ABSTRACT BOOK

Second Clinical Congress of the Gulf Chapter of the American Association of Clinical Endocrinologists, October, 23rd-25th 2014, Abu Dhabi, United Arab Emirates.

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Abstract

These are the advance abstracts of the second clinical congress of the Gulf Chapter of the American Association of Clinical Endocrinologists to be held on 23-25 of October 2014. The declared educational objectives of the congress is to give a "state of the art in endocrine practice". To this end, the organizing committee invited international and regional key opinion leaders to meet the objectives of the congress. We present the abstracts of the congress as submitted by the authors after minimal restyling and editing to suit the publication requirements of the journal. Many major issues and topical themes with wide interests in the profession were addressed in 5 plenary lectures. A clinical practice debate was included to highlight the pros and cons of the recently published lipid lower guidelines from both sides of the Atlantic. More focused issues were included in 12 clinical practice symposia to suite the specific educational needs of the target audience subgroups. Practical issues were addressed in "Meet the Expert"-type of interactive workshops. A selection of free communications from abstracts submitted by delegates, reflecting mostly the regional epidemiology and clinical practice in diabetes care and endocrinology, were selected for presentation as either oral or poster presentations.

We hope that by publishing them in this journal we extend the benefit to those who could not make it to the live presentations. The focus of this year's congress included bone health, molecular endocrinology, pituitary and adrenal disease, new advances in diabetes care, nuclear medicine in endocrinology and select topical issues in addition to many other day to day concerns in diabetes care and clinical endocrinology.

Introduction

In 2012, members and fellows of The American Association of Clinical Endocrinologists (AACE) practicing in the Arabian Gulf Cooperation Council Countries formed and "international chapter". The mission of the chapter is to promote better endocrine care through the support of education, research and

patient advocacy. The bylaws, membership and activities of the chapter may be followed on its official website: www.aacegulf.com. One of its regular activities is hold an annual clinical congress and chapter meeting. The first clinical congress of the Gulf chapter was held in the first week of October 2013 in Abu Dhabi, UAE.

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The main focus areas of this year's congress include bone health, molecular endocrinology, pituitary and adrenal disease, recent advances in diabetes care, nuclear medicine in endocrinology and select topical issues in addition to many other day to day concerns in diabetes care and clinical endocrinology.

The abstracts are presented under their relevant groups; plenary sessions, clinical practice symposia, meet the expert session and free communications. We hope that by publishing them in this journal we extend the benefit to those who could not make it to the live presentations.

Abstracts of Presentations

I. Plenary Lectures and Debates (L1-L6).

L1. Key Note Address: Thyroid Cancer and Molecular Markers 11/2014

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Over 62,000 Americans will be diagnosed with thyroid cancer in 2014. 50% of all females in the United States over the age of 50 have ultrasonographically detectable thyroid nodules. Only 5-10% of patients with detectable nodules actually have thyroid cancer. Thus endocrine physicians are faced with the arduous task of evaluating large numbers of patients with benign thyroid nodules and carefully selecting only higher risk patients for surgical intervention in an effort to definitively diagnose those with clinically important thyroid cancer. The use of thyroid fine needle aspiration biopsy (FNA) revolutionized the patient selection process in the 1970's and steady improvement in cytologic diagnostic acumen led to the Bethesda criteria for interpretation of FNA by the early 2000's. Unfortunately, using the Bethesda criteria, 10-30% of all FNA's still fall into an "indeterminate" category that is not clearly benign or malignant (Bethesda 3 AUS/FLUS or Bethesda 4 Follicular Neoplasm). With the advent of advanced molecular genetic technology, 21st century scientists began using positive predictive value mutational or rearrangement analysis (BRAF, RAS mutations and RET-PTC, PAX8/PPARgamma rearrangements) to delineate thyroid biopsy specimens with malignancy associated DNA changes. But sadly, diagnosticians remain frustrated by the fact that only 60% of thyroid cancers have detectable mutations, and, at present, positive predictive value mutational testing of FNA material does not have the sensitivity or specificity to improve surgical decision-making in the patient with an indeterminate FNA result. The Veracyte Afirma molecular genetic strategy involves negative predictive value gene expression testing with a

