss, tachycardia, and heat intolerance. Examination revealed an abnormal mass. Laboratory evaluation revealed a low TSH, high total T3, and high free T4—results similar to five years prior. Radioiodine imaging revealed no appreciable neck uptake but extensive uptake in the abdomen. CT of the abdomen showed a large 11.1 x 11.5 x 15 cm mass. A diagnosis of struma ovarii was made. She underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy with the pathology showing a teratoma consistent with struma ovarii. Following the surgery, the patient had resolution of her symptoms, and her labs normalized.

Discussion: This patient is a 54-year-old female who was initially diagnosed 5 years prior with thyroiditis when she presented with symptoms of weight loss, tachycardia, and heat intolerance. Evaluation at that time showed a low TSH and a high free T4. A radioactive I123 uptake scan at that time was read as showing minimal uptake in the thyroid. She was diagnosed with thyroiditis when she presented with symptoms of weight loss, tachycardia, and heat intolerance. Examination revealed an abnormal mass. Laboratory evaluation revealed a low TSH, high total T3, and high free T4—results similar to five years prior. Radioiodine imaging revealed no appreciable neck uptake but extensive uptake in the abdomen. CT of the abdomen showed a large 11.1 x 11.5 x 15 cm mass. A diagnosis of struma ovarii was made. She underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy with the pathology showing a teratoma consistent with struma ovarii. Following the surgery, the patient had resolution of her symptoms, and her labs normalized.

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Discussion: Struma ovarii was first described by Boettlin in 1899 and it literally can be translated to goiter of the ovary. A struma ovarii is found within a teratoma of the ovary. There is increased incidence during the 5th and 6th decade, and the tumors are rarely bilateral and rarely functional. In fact, only about 5-8% of struma ovarii tumors actually manifest with biochemical abnormalities and true hyperthyroidism.
Conclusion: Though struma ovarii is a rare tumor, it can be often misdiagnosed. It is important to consider it in a differential diagnosis of hyperthyroidism, especially in the context of low uptake on an I123 radioiodine scan. This suspicion should have been increased with long standing hyperthyroidism beyond one year—unlikely to be a thyroiditis.

Abstract #1026

COMPLIANCE WITH SCREENING DIABETIC PATIENTS FOR MICROALBUMINURIA IN PRIMARY CARE PRACTICE

Abeer W Anabtawi, MD, L. Mary Mathew, MD

Objective: Studies demonstrated suboptimal compliance of primary care physicians (PCP) with microalbuminuria screening of diabetic patient. Electronic medical records (EMR) enabled with physician reminder system have gained interest in recent years as a method of improving PCP compliance. This study evaluated compliance rate of microalbuminuria screening after two years of introducing an EMR enabled with computer-generated reminder. It also evaluated impact of combining EMR with quality improvement monitoring (QI) in enhancing compliance.

Methods: Retrospective analysis of diabetic patients registered at Unity Faculty Partners (UFP) primary care facility between January, 2008 and December, 2009. Patients with CKD stage IV or more and have been followed by nephrologists were excluded. EMR was enabled with a computer generated physician reminder that highlights the recommended screening tests and due dates. Two years after the introduction of EMR, step 1 study included a QI project evaluating microalbuminuria screening compliance rate. Results were disseminated to UFP physicians. One year later, a repeat QI project was performed in step 2 of study. Mantel-Hanzel test was used to calculate the odds ratio and 95 % CI.

Results: 259 diabetic patients were registered at UFP. Twenty seven patients (10.4%) were excluded due to CKD ≥ stage IV. The remaining 232 patients (140 males, 92 females) had a median (interquartile) age of 61 years (52-72). Five of these patients were included only during step 1 due to the date of leaving or joining UFP clinics. In step 1 [n=213]; microalbuminuria screening was ordered in 120 patients (56.3%). The test was completed in 101 patients (84.2%). In step 2 [n=227]; the test was ordered in 158 patients (69.6%) and 134 of these patients completed the test (84.8%). Compliance with microalbumin screening significantly improved during step 2 compared to step 1 [OR 1.556, 95% CI 1.251-1.935, p=0.006].

Discussion: Study shows even with the use of EMR and physicians reminders the compliance rate is still suboptimal. A recent Cochrane review concluded that computerized point of care reminders have small to modest effect on the quality of health care. The significant improvement in compliance rate in step 2 reinforces the power and concept of continuous quality monitoring with EMR adding the advantage of easy data accessibility and monitoring.

Conclusion: Facilitation of quality control monitoring by the use of EMR played a more important role in improving compliance with microalbuminuria screening than computer generated physician reminder system.

Abstract #1027

INCIDENCE OF POSTOPERATIVE HYPOTHYROIDISM FOLLOWING LESS THAN TOTAL THYROIDECTOMY: AN INSTITUTIONAL EXPERIENCE

Shannon Calhoun Eastham, MD, Michael Weingarten, Deanna Mansker, MD, Jyotika Fernandes, MD, James Alele, MD, Denise Carneiro-Pla, MD

Objective: The goal of this study is to evaluate the incidence and risk factors for developing hypothyroidism following less than total thyroidectomy in our institution.

Methods: 149 patients who underwent hemithyroidectomies, total thyroid lobectomies with partial contralateral lobe excisions and partial lobectomies from 2007 to 2010 performed by a single surgeon were selected for chart review. Patients with known preoperative hypothyroidism, pre or immediate postoperative hormone supplementation, diagnosis of thyroid cancer or incomplete postoperative data were excluded. In the 67 patients who met criteria, serum TSH levels measured preoperatively, 7-10 days and 2-4 months postoperatively were retrospectively reviewed. Hypothyroidism was defined as TSH level >5.5mU/L. Surgical pathology, extent of thyroidectomy and different levels of preoperative TSH were analyzed in an attempt to identify risk factors for postoperative hypothyroidism.

Results: Female to male ratio 4:1, mean age 51 years. Postoperative hypothyroidism was diagnosed in 16/67 cases (24%). When stratified into groups according to preoperative TSH values, levels ≥1.5mU/L predicted postoperative hypothyroidism with a sensitivity of 64% and specificity of 71% while TSH ≥2.5mU/L had a sensitivity of 43% and specificity of 94%. Higher incidence of postoperative hypothyroidism becomes statistically significant when patients have preoperative TSH levels ≥1.5mU/L (60%) when compared to TSH
<1.5 mU/L (14%) (p<0.02). Although the incidence of hypothyroidism was higher in patients with thyroiditis (43%) when compared with patients without this condition (22%), this was not statistically significant (p=0.34). The extent of resection did not have an influence in the incidence of postoperative hypothyroidism.

**Discussion:** Following thyroid lobectomy, the tissue left in situ should function to compensate for the resected portion of gland. However, postoperative hypothyroidism is not uncommon. Postoperative hypothyroidism can lead to lifelong hormone replacement, which can be a crucial factor in patients’ decision process in the treatment of benign thyroid disease.

**Conclusion:** Postoperative hypothyroidism occurred in 24% of patients who underwent less than total thyroidectomy. Although, patients with thyroiditis are more likely to develop postoperative hypothyroidism, this higher incidence is not statistically significant. Conversely, preoperative TSH levels ≥1.5mU/L is a predictor of postoperative hypothyroidism with specificity directly proportional to preoperative TSH levels.

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**Abstract #1028**

**PAPILLARY THYROID CARCINOMA PRESENTING AS RECURRENT INTRATHYROIDAL HEMORRHAGE**

Angela Boldo, MD, Allan Golding, MD, Brian Paul, MD, William B. Kinlaw, MD

**Objective:** To discuss the first reported case of papillary thyroid carcinoma presenting as intrathyroidal hemorrhage.

**Case Presentation:** Papillary thyroid cancer (PTC) is frequent in our population and its incidence has been increasing over the last decades. Hemorrhage secondary to PTC is very rare and only a few cases of hemorrhagic metastasis, to lung, liver and brain have been reported in the literature. This is the first case of recurrent intrathyroidal hemorrhage as a presentation of papillary thyroid carcinoma. Our patient is a 58-year-old female who presented to the endocrinology clinic with a history of a 1 cm left sided thyroid nodule. Over the following 8 years she had 4 episodes of acute left sided thyroid pain and swelling that improved after a few days, symptoms consistent with thyroid hemorrhage. During her 4th episode an ultrasound (US) was performed and images were consistent with a 3x5.4x2.3 cm intrathyroidal hemorrhage. On a follow up thyroid US 3 months later, a 1 cm hypoechoic nodule was visualized adjacent to the resolving hematoma. Fine needle aspiration suggested a diagnosis of PTC and this was confirmed after thyroidectomy.

**Discussion:** Review of the literature regarding PTC and hemorrhage revealed only a few cases of hemorrhagic metastases. Hemorrhagic PTC metastases include cerebellar metastases and multiple brain metastases. One case of hepatic metastasis that presented with periumbilical hemorrhage was reported, as were 3 reports of hemoptysis from lung metastases.

**Conclusion:** To the best of our knowledge, this is the first case of primary PTC presenting as intrathyroidal hemorrhage and in this case it presented as recurrent bouts of bleeding. Considering that this is the only reported case of which we are aware, we consider it premature to recommend an evaluation for possible cancer in every case of spontaneous hemorrhage in the thyroid.

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**Abstract #1029**

**SYNCHRONOUS OCCURRENCE OF MEDULLARY-FOLLICULAR-PAPILLARY THYROID CARCINOMA IN A PATIENT WITH GOITER**

Maria Isabel Davila, MD, Rudabah Hasan, MD, Monica Schwarz, MD, Liying Han, MD, PhD, Osama Khan, MD

**Background/Objective:** Papillary thyroid carcinoma (PTC) is the most common thyroid malignancy, constituting 50-90% of differentiated thyroid carcinomas worldwide. The second most common thyroid malignancy is follicular thyroid carcinoma, constituting 5-50% of differentiated thyroid cancers. Medullary thyroid carcinoma, represents only 3-10% of all thyroid cancers. We present a very rare occurrence of a patient with goiter, found to have synchronous medullary, follicular and papillary thyroid carcinoma.

**Case Presentation:** A 64-year-old female was evaluated in our ENT Clinic for multinodular goiter, with dominant right sided thyroid nodule. Medical history was also significant for pulmonary sarcoidosis and diabetes. She had no family history of thyroid cancer or exposure to radiation. Fine needle aspiration of the nodule showed suspicious cells for papillary neoplasm and she underwent total thyroidectomy. Pathology described a 2cm medullary carcinoma of the left lobe of the thyroid extending to the margins along with a 4.5cm minimally invasive follicular carcinoma in the right lobe of the thyroid. In addition, a 3mm papillary carcinoma was present in the left lobe. The patient subsequently received I131 radioactive iodine therapy, TSH suppression and external beam radiotherapy. Stimulated I131 whole body scans at 1, 3 and 6 years postoperatively did not demonstrate abnormal level. Serum thyroglobulin, thyroglobulin antibody, and calcitonin have remained in the past six years.
**Discussion:** Mixed medullary, follicular and papillary carcinoma of the thyroid, although rare, has previously been described in case series. They account for up to 0.13-0.15% of all thyroid tumors. Even more unusual, is the presentation of synchronous, but separate, papillary, follicular and medullary carcinoma in the same gland, and has only been reported twice before our case. There are several genetic alterations involved in the tumorigenesis of each type of thyroid cancer, but there is no known common mutation involved in the pathogenesis of the three tumor types. Thus, our patient’s findings appear to be due to simple chance. The presence of pulmonary sarcoid in our patient could have played a role in the development of thyroid cancer. It appears that regulatory T-lymphocytes in the periphery of sarcoid granulomas suppress IL-2 secretion which is hypothesized to cause a state of anergy by preventing antigen-specific memory responses. The anergy may be responsible for the increased risk of infections and cancer. Although sarcoidosis has been reported in 7 patients with PTC, it remains unclear whether an association exists between the two conditions.

**Abstract #1030**

**A LARGE PAPILLARY THYROID CARCINOMA PRESENTING AS A TOXIC NODULE**

Nesreen Saadeh, MD, Mohammed Hammoude, MD, Abdul B. Abou-Samra, MD, PhD

**Objective:** To describe a case of a large toxic nodule that has later proved to be papillary thyroid carcinoma.

**Case Presentation:** A 39-year-old woman consulted for goiter. She was diagnosed with thyrotoxicosis 2 years ago and treated with Methimazole 5 mg daily. She was clinically euthyroid at presentation and denied any compressive neck symptom. On examination, pulse rate was 105 /min, and the thyroid gland was enlarged with a prominent nontender mass (approximately 5 cm) in the right lobe near the isthmus. No lymph nodes were palpable in the neck. Free T4 level was 1.4ng/dL (0.8-1.8) and TSH was 0.002mIU/L (0.2-4.7). A thyroid scan with 123I showed a dominant hot nodule in the isthmus with an uptake in the hyperthyroid range (46.6% at 6 hrs); causing significant suppression of the remainder of the thyroid gland. Ultrasound study of the thyroid showed a dominant well-circumscribed complex nodule occupying most of the right lobe about 4.5 cm in its largest diameter with uniform intense vascularity on Doppler. FNA biopsy of the nodule was positive for cellular follicular lesion. She underwent right hemi-thyroidectomy, which revealed a 5.2 cm papillary carcinoma of follicular variant; the margins were free of the lesion. A completion thyroidectomy was performed two weeks later. The pathology of the left lobe showed benign thyroid tissues with focal septal fibrosis. Thyroglobulin level after 5 wks of thyroxine withdrawal was < 0.2 ng/mL, when TSH level was 50.4 mU/L. There was no scintigraphic evidence for functioning distant thyroid neoplasm.

**Discussion:** Well-differentiated thyroid carcinoma causing thyrotoxicosis is rare and is usually due to excessive production of thyroid hormone by metastatic lesions. The majority of these cases were due to follicular carcinoma. However, nonmetastatic hyperfunctioning thyroid carcinoma is extremely rare, and most of the cases reported in the literature are papillary thyroid carcinoma. This case of a large toxic nodule has proved to be a quite large papillary thyroid carcinoma of the follicular variant. The nuclear study supports the presence of a large hot nodule with suppression of the rest of the gland. No cold areas were seen within the hot nodule. As the nodule was large, FNA biopsy was done before deciding on surgery as a treatment option. The result further supported the decision for surgery.

**Conclusion:** This case and others we reviewed suggest the need to exclude malignancy even in toxic nodules before deciding on further management as it may be on rare occasions a functioning thyroid carcinoma.

**Abstract #1031**

**SUNITINIB-ASSOCIATED THYROTOXICOSIS AND HEART FAILURE**

Ritu Madan, MBBS, Jaya Kothapally, MD, Manu Kaushik, MD, Andjela Drincic, MD, Robert Anderson, MD

**Objective:** To report a case of Sunitinib-associated thyrotoxicosis presenting as heart failure.

**Case Presentation:** A 73-year-old female with history of left nephrectomy for renal cell carcinoma (RCC) presented with new onset progressive breathlessness and palpitations for two weeks. She also complained of muscle soreness, pedal edema and abdominal distension. Five months earlier, she was started on Sunitinib 50mg/day for 4 weeks within a 6-week cycle after being diagnosed with metastatic RCC. Her past medical history was significant for coronary artery disease with preserved LV ejection fraction (EF) prior to Sunitinib. Physical examination revealed tachycardia, jugular venous distension, left ventricular gallop, mild hepatomegaly, ascites and pitting pedal edema. Echocardiogram showed EF of 20-25% without regional wall motion abnormalities and stress echocardiogram revealed no ischemia. Further testing revealed elevated fT4 (2.93ng/dL), fT3 (8.5pg/mL), thyroglobulin (947ng/mL) and depressed TSH (0.04µIU/mL). TSI was normal. Her previous thyroid function was normal. On ultrasound the gland was heterogeneous and
symmetrically enlarged with blood flow that was not increased. RAIU at 4 and 24 hours was decreased at 3.2% and 9.6%, respectively. She was not exposed to iodinated contrast. Dexamethasone (DEX) 2 mg every 6 hours was initiated, and was tapered as thyroid hormone levels improved. On DEX 1mg every 12 hours, the fT3 and fT4 levels began to increase. On 1 mg every 8 hours, the values improved. Hyperthyroidism and cardiomyopathy were attributed to Sunitinib that was stopped. DEX was tapered off in a month, but subclinical hyperthyroidism persisted. RAIU was 4% at 4 hours and 13% at 24 hours. Her repeat echocardiogram was unchanged.

**Discussion:** Sunitinib is a multi-targeted tyrosine kinase inhibitor used for treatment of renal cell carcinoma and gastrointestinal stromal tumors. Thyroid dysfunction, the mechanism of which is unclear, has been described with its use. Isolated hypothyroidism is most frequent (53% to 85%) form of thyroid dysfunction seen with Sunitinib. Hyperthyroidism is less common and is attributed to destructive thyroiditis. It is usually followed by a stage of hypothyroidism. However, this patient had features suggestive of persistent thyrotoxicosis for more than four months despite discontinuation of the offending drug. Typically, thyroid abnormalities with Sunitinib have been described early in the course of therapy unlike in this case. Severe thyrotoxicosis requiring treatment occurring late in the course of therapy has not been reported earlier.

**Conclusion:** Thyroid functions should be measured prior to treatment and during therapy with tyrosine kinase inhibitors.

Abstract #1032

POORLY DIFFERENTIATED THYROID CANCER

Mohammed Ahmed, MD, FACP, FACE,
Hadeel Al-Manea, MD

**Objective:** To draw attention that poorly differentiated thyroid cancer (PDTC) originates from differentiated thyroid cancer (DTC) lineage rather than denovo, and to recognize it as an aggressive distinct clinicopathological entity.

**Case Presentation:** Case A: A 74-year-old man presented with metastatic scalp lesion of PTC. W/U: disseminated metastases: vital organs: lungs, pleura, bones, brain, vertebrae with cord compression. Initial suppressed TG1050 ug/l, underwent TT: 63 G rt lobe multifocal PTC, largest 5 cm vascular invasion, areas of poor differentiation. 5 yrs later TG >5000, had 2nd surgery for recurrence (PDTC in the background of DTC, spindle cells and myxoid differentiation that comprised 25% tumor mass), developed 3 enhancing lesions liver, kidneys, and rt adrenal, suspected for metastases: given I 131 cumulative dose 590 mCi ; pt deceased. Case B: 68-year old lady presented with painful immobile 12 cm highly vascular mass surrounding pathological fracture of rt humerus, 5 cm lt thyroid lesion, metastases in lungs, disseminated skeletal (also dorsal spine with spinal cord enroachment). Serum Tg > 5000 ug/l, had invasive thyroid tumor encircling esophagus, adherent to trachea. Histopathology: poorly differentiated insular variant, in the background of DTC, extensive vascular, and perithyroidal involvement: Ki 67 Index 20%. I 131 (211 mCi) and XRT given,14 cm poorly diff. TC humeral metastases resected following embolizationX3 and insertion of a metal prosthesis with relief of pain & mobility. Patient is alive.

**Discussion:** We have reported previously a case of DTC that transformed to PDTC after 23 years follow-up (Endocrine Society meetings 2010). Here we describe 2 cases of PDTC in the background of DTC with an aggressive behavior. Poorly differentiated thyroid cancer is justifiably recognized as an aggressive distinct clinicopathological entity based on large series of tumors sharing structural and histopathological criteria. It falls between classical DTC and anaplastic Ca with regards to the clinicopathological behavior and aggressiveness. It was included in the WHO classification of thyroid tumours in 2004. A diagnostic algorithm based on the presence of a solid/trabecular/insular growth pattern was suggested. A confounding factor has been the recognition of geographical differences.

**Conclusions:** Our cases are suggestive of the notion regarding tumorogenesis of PDTC that it originates from DTC lineage rather than denovo. A FU of such cases can substantiate the view that DTC can progress into PDTC and finally to anaplastic cancer.

Abstract #1033

ALEMTUZUMAB INDUCES RECONSTITUTION GRAVES’ DISEASE IN A PATIENT WITH MULTIPLE SCLEROSIS

Mohammad Hammoude, MD,
Nandalal Bagchi, MD, PhD

**Objective:** To report a case of reconstitution Graves’ disease due to Alemtuzumab treatment in a patient with multiple sclerosis.

**Case Presentation:** A 25-year-old African American female referred to our clinic for symptoms of thyrotoxicosis. She complained of palpitation, tremors, heat intolerance with increase in the size of her neck. The patient had no history of thyroid disease. She had a history of multiple sclerosis diagnosed in 2002, received two annual cycles of Alemtuzumab in May 2008 and May 2009. On examination she had tachycardia of 114 per minute, en-
Thyroid Disease

Abstract:

Largely thyroid gland (3 times normal size) and hyperactive deep tendon reflexes. She did not have any exophthalmos. Thyroid function test in April 2010, one year after receiving the second dose of Alemtuzumab, showed suppressed TSH 0.002 (0.5-5 mIU/L) and elevated free T4 2.6 (0.8-1.8 ng/dL). Her TSH level before the treatment with Alemtuzumab in March 2007 was 0.668 (0.8-1.8 ng/dL). Thyroid radioactive iodine uptake was 26% and 47.2% at 2 and 24 hours respectively. The Technetium scan showed an enlarged gland with uniform uptake. A provisional diagnosis of reconstitution Graves’ disease was made, and the patient was started on Methimazole 30 mg daily and Propranolol 40 mg twice a day.

Discussion:

Reconstitution Graves’ disease occurs in three settings. First, after bone marrow transplantation from a donor with Graves’ disease as a result of adoptive immunity. Second, post treatment with highly active antiretroviral therapy for human immunodeficiency virus infection. Finally, Alemtuzumab treatment for multiple sclerosis leads to the development of Graves’ disease in up to a third of patients during the phase of naive T-cell expansion, which follows therapeutic lymphocyte depletion. Reconstitution Graves’ Disease is believed to be part of an immune reconstitution syndrome, which is a broader spectrum of immunoregulatory disturbances. The mechanisms responsible for reconstitution Graves’ disease are at present unclear, but may include a relative bias towards a Th2-mediated immune response and reduced competition for autoreactive lymphocytes to expand during the time when recovery from lymphopenia commences.

Conclusion:

Alemtuzumab is a promising therapy for multiple sclerosis. Graves’ disease is a common adverse event during and after the treatment. This case highlights the importance of long term monitoring for the thyroid function in multiple sclerosis patients receiving Alemtuzumab.