cassette of 142 mRNA's that are mathematically associated with benignity. Using matrix analysis of mRNA obtained simultaneously with the cytologic specimen, patients with indeterminate cytology are mathematically classified as having a benign Afirma test or a suspicious one. Suspicious Afirma patients are sent to surgery, while those with benign Afirma results can be followed sequentially with US to look for nodule growth. Unfortunately, the negative predictive value of the Afirma test depends on the cytologist's ability to segregate patients into the proper Bethesda category based on cytologic findings and on the overall cancer prevalence in the population studied. The higher the cancer prevalence in the the "indeterminate" population tested, the lower the negative predictive value of the Afirma test. In addition, it is likely that the Afirma test was not adequated trained again Hurthle Cell pathologic conditions, since, in our experience, nearly 90% of patients with Hurthle Cell dominant indeterminate cytology are Afirma suspicious but only a 35% percent of these have cancer on final pathology. Thus, the contemporary thyroidologist is left with history, physical exam, ultrasound, FNA and molecular genetic technologies to ascertain the proper patients for thyroid surgery, but his/her most important clinical tool remains carefully honed "clinical judgement"

L2. State of the Art I. Endocrine Hypertension 2015

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Approximately 1 out of 4 adults are estimated to be hypertensive. In the majority, the hypertension is “essential” or “idiopathic”, but a subgroup group of approximately 15% has secondary hypertension. The secondary causes of hypertension can be divided into renal (e.g., renal parenchymal or renovascular disease) and endocrine causes. There are at least 14 endocrine disorders in which hypertension may be the initial clinical presentation. An accurate diagnosis of endocrine hypertension provides the clinician with a unique treatment opportunity, that is, to render a surgical cure or to achieve a dramatic response with pharmacologic therapy. The diagnostic and therapeutic approaches to 2 main forms of endocrine hypertension - pheochromocytoma and primary aldosteronism are reviewed in this presentation.

Catecholamine-secreting tumors are rare, with an annual incidence of 2 to 8 cases per million people. Based on screening studies for secondary causes of hypertension in outpatients, the prevalence of pheochromocytoma has been estimated at 0.1% to 0.6%. Nevertheless, it is important to suspect, confirm, localize, and resect these tumors because 1) the associated hypertension is curable with surgical removal of the tumor, 2) a risk of lethal paroxysm exists, 3) at least 10% of the tumors are malignant, and 4) 10-20% are familial and detection of this tumor in the proband may result in early diagnosis in other family members. Catecholamine-secreting tumors occur with equal frequency in men and women, primarily in the third, fourth, and fifth decades. These tumors are rare in children, and when discovered, they may be multifocal and associated with a hereditary syndrome. Pheochromocytoma should be suspected in patients who have one or more of the following: hyperadrenergic spells (eg, self-limited episodes of nonexertional palpitations, diaphoresis, headache, tremor, or pallor); resistant hypertension; a familial syndrome that predisposes to catecholamine-secreting tumors (eg, MEN 2, NF1, VHL); a family history of pheochromocytoma; an incidentally discovered adrenal mass; hypertension and diabetes; pressor response during anesthesia, surgery, or angiography; or onset of hypertension at a young age (eg, <20 years); idiopathic dilated cardiomyopathy. At Mayo Clinic, the most reliable case-detection strategy is measuring fractionated metanephrines and catecholamines in a 24-hour urine collection (sensitivity, 98%; specificity, 98%). Hypertension, suppressed plasma renin activity (PRA), and increased aldosterone excretion characterize the syndrome of primary aldosteronism, first described in 1955. Aldosterone-producing adenoma (APA) and bilateral idiopathic hyperaldosteronism (IHA)

are the most common subtypes of primary aldosteronism. In the past, clinicians would not consider the diagnosis of primary aldosteronism unless the patient presented with spontaneous hypokalemia, and then the diagnostic evaluation would require discontinuing antihypertensive medications for at least 2 weeks. The spontaneous "hypokalemia/no antihypertensive drug" diagnostic approach resulted in predicted prevalence rates of less than 0.5% of hypertensive patients. However, it is now recognized that most patients with primary aldosteronism are not hypokalemic and that screening can be completed with a simple blood test (plasma aldosterone concentration [PAC]-to-plasma renin activity [PRA] ratio) while the patient is taking antihypertensive drugs. Using the PAC/PRA ratio as a case-detection test, followed by aldosterone suppression confirmatory testing, has resulted in much higher prevalence estimates (5%–13% of all patients with hypertension) for primary aldosteronism. . Patients with hypertension and hypokalemia (regardless of presumed cause), treatment-resistant hypertension (3 antihypertensive drugs and poor control), severe hypertension (>160 mm Hg systolic or >100 mm Hg diastolic), hypertension and an incidental adrenal mass, and onset of hypertension at a young age should undergo case detection testing for primary aldosteronism.

L3. Second Annual AACE GC Lecture: Personalized Endocrinology: The Lab in the Clinic.

Ali Alzahrani, Department of Medicines and Endocrinology at Al Faisal University and King Faisal Specialist Hospital & Research Centre, Riyadh, KSA.

Over the last four decades, major advances in the fields of molecular biology and genetics are rapidly changing the way we practice medicine. These disciplines have evolved from pure academic to clinically practiced fields. The basis for this paradigm shift is the major advances in our understanding of diseases at molecular level and the application of molecular techniques in their diagnosis and management. The terms translational research and personalized medicine are now in common use. They refer to clinically relevant basic research and the use of molecular data in clinical medicine. Of the many advances that took place over the last 30-40 years, two had a major impact on the progress of this discipline, the completion of the Human Genome Project in the early 2000 and the development of the Next Generation Sequencing technology. Whole genome sequencing and exomic sequencing have almost reached a routine practice at affordable prices and are likely to be part of the evaluation, diagnostic procedures, choice of therapy and monitoring of patients. Personalized medicine has positively affected all disciplines of clinical medicine and endocrinology is not an exception. In fact, endocrinology is by its nature, a field of molecules, receptors and hormones. Genomics, proteomics and metabolomics have added much to it molecular flavor. In this presentation, I will briefly review the history of molecular medicine, describe the major advances that took place lately and illustrate my presentation with some interesting cases in which the use of molecular techniques made major differences either in their diagnosis, choice of therapy or prognosis and follow up.

L4. State of the Science 2014: Pathogenesis of Hypopituitarism

Baha M. Arafah, Division Chief of Molecular Endocrinology, Case Western Reserve University, Cleveland, Ohio, USA,

Hypopituitarism is a disease complex with variable clinical manifestations. Recent studies have improved our understanding of its pathophysiology, particularly in patients with pituitary adenomas and other para-sellar mass lesions. In that setting, hypopituitarism was previously considered a permanent and irreversible process, requiring life-long hormone replacement therapy. While this could be true in some instances, recent data demonstrated recovery of pituitary function in a large number of patients with hypopituitarism following surgical decompression. Considering the physiology of normal pituitary hormone secretion and their dependence on hypothalamic regulation, one can

conveniently think of at least 3 different mechanisms leading to the development of hypopituitarism. Postulated mechanisms include the following: 1) Diminished release and/or secretion of hypothalamic hormone(s), 2) Interruption of the delivery of hypothalamic hormones to the anterior pituitary by perisellar mass lesions or through damage or injury of the pituitary stalk and 3) Ischemic necrosis or destruction of hormone-producing cells of the pituitary gland. At times, the latter can be selective to a certain population of cells within the pituitary and not associated with an ischemic event. A typical example of this entity would be autoimmune hypophysitis where corticotroph (and at times Lactotroph) functions are uniquely affected while other pituitary hormone secretion (e.g., FSH and LH) are preserved.

Although there are specific examples that apply to each and every one of the first three mechanisms, it is important to point out that in most patients more than one mechanism contributes to the development of hypopituitarism. In each instance, there is often a predominant mechanism that dictates not only the degree of impairment but also whether the process is potentially reversible. The pathophysiology of hypopituitarism in patients with large adenomas has been of special interest. Mechanical compression of portal vessels and the pituitary stalk, by the expanding adenoma was postulated to be the predominant mechanism causing hypopituitarism in this setting. The presence of mild hyperprolactinemia in addition to the associated partial or complete loss of other pituitary function, clearly support that mechanism. If compression of the portal vessels and the stalk were the sole mechanism explaining hypopituitarism in patients with pituitary macroadenomas, one would have expected complete recovery of pituitary function after surgical decompression. This was indeed documented in some but not all patients. The fact that recovery of pituitary function was incomplete in most patients suggested that other mechanisms are involved in the pathogenesis of this disorder. Since portal vessels also provide blood supply to the anterior lobe, it is possible that ischemic necrosis of portions of the pituitary occur as a result of increased and prolonged compression by the expanding adenoma. We have recently demonstrated increases in intrasellar pressure in patients with pituitary macroadenomas, particularly those with hypopituitarism. The study also showed that the intrasellar pressure measurements correlated positively with the serum prolactin levels but not with tumor sizes. The data indicate that increased intrasellar pressure has a predominant role in the pathogenesis of hypopituitarism in patients with pituitary adenomas. An additional factor contributing to pituitary failure in this setting, could be the development of ischemia and/ or necrosis in the normal gland. As the pituitary gland cannot regenerate, recovery of pituitary function would not be expected in the latter instances, even though the pressure was relieved. Thus, depending on the presence of viable pituitary cells, recovery of pituitary function might occur after selective adenomectomy. Similar mechanisms have been postulated to explain the hypopituitarism seen in patients with other sellar masses such as carotid artery aneurysm or meningioma. The hypopituitarism seen in most patients with metastatic cancer to the sella is mechanistically multi-factorial as it is associated not only with mechanical effects of the tumor mass but also with invasion and loss of hypothalamic and/or pituitary tissue. As such, the hypopituitarism seen in patients with sellar metastasis is clinically characterized by rapid onset and is commonly associated with the development of diabetes insipidus.