Abstract #1034

THYROID HEMIAGENESIS IN A NEPALI US IMMIGRANT MAN

Saleh A. Aldasouqi, MD, FACE, ECNU, Ved Gossain, MD, FACE, FACP, Deepthi Rao, MD, Nazish Ismail, MD, Lily Kristine Sunio, MD, Shaza Khan, MD, Srujan Ameda, MD

Objective: Thyroid hemiagenesis is a rare congenital anomaly characterized by the absence of one lobe with or without involving the isthmus. The prevalence in published studies ranges from 0.05% to 0.25, with female preponderance. The condition has been reported in various ethnic populations. We report a case of thyroid hemiagenesis in a Nepali US immigrant man, which was detected incidentally after he presented with hypothyroidism.

Case Presentation: A 42-year-old male was referred to our clinic for incidental TSH elevation. The patient denied any specific hypo or hyperthyroid symptoms. He reported no goiter or neck masses. His past medical history included depression thought to be related to cultural adaptation. He was a farmer but currently unemployed. The status of Iodine intake prior to immigration is unknown. The patient was clinically euthyroid, and examination of the thyroid did not reveal any nodules, masses, tenderness, or enlargement. Significant laboratory values include TSH of 30.83 uIU/mL (Ref.0.35-5.50); T4, Total 6.9 mcg/dL (Ref.4.5-10.9); T4, Free 0.72 ng/dL (Ref.0.80-1.80); T3, Free 3.1 pg/mL (Ref:2.3-4.2). An ultrasound of the thyroid gland showed no definitive left lobe, but only the right side of the isthmus connected to a normal right lobe measuring 4.39 x 1.24 x 0.94 cm, with a volume of 2.40 ml (Image). The patient was started on Levothyroxine 75 mcg once daily, became euthyroid, and remained stable on follow up.

Discussion: Hemiagenesis is a rare congenital malformation of the thyroid gland and is a part of the disease spectrum of thyroid dysgenesis, which also encompasses ectopy and athyreosis. Although the exact pathogenesis of thyroid hemiagenesis is unknown, some genetic alterations in transcriptional control of thyroid development and in the control of migration of the median thyroid bud during embryogenesis have been implicated. Females are affected more than males, and in 80% of cases the left lobe is the affected side. Thyroid hemiagenesis has been reported in various ethnic populations, and over 350 cases have been reported. Our patient is an immigrant male from Nepal, and to our knowledge, this is the first case of thyroid hemiagenesis to be reported in a Nepali patient. Most patients with thyroid hemiagenesis remain euthyroid, and usually the condition is diagnosed incidentally by ultrasound imaging. However, patients with thyroid hemiagenesis are vulnerable to any thyroid illness/malignancy, similar to the general population, and some cases may pose diagnostic challenges.

Conclusion: Clinicians should be aware of this rare congenital condition in the course of evaluation of patients with thyroid or neck disorders.
Abstract #1035

INCREASED RISK OF PAPILLARY THYROID CANCER IN GRAVES’ DISEASE: A CASE REPORT AND REVIEW OF THE LITERATURE TO DRAW ATTENTION TO UNDERUTILIZATION OF THYROID ULTRASOUND IN GRAVES’ DISEASE IN CLINICAL PRACTICE

Saleh A. Aldasouqi, MD, FACE, ECNU, Srujan Ameda, MD, Nazish Ismail, MD, Shaza Khan, MD, Deepthi Rao, MD, Lily Kristine Sunio, MD

Objective: Recent studies have shown a 2-3 folds increased prevalence of thyroid nodules and papillary thyroid cancer (PTC) in Graves’ disease (GD). Due to misconception, clinicians pay less attention to thyroid anatomy in GD, and hence an observed underutilization of thyroid ultrasonography (TUS) in GD has been reported. If imaging is used in the work up of GD, radioactiveiodine nuclear scans RAI are more routinely utilized. We report a case of PTC in a patient with GD and review the literature to draw attention to potentially missed cases of PTC in patients with GD.

Case Presentation: A 28-year-old woman was referred for evaluation of hyperthyroidism. She had a family history of PTC. She had a small firm goiter with no palpable nodules, and she was clinically mildly hyperthyroid. Thyroid function tests (TFTs) were consistent with hyperthyroidism, and a previously ordered RAI scan was homogenous, non-focal, and consistent with GD. TUS was ordered which revealed an 8 mm left thyroid nodule with micro-calcifications and increased vascualrity (Figures). FNA was consistent with PTC. Total thyroidectomy was performed and pathology confirmed PTC in the nodule as well as multi-focal PTC tumors in the left lobe.

Discussion: The recently reported increase in PTC prevalence in GD is believed to be due to growth stimulating effects of Thyroid Stimulating Immunoglobulin. Clinicians have traditionally underutilized TUS in patients with GD, in favor of RAI scans. It is difficult to understand the rationale of this tradition, since patients with GD tend to have large and firm goiters, and it is quite easy for small nodules and cancers to escape clinical detection. Furthermore, the intense RAI uptake in GD makes it difficult to detect small cold nodules. As interestingly, studies have shown the unreliability of clinical examination in the detection of thyroid nodules, with high false positive and false negative rates. Our patient did present with traditional risk factors for PTC and her nodule, while considered sub-centimeter, did present a suspicious features; therefore FNA was clearly warranted. Nevertheless, and in view of the aforementioned indications, Capelli and others recommended TUS in all patients with GD. Besides detecting subtle nodules, TUS provides an additional diagnostic advantage in GD by depicting classical pathognomonic vascular features.

Conclusion: We echo the recommendations by Capelli and others that all patients with GD should undergo diagnostic TUS. These recommendations are based on increased prevalence of PTC in GD, and the ease with which physical exam and RAI scans may miss thyroid nodules, especially in patients with large goiters.

Abstract #1036

RECURRENTENCE OF INTERMITTENT FOREIGN ACCENT SYNDROME ASSOCIATED WITH THE DEVELOPMENT OF GRAVES’ DISEASE: A CHANCE ASSOCIATION OR MORE?

Saleh A. Aldasouqi, MD, FACE, ECNU, Brooke Frommyer, CCC, MA, SLPA, Geraud Plantegenest, MA, Srujan Ameda, MD, David Solomon, PhD, Julie Topin, CCC, MA, SLPA, Rany Aburashed, MD, Lily Kristine Sunio, MD

Objective: Foreign accent syndrome (FAS) is an extremely rare speech disorder that was first described a century ago. FAS is the sudden onset of altered speech that is perceived as a foreign accent by listeners of the native language of the patient’s. FAS has been attributed to cerebrovascular accidents (CVA) and brain injuries, but sporadic cases were attributed to psychosis, migraine, and developmental causes. FAS has been reported in various languages from around the world. FAS is often transient but can persist, and less often FAS becomes intermittent. We report a new case of CVA-induced intermittent FAS in an American woman, who recently developed Graves’ disease (GD), which appeared to have triggered a recurrence of her FAS. To our knowledge, FAS has not been reported in association with GD.

Case Presentation: A 40-year-old American woman was admitted with severe symptomatic hyperthyroidism. She had a hemorrhagic CVA, 12 year previously, following which she developed FAS (Swedish-like accent) that has been intermittent, usually triggered by stress, with episodes lasting days to weeks. Born in Michigan, she has never traveled abroad, nor spoken a foreign language. Physical examination and laboratory evaluation were consistent with severe hyperthyroidism, and GD was diagnosed. Further observation revealed a stuttering speech, and to all listeners, her English had a distinct foreign accent. Her daughter reported a recurrence of her mother’s FAS few days prior to admission. She was started on methimazole and propranolol, and improved, and her FAS persisted for 2 months, and then resolved.
**Discussion:** FAS is a distinct speech disorder that occurs most commonly in patients recovering from CVA-associated aphasia or dysphasia. The etiology of FAS is still elusive, and defects in certain speech-related areas have been implicated. FAS has captured the interest of clinicians and the public for decades. Famous cases have been broadcasted in public media, with the most famous being an earlier case of a Norwegian woman who suffered ostracism when she began speaking in a German accent during World War II. Fewer than 100 cases have been reported, and many have involved English speaking patients who suddenly begin speaking in a new accent, mostly described as Eastern or Northern European. Our patient’s accent appeared to her family as a Swedish accent. We are not certain if hyperthyroidism has triggered the recurrence of her FAS.

**Conclusion:** We report herein the first case of intermittent FAS presenting with a recurrence in association with the onset of severe hyperthyroidism due to GD. We are uncertain if this is a chance association or it represents a correlation.

**Abstract #1037**

**MYXEDEMA COMA IN A PATIENT TREATED WITH SUNITINIB FOR RENAL CELL CARCINOMA**

Bhavika Bhan, MD, Leigh Eck, MD

**Background/Objective:** Myxedema coma, a severe manifestation of hypothyroidism, is associated with a high mortality rate. It is usually accompanied by a subnormal temperature, bradycardia, and severe hypotension. Although the pathogenesis of myxedema coma is not clear, factors that predispose to its development include exposure to cold, infection, trauma, central nervous system depressants and anesthetics. Alveolar hypoventilation, leading to carbon dioxide retention and narcosis, may also contribute to the clinical state. We describe a case of sunitinib induced myxedema coma in a patient with renal cell carcinoma following an elective surgery.

**Case Presentation:** A 59-year-old female with a history of multinodular goiter s/p left thyroidectomy two years ago for benign thyroid nodule presented with progressive shortness of breath, hoarse voice and enlarging right neck mobile tender mass over one week. On admission, she had shortness of breath, hoarse voice and enlarging right neck mobile tender mass over one week. On admission, she had low TSH 0.02mIU/L (0.35-5.5), elevated free T4 2.09ng/dL(0.9-1.8), and free T3 36pg/mL(2.3-4.2). Microsomalous antibody was negative. Corrected calcium was 11.4mg/dL (8.6-10.4), PTH was 125pg/mL(12-88) with Vitamin D25 hydroxy of 12ng/mL(30-80) and creatinine 1.8mg/dL(0.5-1.2). There was no exposure to iodine. CT neck without contrast showed a heterogeneous mass in the right neck with deviation of the trachea from right to left without invasion of the trachea. Subsequent thyroid ultrasound revealed a heterogeneous mass in the right thyroid lobe measuring 4.7 x 5.5 x 4.5cm³ with a hyperechoic nodule measuring 1.3 x 1.4 x 1.6cm³ in the right thyroid lobe and a hyperechoic nodule measuring 1.0 x 1.3 x 1.1cm³ in the left thyroid lobe. Fine needle aspiration of the thyroid nodules revealed scant cells consistent with nodular goiter requiring re-intubation. In addition, she was found to be hypothermic, hypotensive, and hypocapnic. Pertinent laboratory included an elevated TSH of 27.562 mcu/ml (0.35-5 mcu/ml). Due to a clinical presentation consistent with myxedema coma in a patient with known thyroid dysfunction, a transfer to the ICU was undertaken as well as the initiation of intravenous levothyroxine. The patient’s clinic picture rapidly improved, and she was successfully extubated.

**Discussion:** Sunitinib is an oral multikinase inhibitor which exhibits antitumor and antiangiogenic properties by inhibiting multiple tyrosine kinase receptors. It is utilized for the treatment of RCC, gastrointestinal stromal tumor (GIST), pancreatic neuroendocrine tumors, soft tissue sarcoma, non-GIST, and refractory thyroid cancer. Sunitinib has been shown to induce hypothyroidism in approximately 50% of patients. The mechanism of the antithyroid effect appears to be inhibition of peroxidase activity. To our knowledge, there has been only one report of myxedema coma in a patient on sunitinib treatment. This case highlights the importance of vigilant thyroid function monitoring in patients being treated with tyrosine kinase inhibitors.

**Abstract #1038**

**SUBACUTE THYROIDITIS PRESENTING WITH VOCAL CORD PARALYSIS AND HYPERCALCEMIA**

Cindy Huang, MD, Xiangbing Wang, MD, PhD, FACE

**Objective:** To describe a case of subacute thyroiditis presenting with vocal cord paralysis and hypercalcemia.

**Case Presentation:** A 65-year-old woman with history of multinodular goiter s/p left thyroidectomy two years ago for benign thyroid nodule presented with progressive shortness of breath, hoarse voice and enlarging right neck mobile tender mass over one week. On admission, she had low TSH 0.02mIU/L (0.35-5.5), elevated free T4 2.09ng/dL(0.9-1.8), and free T3 36pg/mL(2.3-4.2). Microsomalous antibody was negative. Corrected calcium was 11.4mg/dL (8.6-10.4), PTH was 125pg/mL(12-88) with Vitamin D25 hydroxy of 12ng/mL(30-80) and creatinine 1.8mg/dL(0.5-1.2). There was no exposure to iodine. CT neck without contrast showed a heterogeneous mass in the right neck with deviation of the trachea from right to left without invasion of the trachea. Subsequent thyroid ultrasound revealed a heterogeneous mass in the right thyroid lobe measuring 4.7 x 5.5 x 4.5cm³ with a hyperechoic nodule measuring 1.3 x 1.4 x 1.6cm³ in the right thyroid lobe and a hyperechoic nodule measuring 1.0 x 1.3 x 1.1cm³ in the left thyroid lobe. Fine needle aspiration of the thyroid nodules revealed scant cells consistent with nodular goiter.
with abundant colloid and negative for malignancy. Both the 4-hour and 24-hour radioactive iodine uptakes were 1.7%. She underwent a flexible laryngoscopy that revealed right vocal cord paralysis. She was treated with prednisone 20mg daily for two days, then 10mg daily for two days for subacute thyroiditis. After the trial of steroids, her calcium level returned to normal, her voice improved, and she was discharged home without surgical removal of right neck mass. She also started taking Vitamin D3 for Vitamin D deficiency. Four months after initial presentation, thyroid hormone levels became normal, patient was clinically euthyroid with decreased size of her goiter, and a full recovery of her voice. Her calcium level was within normal 9.8mg/dL with a near normal PTH 90pg/mL. Vitamin D level and creatinine were also normal.

**Discussion:** To our knowledge, this is the only case of subacute thyroiditis presenting with both vocal cord paralysis and hypercalcemia. The diagnosis of subacute thyroiditis is suggested by low TSH, high freeT4, low 123 iodine uptake and responsiveness to steroid treatment. A few case reports have suggested that vocal cord paralysis can be the result of benign thyroid disease, but the mechanism remains unclear. There was one case report on the association between subacute thyroiditis and hypercalcemia.

**Conclusion:** This case illustrates that subacute thyroiditis can present with thyroid mass, vocal cord paralysis and hypercalcemia. A trial of steroids treatment can significantly improve clinical symptoms and thus avoiding unnecessary surgery.

**Abstract #1039**

**SARCOIDOSIS MASQUERADING AS PAINLESS THYROIDITIS**

Pooja Sherchan, MD, Kamal Shoukri, MD, Frida Rosenblum, MD, Katya Ford, MD, John Landis, MD, Burritt Haag, MD

**Objective:** To report a case of sarcoidosis that presented as painless thyroiditis.

**Case Presentation:** A 44-year-old female presented with “lump in her throat” and 3 months complaint of dry cough, night sweats and 5 lbs of weight loss. On examination, the thyroid gland was 1 ½ times normal size, non-tender with a firm, 2 cm x 1 cm nodule in the isthmus. TSH was <0.02 mIU/ml and FT4 was 1.59 ng/dL (0.7-1.8) suggesting subclinical hyperthyroidism. TPOAb and TRAb were negative. 24 hr 123I Thyroid uptake was <0.5% consistent with thyroiditis. Thyroid U/S showed heterogenous echogenicity with multiple ill-defined hypechoic areas and a 2 cm x 0.9 cm hypechoic nodule at the junction of the isthmus and the right thyroid lobe. FNA biopsy of the nodule showed granulomatous change with epithelioid histiocytes forming sheets, giant cells, nodular aggregates and morphologically benign follicular cells. Chest X-ray showed diffuse infiltrative disease. CT chest revealed diffuse centriflobular nodular opacities. Transbronchial biopsy revealed non-necrotizing interstitial granulomatous inflammation consistent with sarcoidosis. ACE level was 134 U/L (12-68). She was started on Prednisone 30 mg per day. A month later, her TSH was 26 mIU/ml and FT4, 0.5 ng/dL. Levothyroxine was started. Repeat U/S 2 months after initiation of prednisone showed resolution of the isthmic nodule and near-normalization of the gland. She was tapered off prednisone and levothyroxine over a year, remained euthyroid for 6 months, and then became hypothyroid again. No relapse of sarcoidosis has occurred in 4 years of follow-up.

**Discussion:** Prevalence of thyroid gland involvement in systemic sarcoidosis is reported to be approximately 4%. Thyroid conditions associated with sarcoidosis include Hashimoto’s thyroiditis, Grave’s disease, cold nodules, de Quervain’s thyroiditis, thyroid cancer and increased prevalence of thyroid antibodies. Our case presented with painless thyroiditis, initially with subclinical hyperthyroidism followed by hypothyroidism, euthyroidism and eventually hypothyroidism. FNA biopsy revealed non-caseating granulomas, differential being tubercular/fungal infections, de Quervain’s thyroiditis, palpation thyroiditis and sarcoidosis. The absence of pain makes de Quervain’s thyroiditis highly unlikely. Acid fast and methenamine silver stains were negative for microorganisms. The pathology on transbronchial biopsy corroborated the diagnosis of systemic sarcoidosis.

**Conclusion:** This case illustrates that sarcoidosis should be considered in the differential diagnosis of painless thyroiditis.

**Abstract #1040**

**A CASE OF PAPILLARY THYROID CANCER WITH TRABECULAR AND SOLID GROWTH PATTERN IN A HOT NODULE**

Diana Wagner, MD, Runhua Hou, MD, Ellen Giampoli, MD, Vaseem Chengazi, MD

**Objective:** To describe a case of papillary thyroid cancer identified in a hyperfunctioning thyroid nodule.

**Case Presentation:** A 35-year-old female was found to have a large right thyroid nodule during a routine physical exam. Her only symptom was 2-3 months of discomfort on the right side of the neck during singing. There were no hypothyroid, hyperthyroid or compression symptoms. One aunt had thyroidectomy for an unclear reason and another
A 73-year-old male was found to have a large left thyroid nodule in 2005 at another institution. He underwent thyroid ultrasound and fine needle aspiration of the nodule. Cytology was indeterminate, and he was referred for a left lobectomy. His surgical pathology at the time was interpreted as a follicular adenoma. In September 2010, the patient was noted to have a small superficial growth in the left side of his neck. This was excised and the pathology was consistent with a thyroid follicular neoplasm within the dermis. The patient then underwent neck ultrasound which showed an absent left lobe, and an unremarkable right lobe and lateral neck. In addition, it showed a 1cm solid, hypoechoic lesion just left of the mid-line of his neck around the site of the surgical scar. This lesion was biopsied with a fine needle aspiration and the cytology was similar to his previously excised skin lesion. The patient’s original pathology slides from his hemithyroidectomy were then retrospectively reviewed. One site of capsular invasion and two sites of possible vascular invasion were identified, consistent with follicular carcinoma. The patient was subsequently referred for completion thyroidecetomy together with dissection of the recurrence.

Discussion: The diagnosis of follicular thyroid cancer was not recognized initially and further therapy and long-term follow-up was not offered. The patient subsequently presented with two dermal implants of follicular thyroid cancer at the site of his thyroidectomy incision. Cutaneous metastases from thyroid cancer are possible, but given their location at the surgical scar, these lesions were likely the result of seeding of the incision at the time of the original thyroid operation. The separation of the two lesions makes seeding of the needle track during the fine needle aspiration very unlikely.

Conclusion: Although rare, cutaneous recurrence of thyroid cancer around the surgical scar is a possibility. Clinicians should be aware of this rare type of recurrence. Thorough examination of surgical scars should be a part of thyroid cancer follow-up, and dermal lesions should be investigated further.

Abstract #1042

NON-THYROIDAL ILLNESS SYNDROME AND SHORT-TERM SURVIVAL IN ACUTELY ILL ELDERLY POPULATION

Ankit Shrivastav, MD, Tapas Das, MD, Jyotirmoy Pal, MD, Anirban Sinha, MD, DM, Subhankar Chowdhury, MD, DM, MRCP

Objective: Non-thyroidal illness syndrome (NTIS) is associated with poor clinical outcome. However its importance in elderly population has been overlooked. This study was undertaken to evaluate the prevalence of NTIS in elderly population, its pattern and its impact on patients’ survival.

Methods: This was an observational cross-sectional analysis. One hundred and fifty (150) acutely ill elderly
patients (median age 74 years, range 60–82), consecutively admitted to Intensive Care unit of a tertiary care hospital were enrolled in the study. Serum Total T3, Total T4, free T4 and TSH and C reactive protein were measured on admission. APACHE III score was calculated for every patient. All the patients were followed up for 6 months to observe short term mortality.

**Results:** The prevalence of NTIS in elderly population was 74.3% which is significantly higher than the younger age group (29%). Serum Total T4 (TT4) and Total T3 (TT3) were found to be inversely related to disease severity as assessed by APACHE scores with lower values being associated with more severe diseases. Serum fT4 and TSH had no relation with disease severity. The mortality was higher in patients with NTIS (44.2 %) than those with normal Thyroid hormone measurements (6.4 %). Statistically significant correlation was found between Serum TT4 and disease outcome. Serum TT4 values correlated inversely with serum C-reactive protein (P < 0.01). The correlation between Serum TT4 and disease mortality was found to be more significant than APACHE III scores. Serum TT4 was also found to be significantly associated with mortality after discharge from hospital which had no relation with admission APACHE score. Follow up Thyroid hormone tests were normal in majority (97 %) of survivors at 6 months.

**Conclusions:** NTIS is very common in the hospitalized elderly population. The outcome of patients with low TT3 and TT4 serum levels was worse compared with patients who had normal thyroid hormone parameters. Serum TT4 appears to be sensitive and independent predictor of short-term survival after hospital discharge. However more studies are needed for confirmation. Serum TT4 determination should be included in the assessment of short-term prognosis of acutely ill elderly patients and patients with lower values must be put on more intensive follow up schedule post hospital discharge.