L5. State of the Art II. Cardiovascular Outcome In Type 2 Diabetes: Where We Stand Now?
Naveed Sattar, Institute of Cardiovascular and Medical Sciences, Glasgow, Scotland, UK.

This talk will explain why recent trial and epidemiology data have led to revisiting the relationship between glucose and cardiovascular disease. We appreciate now that lipid-lowering with statins and targeting blood pressure are better means to lower cardiovascular disease in terms of number need to treat than are glucose-lowering

regimens. With this in mind, as cholesterol, blood pressure and smoking levels have been declining in diabetes, cardiovascular mortality in diabetes has been reduced over the last three decades. This talk will cover these areas as well as put into a similar context the results of several recent cardiovascular outcome trials in diabetes inclusion LOOK-AHEAD, ORIGIN and the recent DPP4 trials. The summary is that to reduce CVD risk in diabetes, targeting usual risk factors well is paramount whereas glucose control remains important in particular to prevent microvascular complications.

Sattar N. Revisiting the links between glycaemia, diabetes and cardiovascular disease. Diabetologia. 2013;56 (4):686-95.

L6. AACE-GC Clinical Debate 2014: Lipid Guidelines 2014: Which One to Follow?

L6.1 AACE-GC Clinical Debate 2014: Lipid Guidelines 2014 - Which One to Follow? For the European Guidelines.

Eric Kilpatrick, Department of Chemical Pathology, Hull York Medical School, Heslington, York, UK.

The American College of Cardiology/American Heart Association guidance for treating lipids contrasts to most European guidance by dispensing with the need to aim for a target lipid level. Rather, the AHA guidance suggests starting patients on a fixed statin drug dose with the intention to only lower LDL cholesterol by a specific percentage. Their rationale for this approach is that while studies exist comparing statins with placebo, comparing one statin with another and comparing different doses of the same statin, no trial has purely compared the outcomes of patients where one lipid target was aimed for rather than another. Taking the view that this absence of evidence means there is evidence for ignoring targets altogether belies the overwhelming evidence that greater reductions in LDL leads to a greater reduction in cardiovascular risk. Indeed, taking the AHA approach could potentially lead to difficulties with many patients. One situation would be in patients with particularly high cholesterols, where their very high cardiovascular risk may well be reduced by a fixed statin dose, but if their resultant lipids remain raised then they may continue to be at higher risk than if their treatment was intensified further to meet a specific target. Difficulties may also arise in knowing what is best for patients whose lipids respond unusually poorly or unusually well to standard statin doses. An added complication exists when a percentage reduction in LDL is pursued as opposed to a specific lipid target because with the former approach the initial lipid values become of the utmost importance. Knowing what the baseline lipids were for all the patients already taking statin treatment could prove challenging as might knowing whether these baseline values should be from a very first sample or only after lifestyle measures have been implemented. In summary, by being guided more by the evidence that does not exist rather than by that which does, I fear these American guidelines may have fallen victim to being too evidence based.

L6.2 AACE-GC Clinical Debate 2014: Lipid Guidelines 2014 - Which One to Follow? For the American Guidelines.