**Abstract #1043**

**MARINE-LENHART SYNDROME- A CASE REPORT**

*Miguel E. Pinto, MD, FACE, Helard A. Manrique, MD*

**Objective:** To report a case of a young woman with hyperthyroidism because of Graves’ disease and functioning thyroid nodule

**Case Presentation:** A 34-year-old woman presented with recent history of asymptomatic diffuse thyroid enlargement and normal thyroid profile. Physical examination showed a palpable thyroid nodule in the left lobe. Thyroid ultrasound confirmed a solid nodule in the left lobe with increased Doppler color flow. Further work-up demonstrated that the anti-TPO antibodies were positive, and FNA biopsy showed no suspicious cells. After 6 months, she presented with weight loss, palpitations, heat intolerance, and hand tremor. Repeated thyroid hormones were TSH 0.01 mIU/dL and fT4 4.59 ng/dL. Thyroid scan identified homogeneously increased uptake throughout the gland, especially in the middle of both lobes. Treatment was started with methimazole and propanolol. Her clinical evolution was good, her last thyroid hormone levels were normal, and she received a high dose of I-131.

**Discussion:** Graves’ disease with functioning nodules is known as Marine-Lenhart syndrome. The frequency of this syndrome is rare, and only 1% to 2.7% of patients with Graves’ disease have concomitant functioning nodules. However, up to 12.8% of patients with Graves’ disease present with or may develop nodules, most of them are benign expression of autoimmune changes and coexistent nodular goiter. Toxic thyroid nodules are clonal in origin, and activity in toxic nodules can be enhanced by stimulating TSH receptor antibodies. Thus, the existence of stimulating autoantibodies in patients with Graves’ disease may play a role in the development of Marine-Lenhart syndrome.

**Conclusion:** Functional nodules may be more resistant to radioiodine-131 than the extranodular tissue, so patients with this syndrome generally are radio-resistant and require a higher dose of radioactive iodine for ablation.

**Abstract #1044**

**PREDICTING THYROTROPIN RECEPTOR ANTIBODY LEVEL WITH THYROID DOPPLER SONOGRAPHY AND DIGITAL INFRARED THERMAL IMAGING IN PATIENTS WITH GRAVES’ DISEASE**

*Shyang-rong Shih, MD, Chung-Ming Chen, PhD, Tien-Chun Chang, MD, PhD*

**Objective:** Thyrotropin receptor (TSHR) is the primary autoantigen of Graves’ disease (GD). TSHR antibodies (TSHRAbs) level is important for predicting recurrence, and affects the decision of discontinuing antithyroid drugs or not. In our hospital, we checked thyrotropin binding inhibitory immunoglobulin (TBII), standing for TSHRAbs. However, this test took time, not cheap, and also unavailable in most local clinics. Sonography is a very common and fast examination in Taiwan. Digital Infrared thermal imaging (DITI) is a fast and newly developed diagnostic tool. According to the pathogenesis of GD, intrathyroid vascularity (TV) may increase and surface temperature (ST) of the neck may be elevated. Therefore, we tried to analyze the relationship
between TBII, thyroid duplex sonography (DS) and neck ST. We hoped this would be helpful in general practice.

**Methods:** We prospectively recruited 75 GD patients in Endocrine clinics of National Taiwan University Hospital. Thyroid DS of color flow mode at a fixed setting was obtained and analyzed. TV was defined as (the average of right and left side of color flow area in the thyroid/total thyroid area in transverse view) x 100. ST was defined as the average of right and left side of the skin temperature measured between the upper and lower poles of thyroid glands with DITI. Stata 9.0 was used for statistic analysis.

**Results:** The average of TBII, TV and ST was 42.7% (range: -2.4%–94.4%, SD: 31.1), 24.4 (range: 0.6–75.2, SD: 18.3) and 29.32[(range: 22.24–34.93, SD: 3.05)], respectively. TV positively and significantly correlated with TBII (regression coefficient (CO): 1.00, p<0.001). If we set the TV cutoff point at 15.8 to predict TBII being more or less than 20%, area under the ROC curve was 0.85 (sensitivity and specificity were both: 82.6%). ST positively correlated with TBII (CO: 1.94, p: 0.119). We adjusted ST with ear temperature (ET) according to CO of the regression model using TBII as dependent variable, and ST and ET as independent variables. Adjusted surface temperature (AST) was defined as (2.4 x ST - 7.09 x ET). AST positively and significantly correlated with TBII (CO: 1.00, p: 0.045).

**Discussion:** TV and AST both positively and significantly correlated with TBII because they all related to thyroid activity in GD.

**Conclusion:** TBII could be predicted with thyroid duplex sonography and neck surface temperature. This may help clinically in the fast decision of discontinuing antithyroid drugs or not.

Abstract #1045

SIMULTANEOUS MEDULLARY AND PAPILLARY MICROCARCINOMA OF THE THYROID WITH LYMPH NODE METASTASIS

Tariq Abdulrahman Nasser, MD, Salh Jaser, MD, Abdullah Karawagh, MD

**Objective:** To report the simultaneous occurrence of medullary thyroid carcinoma (MTC) and papillary thyroid carcinoma (PTC), presenting as spatially distinct and well-defined tumour components.

**Case Presentation:** A 58-year-old Saudi man without any family history of thyroid cancer presented with neck swelling that he had first noticed 2 months earlier. Ultrasound of the neck showed a solid and focally cystic mass measuring 3.0 cm in diameter and focal calcification in the thyroid. Technetium- 99m scanning of the thyroid gland indicated an irregular defect. Fine-needle aspiration cytology demonstrated medullary carcinoma, and total thyroidectomy and cervical lymph node dissection was performed. Gross examination revealed a round yellow-white nodule (4.6 x 2.8 x 2.0 cm) occupying the right lobe of the thyroid and a small white nodule (0.5 cm in diameter) at the bottom of the lobe. Microscopically, the yellow-white nodule in the right lobe consisted of spindleshaped cells and its stroma contained amyloid, findings typical of medullary carcinoma. The small white nodule at the bottom of the lobe was follicular variant of papillary carcinoma. In addition, four seven nodes contained tumor metastases from medullary thyroid cancer only. Genetic analyses showed The MTC tissue was negative for the BRAF substitution and the PTC foci were negative for the RET mutation. Both mutations were absent in the surrounding normal tissue, thus excluding the diagnosis of MEN 2 and indicating a sporadic MTC.

**Discussion:** The synchronous occurrence of medullary and papillary carcinoma in the thyroid gland is very unusual, and it is remarkable because these two neoplasms are thought to be derived from different cells of origin. However, several other possibilities such as a common precursor cell as well as the effect of immunosuppression and that of chronic replicative hepatitis C offer interesting perspectives for speculation. The cause of both malignancies in our case patient remains unclear. Actually, recent study by using laser-based microdissection revealed that the medullary and follicular components in mixed medullary–follicular carcinomas are not derived from a common stem cell.

**Conclusion:** Genetic analysis strongly argues against a role of RET germline mutations in the genesis of these collision tumours. Previous hypotheses of a common genetic drive to be at the basis of these tumours were not confirmed due to the finding of different mutations in the two histological types. It is tempting, however, to speculate that these coexisting neoplasms arise in thyroid glands rendered more prone to various genetic events by still unknown mechanisms.

Abstract #1046

LUPUS-LIKE SYNDROME BY THIAMAZOLE- A CASE REPORT

Miguel E. Pinto, MD, FACE

**Objective:** To report a case of a girl with Graves’ disease who developed lupus-like syndrome because of thiamazole.

**Case Presentation:** A 14-year-old girl presented with recent history of heat intolerance, sweating, hand tremor, palpitations, and fatigue. Physical examination showed a diffuse goiter (3N). Laboratory results were TSH 0.20 mIU/dL (normal range: 0.3 – 5) and total T4 >24 mg/dL.
(normal range: 4.5 - 12). The anti-TPO and anti-TG were positive. Graves’ disease diagnosis was established, and treatment with thiamazole 20 mg once a day and atenolol 50 mg twice a day was started. After twenty days, she presented with fever (40°C), malaise, generalized joint pain, headache, depression, breathlessness, and peripheral edema. Physical examination showed synovitis in several joints, disseminated erythematous maculopapular rash, and hyperreflexia. Thiamazole was immediately stopped, and prednisone 50 mg once a day and propanolol 40 mg thrice a day was added. Repeated thyroid profile showed suppressed TSH and elevated fT4 and T3. Further work-up demonstrated no proteinuria, hematocrit and leucocytes were normal. ANA, anti-dsDNA, and serum rheumatoid factor were negative. ANCA antibodies were not performed. After ten days, patient received I-131 (5mCi), and developed hypothyroidism. Her clinical evolution was good, and she is receiving levothyroxine 100 µg per day.

Discussion: Antithyroid drugs remain cornerstones in the management of hyperthyroidism, especially in young women with Graves’ disease. Thionamides are actively concentrated by the thyroid gland, where their primary effect is to inhibit thyroid hormone synthesis. These drugs are associated with a variety of minor side effects that included cutaneous reactions, arthralgia, and gastrointestinal upset. The development of arthralgias could be related to a severe transient migratory polyarthritis known as “the antithyroid arthritis syndrome”. On the other hand, agranulocytosis is the most feared side effect of antithyroid drug therapy, but it is a rare complication. Vasculitis is another major toxic reaction seen with these drugs, more commonly found in connection with propylthiouracil than with methimazole. In some cases, serologic evidence consistent with lupus erythematosus develops (drug induced lupus). Also, antineutrophil cytoplasmic antibodies positive vasculitis has been reported. Although this syndrome generally resolves after drug cessation, glucocorticoid therapy or cyclophosphamide may be needed in severe cases. In these cases, treatment with radioiodine is mandatory.

Conclusion: Thionamides are common medications in patients with Graves’ disease, and drug-induced ANCA positive vasculitis has been reported. In some cases, immunosuppressive therapy is needed, and radioiodine must be administered.

Abstract #1047

SUBCLINICAL HYPOTHYROIDISM IN PREGNANCY: INCIDENCE, PERSISTENCE AND DEMOGRAPHICS

Ellie Simpson Ragsdale, MD, Steven Hokstein, MD, Shari Gelber, MD, PhD

Objective: The purpose of this study was to ascertain the incidence of subclinical hypothyroidism in an unselected patient population and determine difference in antepartum and postpartum thyroid function in these patients.

Methods: Antenatal records of a single provider that routinely screens for thyroid dysfunction in pregnancy were reviewed for an 18 month period. Serum TSH was collected on all patients during their first prenatal care visit. Subclinical hypothyroidism was defined as a TSH of ≥ 2.5. Inclusion criteria: no prior history of thyroid disease or thyroid surgery, antenatal TSH collected prior to 14 weeks gestational age. Pearson correlation and Wilcoxon signed ranks tests were used in statistical analysis.

Results: 256 patients with a mean age of 33.39 ± 4.23 years, mean body mass index of 22.76 ± 3.79, and mean TSH of 1.51 ± .82 were included in the analysis. Subclinical hypothyroidism was found in 31/256 (12.1%) of women. There was no difference in age between women with and without subclinical hypothyroid (33.87 vs. 33.32yrs, p = .501). BMI was significantly less in the subclinical hypothyroid group (21.34 vs. 22.95, p = .027). Postpartum TSH (without levothyroxine supplementation) in the subclinical hypothyroid group collected at 6-12 weeks postpartum was less than antepartum TSH in 30/31 cases (96.8%). One case of overt hypothyroidism was identified in the subclinical hypothyroid group in the postpartum period.

Discussion: Prior studies have suggested that subclinical hypothyroidism during pregnancy affects the neuropsychological development of children. However, the American College of Obstetrics and Gynecology does not currently recommend routine screening for thyroid dysfunction in pregnancy. This study suggests that the incidence of subclinical hypothyroidism in pregnancy is significant. Therefore a consensus should be established for the antepartum management of these patients.

Conclusion: Subclinical hypothyroidism (TSH ≥ 2.5) was identified in 12.1% of screened antepartum patients. BMI was lower in patients with subclinical hypothyroidism. Presence of subclinical hypothyroidism during pregnancy was not indicative of overt hypothyroidism in the postpartum period.
Abstract #1048

DIAGNOSTIC OUTCOME OF THYROID NODULE FINE NEEDLE ASPIRATION USING THE BETHESDA CLASSIFICATION SYSTEM

Abeer W Anabtawi, MD, Keith Schroeder, MD, KK Rajamani, MD

Objective: Fine-needle aspiration (FNA) is recommended for the initial evaluation of most thyroid nodules. The Bethesda System (TBS) for Thyroid Cytopathology was introduced to provide universally accepted terminology for FNA results. A limited number of studies have evaluated TBS in clinical practice. Two studies have evaluated TBS in institutions with high volume of FNA. This study evaluated TBS in a community hospital with low volume of FNA.

Methods: Prospective study of all consecutive thyroid nodule FNAs that were performed at Unity hospital between January 2008 and December 2009. All FNAs were performed under ultrasound guidance. Cytologic findings were classified per TBS: benign, atypia of undetermined significance/follicular lesion of undetermined significance (AFLUS), follicular neoplasm/ suspicious for follicular neoplasm (SFN), suspicious for malignancy (SM), malignant, and nondiagnostic. Patient who underwent thyroid surgery had their histopathology (HP) findings correlated to FNA.

Results: A 281 thyroid nodules were evaluated with FNA in 203 patients (33 Males, 170 Females), median (interquartile) age 54 years (47-67). FNA results included: Benign 147 (52.3%), AFLUS 55 (19.6%), SFN 37 (13.2%), SM 9 (3.2%), malignant 17 (6.0%), nondiagnostic 16 (5.7%). A total of 63 thyroid nodules were surgically excised. Correlation with HP showed [7 benign FNA: 5 benign HP, 2 papillary carcinoma], [21 AFLUS FNA: 14 benign HP, 6 papillary and 1 Hurthle carcinoma], [14 SFN FNA: 13 benign HP and 1 follicular cancer], [9 SM: 1 benign HP, 7 papillary and 1 Hurthle carcinoma], [12 malignant FNA: all had papillary carcinoma on HP]. Considering FNA of SM and malignant cells combined; FNA had a specificity of 94.5% (95% CI 0.66-0.99) with a positive predictive value of 93.3% (95% CI 0.66-0.99). Calculations of sensitivity and negative predictive value were not feasible in view of the small number of patients with benign lesions on FNA who underwent surgery.

Discussion: Study emphasizes the high specificity and positive predictive value of FNA in detecting malignant thyroid nodules. However, it also underscores the fact that a negative biopsy does not exclude the possibility of a malignancy. This study reports a higher percentage of AFLUS lesions compared to that reported from institutions with a high volume of FNA.

Conclusion: Variation in reporting AFLUS reflects its heterogeneity which may result in variations between institutions. Guidelines advocate for limiting the use of this category to less than 7% of all FNAs. Quality control measures and consultation with an expert cytopathologist in difficult cases are options to ensure meeting this requirement.

Abstract #1049

PAPILLARY THYROID CARCINOMA PRESENTING AS A HOT THYROID NODULE

Sameh M Said, MD, Melanie L. Richards, MD, Vahab Fatourechi, MD

Objective: Radioiodine imaging is the first test of choice in the evaluation of a patient with a thyroid nodule associated with a suppressed TSH. According to the American Thyroid Association guidelines, fine needle aspiration cytology (FNAC) is not mandatory due to the low likelihood of malignancy in a hyperfunctioning nodule. However, there are isolated reports of papillary thyroid cancer associated with hyperfunctioning nodules. We report a case of papillary thyroid cancer presenting with hyperthyroidism due to a hyperfunctioning thyroid nodule.

Case Presentation: A 42-year-old man presented with a 3-month history of weight loss and tremors. He had undetectable thyroid stimulating hormone level (TSH) and free thyroxine (T\textsubscript{4}) level of 2.0ng/dl (normal, 0.8-1.8). Thyrotropin receptor antibodies level was less than 1.0 IU/L (normal, 0-1.75). His family history was positive for Graves’ disease. Neck ultrasound showed a 3.5-cm nodule occupying the right lobe of the thyroid gland with multiple punctate calcifications. He was referred for radioactive iodine-123 (RAI) uptake scintigraphy, which demonstrated marked enlargement of the right lobe of the thyroid with a suggestion of a hyperfunctioning mass or nodule in the lower pole. The left lobe of the thyroid had decreased activity and suggested suppression. The 4.5 hour RAI uptake was 16.8% (normal range at 6 hours is 3 to 16%) FNAC of the mass was suspicious for papillary thyroid carcinoma. He underwent total thyroidectomy with central compartment lymphadenectomy. Histopathological examination confirmed the presence of papillary thyroid carcinoma, grade 1 (of 4), forming a mass (1.4 x 1.3 x 0.6 cm) located in the lower portion of the right lobe corresponding to the same hot area visualized on the preoperative RAI study. The tumor was confined to the thyroid. All surgical resection margins were negative for tumor. There were Multiple (13 of 15) lymph nodes that were positive for papillary thyroid carcinoma. He is being followed regularly with TSH, free T4, and thyroglobulin
levels. The patient is doing well at 6-months follow-up.

**Conclusion:** Evaluating solitary thyroid nodule by measuring TSH level, followed by isotopic thyroid scan if TSH is suppressed are still the appropriate recommendations. The need for FNAC is low in the presence of a hot nodule on isotopic scans. However, in the light of the present case and rare similar reported cases, we suggest that ultrasound characteristics should be considered if biopsy is not planned.

**Abstract #1050**

**AN ASYMPTOMATIC PATIENT WITH NON-SUPPRESSIBLE TSH MOST LIKELY FROM A TSH SECRETING PITUITARY ADENOMA**

Smita Kargutkar, MD, Sudha Ganne, MD

**Objective:** Inappropriate secretion of TSH usually results from either a TSH-secreting pituitary adenoma or thyroid hormone resistance. We report a case of a woman with elevated serum thyroid hormones and non-suppressed TSH levels, with no clinical symptoms of hyperthyroidism, most likely associated with a TSH-secreting pituitary adenoma.

**Case Presentation:** A 44-year-old woman was referred for evaluation for elevated free T4 and free T3 levels with a normal TSH that was noted for several years on routine blood work. The patient denied any symptoms suggestive of hyperthyroidism. Physical examination was normal except for an easily palpable thyroid gland and severe hearing impairment. Repeat blood work showed a TSH 2.640 uIU/mL, total T4 12.7 ug/dL, free T4 2.02 ng/mL, and total T3 209 ng/dL. Additional work-up to evaluate for thyroid hormone resistance revealed a free alpha subunit of 0.60 ng/mL, thyroid peroxidase (TPO) antibodies <10 units/mL, thyroid stimulating immunoglobulin 31, T3 uptake 34%, and free Thyroxine index 4.3. A 24-hour RAI uptake and scan showed elevated homogeneous thyroid uptake of 31.3% suggestive of hyperthyroidism. FSH, LH, IGF-1, cortisol, ACTH, and prolactin levels were all within normal limits. MRI of the brain showed a 1.2 x 0.7 x 1.1 cm pituitary adenoma; the optic chiasm was unaffected. Visual field testing was within normal limits. Liothyronine suppression test lowered the patient’s TSH to 0.926 uIU/mL with total T4 8.1 ug/dL, and total T3 >651 ng/dL, but could not entirely suppress the TSH even at maximal doses (TSH 0.589 uIU/mL, total T4 6.5 ug/ dL, and total T3 >651 ng/dL). Follow-up MRI after 9 months showed no significant interval change in size of the pituitary adenoma and it was decided to monitor her closely as she remained asymptomatic.

**Conclusion:** In the differential diagnosis of a non-suppressed TSH, a TSH-secreting pituitary adenoma or thyroid hormone resistance should always be considered, especially in those with a diffuse goiter and no extra-thyroidal manifestations of Graves’ disease. Failure to do so may result in dramatic consequences, such as improper thyroid ablation that may cause the pituitary tumor volume to further expand. In patients with TSH secreting pituitary adenomas, the most definitive treatment is trans-sphenoidal resection of the tumor and restoring euthyroidism. Medical treatment with somatostatin analogues, such as octreotide and lanreotide, can reduce TSH secretion in >90% of patients, leading to restoration of the euthyroid state.

**Abstract #1051**

**AN UNUSUAL GOITER**

Olubiyi Fidelis Adesina, MBChB, FMCP, O Oguntuyinbo, MD

**Objective:** To present an unusual case of a Toxic Goiter coexisting with bilateral Thyroglossal fistula.

**Case Presentation:** AF, a 32-year-old male presented with 4 years history of an anterior neck swelling associated with palpitations, heat intolerance, protrusion of the eyeballs, weight loss, tremors of the hands and generalized weakness. Prior to onset of the neck swelling, he had noticed since childhood that whenever he drinks any fluid, some of the fluid drips out from two points on either side of the lower part of his neck. No associated history of neck pain, no family history of thyroid disease. No associated ear or nasal symptoms. An examination of a young man with thyroid stare, bilateral proptosis, diaphoretic, with tremors of the outstretched hands and warm and moist palms was completed. Neck: Anterior neck mass about 80g in size, with scarification marks, soft, non-nodular, non-tender, with discharge of clear fluid from the inferior region bilaterally. CVS: Pulse rate 104 beats per minute, Blood pressure 120/70 mmHg. Precordium was hyperactive. Cardiac apex was not displaced. First and second heart sounds were heard. Assessment of exam was Toxic Goiter co-existing with bilateral thyroglossal fistula.

**Results:** Ultrasound: Diffuse goiter. No nodule or cyst demonstrated. Thyroid function test: Test: T3, Result: 7.5, Range: 0.8-2.0 ng/mL. Test: T4, Result: 415, Range: 45-115ng/ml. Test: TSH, Result: 0.1, Range: 0.5-3.7mIU/L. He was commenced on anti-thyroid medications and is scheduled for Fistulography.

**Conclusion:** Goiter coexisting with bilateral thyroglossal fistula is an uncommon presentation. Clinicians need to be aware of the possibility of such a presentation and then investigate and treat appropriately.
Abstract #1052

THYROID DYSFUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS AND ITS RELATION TO CARDIOVASCULAR RISK

Aziza Abdel Moez Hammad, MD, Mohammad Salah Eldin Abdel-Baki, MD, Dalia Fayez, MD, Amr Abdel Mageed, MD

Objective: Rheumatoid Arthritis (RA) patients have an increased risk of developing cardiovascular diseases (CVD). Hypothyroidism may further boost CVD risk in RA patients; however, there are no controlled studies on the prevalence of thyroid dysfunction in Egyptian patients with RA. Our objective was to determine the pattern of thyroid dysfunction associated with RA patients, and to study the risk of CVD in RA patients with hypothyroid abnormalities.

Methods: Thyroid hormonal levels were assessed in seventy RA patients, mean age 43.6 years and mean disease duration 7.6 years, and seventy age and sex matched healthy controls. Atherosclerosis was defined by carotid duplex finding of intima-media thickness >0.9 mm and/or presence of one or more atheromatous plaques.

Results: Clinical hypothyroidism was observed in 5 out of 70 RA patients (7.1%), while no one of the control group had clinical hypothyroidism. Subclinical hypothyroidism was detected in 4 out of 70 RA patients (5.7%) which is significantly higher than the control group (1.7%) (p<0.05). No one of RA patients had hyperthyroidism, while subclinical hyperthyroidism was detected in 1.7% of the control group. Long disease duration is associated with increased incidence of hypothyroidism in RA patients (P<0.01). Hypothyroid RA patients have a more unfavorable cardiovascular risk profile, reflected by an increased prevalence of diabetes, hypertension, hyperlipidemia and obesity compared to euthyroid RA patients. Higher prevalence of atherosclerosis was found in hypothyroid RA patients (44.4%) compared to euthyroid RA patients (16.4%) (P<0.05). The odds ratio for CVD comparing hypothyroid RA patients with euthyroid RA patients was 1.9 (95% CI 0.4 – 8, P<0.01) after adjustment for sex, age, diabetes, smoking, hypertension, statin use, renal insufficiency and disease duration.

Conclusion: Hypothyroidism is the most frequent thyroid disorder in RA patients. Hypothyroid RA patients have worse cardiovascular risk profile and higher prevalence of atherosclerosis compared to euthyroid RA patients suggesting a greater need for cardiovascular risk management in these patients to prevent future CVD events.

Abstract #1053

PERSISTENT HYPERCALCITONINEMIA AFTER TOTAL THYROIDECTOMY FOR MEDULLARY THYROID CANCER IN A PATIENT WITH MULTIPLE ENDOCRINE NEOPLASIA 2A

Saumya Kumar, MD, Lyndell Horine, MD, Shyam Dang, MD, Fred Faas, MD

Objective: Serum calcitonin level is an excellent biochemical marker for both the diagnosis and follow-up of patients with medullary thyroid carcinoma (MTC), which is a part of MEN (Multiple Endocrine Neoplasia) 2A syndrome complex. We report a case of persistently elevated levels of serum calcitonin after total thyroidectomy of medullary thyroid cancer in a patient with MEN2A, without any evidence of recurrence of disease on appropriate further testing.

Case Presentation: A 26-year-old white female with history of MTC and pheochromocytoma in grandmother, and MTC in mother presented to ambulatory clinic with dizziness, tremors, sweating, and palpitations and was found to have a thyroid nodule. Radiological testing revealed an elevated serum calcitonin level of 1476 pg/ml (normal<5.1 pg/ml). Plasma and urine catecholamines and metanephrines, serum ionized calcium and intact parathyroid hormone levels were also elevated. Thyroid nodule biopsy showed medullary thyroid cancer, and right adrenal biopsy showed pheochromocytoma. Genetic testing showed RET C634Y mutation. MEN2A syndrome complex was diagnosed. She subsequently underwent total thyroidectomy with bilateral radical neck dissection, right adrenalectomy, and partial parathyroidectomy. Post operatively, serum calcitonin levels remained elevated. Follow up radiological scans showed multiple enlarged lymph nodes in right level IIB neck area and a new left adrenal mass. She underwent repeat bilateral neck dissection with multiple lymph node excision, and left adrenalectomy. Lymph node pathology returned as benign, and adrenal mass showed recurrence of pheochromocytoma. Calcitonin levels remained elevated over a follow up course of three years.

Discussion: Initial treatment of MTC involves total thyroidectomy with radical neck dissection. Controversy exists with the management of patients who have seemingly adequate initial surgical treatment with no demonstrable clinical or radiologic disease, but continue to have elevated levels of serum calcitonin. Some authors suggest excision of demonstrable recurrent disease, where as some suggest a more radical approach with extensive removal of nodal and soft tissue that may or may not be macroscopically abnormal. Many reports have described
excellent outcomes in patients with conservative follow up despite continuously elevated calcitonin, in whom recurrence of disease cannot be localized.

Conclusion: Managing persistent hypercalcitoninemia without demonstrable clinical or radiological disease in postoperative medullary thyroid cancer is still a matter of debate.

Abstract #1054

PULMONARY HYPERTENSION & GRAVES’ HYPERTHYROIDISM: A RETROSPECTIVE OBSERVATIONAL STUDY

Soe Naing, MD, MRCP, Abhishek Sawant, MD, MPH, Muhammad Bajwa, MD, Eric Wilson, MD
Paul K. Mills, PhD, MPH, Vijay Balasubramanian, MD, FCCP

Objective: To determine the prevalence of pulmonary hypertension (PH) in Graves’ hyperthyroidism (GH).

Methods: This retrospective study was conducted at a community hospital. Patients, who were diagnosed with hyperthyroidism from 2006 to 2010, had Thyroid Stimulation Immunoglobulin (TSI) measurement and/or thyroid uptake scan and had an echocardiogram performed at the time of diagnosis, were included in the study. PH was defined as Estimated Right Ventricular Systolic Pressure (RVSP) of ≥35 mmHg by transthoracic echocardiography. Patients with biochemical evidence of hyperthyroidism were considered to have GH if they had elevated TSI and/or diffusely increased uptake at radioactive iodine thyroid uptake scan and had an echocardiogram with over the counter remedies. She reported that the neck pain had been worsening over the past several days, with progressive odynophagia, and hoarseness of voice. On physical examination, she was febrile, unable to open her mouth and had poor dentition and hygiene. The thyroid gland was enlarged and tender to palpation. A CT scan of the neck revealed acute inflammatory changes with retropharyngeal edema and a cystic mass in the thyroid gland. Her white blood cell count was 24,550/µL with neutrophilia (22,800/µL and 48% bands). Her TSH was 0.09 mU/L; free thyroxine was 7.8 ng/dL and thyroid stimulating immunoglobulin (TSI) index was 89% (normal<129%). A flexible laryngoscopy revealed no edema of the larynx or lower airways. She underwent fine-needle aspiration of the cystic thyroid mass by palpation. Due to the purulent nature of the aspirate, cytology was not performed and she was discharged to a nursing facility for parenteral antibiotic therapy. She failed to return for follow up.

Results: Of 35 patients included in the study, 25 (71%) were female; and Caucasian, Hispanic, African American and Asian were 23%, 29%, 17% and 29%, respectively. Mean age was 50.8±16 years with mean BMI of 26.8±9.4, mean TSH of 0.01±0.01 µIU/ml (NR: 0.35-5.5), mean free T4 of 4.14±2.56 ng/dl (NR:0.89-1.76) and mean RVSP of 42.1±13.2mmHg. 28 (80%) had GH and 7(20%) had non-autoimmune hyperthyroidism. Further studies with larger number of cases are needed to confirm the findings.

Abstract #1055

AN UNUSUAL CASE OF GROUP A STREPTOCOCCAL SUPPURATIVE THYROIDITIS IN A PATIENT WITH HIV

Devendra Wadwekar, MD, Devaprabu Abraham, MD

Objective: We report a unique case of suppurative thyroiditis in a HIV patient and review the literature.

Case Presentation: A 40-year-old multiparous woman was seen for throat pain 24 hours after an uncomplicated delivery. Upon further questioning, she described 4 week history of neck pain and sore throat which she was treating with over the counter remedies. She reported that the neck pain had been worsening over the past several days, with progressive odynophagia, and hoarseness of voice. On physical examination, she was febrile, unable to open her mouth and had poor dentition and hygiene. The thyroid gland was enlarged and tender to palpation. A CT scan of the neck revealed acute inflammatory changes with retropharyngeal edema and a cystic mass in the thyroid gland. Her white blood cell count was 24,550/µL with neutrophilia (22,800/µL and 48% bands). Her TSH was 0.09 mU/L; free thyroxine was 7.8 ng/dL and thyroid stimulating immunoglobulin (TSI) index was 89% (normal<129%). A flexible laryngoscopy revealed no edema of the larynx or lower airways. She underwent fine-needle aspiration of the cystic thyroid mass by palpation. Due to the purulent nature of the aspirate, cytology was not performed and the fluid sent for culture. She was treated with intravenous vancomycin, clindamycin, and piperacillin-tazobactum. The culture grew group A beta hemolytic Streptococcus that was sensitive to penicillin. Following these results, her antibiotic coverage was narrowed to penicillin G 18 million units and clindamycin for 2 weeks. Further investigations revealed her to have HIV and Hepatitis C infections. Her CD4 count was 699/µL. Her fever subsided 3 days later and she was discharged to a nursing facility for parenteral antibiotic therapy. She failed to return for follow up.
**Discussion:** This is the first reported Group A Streptococcal infection of thyroid gland in a HIV positive individual. Previously published reports in HIV patients with suppurative thyroiditis have indentified the following microorganisms: 4 cases of Pneumocystis carinii, 1 case of Salmonella, 1 case of Proteus, 2 cases of Staphylococcus, 1 case of Mycobacterium tuberculosis and Cryptococcus neoformans, 15 cases of Pneumocystis jiroveci and 1 patient with unknown organism. To date, no case of Group A Streptococcal infection of thyroid gland in a HIV positive patient has been reported in published literature.

**Conclusion:** HIV suppurative thyroiditis is a rare disease which can be caused by common and atypical microorganisms that require a high index of suspicion for prompt diagnosis and treatment.

**Abstract #1056**

RIEDELS THYROIDITIS IN A PATIENT WITH PREVIOUSLY DIAGNOSED PERIAORTIC MYOFIBROBLASTIC TUMOR

Rachael Bendele, MD, Archana Bindra, MD, Sunita Bhuta, MD, Andre Van Herle, MD

**Objective:** To report a case of Riedel's thyroiditis, a rare fibrosing disorder involving the thyroid, in a patient with a previously diagnosed periaortic inflammatory myofibroblastic tumor.

**Case Presentation:** A 50-year-old woman presented with constitutional symptoms and a large mediastinal/periaortic mass. The diagnosis of Castleman’s disease was initially suspected. She was treated with pulse dose dexamethasone and thalidomide for 6 months with marked improvement in her symptoms and near resolution of the periaortic mass on CT scan. She then presented 6 years later with a firm thyroid mass. CT scan done at that time demonstrated a solid hypoenhancing nodule involving the left lobe of the thyroid gland measuring 3.5 cm x 2.6 cm x 1.5 cm as well as an interval increase in size of the mediastinal mass. Thyroid peroxidase antibody was negative. A fine needle aspiration biopsy of the thyroid nodule revealed a mixed population of lymphoid cells. Left thyroid lobectomy was planned but aborted due to the infiltrative nature of the thyroid mass. Instead an excisional biopsy was performed and the diagnosis of Riedel's thyroiditis was made. Pathologic examination of both the periaortic mass and the thyroid mass showed similar findings consisting of sclerotic fibrous tissue and inflammatory infiltrate. Based on the histopathological findings the initial mediastinal mass and the thyroid mass appear to be manifestations of the same disease process, idiopathic multifocal fibrosclerosis.

**Discussion:** The etiology of both Riedel’s thyroiditis and multifocal fibrosclerosis is unknown. Recently, it has been proposed that Riedel’s thyroiditis and multifocal fibrosclerosis are part of the IgG4-related systemic disease spectrum. Patients with multifocal fibrosclerosis and Riedel’s thyroiditis have been shown to have elevated IgG4 in the involved tissues. In this case, the serum IgG4 was normal at the time of the thyroid mass work-up although total serum IgG was markedly elevated at initial presentation. The surgical thyroid tissue specimen had an increased number of IgG4 plasma cells however they accounted for less than 5% of the total plasma cell population. It has been proposed that the IgG4 level may be elevated in the early stages of the disease due to the strong inflammatory component and normal or low in the later stages as fibrosis becomes the prominent finding.

**Conclusion:** In patient’s presenting with Riedel’s thyroiditis it is important to assess for other areas of fibrosis and to check an IgG4 serum level as well perform IgG4 immunostaining in the involved tissue.

**Abstract #1057**

THE DIAGNOSTIC ACCURACY OF ULTRASOUND GUIDED FINE-NEEDLE ASPIRATION BIOPSY AND INTRAOPERATIVE FROZEN SECTION EXAMINATION IN NODULAR THYROID DISEASE

James Young, MD, Roberto Mirasol, MD, Cherrie Gail Lumapas-Gonzalez, MD

**Objective:** To determine the diagnostic accuracy of combined ultrasound-guided fine needle aspiration biopsy (USG-FNAB) and intraoperative frozen section examinationin (FSE) in diagnosing malignant thyroid nodules.

**Methods:** A retrospective review of patients undergoing thyroidectomy with intraoperative frozen section examination following ultrasound guided fine-needle aspiration biopsy. Sensitivity, specificity, positive and negative predictive values and accuracy were calculated with respect to final histology.

**Results:** A total of 2,239 nodules were subjected to USG-FNAB at Diabetes, Thyroid and Endocrine Center, St. Luke’s Medical Center between January 2007 and December 2009. Two hundred fifty-one nodules were surgically excised following USG-FNAB. Frozen section examinations were taken from 90 of 251 nodules. The USG-FNAB yielded 90.3% (n=1,721) adequate specimen and 9.7% (n=185) inadequate specimen. The histologic examination of the 251 surgically excised nodules were benign in 182 (73%) and malignant in 69 (27%) nodules.
The sensitivity, specificity, positive and negative predictive values and accuracy rate of USG-FNAB cytology are 70.3%, 92.8%, 76.5%, 90.4% and 87.2%, respectively. The diagnosis by frozen section was benign in 56 cases (62%), malignant in 10 cases (11%) and deferred in 24 cases (27%). By FSE, the sensitivity, specificity, positive and negative predictive values and accuracy rate are 83.3%, 100%, 100%, 96.4% and 96.7%, respectively. A diagnostic accuracy of up to 97.2% was achieved when USG-FNAB and FSE were combined and when their findings were concordant. When USG-FNAB and FSE diagnoses were discordant, the FSE showed superior accuracy (83.3%) than cytology (16.7%). In the group of nodules with indeterminate or inadequate cytology, the diagnostic accuracy of frozen section is 100%.

**Conclusion:** Ultrasound guided fine-needle aspiration biopsy is an accurate preoperative test for the evaluation of nodular thyroid disease. It helps to distinguish malignant from benign lesions. The intraoperative frozen section is a valuable test for confirming the cytologic diagnosis. It is especially important in identifying malignant thyroid nodule in cases with indeterminate cytology. The combination of USG-FNAB and FSE greatly improves the accuracy rate in thyroid cancer detection.

**Abstract #1058**

**RAPID REVERSAL OF PULMONARY HYPERTENSION IN Graves’ DISEASE**

Sruti Chandrasekaran, MBBS, Sheila Ramirez, MD, Elizabeth A. Streten, MD

**Background/Objective:** Pulmonary hypertension (PH) has been described in 30-60% of patients with hyperthyroidism but the time course of resolution following treatment is unclear. We describe a case of near normalization of pulmonary hypertension (PH) within 5 weeks of treatment with antithyroid drugs.

**Case Presentation:** 59-year-old caucasian female with known history of Graves’ disease was hospitalized for inter-trochantric hip fracture. She had stopped taking methimazole eight months previously. Her past history was notable for low impact fragility fractures of left wrist, right ulna and right shoulder. Her outpatient medications included multiple herbal supplements only. Family history was significant for hyperthyroidism in her mother. Review of system was positive for shortness of breath. On examination she was tachycardic, tachyypnoeic and hypertensive. Her thyroid was enlarged (60 g) with a palpable thrill. On cardiac exam there was an accentuated pulmonary component of the second heart sound. Thyroid function test (TFT) showed TSH 0.02 mcIU/mL (nl 0.34-5.60), Total T3 696 ng/mL (nl 45-137) and free T4 > 6.0 ng/mL (nl 0.6-1.9). A 2D echocardiogram showed severe pulmonary hypertension with a pulmonary arterial pressure (PAP) of 72 mmHG (nl 15-30), normal right and left ventricular function. After 48 hours of intensive treatment with propylthiouracil, metoprolol, dexamethasone and potassium iodide, her blood pressure and tachycardia improved and surgical fracture repair was performed. Two days after surgery, echocardiogram showed mild improved PAP of 64 mmHG. She was discharged on methimazole and 5 weeks after discharge she was clinically euthyroid. TFT showed TSH 0.01, Free T4 0.8 and Free T3 2.6 and echocardiogram showed PAP of 36 mmHG.

**Discussion:** Pulmonary hypertension is a common but not well recognized complication of hyperthyroidism. The mechanism of PH in hyperthyroidism is unclear. Autoimmunity has been postulated as a possible mechanism. Our case illustrates that dramatic improvement in PAP can occur within weeks of treating hyperthyroidism suggesting a direct effect of thyroid hormone. A similar case was reported with improvement in PH in 4 weeks and normalization of PAP in 9 weeks.

**Conclusion:** PH associated with hyperthyroidism can improve rapidly after normalization of TFT.

**Abstract #1059**

**TOTAL THYROIDECTOMY AS PRIMARY DEFINITIVE TREATMENT FOR Graves’ HYPERTHYROIDISM**

Samuel Kevin Snyder, MD, FACS, Cara Govednik-Horny, MD, Terry Lairmore, MD, Da-Shu Jiang, BS, Juhee Song, PhD

**Objective:** To compare the results of total thyroidectomy (TT) for hyperthyroidism secondary to Graves’ disease (GD) to total thyroidectomy for other benign thyroid disease, including other causes of hyperthyroidism, to determine if TT should be considered more often as first line therapy for GD.

**Methods:** Seven hundred and eighty patients underwent TT for benign disease: 203 for GD, 56 for other hyperthyroidisms and 521 for other benign diseases from March 1, 2003 to December 31, 2009. The perioperative results of these 3 groups were compared for demographics, blood loss, operative time, complications, and hospitalization.

**Results:** There were no significant differences between the 3 groups of TT for mean thyroid size, operative time, asymptomatic or symptomatic hypocalcemia. The GD patients were significantly more likely to be younger (42 vs 56 vs 57 yrs.; P<.001), have more blood loss (154 vs 99 vs 110 ml; P=.05), and permanent hypoparathyroidism...
with other hyperthyroid patients (1.0% vs 1.8% vs 0%; P=.03). Permanent recurrent laryngeal nerve injury did not occur in the GD group (0% vs 0% vs 0.4% nerves-at-risk; P=.69), with transient recurrent laryngeal nerve injury occurring in (1.7% vs 2.7% vs 3.1% nerves-at-risk P=.35). The lack of a euthyroid state preoperatively had no influence on surgical outcomes or complications. Eighty percent of the TTs for GD were done as same-day outpatient procedures.

**Discussion:** The American Association of Clinical Endocrinologists medical guidelines emphasize thionamides and radioactive iodine ablation as a first line therapy for hyperthyroidism secondary to GD, reserving surgical treatment for only certain patient populations. The rapid resolution of Graves’ hyperthyroidism with TT and improved operative outcomes with current surgical techniques may necessitate reevaluation of these treatment priorities in selected patients. TT for Graves’ hyperthyroidism can be performed with low morbidity and excellent outcomes.

**Conclusion:** TT offers a safe, low-risk, and rapid cure for GD to justifiably be considered as a reasonable first line therapy in selected patients with Graves’ hyperthyroidism.

**Abstract #1060**

**AN UNUSUAL CASE OF INCIDENTAL MALIGNANT STRUMA OVARII**

Devaprabu Abraham, MD

**Objective:** We present a case of malignant struma ovarii and review the literature.

**Case Presentation:** A 54-year-old female presented to her primary care physician with complaints of irregular menstrual bleeding. A pelvic ultrasound was done and revealed a cystic ovarian mass in the right ovary. She underwent right oopherectomy and pathology showed a mature cystic teratoma with focal malignant transformation. Sections of the ovary had mature respiratory epithelium, sebaceous glands, adipose tissue, squamous and columnar epithelium, gastrointestinal type mucosa, bone, and thyroid tissue. A 3mm microscopic focus of papillary thyroid carcinoma was also identified. She is being evaluated for additional disease burden.

**Discussion:** Malignant struma ovarii is an extremely rare disease with less than 200 cases reported in literature. The incidence of struma ovarii is about 0.4% of all ovarian tumors of which only 5-10% becomes malignant. The most common type of malignant struma ovarii is follicular variant of papillary thyroid carcinoma (54%) followed by papillary thyroid carcinoma (21%), and finally mixed follicular/papillary carcinoma (12.5%) or follicular carcinomas. These tumors present commonly as abdominal mass (78%) or pelvic pain. The overall survival rate is 89% and 84% at 10 and 25 years respectively and only five lethal cases have been reported in literature. Optimal management includes total thyroidectomy followed by radioiodine ablation and periodic whole body scans to detect local recurrences.

**Conclusion:** Malignant struma ovarii is an extremely rare disorder requiring the same level of aggressive management as traditional thyroid cancer therapy.

**Abstract #1061**

**A CASE OF OXCARBAZEPINE INDUCED CENTRAL HYPOTHYROIDISM**

Mahima Gulati, MD, Robert E Jones, MD

**Background/Objective:** It is well-known that several antiepileptics (e.g. Carbamazepine) can induce abnormalities in thyroid function, by accelerating the hepatic clearance of thyroxine, thereby lowering circulating thyroxine (T4) levels. Oxcarbazepine is a derivative of carbamazepine which does not induce hepatic cytochrome P450 enzymes, and therefore, does not increase hepatic metabolism of T4. We report a case of central hypothyroidism in an adult female patient who was administered oxcarbazepine for treatment of severe bipolar disorder.