In 2013 the American Heart Association (AHA) and the American College of Cardiology (ACC) issued new guidelines for treatment of hypercholesterolemia. In terms of primary prevention of atherosclerotic cardiovascular heart disease (ASCVD), these represent a major departure from previous guidelines which relied on LDL measurements, specific targets and use of various lipid-lowering agents. Instead, the AHA/ACC guidelines recommend 1) abandoning LDL measurements as targets for treatment decisions, 2) using a 10 year ASCVD risk calculator (pooled cohort equations [PCE]) to determine whether, in addition to lifestyle modification, individuals should be placed on high intensity statin therapy (>7.5% risk) aimed at reducing LDL >50% or moderate intensity statin therapy (>5.0 <7.5% risk) aimed at reducing LDL 30-50% and 3) de-emphasizing non statin treatments because of lack of randomized controlled trial (RCT) evidence of efficacy. The new recommendations questioned the rationale for

the previous ones since the latter were based on post hoc analyses of studies comparing different statins or different statin doses and not on ones titrating therapy to specific LDL targets. i.e., no RCT has shown that baseline or on-treatment LDL levels alter the beneficial effects of statin therapy. The Canadian Diabetes Association, the American Association of Clinical Endocrinologists and the American Diabetes Association have not endorsed these recommendations which have been criticized on the grounds that 1) the PCE overestimates risk, 2) the approach ignores RCT results demonstrating lower LDL levels are better, 3) eliminating LDL targets will reduce motivation and patient adherence to medication and 4) no RCTs randomized subjects by ASCVD risk and targeted different % LDL reductions. Regarding these criticisms, the risk overestimation occurs primarily in higher risk patients who would normally be put on high intensity statin therapy. Secondly the new guidelines will lower the threshold for initiating statin therapy which should lower the lifetime LDL burden. In conclusion, these guidelines could be improved if, instead of targeting % LDL reductions, a specific risk-based target were chosen for individual patients and LDL levels routinely measured to assess efficacy and compliance.

II. Clinical Practice Symposia

Clinical Practice Symposium A: Bone Health Update: Basic and Clinical.

S1.1 Osteoporosis Diagnosis in MENA and GCC and FRAX Based Guidelines

Ghada El-Hajj Fuleihan, The Calcium Metabolism and Osteoporosis Program and WHO Collaborating Center for Metabolic Bone Disorders, American University of Beirut, Beirut, Lebanon.

The "Middle East & Africa Regional Audit" examined the epidemiology, costs and burden of osteoporosis in 17 countries across the MENA region. By 2020 it is expected that 25% of the population in the region will be over the age of 50 years, and up to 1/4-1/3 will suffer an osteoporotic fractures, incurring enormous burden for healthcare systems. Older people who suffer hip fractures are often faced with long-term disability, loss of independence and higher risk of death. Prevention is therefore key. Since its launch in 2008, FRAX® has resulted in a major paradigm shift in the assessment of the patient at risk for osteoporosis. It adopts a case finding strategy based on clinical risk factors, with and without Bone Mineral Density (BMD), and estimates an absolute fracture risk, identifying high risk individuals who should receive pharmacologic therapy. FRAX® takes into account population-specific life expectancy as well as hip fracture incidence rates, and has become the cornerstone for the development of national care pathway models. It has encouraged many national and international organizations to revisit their previous osteoporosis guidelines based on information derived from FRAX.

The FRAX based Lebanese guidelines, revisited the initial set of national osteoporosis guidelines developed in 2002 and updated in 2007, and capitalized on the availability of a FRAX Lebanon model, to develop a unique model for FRAX-based guidelines. They retain four of the original definite indications on "Who to Test": presence of a fragility fracture, age older > 65 years, bone demineralization by x-ray, chronic steroid therapy for a duration exceeding 3-6 months at doses exceeding the equivalent of a prednisone dose of 7.5 mg daily. Newly added is the indication of use of an aromatase inhibitor or chronic androgen deprivation therapy. For all other conditions, the recommendations are to run a FRAX calculation based on clinical risk factors, and to request a BMD with DXA if the 10-year fracture risk estimate for overall fractures approaches 10%. Indications for “Who to Treat" retain the original indication of a history of fragility fracture, but with specification for the skeletal site, at the spine or hip, or the presence of more than one other fragility fracture. For subjects who have not experienced any fragility fracture, a hybrid model was developed. The intervention threshold in the hybrid model is set at ≥ 10% for the 10-year overall risk of fractures for individuals up to age 70 years, and for individuals above age 70 years, the threshold increases with age: 15% at 75 years, 21% at 80 years,

27% at 85 years, and 30% at 90 years. A BMD T-score ≤ -2.5, in the absence of additional risk factors, is no longer an indication for treatment by itself, due to the very low estimated 10-year risk for fractures, that is less than 10%, in women up to age 70 years, and men up to age 90 years. These Lebanese FRAX-based guidelines provide a major advance in the management of osteoporosis in Lebanon, and are a useful model for the development of similar country specific guidelines in the region.