**Case Presentation:** A 37-year-old woman with a history of refractory bipolar illness and anorexia nervosa was referred to this university specialty clinic for evaluation of fatigue, weight gain, constipation, cold sensitivity, and decreased exercise tolerance. Ten months prior and before she was started on oxcarbazepine, her thyroid functions were normal (TSH 1.84 mU/L; normal 0.3-4.0 and free T4 0.86 ng/dL; normal 0.8-1.7). Because of her new symptoms and after she had been on oxcarbazine for several months, thyroid levels were re-measured; her free T4 was found to be low (0.66 ng/dL) in the face of a normal TSH (2.77 mU/L). She continued on oxcarbazepine, and 3 months later, thyroid functions were reassessed and were still consistent with central hypothyroidism (TSH 2.26 mU/L; FT4 0.51; free T3 1.9 pg/mL; normal: 2.4-4.2 pg/mL). Her remaining pituitary axes were assessed and were found to be completely normal. Her rest pituitary labs were normal (8 AM Cortisol; Prolactin, FSH, LH, Estradiol, IGF-1); and she had regular, normal menstrual cycles. Due to her persistently low thyroid hormone levels and presence of symptoms, we decided to start her on levothyroxine. Her symptoms have resolved; unfortunately, she has not had a repeat measurement of thyroid hormone levels. Discontinuation of oxcarbazepine was discussed with the patient but was deemed unethical due to the psychiatric benefit she has achieved on oxcarbazepine.
**Objective:** It was reported that LNAB is a safe technique useful for the preoperative selection of indeterminate follicular nodules and for the nodules inadequate at FNAB. LNAB of thyroid may be considered more painful than FNAB because it uses larger nodules (18-20 gauge versus 22-25 gauge).

We compared by a survey the pain referred by two groups of patients examined with FNAB or FNAB+LNAB.

**Methods:** Seventy-nine patients (87.3% women, mean age 59 years) had a palpable nodule examined only by FNAB. Forty-one patients (90% women, mean age 60 years) had nodules examined by FNA cytology + LNAB histology. At a successive visit each patient was asked to be clear whether he or she experienced: a) no unpleasant feeling - sensation; b) unpleasant sensation; c) mild pain (no analgesic used); or d) pain (analgesic used). The pain was scored as an ordinal variable (0-3).

**Results:** Sex and age were not significantly different in two groups (Fisher’s exact test p= 0.77 and unpaired Wilcoxon test p=0.47 respectively). Subgroup a) included 32% of the patients examined only by FNAB and 29% of those examined by FNAB +LNAB. Subgroup b) included 38% and 44% of the patients, respectively. Subgroup c) included 29% and 24% of the patients, respectively. Subgroup d) included one patient per group. The pain score in the FNAB or FNAB + LNAB group was 1 ± 0.8 or 1 ± 0.8 (ordinal logistic regression; p= 0.972).

**Discussion:** It should be considered to extend the clinical use of LNAB also because, compared to FNAB, it provides a much better substrate for thyroid tumor marker determination.

**Conclusion:** These data confirm our long standing experience that LNAB is not more painful than FNAB.

**Abstract #1063**

**THYROTOXIC PERIODIC PARALYSIS- A CASE SERIES**

Meera Shah, MBCHB, Ambika Babu, MD

**Objective:** Thyrotoxic periodic paralysis (TPP) is a rare disorder causing temporary episodes of muscle weakness or paralysis associated with hypokalemia and hyperthyroidism. This association between hyperthyroidism and periodic paralysis has been known since 1931 and is most often reported in young males of Asian descent. Here, we aim to summarize the clinical presentation, pertinent laboratory values, clinical course and management of six patients with TPP in an urban teaching center.

**Case Presentation:** Six patients who first presented to the ER with symptoms of weakness and/or paralysis, and were eventually found to be hypokalemic and thyrotoxic over a 2 year period, were analyzed. All six patients were males of Hispanic descent and the mean age was 31.6 years (27-36 years). Three patients had Graves disease and were clinically and biochemically hyperthyroid on presentation. In two patients, this was the initial presentation of hyperthyroidism while the sixth patient, though clinically euthyroid, was found to be biochemically hyperthyroid. The mean serum free T4 was 4.65ng/dL (0.58- 1.64ng/dL). The mean serum potassium concentration was 2.67mEq/L (3.5-5.0mEq/L). Five patients presented with symptoms of paralysis on waking up in the morning; time of symptom-onset in the sixth patient was unknown. A history of precipitating factors like carbohydrate-loading was obtained in two patients. There was no known family history in any patient. The majority of patients in this series had weakness confined to bilateral lower extremities. All patients responded to potassium supplementation with complete resolution of symptoms. Once treated with RAI and rendered euthyroid, there was no recurrence of symptoms.

**Discussion:** The severity of paralysis correlates with the degree of hypokalemia but not to the severity of thyrotoxicosis or thyroid hormone levels. The onset of symptoms on waking seen in our series is a characteristic feature; 84% of all patients with TPP have symptoms between 1 and 6 am. Muscle weakness in TPP is more common in the proximal muscle groups and in the lower rather than the upper extremities, again consistent with the findings in our series. There is also an associated decrease in muscle tone and loss of reflexes which responds well to potassium replacement and anti-thyroid medications.

**Conclusion:** There should be a high index of suspicion...
for TPP in young male Hispanic patients presenting with paralysis or lower extremity weakness in the early hours of the morning, even in the absence of clinical hyperthyroidism. These symptoms do not recur once the patient is biochemically euthyroid.

Abstract #1064

ACUTE HYPOTHYROIDISM IN THE SETTING OF INTERLEUKIN-2 IMMUNOTHERAPY

Reshmi Iyengar Srinath, MD

Objective: To describe a case of acute thyroid dysfunction in the setting of Interleukin-2 (IL-2) administration for metastatic renal cell carcinoma.

Case Presentation: A 51-year-old female with metastatic renal cell carcinoma and stable lung metastasis presents for her second cycle of IL-2 therapy with complaints of facial and upper extremity swelling and numbness for one week. On evaluation, this is an obese middle aged caucasian female who is afebrile, normotensive, with a hoarse voice. Head and neck exam shows periorbital edema with neck fullness, without palpable thyroid nodules or lymphadenopathy. Upper extremities demonstrate 4/5 strength, diminished sensation to light touch, and normal deep tendon reflexes. Physical exam was otherwise unremarkable.

Discussion: Thyroid dysfunction can occur in the setting of Interleukin-2 immunotherapy. Close monitoring of thyroid function and further workup including thyroid ultrasound and FNA of amenable lesions is necessary.

Abstract #1065

THYROTROPIN SECRETING PITUITARY ADENOMA IN A PATIENT WITH MINIMAL SYMPTOMS

Naga Nalini Tirumalasetty, MBBS, Michelle Cordoba-Kissee, MD, Hussein Yassine, MD, Craig Stump, MD, PhD

Objective: Hyperthyroidism secondary to thyrotropin (TSH) secreting pituitary adenoma is exceedingly rare. We endeavor to present a case of hyperthyroidism secondary to a pituitary macroadenoma in a patient with minimal signs or symptoms.

Case Presentation: A 40-year-old man with no past medical history was evaluated for abnormal thyroid function tests (TFTs). He denied weight change, diarrhea, palpitations, tremor or vision changes. His primary provider started him on low-dose levothyroxine, but discontinued it shortly after. Repeat TFTs showed elevated free thyroxine (FT4) 2.8 ng/dL, total T4 15 ng/dL, and TSH 6.2 mU/L. Other pituitary axis hormones were normal. Physical examination was unremarkable for tachycardia, tremor, hyperkinesia, or goiter. Because of the minimal clinical presentation syndrome of resistance to thyroid hormone (RTH) was entertained. However, α-subunit level was found to be elevated 0.7 ng/mL (<0.6), and MRI of the brain revealed a 1.8 x 1.7 x 1.2 cm pituitary adenoma extending inferiorly into the sphenoid sinuses. The patient was referred to neurosurgery and transsphenoidal endoscope-assisted microsurgical excision of the pituitary tumor was performed. A frozen section aggregate specimen (0.9 X 0.2 cm) was confirmed to be a pituitary adenoma. The most prominent positive marker was α-subunit with scattered cells reactive for luteinizing hormone and growth hormone. The tumor was negative for adrenocorticotropic hormone and TSH immunoreactivity. Lab tests one week after surgery indicated decreased TSH 0.02 mU/L and FT4 0.56 ng/dL.

Discussion: The differential diagnosis for patients with elevated TSH and FT4 includes RTH and TSH secreting pituitary adenoma. Both α-subunit and sex hormone binding globulin levels are usually elevated in central hyperthyroidism, but normal in RTH. Imaging studies are not entirely reliable for diagnosis since 10%
of patients will have incidental pituitary findings, usually microadenomas. Conversely, most TSH secreting pituitary adenomas are >1.0 cm when diagnosed. A majority of patients with TSH secreting tumors exhibit the usual signs and symptoms of hyperthyroidism, though in some cases, such as our patient, they have minimal symptoms. Treatment includes transsphenoidal resection, although many cases require dopamine agonist or somatostatin analogue therapy post-operatively.

**Conclusion:** Hyperthyroidism secondary to a TSH-secreting pituitary adenoma is a rare condition that may occur in patients exhibiting minimal signs and symptoms. TSH immunoreactivity of the pathological specimen is not requisite for diagnosis.

**Abstract #1066**

**CASE OF METHIMAZOLE ASSOCIATED CRESCENTIC GLOMERULONEPHRITIS COMPLICATED BY PULMONARY HEMORRHAGE**

Cheryl Denise Givens, MD, Daryl Cottrell, MD, FACE

**Objective:** Describe a case of methimazole associated vasculitis with crescentic glomerulonephritis and alveolar hemorrhage.

**Case Presentation:** 47-year-old female presented with thyrotoxicosis. Methimazole and atenolol were initiated. Creatinine was 1.0 mg/dL (0.4-1.1). One month later, patient presented with nausea and vomiting and was found to have renal failure with BUN 49 mg/dL (8-25), Cr 3.2 mg/dL. Renal biopsy revealed linear IgG deposition of the glomerular basement membranes and crescent glomerulonephritis, affecting 30% of glomeruli. C-ANCA was weakly positive, P-ANCA, ANA and MPO and PR3 antibodies negative. Methimazole was discontinued. Prednisone and cyclophosphamide were initiated. Radioactive iodine ablation was successful. Patient was non-compliant with immunosuppressant therapy. She returned three weeks later with Cr 11.0 mg/dL, BUN 141 mg/dL. Hemodialysis was initiated. Repeat renal biopsy showed crescentic glomerulonephritis with 90% of glomeruli involved and sclerosis. The patient developed acute respiratory failure requiring mechanical ventilation. Chest x-ray showed diffuse pulmonary infiltrates. Bronchoscopy showed hemosiderin laden macrophages, consistent with pulmonary hemorrhage. Given renal and pulmonary involvement, Goodpasture’s disease was suspected. Patient underwent plasmapheresis for two weeks and restarted cyclophosphamide and prednisone. In previous case reports, glomerulonephritis associated with anti-thyroid therapy resolved with removal of drug alone or combined with immunsuppressive therapy. However, our patient remained dialysis-dependent.

**Discussion:** With recent increased recognition of hepatic failure as a consequence of propylthiouracil (PTU) therapy, methimazole is generally preferred as first-line anti-thyroid treatment in non-pregnant adults and children with hyperthyroidism. Autoimmune vasculitis has been reported in rare instances, most frequently associated with PTU and reversible. The mechanism is unknown; hypotheses include interaction of PTU with MPO producing an immunogenic structure, similarities in MPO and thyroid peroxidase, and multi-factorial with viral trigger. As methimazole is prescribed more frequently, it is important for physicians to be aware of the less reported complication of vasculitis, which in this case was not reversed on discontinuation of the drug.

**Conclusion:** Although less reported vs PTU, methimazole therapy for Grave’s hyperthyroidism may be associated with autoimmune vasculitis such as Goodpasture’s syndrome, which may not reverse on discontinuation of the drug.

**Abstract #1067**

**GRAVES’ DISEASE AFTER IMMUNE RECONSTITUTION FROM HAART**

Vivien Leung, MD, Helen Karakelides, MD, Sian Jones, MD

**Objective:** To describe a case of Graves’ disease following the initiation of highly active antiretroviral therapy (HAART) for HIV infection.

**Case Presentation:** A 44-year-old male with HIV was referred for evaluation of thyrotoxicosis. He had been treated with a combination HAART regimen achieving virologic suppression and an increase in CD4+ count from a nadir of 500 to 1119 cells/mm³. Approximately 22 months after commencement of HAART, he developed loose stools, mild nausea and weight loss. Extensive GI work-up was unrevealing. TFTs were consistent with thyrotoxicosis: TSH 0.04 mU/L, fT4 2.44 ng/dL, T3 2.68 mg/L. TPOAb was elevated at 77.8 IU/L and TSHRAb was in the upper range of normal at 1.53 IU/L. He had a mild hand tremor. Ultrasound showed an enlarged, hypervascular thyroid gland. Thyroid uptake/scan demonstrated homogeneously increased uptake of 74%. Radioiodine ablation was recommended for Graves’ disease. However, he declined treatment and self-discontinued HAART against medical advice. Three months later without intervention for his hyperthyroidism, his TSH was 0.01 mU/L and fT4 was down to 1.62 ng/dL. GI symptoms improved. During this period, his CD4 count dropped to 555 cells/mm³.

**Discussion:** Autoimmune diseases, including Graves’
disease (GD), have been reported in the setting of immune reconstitution after HAART therapy. An earlier report of 5 patients with HIV demonstrated the novel appearance of TPOAb and TSHRAb after CD4 count had risen on HAART (Jubault et al, JCEM 2000: 85; 4254-7). Clinical hyperthyroidism manifested 14-22 months after the commencement of therapy. Our patient developed GD 22 months after initiation of HAART, which is consistent with other published reports. The occurrence of thyroid autoantibodies is thought to be coincident with the second phase of T-cell repopulation during immune reconstitution, in which naïve T cells reappear in the circulation. Unlike other reports, our patient did not have a profoundly low CD4+ count at baseline, but it is possible that the degree of rise in CD4+ cells (619 cells/mm³) played a role in the development of GD rather than the rise above a threshold level. Of interest, our patient’s drop in CD4+ count after HAART discontinuation correlated temporally with an improvement in his hyperthyroidism, providing further evidence for the link between immune regulation and autoimmune disease.

**Conclusion:** GD can occur several months to years after initiation of HAART due to the sequential production of thyroid autoantibodies during immune reconstitution. The degree of rise in CD4+ count may play a role in the pathogenesis of reconstitution GD.

Abstract #1068

**PAPILLARY THYROID CANCER PRESENTING AS CORD COMPRESSION**

Yemul Almecci, MD, Isabelle Zamfirescu, MD, Harmeet Narula, MD

**Objective:** To report a case of papillary thyroid cancer presenting as spinal cord compression.

**Case Presentation:** A 53-year-old female presented with suboptimally controlled diabetes and a Multinodular Goiter in 2004. She had a 3 cm left and 1.8 cm right thyroid nodules and was recommended an FNA, however, she did not follow-up. The patient presented one year later to the ER with bilateral lower extremity weakness. An MRI of the thoracic spine showed a mass involving the vertebral body of T8 causing severe spinal stenosis and moderate compression of the spinal cord. Patient underwent urgent surgical decompression and spinal stabilization. The pathology report of the mass revealed metastatic adenocarcinoma well differentiated, most consistent with metastatic thyroid cancer. She subsequently underwent total thyroidectomy which revealed a 4 cm, mixed follicular variant and classical type papillary thyroid carcinoma confined to the left thyroid lobe (T2, Nx, M1). She then received external beam radiotherapy (EBRT) from T4 to T10 and 200 mCi I-131. Post treatment thyroid carcinoma survey (WBS) revealed no iodophilic metastasis despite her thyroglobulin (Tg) being 13,700 with negative antibodies. The patient was recommended chemotherapy and/or experimental Tyrosine Kinase Inhibitor (TKI) therapy, but she declined. On follow-up, she had persistently elevated Tg and did have uptake in her spinal metastases on I-131 WBS, and as she repeatedly declined chemotherapy and/or TKIs, she was given three more treatments of 200 mCi of 131-I for persistent bone metastasis (cumulative dose 800 mCi). Despite this, she had progression of her disease and developed new bone metastases (skull & ribs). Additionally, the Tg had increased from 1000s to 8000s while on suppression. The skull tumor was initially treated with EBRT and then was surgically removed. The patient was again advised treatment with TKI therapy or chemotherapy but she declined.

**Discussion:** Less than 5% of patients with PTC present with bone metastases. Aggressive surgical therapy, EBRT & possibly TKI should be employed in the treatment of PTC with bone metastases. I-131 has a limited role, as most bone metastases are refractory to I-131.

**Conclusion:** PTC rarely presents with bone metastases and newer therapies with TKI/chemotherapy should be offered to patients with progressive and/or iodine resistant thyroid cancers.

Abstract #1069

**RARE CASE OF PERICARDIAL TAMPONADE SECONDARY TO CENTRAL HYPOTHYROIDISM**

Maha Jawad Abu Kishk, MD, Tahira Yasmeen, MD, FACE, Farah Hassan, MD

**Objective:** To report a rare case of central hypothyroidism causing massive pericardial effusion and tamponade within two months of the diagnosis.

**Case Presentation:** This is a 59-year-old African American lady who underwent trans-sphenoidal resection of nonfunctional pituitary macroadenoma. Preoperative work up included thyroid function tests, Echocardiography and chest X ray that all were normal. Unfortunately, she neither followed up with her endocrinologist nor refilled her prescriptions for levothyroxine and hydrocortisone after discharge. Two months later she presented to the emergency department with shortness of breath and chest heaviness. Physical exam revealed hypotension, tachycardia, distended neck veins, and distant heart sounds. Electrocardiogram, chest X ray, and Echocardiography showed sinus tachycardia with low voltage, cardiomegaly, and pericardial effusion with tamponade, respectively. Immediate pericardiocentesis and pericardial window
Thyroid Disease was performed, 500 ml of straw colored pericardial fluid was drained and sent for Gram stain and microbiology analysis that was negative for infectious etiology. Further work-up revealed central hypothyroidism, adrenal insufficiency, hypogonadism and hypoprolactinemia consistent with pan-hypopituitarism. She was started on hormonal replacement therapy including levothyroxine and hydrocortisone. A follow up echocardiography few months later was normal without pericardial effusion.

Discussion: Hypothyroidism is well known to cause small, slowly accumulating, exudative and asymptomatic pericardial effusion. The mechanism is increased capillary permeability, and decreased lymphatic drainage. The amount of pericardial effusion directly correlates with the severity and duration of hypothyroidism. Cases of moderate to severe pericardial effusion from hypothyroidism are rarely reported, develop many years rather than few months after the diagnosis, rarely result in tamponade, and are cases of primary rather than central hypothyroidism. A distinctive laboratory finding in these cases is high protein content of the pericardial fluid; unfortunately this was not documented in our case. The normal echocardiography before the surgery and development of the tamponade two months later was highly suggestive of hypothyroidism as the cause.

Conclusion: Central hypothyroidism is an exceedingly rare cause of cardiac tamponade, but should be considered as an etiology if given the clinical scenario. Pericardiocentesis with pericardial window in addition to hormonal replacement was a successful approach in our case.

Abstract #1070

AN UNCOMMON PRESENTATION OF AUTOIMMUNE THYROIDITIS

Chaithra Prasad, MD, Gabriel Sciallis, MD, Bryan McIver, MD

Objective: To illustrate an uncommon presentation of autoimmune thyroiditis and highlight the importance of a thorough clinical evaluation into the etiology of skin conditions not responsive to common therapies.

Introduction: Hypothyroidism is a common disorder that can have an array of systemic effects. A variety of skin findings have been described with hypothyroidism but palmoplantar keratoderma is rare and completely reversible with thyroid hormone replacement.

Case Presentation: A 66-year-old gentleman presented for evaluation of a 1-year history of profound skin dryness with painful fissures as well as crusting and darkening of the palms, forearms, and soles of his feet. He had no improvement with an array of moisturizers and creams. A dermatologist had diagnosed palmoplantar keratoderma but the patient had no relief with 40% urea or antifungal creams. On further questioning, the patient admitted to a slew of progressive symptoms including profound fatigue, anhedonia, slowed speech and movements, somnolence, cold intolerance, 20-lb weight gain, constipation, and hair thinning/loss. The examination was striking for a dull, expressionless man with puffy eyelids. He had severely dry, pale skin with hyperkeratotic palms and soles. Mentation, speech, and reflexes were slowed. Labs showed a normocytic normochromic anemia and high cholesterol; infectious/autoimmune testing was negative; TSH was 236 mIU/L, T4 0.2 ng/dL, and TPO 851.9 IU/L. After 6 months of thyroid hormone replacement, the patient had gone from a man with profound psychomotor retardation to an animated and jovial man. He had complete resolution of his skin and systemic complaints. His anemia and hyperlipidemia also resolved.

Discussion: Thyroxine is a pleiotropic hormone not only important for energy and mood but also for an array of physiologic processes, including hematopoiesis, lipid metabolism, intestinal motility, and skin functioning. Common cutaneous findings in hypothyroidism include dry skin, myxedema, and carotenodermia. Rarely, hypothyroidism is associated with palmoplantar keratoderma, characterized by abnormal thickening of the palms and soles that is unresponsive to moisturizers, topical corticosteroids, and even keratolytics. The systemic complaints of this patient had initially been inappropriately dismissed and were actually instrumental in the diagnosis and treatment of a patient whose initial complaint was a skin problem.

Conclusion: This case illustrates the importance of thyroid hormone not only in metabolism but also other areas such as skin physiology. The endocrinologist should be aware of uncommon presentations of autoimmune thyroiditis.

Abstract #1071

GRAVES’ OR THYROIDITIS THYROTOXICOSIS: ETIOLOGIC MYSTERY SOLVED BY ULTRASOUND

Mala Ramnaraine, MD, Amit Seth, MD, Carla M Romero, MD, Maria Bouzouki, MD, Adrienne M Fleckman, MD

Objective: To present a case in which thyroid ultrasound clarified the etiology of thyrotoxicosis.

Case Presentation: A 66-year-old man with bipolar disorder on lithium, cardiovascular disease, COPD and hypertension presented with 4 days of acute delirium. He had cough and diarrhea for one week. On exam, he
was tachycardic to 110, febrile (100.9 F), oriented to person only, agitated, tremulous, hyper-refexive, and had a normal thyroid exam. Lithium level was 1.9 mEq/L (normal, 0.6-1.2), WBC 14,400/mm³, TSH 0.01 mU/L, free T4 (FT4) 5.4 ng/dL, total T4 13.3 ug/dL, T3 285 ng/dL. Lithium was held and empiric antibiotics begun. He was started on potassium iodide (KI), methimazole and propranolol for possible thyroid storm. Initially unable to undergo thyroid imaging due to severe agitation, one week after admission he was finally able to have a technetium99 (Tc99) scan. Heterogeneous uptake was interpreted as consistent with either a toxic multi-nodular goiter or a solitary hot nodule. TPO 200 IU/mL and TSI antibodies 156% were elevated. Radioactive iodine (RAI) scan done 3 days after KI was discontinued showed decreased tracer uptake as expected. Subsequent thyroid ultrasound (US) showed no discrete nodules, no increased vascularity of the thyroid parenchyma on color Doppler, and only slight vascular flow in a patchy hypoechoic area in the right lobe; findings most consistent with thyroiditis. Methimazole and propranolol were tapered as FT4 and T3 decreased. Mental status slowly improved after several weeks.

**Discussion:** Following a diagnosis of thyrotoxicosis, RAI uptake and scan usually help determine the underlying cause. Reports of lithium associated thyrotoxicosis implicate both Graves’ and silent thyroiditis as etiologies. Diagnosis in our case was confounded by the delay in scanning due to severe agitation, requiring administration of KI prior to RAI scan; and by conflicting Tc99, serologic and US results. Since Tc99 may inaccurately characterize thyroid function, TPO is non-specific and TSI has been reported to be elevated in up to 15% of patients with silent thyroiditis, we feel that a diagnosis of thyroiditis, supported by the US findings, is most likely.

**Conclusion:** Thyrotoxic patients frequently have contrast studies compromising uptake and rendering RAI inaccurate. Tc99 is known to demonstrate enhanced uptake in nodules that are functionally “cold”. An increasing number of studies suggest that thyroid ultrasound may be an important tool to determine the etiology and guide treatment in complicated thyrotoxicosis cases.

**Abstract #1072**

**UNUSUAL CASE OF ANCA-NEGATIVE VASCULITIS DUE TO METHIMAZOLE**

Richard W. Pinsker, MD, FACE, Abhay Vakil, MD, Prakashkumar Patel, MD, Farshad Bagheri, MD, Kelly Cervellione, MA, MPh, ABD

**Objective:** To report an interesting case of ANCA-negative vasculitis in a patient being treated with methimazole for Graves’ disease.

**Case Presentation:** A 50-year-old female with a history of diabetes mellitus type 2, hypertension, CAD, ischemic cardiomyopathy and Graves’ disease presented to ER with progressively worsening fatigue, lightheadedness and weakness for four days. She reported swelling and tenderness on the left wrist and multiple proximal interphalangeal joints. She had a hemorrhagic purpuric rash and blisters over both forearms and legs. She denied weight loss, hemoptysis, hematuria or fever. Urine analysis showed microscopic hematuria and pyuria with 15-20 erythrocytes, 80-90 leukocytes and nephrotic range proteinuria. Upon admission, creatinine increased from 1.3 to 4.5 with hyperkalemia and high anion gap metabolic acidosis. Patient was dialyzed and methimazole was discontinued due to suspected vasculitis. She was then started on prednisone 40 mg daily. Further laboratory studies revealed ESR=118 and C-reactive protein=27. ANA, myeloperoxidase (MPO) and proteinase-3 antineutrophilic anticytoplasmic antibodies (ANCA) were all negative. She responded to steroid treatment and the rash resolved in four days before skin biopsy could be completed. After one week creatinine returned to baseline, hemodialysis was discontinued, and steroids were tapered off. Patient was scheduled for treatment with radioactive iodine.

**Discussion:** Vasculitis is a possible toxic side effect of antithyroid drugs. The incidence of vasculitis from these drugs is very low. Most of the previously reported cases of patients with Graves’ disease on antithyroid drugs developing vasculitis were ANCA positive. Methimazole is known to accumulate in neutrophils and bind and alter MPO antigen. This leads to formation of anti antibodies in susceptible individuals. The reason for absence of ANCA positivity in our patient is unknown. One case with ANCA negative vasculitis has been reported in a patient with amiodarone-induced thyrotoxicosis treated with methimazole.

**Conclusion:** Vasculitis should be suspected in any patient on antithyroid drugs presenting with fever, rash, weight loss, joint pain, hemoptysis or hematuria. Most patients respond to early withdrawal of antithyroid medication and long term prognosis is good. If untreated, worsening renal failure requiring hemodialysis or pulmonary involvement may result. Very few patients require immunosuppressive therapy with steroids or cyclophosphamide. Early recognition and withdrawal of antithyroid medication is critical.
Abstract #1073

A CASE OF FAMILIAL DYSALBUMINEMIC HYPERTHYROIDOXINEMIA (FDH) - A SYNDROME THAT CAN BE CONFUSED WITH HYPERTHYROIDISM

Gauri Dhir, MD, Elias S. Siraj, MD

Objective: Many conditions result in increases in serum total T4 (TT4) and/or T3 (TT3) but little change in serum free T4 (FT4) and/or free T3 (FT3). Familial Dysalbuminemic Hyperthyroxinemia (FDH) is one such condition which is often confused with hyperthyroidism. To highlight the significance of this condition, we present a case of FDH that was misdiagnosed and treated for hyperthyroidism.

Case Presentation: A 50-year-old African American female with history of anxiety, fibromyalgia, and hepatitis C presented to her internist with complaints of worsening anxiety, sweating, and palpitations. Laboratory tests showed a TSH of 0.22 mIU/L (NL: 0.4-4.5), TT4 of 14.4 mcg/dl (NL: 4.5-12.5), FT4 of 1.1 ng/dl (NL: 0.8-1.8), T3 Uptake of 22% (NL: 22-34), and TT3 of 163 ng/dl (NL: 76-181). Her 24 hour RAI uptake was 23% and scan showed diffusely enlarged gland. With the impression of hyperthyroidism, she was treated with methimazole followed by RAI treatment. On the 4th day following RAI treatment she presented to the emergency room with severe neck pain/swelling, palpitations and sweating. Subsequently, she was referred to us for further management. We made a diagnosis of radiation thyroiditis and moderate hyperthyroidism. This necessitated management with prednisone which led to resolution of her local symptoms. Ultimately the patient developed postablative hypothyroidism requiring LT4 replacement. Careful review of all her previous thyroid tests revealed that all along, the patient had high TT4 but normal TT3 and FT4. Her TSH was also slightly low.

Discussion: We believe that the patient has FDH, which led to a misleading diagnosis of hyperthyroidism and subsequent treatment with RAI. This is an autosomal dominant condition, whereby mutant albumin molecules have low affinity but high capacity for T4 while maintaining normal behavior to T3. This leads to a high TT4 (but normal TT3) levels, but FT4 as well as TSH levels are generally normal, indicating an essentially euthyroid state. In contrast, in patients with TBG excess, both TT4 and TT3 are elevated where as both FT4 and FT3 are normal. The slightly low TSH levels in our patient may indicate an independent subclinical hyperthyroidism which is relatively common in our population of patients with goiter. Although FDH is harmless, the mistaken diagnosis of thyrotoxicosis is not. Patients with FDH commonly undergo unnecessary diagnostic and therapeutic procedures, including thyroid ablation.

Conclusion: Elevated TT4 level not accompanied by elevated FT4 (and FT3) levels does not always indicate hyperthyroidism and should prompt some one to look for causes of euthyroid hyperthyroxinemia, which include FDH.

Abstract #1074

TRANSTHORACIC ECHOCARDIOGRAM: AN IMPORTANT EARLY DIAGNOSTIC TOOL IN THYROID STORM

Gregory Dodell, MD, Eitan Klein, MD, Jeanine B. Albu, MD

Objective: Thyroid storm is a well known endocrine emergency that requires early diagnosis and prompt treatment. If unrecognized and untreated, thyroid storm can be fatal with mortality as high as 10-20%. Cardiovascular consequences of thyrotoxicosis such as congestive heart failure (CHF) and atrial fibrillation (AFIB) require additional attention in the setting of thyroid storm.

Case Presentation: The endocrine team was consulted for a 32-year-old male with a history of hyperthyroidism who was admitted one day prior with substernal chest pain and worsening shortness of breath. The patient was diagnosed with hyperthyroidism by his internist 6 months previously but had not taken the prescribed methimazole 30 mg daily for the last 5 months due to gastrointestinal side effects. At admission the patient was in AFIB with rapid ventricular response (RVR). On the initial exam by the endocrine service the patient was diaphoretic, anxious and complained of abdominal pain. On the Burch and Wartofsky diagnostic criteria scale for thyroid storm, the calculated value was 45, highly suggestive of storm. Based on the AFIB with RVR and physical exam findings consistent with CHF, the patient was immediately screened for the cardiac care unit (CCU). An urgent transthoracic echocardiogram (TTE) demonstrated an ejection fraction (EF) of 5-10% with a severely dilated and hypokinetic left ventricle. In the CCU, the patient was started on an esmolol drip for rate control, lovenox 120 mg Q12h and propylthiouracil 200 mg PO Q6h. The thyroid function tests results were consistent with the clinical diagnosis: TSH <0.03 mU/l, T4 free 2.3 pg/dl (0.7-1.7) and T3 free 6.8 pg/dl (2.3-4.2). Throughout the hospital course, the patient improved both clinically and biochemically. As an outpatient, he underwent radioactive iodine treatment and due to persistent and symptomatic AFIB he was cardioverted. The last EF was 25% and clinically he remains without signs or symptoms of heart failure or hyperthyroidism.
Discussion: As demonstrated in this case, the cardiovascular effects of hypothyroidism can be life threatening. A TTE done early in the management of this patient prevented a potentially worse outcome. Based on the diagnosis, metoprolol was used in place of propranolol because of the known mortality benefits in CHF. Additionally, the patient was started on an ACE inhibitor, an important medication for heart failure management.

Conclusion: In the setting of thyroid storm, which is a known risk factor for decompensated CHF, a prompt TTE will guide management and potentially improve outcomes.

Abstract #1075

ACUTE HYPOTHYROIDISM PRESENTING WITH MYOPATHY FOLLOWING RADIOIODINE THERAPY FOR GRAVES’ DISEASE

Esti Charlap, MD, Amit Seth, MD, Anastasios Manessis, MD

Objective: To report a case of acute hypothyroidism that presented with myopathy following radioiodine therapy for treatment of Graves’ disease.

Case Presentation: A 52-year-old woman with a history of Graves’ disease that was treated with radioiodine therapy six months earlier was admitted to the hospital with severe diffuse proximal muscle pain for 1 month. Pain was more pronounced in both hips and shoulders, and aggravated by lifting objects and walking uphill. Associated symptoms included fatigue, depressed mood, 20 lb. weight gain, and upper and lower extremity swelling. No history of recent trauma, falls or immobilization. She was not taking any medications. Prior to admission, evaluation by rheumatology revealed normal SS-A, SS-B, Anti-Smith antibody, rheumatoid factor, and C - reactive protein. On physical exam she was noted to have mild peri-orbital edema, and bilateral trace edema of her upper and lower extremities. Patient had a delayed relaxation phase of knee tendon reflexes. Muscular exam revealed 4+ bilateral lower extremity muscle strength. Exam was otherwise normal. On admission, the patient was found to have a CPK of 3887 U/L (normal 30-135 U/L), AST of 100 U/L (normal 15-46), and ALT of 90 U/L (normal 13-69 U/L). Creatinine increased from a baseline of 0.67 mg/dl to 1.19 mg/dl (normal 0.52 – 1.04 mg/dl). Electrolytes were normal. There was no evidence of myoglobinuria. Thyroid function tests showed a TSH of 77.53 mU/L (normal 0.55-4.78 mU/L), free T4 of 0.2 ng/dl (normal 0.7-1.7 ng/dl), and T3 of <59 ng/dl (normal 60-180 ng/dl). EKG showed sinus rhythm with normal voltage, and no evidence of ischemia. Aggressive intravenous hydration with normal saline was initiated, and patient was started on levothyroxine 100mcg daily. Muscle pain and weakness improved after 1 week of treatment. Patient reported a significant reduction in pain at discharge, with complete resolution one month later.

Discussion: In this case, rheumatological and neurological evaluation did not reveal a specific cause of this patient’s myopathy. The patient’s abnormal thyroid function, previous history of radioiodine ablation, and associated signs and symptoms of hypothyroidism suggest acute hypothyroidism as the specific cause of her myopathy.

Conclusion: Acute hypothyroidism can be associated with myopathy and rhabdomyolysis, which can resolve after adequate treatment with levothyroxine. This report emphasizes the importance of assessing thyroid function in patients presenting with myopathy and rhabdomyolysis following radioiodine therapy for Graves’ disease.

Abstract #1076

LINGUAL THYROID-TO KEEP, OR NOT TO KEEP

Adina F. Turcu, MD, Diana S. Dean, MD

Objective: Lingual thyroid is a rare embryological anomaly; there is no consensus on its management. Our scope is to determine advantages and pitfalls of the available treatment options.

Methods: A retrospective review of lingual thyroid cases seen at Mayo Clinic Rochester, MN between 1976 and 2010 was performed. Demographics, clinical presentation, imaging, laboratory, operative, and pathology results were reviewed. Results are reported using descriptive statistics.

Results: 30 cases of lingual thyroid were included in our review. Age of presentation varied widely (2 weeks to 74 years old); 83% were females. Many were diagnosed incidentally, on routine exam, during evaluation for upper respiratory infections or tonsillectomy. In those symptomatic (~1/3), cough and hoarseness were the commonest complaints; one had severe obstructive sleep apnea from a 7 cm thyroid gland. None had orthotopic thyroid tissue present. 18 of 23 (78%) cases in which thyroid function assessment was available to us, eventually became hypothyroid. None developed thyroid cancer. 6 patients underwent thyroidectomy, 2 radioactive iodine ablation, 2 observation and 20 received thyroid hormone treatment. Of surgically treated patients, one had significant difficulty swallowing post Da Vinci transoral thyroidectomy, and tongue base mucosal bleeding, requiring cauterization. All underwent intubation for airway protection and one received a temporary tracheotomy. One patient developed hyperthyroidism while on thyroid hormones, and gland enlargement when off treatment. Two others reported palpitations and anxiety, respectively, while on
levothyroxine, despite documentation of normal thyroid function tests.

**Discussion:** Lingual thyroid results from complete failure of the gland to descend from the foramen caecum to its orthotopic pre-laryngeal site. It may cause local symptoms. Up to 80% of patients may have hypothyroidism. Carcinoma arising in a lingual thyroid is rare. Management of lingual thyroid has been controversial. No treatment is required when the lingual thyroid is asymptomatic and the patient is euthyroid. For patients with mild clinical symptoms and elevated TSH, substitutive therapy with thyroid hormone is most often successful. Ablative radioiodine therapy is an alternative approach, recommended in patients unfit for surgery. In severely symptomatic cases, surgery is the treatment of choice, but not devoid of complications.

**Conclusion:** Most lingual thyroid cases are manageable with conservative measures. Treatment should be individualized and options reconsidered when needed.

**Abstract #1077**

**SEVERE HYPOTHYROIDISM TRIGGERS STATIN-INDUCED RHABDOMYOLYSIS**

Mohammad Hammoude, MD, Nandalal Bagchi, MD, PhD

**Objective:** To report a case of statin-induced rhabdomyolysis as a rare, life-threatening complication of severe hypothyroidism.

**Case Presentation:** A 65-year-old lady presented with a six week history of progressive myalgia, most severe in the lower back and lower extremities, with no recent trauma, fall or strenuous physical activity. She had a history of chronic kidney disease stage III secondary to hypertension, hypothyroidism due to Hashimoto’s thyroiditis and dyslipidemia. The patient was taking Levothyroxine 100 mcg daily for the last four years and Simvastatin 20 mg daily started two years ago. Review of systems was unremarkable. She was clinically euthyroid with no goiter. Musculoskeletal examination was negative for tenderness, weakness and atrophy. Initial investigations revealed TSH 65 (0.5-5 mLU/L), creatinine 2.2 (baseline 1.5 mg/dL) and creatine kinase 4463 (25-240 U/L). A provisional diagnosis of rhabdomyolysis was made. Consequently Simvastatin was stopped and the patient was admitted to the hospital for aggressive hydration. Levothyroxine was eventually titrated up to 150 mcg daily. After 8 weeks treatment with thyroxine her muscle pain improved and repeat blood test showed TSH 0.09 mLU/L, free T4 1.7 (0.8 – 1.8 ng/dL) and CK 77 U/L.

**Discussion:** Overt hypothyroidism is a very common endocrine disorder affecting approximately 1-2% of the general population in the United States. The clinical presentation is highly variable and depends on the age at presentation, duration and severity of the disease. Musculoskeletal symptoms are frequent in the hypothyroid patient. Myopathy is usually limited to asymptomatic elevation of serum creatinine phosphokinase, cramps and proximal muscle weakness. Rhabdomyolysis, however, is very rare and only a few cases were reported in the literature. Severe hypothyroidism also could exacerbate statin myotoxicity and trigger rhabdomyolysis. The exact mechanism is unclear but both impaired glycogenolysis and impaired mitochondrial oxidative metabolism had been implicated. Vigorous hydration with isotonic crystalloid is the cornerstone of therapy for rhabdomyolysis, and any underlying condition should be corrected. An awareness of this rare complication of overt hypothyroidism may prevent misdiagnosis and ensure effective therapy.

**Conclusion:** This case highlights the importance of monitoring thyroid function tests and serum creatine kinase in hypothyroid patients who use statins as a treatment for dyslipidemia, especially when they develop musculoskeletal complaints.

**Abstract #1078**

**SURVIVAL AND PROGNOSIS OF A CASE OF PAPILLARY THYROID CANCER**

Harkesh Arora, MBBS, David C. Lieb, MD, Joseph A. Aloii, MD

**Objective:** To describe a case of Stage IV Papillary Thyroid Cancer in a patient with Graves’ disease.

**Case Presentation:** A 49-year-old woman presented to the hospital 10 years ago with chest pain, palpitations, shortness of breath, bulging eyes, and was found to be in thyroid storm complicated by cardiomyopathy (EF= 25%), pleural effusions and atrial fibrillation. She was found to have Graves’ disease with TSI of 370% (0-139%). She was treated with beta blockers and a thionamide but continued to deteriorate. A total thyroidectomy was performed. She experienced a protracted post-operative period. Pathology of the thyroid gland revealed stage-II, 3.2 cm right thyroid well-differentiated follicular variant of papillary thyroid cancer. Two months following surgery an I-123 scan showed foci of residual tissue in the right neck with perithyroidal lymph node and widespread pulmonary metastasis. A total of four doses of I-131(156 mCi each) were given over the next year. Thyroglobulin (TG) levels following withdrawal of levothyroxine therapy after each treatment demonstrated a downtrend. Following the fourth treatment diffuse bilateral lung uptake persisted and she was then lost to follow up. 8 years later she developed seizures. She was on 200 mcg of levothyroxine with a TSH of 0.24 mcU/mL(0.27-4.20 mcU/mL) and free T4 of 1.9 ng/dL (0.9-1.8 ng/dL). A right
Thyroid Disease

frontal lobe mass measuring 2.1 cm x 2.6 cm x 1.7 cm with midline shift and another mass in right paramedical occipital lobe were found on brain imaging. Phenytoin and dexamethasone were started and right frontal craniotomy was performed. Pathology revealed the frontal mass to be metastatic thyroid carcinoma. Pre and post surgery TG concentrations were 8.7 ng/mL and 3.8 ng/mL (0.5-55.0 ng/mL) respectively. Post-operative PET/CT showed low level metabolic activity localizing to left coracoclavicular joint and no other abnormal hypermetabolic activity. Whole brain radiation therapy (3500 CGy) and another dose of I-131 (100 mCi) were given. Post- I-131 scan showed intense uptake to the right parietal brain (7mm) and diffuse uptake in lung. The difference in the two studies could not be explained. Follow up whole body MRI approximately 4 months later showed postsurgical changes in the brain and continued diffuse lesions in the lungs.

Discussion: Thyroid cancer is an unusual finding in patient with Graves’ disease. Literature search suggests an incidence between 0.3%-16%. Patients who develop brain metastasis from differentiated thyroid cancer (DTC) tend to have characteristics of aggressive disease at initial presentation- older age, extrathyroidal spread, locoregional and/or distant metastasis. Patients with distant metastasis of DTC, either at initial presentation or later have a higher disease-specific mortality. This is particularly true for patients who develop brain metastasis (about 1%). Median survival after diagnosis of brain metastasis is typically less than one year (4.7 months). Surgical resection of one or more brain metastasis has been shown to improve the survival by 3 fold.

Abstract #1079

A TALE OF TWO TREMORS
Jon Holland Steuernagle, MD, Diana Dean, MD

Objective: In this case we report new Graves Hyperthyroidism superimposed on a preexisting benign (senile) tremor.

Case Presentation: The patient is a 67-year-old with a multiple year history of essential tremor that was poorly tolerated with regard to activities of daily living. It was so poorly tolerated, in fact, that the patient had a deep brain stimulator (DBS) inserted in 2008. TSH check in 2008 was normal at 1.9, prior to DBS implant. She had done well for a period of approximately 2 years. However, the patient noted increasing fine tremor over the previous 6 months before being seen. Multiple adjustments were made to the DBS with no improvement in the tremor.

Previously her deep brain stimulator was controlling her tremor 100%, but in the several months prior seeing us she noticed her fine tremors started to take over the ability of her deep brain stimulator to control it. From a cardiovascular standpoint, there was no difficulty with palpitations or tachycardia. However, she started noticing fatigue, dyspnea after one flight of stairs, unintentional weight loss, and poor energy levels, overall. Initial studies showed a T4 level of 2.7. Repeat study showed T4 at 2.5. TSH was persistently suppressed at undetectable levels, less than 0.01, and repeat studies confirmed undetectable levels at less than 0.01. Upon repeat the total T4 was 10.2, TSI 4.3. Her physical exam was remarkable for an enlarged thyroid gland (estimated at 30 grams), hyperreflexia noted in all extremities and a fine tremor bilaterally. There was no Graves ophthalmopathy or dermopathy noted. The patient was treated with 13 mCi of radioiodine. At follow-up her labs were T4 0.4, TSH 18.6. Her fine tremor was completely resolved. She was started on 100 mcg levothyroxine, daily. To date she continues to do well with no reemergence of tremor.