S1.2 Osteoporosis Therapies from Bench to Bedside

Ego Seeman, University of Melbourne, Melbourne, Australia.

Treatments reduce vertebral and hip fracture risk by only ~50%. Non-vertebral fractures, 80% of all fractures, are not prevented by treatment. Most studies show no non-vertebral anti-fracture efficacy. The few that do, fracture risk is reduced by ~20%. Compelling evidence for anti-fracture efficacy for any drug is lacking in >75 year-olds (the source of most hip fractures), in women with osteopenia (the source of 60% of all fractures), in men, and in all groups after 3-4 years of any therapy; most trials have violated randomization after this time. Thus, there are many challenges.

Net loss of bone from the skeleton occurs during advancing age for three reasons. (i) Each basic multicellular unit (BMU) deposits less bone than was resorbed during the remodeling cycle. This net negative BMU balance is the necessary and sufficient cause of structural decay. (ii) The rate of remodeling increases after menopause; more BMUs, each replacing less bone than removed, producing more rapid bone loss. (iii) Periosteal apposition slows and is minimal after menopause so that it fails to compensate for bone matrix being removed by unbalanced remodeling upon the internal (intracortical, endocortical, trabecular) surfaces. These cellular changes, and the structural decay produced - cortical porosity and thinning, trabecular perforation and thinning are targets for therapy. Anti-resorptive agents reduce the volume of bone deposited by each BMU and reduce the rate of remodeling. There is no evidence that they increase the volume of bone deposited; they are not anabolic. Reducing the negative BMU balance by reducing the volume of bone resorbed slows, but does not stop bone loss and structural decay. Fragility is not reversed or even stabilized, it worsens, but more slowly, despite compliance with therapy. If BMU balance is restored, bone loss stops, structural decay stabilizes but is not reversed irrespective of the rate of remodeling. If remodeling is stopped, bone loss also stops. Structural decay is again stabilized but does not reverse but increases in tissue mineral density and accumulation advanced glycation end products reduce matrix toughness (ductility). Thus anti-resorptive agents do not reverse or structural decay, they at best halt or slow its progression. The increase in BMD following antiresorptive therapy misleadingly suggests otherwise but this net increase in BMD is due to fewer new BMUs appearing while the many initiated before treatment are in their refilling phase. Continued slow remodeling with a persisting negative BMU balance erodes the bone from the higher BMD; an effect obscured by secondary mineralization of the less remodeled bone observed with powerful antiresorptives. It is clearly seen as a decrease in BMD from its higher value after about 12 months using weak antiresorptives like calcium supplements or selective estrogen receptor antagonists. The challenge is to find agents that reconstruct the skeleton – anabolic agents. Drugs that deposit bone upon (i) the periosteum widening the bone and increasing its resistance to bending, (ii) the intracortical surface of Haversian canals narrowing the canals, reciprocally increasing the matrix volume of the cortex, (iii) the endocortical surface thickening the cortex and (iv) the trabeculae, thickening them and increasing their connectivity as well as synthesizing new trabeculae. The available anabolic agents are PTH molecules like PTH 1-34 and 1-84. Newer molecules are being investigated like PTHrP and the antisclerostin antibody. PTH molecules increase bone matrix volume mainly by acting on bone formation within existing or newly created BMUs, and less so by increasing bone formation upon quiescent bone surfaces. Periosteal apposition does not appear to be a major anabolic

effect of PTH molecules. Development of new anabolic agents, more effective modes of administration, or combinations with antiresorptives are unmet needs created by increasing longevity. The burden of fractures in the community arises in persons with structural decay. Reports of blunting of PTH with antiresorptives are not confirmed by more recent studies and there may be advantages in combining therapy with agents like denosumab or cathepsin K inhibitors that block resorption allowing PTH to target bone formation. The search for effective therapies and new targets is not over.