Abstract #1080

CASE OF THYROID AUTOANTIBODIES ASSOCIATED WITH THYMIC MASS
Mohammad Kawji, MD, Irina Ciubotaru, MD, Tahira Yasmeen, MD, FACE, Farah Hasan, MD, FRCP, FACE, FACP

Objective: The correlation between thymic hyperplasia and subclinical hyperthyroidism in asymptomatic patients.

Case Presentation: A 27-year-old caucasian female who presented to outpatient clinic for management of abnormal thyroid function tests prior to thymectomy. The patient has a history of anterior mediastinal mass, which doubled in size on a recent CT of the chest. She has a history of pulmonary embolism 15 months ago while on oral contraceptives which was treated with anticoagulation for 6 months. A year prior she was worked up for intermittent chest pain and because of her history of pulmonary embolism a CT of the chest was done. It revealed an anterior mediastinal mass of 2.3x0.7x2.5 cm. She denied any compressive symptoms related to the mass. On physical exam, thyroid was palpable and estimated to be 20 grams in size, without any nodules or bruits. Her TSH was < 0.01, free T4 was 1, free T3 was 3.2, these labs were suggestive of subclinical hyperthyroidism. A radionuclide thyroid scan was also performed and showed homogenous distribution of radiotracer within the thyroid.
gland. Thyroid uptake values at 5 and 24 hours were 20.4 and 40.6%, respectively, indicating a hyperthyroid state. Immunological studies showed elevated antithyroglobulin antibody level to 403 (reference range 0-40 IU/ml), TSH receptor antibodies to 14% (reference range < 9%) and thyroid stimulating immunoglobulin’s antibodies to 135% (reference range less than 109%). Her PTH and calcium were all within normal level. She was started on Methimazole before median sternotomy and thymectomy to avoid any worsening of hyperthyroidism. Pathology showed thymic lymphoid hyperplasia.

**Discussion:** The correlation between Graves’ disease and thymic hyperplasia has been described in the literature. Thymic enlargement may be asymptomatic or may cause compression symptoms like pain or dysphagia. The current guidelines recommend treating underlying hyperthyroidism and watching the thymic mass before performing thymectomy. It has been suggested that human thymus expresses TSH receptors. In Graves’ disease anti-TSH receptor antibodies are elevated which can stimulate the growth of thymic tissue. To our knowledge this is one of the few cases reporting the association between an evolving thymic mass before diagnosing Graves’ disease.

**Conclusion:** Thymic hyperplasia has been associated with Graves’ disease and it has been reported that treatment of hyperthyroidism leads to involution of the thymic process. On the other hand, It has also been shown that resection of the thymic mass may improve thyroid function.

**Abstract #1081**

**ULTRASOUND-GUIDED VERSUS PALPATION-GUIDED FINE-NEEDLE ASPIRATION BIOPSIES FOR EVALUATION OF THYROID NODULES: A SYSTEMATIC REVIEW**

Netee Papneja, MB, BCH, BAO (HONS), Ally Prebtani, MD

**Objective:** To perform a systematic review of the literature to identify and summarize all observational studies and randomized controlled trials (RCTs) which have compared the rates of inadequate material and diagnostic accuracy of ultrasound guided FNA (USGFNA) with palpation guided FNA (PGFNA) for the evaluation of nodular thyroid disease.

**Methods:** We reviewed the literature for all English language publications from 1950-November 2010 in Pubmed, EMBASE, MEDLINE, and Cochrane database. Trials comparing the rates of inadequate material and diagnostic accuracy of USGFNA with PGFNA in evaluating thyroid nodules of 1 cm or larger were included. We excluded trials that reported on USGFNA only in selected patients (e.g. nonpalpable nodules or unsuccessful PGFNA). Data extraction was carried out by first reviewer and verified by a second reviewer.

**Results:** One small RCT and four observational trials were identified comparing the rates of inadequate material and diagnostic accuracy of USGFNA with PGFNA for the management of palpable thyroid nodules. The rate of inadequate cytology material for USGFNA varied from 7.1%-29% and for PGFNA was 11.2%-50%. Inadequate material rate was significantly lower in USGFNA compared to PGFNA for all palpable nodules in two studies and for only smaller nodules in two other studies. The diagnostic accuracy varied from 60.9%-88.5% for USGFNA and 48%-80% for PGFNA in four studies and was reported to be significantly higher for USGFNA than PGFNA in one study. Six observational trials were identified comparing USGFNA with PGFNA for the evaluation of all palpable and non-palpable thyroid nodules. One study reported higher rate of a nondiagnostic aspirate in USGFNA(23%) compared to PGFNA(14%). In the remaining studies, the inadequate rate for USGFNA was significantly lower and varied from 3.5%-12.5% versus 8.7%-27.2% for PGFNA. The diagnostic accuracy of both methods were only reported in two studies and varied from 75.9%-94% for USGFNA and 72.6%-88% for PGFNA.

**Discussion:** There is a great deal of heterogeneity in studies comparing USGFNA versus PGFNA for thyroid nodular disease. There is a lack of high-quality data comparing the diagnostic accuracy of USGFNA with PGFNA for evaluation of nodular thyroid disease raising the need for large scale RCT’s prior to recommending universal application of ultrasound guidance for thyroid FNA.

**Conclusion:** Observational studies demonstrate that USGFNA is superior to PGFNA for obtaining adequate cytological material for palpable and non-palpable thyroid nodules.

**Abstract #1082**

**TALL CELL VARIANT OF PAPILLARY THYROID CANCER ASSOCIATED WITH NEGATIVE FINDINGS ON WHOLE BODY I-123 SCAN**

Mohammed Ahmed, MD, FACP, FACE, Abdul Raof Al-Mahfouz, MD, Hindi Al-Hindi, MD

**Objective:** The Tall cell variant (TCV) of papillary thyroid carcinoma (PTC) is the most common among aggressive variants and most aggressive of all variants. PTC associated with negative findings on I 123 whole body scan (DX WBS) but detectable thyroglobulin
(Tg) carries poor prognosis. What is the impact of TCV associated with negative DX WBS? We present 2 such cases to indicate that with this combination both patients developed brain and disseminated metastases that eventuated in their demise.

**Case Presentation:** A 72-year-old man underwent thyroidectomy for 8.5 cm PTC (TCV), but declined I 131 RX. A year later he developed 3.5 cm tumor recurrence with bilateral lung metastases and refused 2nd neck surgery, but accepted I 131 Rx (200 mCi.) for Tg positive and scan negative findings. A year later he presented with dysphagia, 30 kg wt. loss & headaches. W/U: thyroid tumor extended into mediastinum involving esophagus, larynx, pharynx, mediastinum, with progression of lung mets. and a large brain (left occipitoparietal) metastatic lesion. Serum unsuppressed Tg remained 3.5-9.6 ug/l, Tg abys 1189 u/ml during the entire FU period. At his late acceptance for FU thyroid resection of recurrent tumor histology showed confluent areas of TCV with transition to anaplastic carcinoma. Craniotomy done; histopathology showed brain metastatic TCV, presence of Psammoma bodies with immunostains positive for Tg and thyroid transcription factor 1. He died a month later. 

**Patient B:** A 69-year-old female underwent resection of recurrent 6x5x4 cm PTC (TCV). She had lung metastasis, negative I 123 DX WBS, unsuppressed Tg<0.1, Tg abys 748. Two years later had resection of a large rt frontoparietal brain metastases and died soon thereafter.

**Discussion:** There is limited experience defining the natural history of TCV, the impact of Rx and FU data. We have encountered 39 patients in our archival clinical/histopathological data with a Dx of TCV out of a total of 3752 thyroid cancer patients over 29-year period (1.0%). Of these, there were only 2 patients with the association of TCV and negative DX WBS who developed brain metastases in conjunction with metastases at other sites. Case A provides answer to a fundamental question regarding tumorogenesis of anaplatic carcinoma that it originates from DTC lineage rather than denovo.

**Conclusion:** TCV of PTC is associated with an aggressive course, poor prognosis, and mortality. There is a need for a nested case-controlled study between TCV versus non-TCV thyroid cancer patients with attention to findings on DXWBS. Patients with TCV and negative findings on DXWBS should be candidates for brain imaging to detect metastases in this unusual location for timely intervention.

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**Abstract #1083**

**TUBULOINTERSTITIAL NEPHRITIS WITH UVEITIS (TINU) SYNDROME PRESENTING WITH THYROIDITIS IN A YOUNG MALE**

Darren Allcock, DO, David W. Gardner, MD, FACE

**Objective:** To report an unusual case of thyrotoxicosis due to thyroiditis in a patient with tubulointerstitial nephritis with uveitis (TINU) syndrome.

**Case Presentation:** A 28-year-old white male presented with a 5-week constellation of symptoms that began while on a business trip. He reported a progressive onset of symptoms, which began two weeks into his trip with fever and night sweats. Deep cough followed. By the end of his trip, he had also developed nausea, vomiting, diarrhea, and polydypsia. The patient denied any unusual foods or contacts. By admission, he reported a weight loss of 40 pounds. High fevers and diarrhea had resolved, but low-grade fever continued. Further questioning revealed that he had begun to experience redness of his left eye with photophobia. Laboratory evaluation demonstrated renal failure, with creatinine 4.03 mg/dL (0.61-1.28 mg/dL), along with anemia and thrombocytopenia. Thyroid studies were obtained secondary to his weight loss. Hyperthyroidism was demonstrated, with TSH 0.08 milliunit/L (0.32-5.00 milliunit/L), free T4 2.77 ng/dL (0.58-1.64 ng/dL), and free T3 7.4 pg/mL (1.5-4.1 pg/mL). Thyroiditis was a strong consideration, given his symptoms. However, it is notable that his mother had a history of Graves’ disease. Thyroid uptake and scan showed 1.0% uptake at both 6 and 24-hours. Uptake was uniformly decreased, suggesting thyroiditis rather than Graves’ disease. Renal function improved somewhat with fluid administration, but did not approach his presumed normal baseline. Renal ultrasound demonstrated mild hyperechoity, suggestive of medical renal disease. Renal biopsy was performed, which gave the diagnosis of acute interstitial nephritis. With this diagnosis, more attention was given to the red eye and photophobia. Laboratory evaluation demonstrated renal failure, with creatinine 4.03 mg/dL (0.61-1.28 mg/dL), along with anemia and thrombocytopenia. Thyroid studies were obtained secondary to his weight loss. Hyperthyroidism was demonstrated, with TSH 0.08 milliunit/L (0.32-5.00 milliunit/L), free T4 2.77 ng/dL (0.58-1.64 ng/dL), and free T3 7.4 pg/mL (1.5-4.1 pg/mL). Thyroiditis was a strong consideration, given his symptoms. However, it is notable that his mother had a history of Graves’ disease. Thyroid uptake and scan showed 1.0% uptake at both 6 and 24-hours. Uptake was uniformly decreased, suggesting thyroiditis rather than Graves’ disease. Renal function improved somewhat with fluid administration, but did not approach his presumed normal baseline. Renal ultrasound demonstrated mild hyperechoity, suggestive of medical renal disease. Renal biopsy was performed, which gave the diagnosis of acute interstitial nephritis. With this diagnosis, more attention was given to the red eye and photophobia. Laboratory evaluation demonstrated uveitis. This cluster of diagnoses is consistent with TINU syndrome. In this patient, the syndrome was accompanied by thyroiditis. Outpatient follow-up at two months showed normalization of free T4 to 0.69 ng/dL. TSH remained mildly suppressed at 0.20 milliunit/L. Unfortunately, he has now been lost to follow-up.

**Discussion:** Hyperthyroidism has been reported in a few cases of TINU syndrome, but is unusual and has been reported in adolescents. Our patient had the rarely documented constellation of TINU syndrome and thyroiditis.
Objective: To report a case of a stable primary hypothyroidism turning into Graves’ disease after 40 years.

Case Presentation: A 71-year-old female was admitted to our hospital with severe hyperthyroidism and atrial fibrillation. She was originally diagnosed with Hashimoto’s disease at age 30 and Addison’s disease at age 45 and had been on levothyroxine 100mcg daily for 40 years. Three months prior to admission, she developed heat intolerance, palpitations, tremors, and increased frequency of bowel movements. Despite appropriate levothyroxine dose adjustments and eventual discontinuation, her symptoms persisted. One month prior to admission, off levothyroxine, the TSH was 0.01 mIU/L and free T4 was 2.7 ng/dL. Thyroid sonogram showed an increased blood flow consistent with Graves’ disease. Methimazole 20mg twice a day and propranolol 10mg twice a day were initiated. Two days after starting methimazole, she was admitted for atrial fibrillation in rapid ventricular response secondary to severe thyrotoxicosis. On admission, her heart rate was 132bpm, BP was 120/67 and temperature was 36.8°C. On exam, she had no exophthalmos and her thyroid was small, non-tender and without bruit. The TSH was <0.004 mIU/L and free T4 was 3.3 ng/dL. Her thyroid receptor antibody, thyroid stimulating immunoglobulin and thyroid peroxidase antibody were all elevated. The methimazole was increased to 20mg three times daily. She was discharged on high doses of a beta-blocker and calcium-channel blocker. Four weeks after discharge, she converted to sinus rhythm after 2 doses of flecainide. The methimazole dose was reduced over the following weeks as her TSH continued to rise. On methimazole 5mg daily, her TSH was 13.4 mIU/L and free T4 was 0.7 ng/dL and her dose was decreased to 2.5mg daily.

Discussion: Hashimoto’s and Grave’s diseases are two common conditions both part of the spectrum of autoimmune thyroid disease, in which there is a diversity of circulating immunoglobulins. The change from hypothyroidism to hyperthyroidism is postulated to be due to a change in the balance of circulating TSH-stimulating antibodies and TSH-blocking antibodies. The incidence of Graves’ disease following hypothyroidism from Hashimoto’s is uncommon. The case reports demonstrating this change in thyroid function show an interval that ranged from 1 to 20 years. Our case is unusual in that this is longest reported interval from diagnosis of hypothyroidism turning to Graves’s disease.

Conclusion: This case illustrates that stable primary hypothyroidism can turn into Graves’ disease after 40 years.

Abstract #1085

A CASE OF HYPERTHYROIDISM AND NEGATIVE I-123 SCINTIGRAPHY: PERSEVERANCE AND COMMON SENSE PAID OFF

Mohammed Ahmed, MD, FACP, FACE, Ahmed Al-Shehri, MD, AbdulRaof Al-Mahfouz, MD

Objective: Describe an unusual cause of hyperthyroidism (HT) but negative iodine scan.

Case Presentation: A 31-year-old single simple-minded female from poor socioeconomic background had a 3 yr hx of HT and poor compliance to anti-thyroid Rx. Patient never received iodine contrast. On examination: Severely emaciated down to skin and bones, wt: 31.4 kg, BMI 12, px. myopathy, diffuse painless/nontender thyromegaly (80 G) w/out nodules, no exophthalmus. Labs: HGB: 87 g/L, nl ESR, WBC-D & low Vitamin D 24 nmol/, Creatinine 25 umlo/L low Albumin: 22 g/L, Celiac disease W/U: negative. TSH:<0.02 mU/L F4:>73 pmol/L(RR:12-22)T3:>10.0 nmol/L(RR 1.5-3.1) thyroglobulin (TG) 60 ug/l, Anti TG/TPO abys : 390U/17 U /ml. I123 Thyroid scan: No tracer detected at 4/24 hr. US :Thyroid enlarged, no discrete nodules, increased hypervascularity. Scan #2: whole body scan failed to detect ectopic thyroid. Scan # 3 done under Endocrinologist’s supervision. Patient was detected holding I 123 capsules under the tongue. Reason: Pt had never taken any capsule in her life and admitted to spitting them at previous scans. Following an explanation she swallowed them: Results: intense, homogeneous uptake of radiotracer within the thyroid w/ uptake at 24 hrs 76%. Pt. received I 131 Rx. Thyroid-Stimulating Immunogloblobulin available post discharge, High TSI index 1.4 (nl<=1.3) confirming Grave’s disease.

Discussion: HT with negative radiiodine uptake indicates either inflammation or destruction of thyroid tissue w/ release of preformed hormone, or an extrathyroidal source of thyroid hormone. These considerations were not applicable to our pt. Indeed, we encountered usual situation wherein a simple pt did cooperate in scan procedure. Surreptitious use of thyroxine was distinctly unlikely because pt had large diffuse thyromegaly, detectable TG, Hi T3 (current formulations of thyroid meds are free of T3),
& a through/persistent personal & patients’ belongings failed to yield possession of any meds/drugs/vitamins/ antithyroid Rx etc. Excess exogenous iodine intake was not the cause. Other causes were considered and ruled out on the basis of a thorough history, exam and labs. These included: Subacute granulomatous thyroiditis, Painless thyroiditis (silent thyroiditis, lymphocytic thyroiditis), Postpartum thyroiditis, Amiodarone-related, contrast-induced, radiation thyroiditis. Ectopic HT (Struma ovarii).

Conclusion: We encountered usual situation wherein a simple-minded pt did not understand/not given adequate explanation of the iodine scintigraphy requiring pt.’s cooperation in swallowing the radioactive material. Once satisfied she complied with providing the missing information. Perseverance and common sense paid off in resolving the dilemma.

Abstract #1086

INTERFERON ALPHA-INDUCED THYROID DYSFUNCTION IN A PATIENT WITH CHRONIC HCV INFECTION

Miguel E. Pinto, MD, FACE, Jose L. Pinto, MD

Objective: To report a case of a man with chronic HCV infection that developed Graves’ disease associated with antiviral therapy with peg interferon alpha-2a and ribavirin.

Case Presentation: A 43-year-old man presented with mild history of dyspepsia and asymptomatic elevation of ALT, which was detected in a routine screening for blood donation. Further work-up showed that serology for HIV and viral hepatitis was negative. On the other hand, results for ANA and AMA antibodies were negative, and abdominal ultrasound was compatible with mild hepatic steatosis. The next step was to perform a qualitative HCV RNA PCR, which was positive for HCV genotype 1a/1b. After two months, a liver biopsy revealed an active chronic hepatitis with significant fibrosis (stage 2), and HCV viral load was over 850,000 copies/mL. Treatment was started with Peg-interferon alpha-2a 180 µg weekly plus ribavirin 1200 mg daily. After four weeks, viral load was under 25,000 copies/mL, and thyroid profile was normal. After twelve weeks of treatment, hemoglobin and leukocytes were decreased, TSH was 0.023 mIU/dL and fT4 was 3.28 ng/dL. Treatment was tapered to Peg interferon alpha-2a 135 µg weekly plus ribavirin 1000 mg daily. At week twenty-four of treatment, ALT, hemoglobin, and leukocytes were normal. The viral load was negative, however, TSH was 26 mIU/dL and fT4 was 0.43 ng/dL. The anti-TPO antibodies were positive. Antiviral treatment was continued up to 48 weeks, and levothyroxine 50 µg daily was started. In the 72 week post treatment control, TSH was suppressed and fT4 was elevated. Anti-TPO remained positive. Graves’ disease diagnosis was established, and levothyroxine was stopped.

Discussion: Thyroid dysfunction is a common side-effect of interferon-based antiviral therapy for chronic hepatitis C, which may lead to dose reduction or discontinuation of therapy. Up to 20% of patients could develop thyroid dysfunction (hypothyroidism, hyperthyroidism or both). On the other hand, ultrasound could reveal a reduction in echogenicity suggestive for a destructive process of the thyroid gland, even before changes in thyroid function. Risk factors for the development of thyroid dysfunction were age, female gender, pretreatment thyroid volume, preexisting anti-TG or anti-TPO antibodies, and viral load. Interferon-induced autoimmune thyroiditis is frequent, and it is characterized by Graves’ disease, Hashimoto’ thyroiditis or the production of thyroid autoantibodies without clinical disease. In the case of Graves’ disease, thyroid ablation with radioactive iodine or surgery is preferred. Anti-thyroid medications could aggravate liver dysfunction.

Conclusion: Antiviral therapy of HCV possibly induces de novo or exacerbates pre-existing silent thyroid dysfunction. Thyroid function tests should be monitored during and after interferon-based therapy. In the case of patients with Graves’ disease, there is a high risk of no remission after treatment is stopped.

Abstract #1087

AMIODARONE-INDUCED HYPOTHYROIDISM: A CASE REPORT

Miguel E. Pinto, MD, FACE, Jorge L. Salinas, MD, Paula M. Solorzano, MD

Objective: To report a case of a woman with amiodarone-induced hypothyroidism.

Case Presentation: A 57-year-old woman presented with an 8-months history of palpitations, hot flashes, weakness, and disturbed sleep pattern. Electrocardiographic studies showed a nonspecific tachyarrhythmia, and amiodarone 200 mg/day was started. With this treatment, palpitations were gone. After six months, patient developed fatigue, constipation, cold intolerance, and muscle weakness. Her thyroid hormones were TSH 247 mIU/dL, fT4 0.46 ng/dL, and fT3 0.68 pg/mL. Physical examination was unremarkable, and no goiter was detected. Amiodarone was discontinued, and levothyroxine 100 µg/day was started. After two weeks, levothyroxine was titrated to 150 µg/day. After eight weeks, patient was asymptomatic, and her thyroid hormones were TSH 0.90 mIU/dL and fT4 1.64 ng/dL. The anti-TPO antibodies were negative.
Toxic Nodular Ultrasound multiple small nodules and a thyroid tests were normal including TSH < 2.0. DX: Non- of goiters, thyroidectomies, but no thyroid cancer. All No prior history of thyroid disease, but family history visible in the mirror. The thyroid was enlarged right onset of difficulty swallowing and fullness in the neck

Objective

Richard B. Guttler, MD, FACP, FACE, ECNU

CYSTS

ETHANOL THYROIDITIS: LATE ONSET

Abstract #1089

THE INTRICATE RELATION BETWEEN THE THYROID GLAND AND THE LIVER IN HEALTH AND DISEASE

Theresa Adadzewa Fynn, MD, Gail Nunlee-Bland, MD, Wolali Odonkor, MD, Vijaya Ganta, MD, Rabia Cherqaoui, MD

Background/Objective: Thyroxine and triiodothyronine are essential for normal organ growth, development and function. These hormones regulate the basal metabolic rate of all cells, including hepatocytes, and thereby modulate hepatic function; the liver in turn metabolizes the thyroid hormones and regulates their systemic endocrine effects. Liver dysfunction may perturb thyroid function, since the liver modulates thyroid hormone metabolism. The aim of this presentation is to highlight this lucid association between the thyroid and the liver.
**Case Presentation:** I present a case of a fifty year old African American female with past medical history significant for partial thyroidectomy due to compressive symptoms in 1992 and congenital left bundle branch block who was admitted to the cardiology service for hypertensive urgency with chest pain. Myocardial infarction was ruled out. She had been in fairly good health prior to being admitted. Her thyroid function was monitored regularly on out patient. She admitted to hot flushes, increased sweating, headaches and palpitations for the last three days prior to coming into hospital. There however was no significant finding suggestive of thyroid disease on physical examination. The Endocrinology Consult team was contacted for abnormal thyroid function test as follows: Total T4 – 11.90mc/dl T3 Uptake – 23.1% Total T3 – 241.9ng/dl TSH – 0.78mu/ml Free Thyroxine Index – 2.618. Her urine drug screen was negative, Liver and kidney function were also normal. Assessment by the Endocrinology team was Euthyroid hyperthyroxinemia and on further evaluation the patient was diagnosed with chronic hepatitis C infection.