S1.3 Challenges in Management of Osteoporosis
Christian Roux, Centre d'Évaluation des Maladies Osseuses, Hôpital Cochin, Paris, France

Osteoporosis is a medical condition characterized by an increased risk of fractures. The consequences of recurrent vertebral fractures are more and more recognized. Hip fractures are the most devastating fractures, but attention must be paid also to some non-vertebral-non-hip fractures which carry an excess mortality in the years following the fracture. Several pharmaceutical treatments exist for the management of osteoporosis that effectively reduce the risk of vertebral fractures, and to a lower extent the risk of non-vertebral fractures. Falls is the main determinant of these fractures, and falls prevention programs must be implemented in frail patients. They are effective in older patients, to decrease the number of falls and fallers and to prevent injuries caused by falls. Moreover the optimization of frail patients care is also based on assessment and correction of poor visual acuity, excess of anti-hypertension drugs or hypnotics… We could miss an opportunity if we go on neglecting the non-pharmacological approach in the osteoporosis treatment. Although it is well-known that fracture begets fracture, most of the patients with a recent fragility fracture do not receive appropriate treatment. The Fracture Liaison Services are effective, and cost effective, for prevention of recurrent fractures. Selection of patients at high risk before the first fracture is a challenge, and tools like FRAX can help is the selection of subjects who should receive the highest priority for treatment. But, after the prescription of the treatment, other issues emerge: there is a failure to perceive the increased risk of fracture, and adherence is low in many patients. Moreover the perception of the risk of side-effects is very high among patients, higher than the risk of the disease itself. The target for the treatment is not yet clear, and thus duration of treatment is not standardized. A comprehensive assessment of the risk of fracture must be performed, at the individual level, all along the treatment, to assess its optimal duration.

Clinical Practice Symposium B: Benefits and Risks of Newer Diabetes Therapies

S2.1 Incretin-Based Therapy
Mario Skugor, Cleveland Clinic Lerner College of Medicine of Chase West Reserve University and The Endocrine and Metabolic Institute, Department of Endocrinology and Metabolism, Cleveland Clinic, Cleveland, Ohio, USA.

Incretin based therapies aim to correct the defect in secretion and action of the native GLP-1 and GIP seen in the patient with type 2 diabetes mellitus. These defects are known for a long time but only recently the practical therapies have been developed. At this point therapies are aimed at enhancing the action of the naturally secreted incretin hormones using the inhibitors of dipeptydyl peptidase – 4 in a pill form, or providing the GLP-1 analogs as injections. Both types of therapies provide glucose dependent stimulation of insulin secretion and glucose dependent glucagon suppression, which leads to drop in fasting and postprandial blood glucose levels, as well as drop in HBa1c over time. Additional benefit of these medications is the protection of the beta cells against apoptosis which leads to increase in beta cell mass in animals. Furthermore, Injectable GLP-1 analogs cause slowing of the gastric emptying and also appear to affect appetite centers in hypothalamus leading to weight loss in majority of the patients. Side effects are mostly related to GI system and include nausea,

diarrhea, and vomiting. More serious side effects include development of acute pancreatitis (even fatal cases have been reported). Patients should be warned to stop treatment and be seen if acute abdominal pain develops while using these medications. Controversy arise after report of higher incidence of pancreatic duct metaplasia in patient using incretin therapies and question of possible increase of risk for pancreatic cancer was raised. However, FDA reviewed all existing information and found no increased risk so far. Finally, patients who have history of medullary thyroid carcinoma or are known to have MEN-2 should not use incretin therapies at this time. Reason for this is the observation in mice and rats of increase in incidence of c-cell derived tumors. So far, from post marketing data it appears that risk is not increased.

S2.2 Sodium-Glucose Transposorters 2 (SGLT2) Inhibitors

John Gerich, Department of Medicine, University of Rochester, School of Medicine, Rochester, New York, USA.