**Discussion:** Today when most clinicians measure serum TSH as a screening test for thyroid function, a normal serum TSH value is usually not followed by measurement of serum T4. As a result, euthyroid hyperthyroxinemia goes undetected, with no harm to the patient. The astute physician however, may be able to clinch the diagnosis of this disorder early and offer treatment to the patient.

**Conclusion:** A complex relationship exists between the thyroid gland and the liver in both health and disease. A multisystem approach to treating patients with diseases affecting the thyroid is vital to avoid missing subtle but clinically relevant abnormalities.

**Abstract #1090**

**THERAPEUTIC OUTCOME OF PATIENTS WITH PAPILLARY THYROID CANCERS IN DIFFERENT RISK GROUPS**

**Jen-Der Lin, MD, Bie-Yu Huang, MD, Tsu-Chieh Chao, MD, PhD, Kun-Ju Lin, MD, Chuen Hseuh, MD, Ngan-Ming Tsang, MD, PhD**

**Objective:** This study is to determine the therapeutic results in patients with papillary thyroid cancer (PTC) in different risk groups in one institute.

**Methods:** For the retrospectively analysis, we collected cases between 1977 and 2008; a total of 1,759 PTC patients (1,394 females and 365 males) underwent total or complete thyroidectomy with or without lymph node dissection and follow-up at Chang Gung Medical Center (CGMC) in Linkou, Taiwan. CGMC is a tertiary referral centre located in Northern Taiwan. For the cases of follicular variant of PTC did not diagnosed in pre-operative cytology or frozen section, complete thyroidectomy were performed in secondary operation. All patients had follow-up at the end of 2009 and were staged by UICC TNM criteria (6th edition). The patients were categorized as follows: TNM stage I and II as low-risk group, excluding the high-aggressive histologic pattern; TNM stage III as intermediate risk, excluding the high-aggressive histologic pattern; and stage IVa or more as high-risk group. Aggressive histologic patterns as multicentric papillary thyroid carcinoma, an insular pattern, columnar cell, tall cell, diffuse sclerosing type, and poorly differentiated components were categorized in high-risk group.

**Results:** Among 1,759, 15.1% were presented with lymph-node metastases, 4.6% with distant metastases at the time of thyroid operations. After 8.0±0.1 years follow-up, there were 73 (4.2%) patients that died of thyroid cancer. Fifty-six of 1,759 cases were categorized as high risk. Among 1,759 cases, male gender has a significantly higher percentage in the intermediate risk and high-risk groups than the female. Fifty-six of 561 high-risk patients (10.0%) died due to thyroid cancer; whereas 144 patients (25.8%) had a recurrence during the follow-up period. Lower recurrence rates of 7.8% and 18.7% developed in the low- and intermediate-risk groups, respectively. Cancer-related deaths occurred in the 0.8% of low-risk group, and 10.7% in the intermediate-risk group. The thyroid cancer-specific survival rates in the low-, intermediate-, and high-risk groups were 99.7%, 91.2%, and 91.8% at 5 years; 99.0%, 85.0%, and 87.5% at 10 years; and 97.5%, 81.0%, and 34.5% at 20 years, respectively. The recurrence-free rates for the 3 groups were 93.5%, 81.1%, and 73.9% at 5 years; 91.4%, 73.1%, and 68.6% at 10 years; and 91.4%, 73.1%, and 60.5% at 20 years, respectively.

**Discussion:** Our data show that 31.9% of patients with PTC were at high risk. Because CGMC is a tertiary referral center, this high-risk percentage may be higher than expected from Taiwan. Although classification criteria were different, these data were lower than the 51.5% advanced thyroid cancer patients reported in Italy, and close to the 27% high-risk patients using the AMES criteria at the Lahey Hitchcock Medical Center in the United States. Our data illustrate similar cancer mortality rates in the high- and intermediate-risk groups, respectively. Otherwise, cancer recurrence was different after similar total 131I therapeutic dose in high- and intermediate-risk groups. Male patients with PTC had a higher percentage in the intermediate and high-risk groups than females.
**Conclusions:** The categorization of risk groups by TNM staging for PTC patients illustrated both intermediate and high risk groups having near 10% cancer related mortality and need aggressive surgical and postoperative adjuvant therapies.

**Abstract #1091**

**AMIODARONE INDUCED THYROTOXICOSIS**

Adedayo David Adegite, MBBS, Ian Ross, MD

**Objective:** To present a case of type 2 amiodarone-induced thyrotoxicosis that was recently managed successfully in our institution.

**Case Presentation:** A 58-year-old gentleman presented with a two week history of weight loss, diarrhoea, anorexia, nausea, vomiting, palpitations, dyspnoea, heat intolerance, diaphoresis, tremulousness, irritability and polyuria. He has a background history of coronary artery disease that was complicated by left ventricular dilatation and inferoseptal aneurysm. This resulted in recurrent monomorphic ventricular tachycardia requiring ICD and amiodarone therapy. He had been on 200mg daily of amiodarone for 3 years prior to presentation. He had fine tremors and sweaty, warm and erythematous palms. He was also restless and fidgety and had global hyper-reflexia. He had a palpable, nontender and soft thyroid gland but without a bruit. He was biochemically thyrotoxic with TSH<0.01 mIU/L(0.27-4.2), fT3 32.0pmol/L(2.8-7.1), fT4>100.0pmol/L(12-22). He also had a deranged liver function test with albumin 34g/L, Alkaline phosphatase (ALP) 176u/L(40-120), gamma glutamate transerase (GGT) 458U/L(0-60), ALT 158U/L(5-45), AST 239U/L(5-40), LDH 237U/L(240-480). Hepatitis screening was negative. The Technetium uptake scan showed NO uptake, thyroid ultrasound with doppler revealed a diffusely enlarged gland with reduced flow. Thyroid auto antibodies were negative. He had been on 20mg neomercazole and 50mg atenolol daily for one week without much clinical or biochemical improvement. Neomercazole was discontinued and prednisone 40mg daily was commenced and tapered gradually over 2 months. He was subsequently maintained on 5 mg daily for 4 months. At 6 month of follow up he was asymptomatic and had gained 13kg weight. The thyroid and liver function tests had normalised with TSH 4.27mIU/L, fT3 4.6pmol/L, fT4 17.1pmol/L albumin 51g/L, ALP 74, GGT 31, ALT 17, AST 25, LDH 72.

**Conclusion:** Amiodarone could have a wide range of unpredictable effect on the thyroid gland and thyroid function. These often depend on the underlying status of the thyroid gland and the dietary iodine intake of the individual. Amiodarone - induced thyrotoxicosis (AIT) has 2 major forms which are often difficult to differentiate and treat. The type 2 AIT occurs commonly in patients with apparently normal thyroid gland. Its onset is often abrupt and unpredictable and is due to destructive thyroiditis with leaking of preformed hormones into the circulation. It often responds to corticosteroid. Careful monitoring and surveillance of patients requiring amiodarone therapy is very essential to avoid or minimise this complication of amiodarone.

**Abstract #1092**

**DIFFUSE LARGE B CELL LYMPHOMA IN THE SETTING OF HASHIMOTO’S THYROIDITIS**

Maha Jawad Abu Kishk, MD, Tahira Yasmeen, MD, Farah Hassan, MD

**Objective:** To report a rare case of diffuse large B cell lymphoma “DLBCL” in the setting of Hashimoto’s thyroiditis in a male patient.

**Case Presentation:** This is a 69-year-old Caucasian gentleman who presented with neck mass and hoarseness over a course of three weeks. Physical exam confirmed a right sided 5 cm hard and non-tender thyroid mass with no neck lymphadenopathy. Thyroid stimulating hormone TSH was elevated 13.4 (0.35-5.0), FNA was done and showed lymphocytic infiltrate consistent with Hashimoto’s thyroiditis. The diagnosis was further supported by detecting antimicrosomal and antithyroglobulin antibodies. Patient was started on levothyroxine 88 mcg daily, and then followed six weeks later with no change in the mass and resolution of hypothyroidism. On a subsequent visit few weeks later, he reported dyspnea, dysphagia, worsening hoarseness, and doubling the size of the neck mass. FNA was repeated and showed diffuse lymphocytic infiltrate consistent with Hashimoto’s thyroiditis. Computed tomography of the neck showed a doughnut effect of the thyroid mass on the trachea and esophagus with enlarged para-tracheal lymph nodes. The patient was admitted for worsening respiratory symptoms that was relieved within hours after dexamethasone 10 mg intravenously. Staging workup for Non-Hodgkin lymphoma included computed tomography of chest, abdomen and pelvis and bone marrow biopsy with no evidence of extra-thyroidal lymphoma. A non-surgical approach with chemotherapy and radiation was preferred by the patient. R-CHOP chemotherapy (rituximab, cyclophosphamide, doxorubicine, and vincristine) was started with good clinical response and shrinkage of the mass after the first cycle.

**Discussion:** Primary thyroid lymphoma is a rare malignancy that constitutes 2% of thyroid malignancies and 2% of extra-nodal non-Hodgkin’s lymphomas. Hashimotos’s thyroiditis and thyroid lymphoma occur
more often in females with 10:1 and 4:1 female to male ratio, respectively. Hashimoto’s thyroiditis increases the risk of DLBCL by 60 folds compared to patients without thyroiditis. Thyroid lymphomas are almost always Non-Hodgkin lymphoma and a rapidly enlarging thyroid mass is the key feature of DLBCL or anaplastic carcinoma. DLBCL of the thyroid compared to anaplastic carcinoma carries better prognosis and is more responsive to chemotherapy. Fine needle biopsy might be helpful in differentiating both entities as in or case, but core needle or excisional biopsy is preferred.

Conclusion: In the setting of Hashimotos thyroidists, clinicians should be very proactive in detecting primary thyroid lymphoma as a potential complication.

Abstract #1093

NORMAL TSH – CAN THE PATIENT STILL BE HYPERTHYROID?

Swapnil Khare, MD, Alok Silodia, MD, Mohammad I Arastu, MD

Objective: TSH is considered a reliable marker for thyroid function and is recommended to be the initial test. Interpretation of TSH is usually straightforward and often leads to correct diagnosis. However in certain conditions there could be discrepancy between TSH and patient’s clinical picture. One such rare condition is thyroid hormone resistance syndrome.

Case Presentation: We present a 78-year-old female with history of persistently high total T4 with normal TSH for more than 20 years. Although asymptomatic for all these years she recently developed tachycardia, heat intolerance, sweating and anxiety. Patient was not on estrogen replacement but she did receive treatment for anxiety. The working diagnosis of autosomal dominant TBG excess was made. Based on her symptoms and total T4 of 17.5, methimazole was initiated even though her TSH was normal. It is at this point that Endocrinology referral was sought because of discrepancy between clinical picture and thyroid function tests. Evaluation by Endocrinologist revealed normal pulse, normal thyroid, no exophthalmos, tremors or brisk reflexes. Family history showed similar thyroid levels in her sister, son and grandson. Further workup included thyroid ultrasound which showed inhomogeneous echogenicity. Also pituitary MRI, TBG and antithyroid antibodies were done which were normal. Methimazole was continued and thyroid functions were followed monthly. Four months later, on methimazole, her free T4 was 1.1, T3 was 294 micrograms (normal) and TSH was 30.90. Her symptoms however markedly improved. Based on this, the Endocrinologist concluded that the patient did not have TBG excess, as was thought earlier. The patient was diagnosed with central thyroid hormone resistance syndrome and was continued on methimazole.

Discussion: Hyperthyroidism with normal TSH could be secondary to TSH secreting pituitary adenoma or thyroid hormone resistance syndrome. Thyroid hormone resistance is a rare autosomal dominant disorder (1 in 45,000 live births). It is caused by either thyroid hormone receptor beta (TR beta) gene mutation or thyroid hormone transporter (MCT8) gene mutation. It is characterized by elevated circulating free hormone levels in presence of measurable serum TSH concentrations. This “inappropriate” TSH elevation contrasts with suppressed TSH in primary hyperthyroidism. It can be either generalized resistance or pituitary resistance. Clinically patients could be euthyroid, hypothyroid or rarely hyperthyroid.

Conclusion: Endocrinology referral should be sought if thyroid function results are confusing or do not match clinical picture.

Abstract #1094

HASHIMOTO’S ENCEPHALOPATHY

Sajid Khan, MD

Background: A triad of findings including acute or subacute encephalopathy, elevated anti-thyroid antibody titers and positive response to steroid therapy has been defined by some authors as a syndrome of HE. Some clinicians have further divided HE into two sub types, vasculitic type, characterized by multiple stroke like episodes and diffuse progressive type, characterized by dementia, and psychiatric symptoms. However in literature, it is still regarded by many as a chance association.

Objective: To report three patients who presented with this triad in our institution, in the setting of a negative laboratory work up except high anti-thyroid peroxidase antibody titers, in order to help define this rather rare entity and to see if these cases would lend support to the notion that HE is indeed a viable syndrome.

Case Presentation: We present three patients with the working diagnosis of Hashimoto’s encephalopathy seen recently in our hospital. All three patients had neuropsychiatric findings including altered mental status and cognitive impairment, negative laboratory workup except increased thyroid peroxidase antibody titers (144 IU/ml, 112IU/ml and 762 IU/ml) and some ischemic changes on radio-imaging of their brains. Patients in the current case series also showed positive response to steroid treatment as is often reported in literature in cases of Hashimoto’s encephalopathy.
Conclusion: Due to the paucity of specific clinical, laboratory, radiological and pathogenetic evidence of this entity, HE may be a disorder which is under-diagnosed in daily clinical practice. As noted by the cases presented in this series and in literature, once a diagnosis of HE is suspected, most patients show a fair response to treatment with steroids. This case series elucidates the need for further improvement of all criteria (clinical and ancillary testing) required in making the diagnosis of Hashimoto’s encephalopathy, a treatable disease with a fairly good prognosis.

Abstract #1095

HAIR LOSS SECONDARY TO TREATMENT OF CONGENITAL HYPOTHYROIDISM

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Objective: To describe the rare side effect of thyroxine therapy in an infant suffering from congenital athyreotic hypothyroidism.

Case Presentation: 7 month old baby girl was referred to us from pediatric colleague with complaints of hair loss following thyroxine therapy, which was initiated 3-4 week back. Patient is a product of non-consanguineous marriage, full term normal vaginal delivery at district hospital. Birth weight/length was not available. She had history of proloned jaundice, was not gaining length and failing back in milestones. Thyroid profile done at the age of 6 months 24 days revealed FT3 1.24 pg/ml (2.0 - 4.4), FT4 0.3 ng/dl (0.6-2.2), TSH 302 mIU/L (0.5-5). Antithyroid antibody titers were within normal limits (anti TPO antibody 31 IU/ml (<50), anti Thyroglobulin Ab15 IU/ml (0-35)). She was initiated with 25 mcg of thyroxine, child became little more alert. After one week of initiating thyroxine therapy the baby developed multiple patches of progressively increasing hair loss, but without loss of eyebrow and eyelashes. She was then referred to us for evaluation. TFT after 3 week of thyroxine therapy show FT3 2.74 pg/ml, FT4 0.77 ng/dl, TSH 126 mIU/L. 99mTc-Pertechnetate scan revealed non-visualization of thyroid gland in neck or elsewhere. Salivary or oral activity was normally visualised. After this dose was stepped upto 50 mcg and reviewed after 3 weeks. On examination (at age 8 & half months) patient is more alert, sitting without support, better recognition of environment, trying to crawl, T3 1.74,T4 12.0,TSH 9.0. Her hair regrowth started. Dose was increased to 62.5 mcg/day. Stands without support and attempts to walk, vocalisation started. Hair density further improved. FT3 2.66pg/ml, FT4 1.34ng/dl, TSH 3.2mIU/L.

Discussion: This patient developed a rare side effect of marked patchy hair loss after thyroxine therapy in an athyreotic congenital hypothyroidism which regrew completely over a period of 5 months with continued therapy.

Abstract #1096

PSYCHIATRIC ILLNESS COMPLICATING THE TREATMENT OF A THYROID TOXIC PATIENT

Crystal Ann Jacovino, DO, Douglas Schwartz, DO

Objective: To report a case of thyrotoxicosis whose treatment was complicated by schizophrenia, Protein C deficiency, HIV, and polysubstance abuse.

Case Presentation: This is a 40-year-old AA female with a history of HIV, CHF, Protein C deficiency with PE, and substance abuse. At each ER visit, the patient complained of chest pain and shortness of breath. She received CT Scans with iodinated contrast to rule out pulmonary embolism during these visits. The patient was placed on PTU and Warfarin. The patient had a previous thyroid ultrasound which showed a 3.2 cm mass in the right lobe with FNA showing clusters of follicular cells with scant colloid, and an iodine uptake with 544mCi of I-123 showed uptake of 79.4% in the right gland with suppression of the left lobe leading to the conclusion of an autonomous right toxic thyroid nodule. Now, the patient noted pleuritic chest pain with SOB, palpitations, psychosis, and suicidal ideation. The patient stated she was living on the street and did cocaine daily. She had not taken her PTU or Warfarin since her last hospital discharge one month prior. On physical exam, the patient was found to be febrile with tachycardia and tachypnea. TSH of 0.008 and UDS positive for cocaine was noted. The patient had a Burch-Wartofsky score of greater than 45 and was treated for thyroid storm with propranolol,
PTU, and steroids. The patient was found to be a poor candidate for thyroidectomy secondary to her frequency thyroid storm, medication non-compliance and active cocaine abuse. Radio iodine ablation could not be done in her hospitalization as she received multiple doses of iodinated contrast to evaluate for pulmonary embolus.

Discussion: The work of Dunlap and Moersch has shown the psychiatric manifestations associated with hyperthyroidism. Additionally, the adrenergic effect of cocaine on the psychiatric state is well known. There has been little demonstrating how the effects of these illnesses effect follow up and treatment in these patients with multiple comorbidities. The patient’s delirium and her illness compliment each other, presenting an unusual Catch-22 for the Endocrinologist.

Conclusion: Psychiatry saw the patient after the acute illness was over, and, though they believed that the patient was decompensated in her schizophrenia, they did not believe the patient lacked capacity. We were not able to commit involuntarily. Knowing the patient would not follow up, she was discharged on PTU, propranolol, and risperidone.

Abstract #1097

CARDIOVASCULAR COLLAPSE ASSOCIATED WITH BETA BLOCKADE IN SEVERE THYROTOXICOSIS

Tariq Abdulrahman Nasser, MD, Ammar Saati, MD, Dala Mehammadi, MD, Abdullah Karawagh, MD

Objective: We describe a patient who developed cardiovascular collapse after the administration of Beta-blocker.

Case Presentation: A 27-year-old Saudi lady presented to the ER complaining of sore throat, fever, palpitation and diarrhea for 1 day. Her initial vital signs were as follows: temperature was 38.3°C, heart rate was 102 beats/min, and blood pressure was 132/34 mmHg. Her respiratory rate was 22/ min and pulse oximetry reading was 100% on room air. A diagnosis of thyrotoxicosis and upper respiratory tract infection was made. Patient was started on Propanolol 40mg tid, cefuroxime 250 mg twice a day and methimazole 20mg daily, and she was treated as an outpatient. 72 hours later the patient presented again to ER complaining of dizziness and breathlessness. She was diaphoretic, anxious and flushed. Her vital signs were as follows: temperature 37°C, heart rate 140 beats/min, blood pressure 80/34 mmHg, respiratory rate 26/ min, pulse oximetry reading was 96% on room air. Her investigations showed serum fT4 level was 33.5 (9.6—19.1 pmol/L), fT3 >12.9 (2.5—5.6 pmol/L) and TSH < 0.011. An electrocardiogram showed sinus tachycardia, chest radiography showed normal cardiac size and features of mild fluid overload and echocardiography showed an EF of 65% with evidence of high output cardiac failure. CT angiogram of the chest was done and showed air space disease with mild right plural effusion and no evidence of PE. She was diagnosed as thyroid storm with high output cardiac failure. Patient was admitted to intensive care unit and she started on hydrocortisone, Methimazole, norepinephrine and empirical antibiotics. Propanolol was stopped and she was started on esmolol and BIPAP as she was tachypenic and had oxygen saturation of 88% on room air. Eventually she recovered and was discharged after 6 days.

Discussion: Arrhythmia is the most common presentation of thyrotoxic cardiac disease. Arterial hypotension is not presenting sign of thyrotoxicosis but is frequent symptoms of hypoadrenalism. Clinically the patient was not in heart failure as shown in the initial chest radiograph at presentation. However, the majority of hyperthyroid patients are in a high cardiac output state in the absence of symptomatic heart failure. This ‘high-output’ heart failure usually occurs in young individuals with severe and longstanding hyperthyroidism in the absence of any underlying heart disease and responds well to treatment with diuretics. The patient deteriorated after being given Propanolol. Her blood pressure fell profoundly and she went into overt cardiac failure but she tolerated esmolol with dramatic response in the heart rate and cardiac failure. Beta-blocker (Propanolol) has been used successfully in the control of tachycardia; even in patients with congestive cardiac failure with tachycardia appeared to be adding to the problem. However, in this patient, possible depression of myocardial contractility by the drug resulting in severe hypotension and fall in cardiac output was outweighed by the benefit derived from controlling the rate. The use of beta blockers should be carefully considered in patients, especially with heart failure because of the risk of exacerbation.

Conclusion: Beta blockade could be harmful in hyperthyroid patients.