The kidney regulates glucose homeostasis in three ways: 1) it produces (via gluconeogenesis) and releases glucose into the circulation, 2) it takes up glucose from the circulation, and 3), and much more importantly, it reabsorbs glucose from glomerular filtrate (~180g/d). Ninety percent of this occurs via sodium glucose transporters 2 (SGLT2) exclusively located in the S1 segment of the proximal convoluted tubule (PCT). The remaining 10% is reabsorbed via sodium glucose transporters 1 located in the S3 segment of the PCT. These transporters are widely distributed in various tissues and are responsible for intestinal glucose absorption. In Type 2 diabetes, renal glucose production, utilization and glomerular filtrate reabsorption are all increased, the last due to increased numbers of SGLT2 transporters. Consequently the maximal reabsorption rate of glucose and the renal threshold for glycosuria (normally ~10mM) are increased so that greater amounts of filtered glucose are reabsorbed and glycosuria may not occur until plasma glucose levels exceed ~ 13mM. Inhibition of SGLT2 transporters in diabetic animals reduces hyperglycemia and glucose toxicity thus improving insulin and glucagon secretion and liver and muscle insulin sensitivity. Three SGLT2 inhibitors are approved in the US and EU for treatment of type 2 diabetes: canagliflozin, dapagliflozin and empagliflozin. As add-ons to metformin, these agents reduce HbA1c as much as sulfonylureas, as and more than DPP4 inhibitors. Moreover, they have added benefits: weight loss (2-3%), systolic blood pressure reductions (3-6mm Hg), reduced proteinuria, low risk of hypoglycemia, and lack of dependence on beta cell function. Most frequent side effects include genital tract infections (vaginal candidiasis and balanitis) (3-4 fold above placebo, i.e., 8-12%), transient polyuria (~400 ml/day), hypovolemic symptoms (e.g., orthostatic hypotension), 2-8% elevation of LDL cholesterol. There are no significant effects on plasma electrolytes, serum calcium or bone metabolism markers and renal function. The efficacy and side effects of these agents are influenced by renal function, age and concomitant medications. Thus, SGLT2 inhibitors represent a major addition to choices available for treating T2DM.

S2.3 Trends of Insulin Management: The Current and Future

Stephen L Atkin, Weill Cornell Medical College in Qatar (WCMC-Q), Doha, Qatar.

Type 2 diabetes is a complex multifactorial disease that represents a serious challenge to achieve optimal glycemic control for the prevention of related morbidity and mortality. Whilst there are an increasing number of therapies for the treatment of diabetes the most potent is insulin that is often used as the last therapeutic resort. Basal insulin is often used an adjunct therapy with its escalation to various forms of a basal bolus regimen should that prove insufficient. Basal insulin therapy with NPH insulin has increasingly been superseded in many practices with insulin glargine that is associated with fewer hypoglycemic though overall glycemic control does not differ. The new long acting basal insulin degludec has a flat profile lasting a full 24 hours and

may be seen to be a further therapeutic advance with fewer hypoglycemic events than glargine and potentially providing better flexibility and safety of insulin dosing.

Clinical Practice Symposium C: Reproductive Endocrinology Update

S3.1 An Update on Polycystic Ovary Syndrome

Stephen L. Atkin, Weill Cornell Medical College in Qatar (WCMC-Q), Doha, Qatar

Recently published guidelines have suggested that the diagnosis of PCOS should be based on the Rotterdam criteria with the caveat that its diagnosis in adolescence and in menopausal women is difficult. The guidelines highlight the need for a holistic approach to the diagnosis with the exclusion of androgen-excess disorders and the evaluation of the risk factors for diabetes, cardiovascular disease, obstructive sleep apnoea, endometrial cancer and mood disorders. Hormone contraceptives are recommended as the first line of treatment, with a place for clomiphene as first line for fertility issues and a limited role for metformin. The etiology of PCOS continues to remain elusive, genetic studies especially in the Chinese populations have identified candidate genes associated with insulin resistance and type 2 diabetes, but no epigenetic changes have been discerned. A plethora of markers associated with increased cardiovascular risk have been described but whether there is accelerated atherosclerosis with an increased morbidity and mortality rate remains unclear. However, one recent study has suggested that there may be an increased prevalence rate for both angina and myocardial infarction. More recent studies have highlighted the role that small non coding RNA (miRNA) may play in PCOS, particularly in insulin resistance, whilst metabolomics studies have opened the door to new biomarkers for diagnosis and prediction of disease progression

S3.2 The Endorcine Aspect of Female Fertility

William Ledger, Obstetrics & Gynecology, School of Women's & Children's Health, University of Southwest Australia, Sydney, Australia.

Anovulation is one of the three major causes of infertility, along with anatomical disruption to the reproductive tract and problems with the male. Problems of anovulation can usefully be broken down into those resulting from dysfunction of the hyperthalamus and pituitary and those arising primarily from the ovary, although it is sometimes difficult to separate out cause and effect. The classical example of hypothalamo-pituitary dysfunction is that of Kallmann's syndrome leading to hypogonadal hypogonadism, the pathogenesis and the genetics of which have now been well investigated. Hypogonadal anovulation in young women is usually straight forward and rewarding to treat since if ovulation can be restored, pregnancy usually follows. The World Health Organisation class II phenomena, most classically polycystic ovary syndrome, can be more difficult to treat. Definition of the polycystic ovary syndrome has been revised according to the Rotterdam criteria but more recently measurement of AMH (Anti-Mullerian Hormone) has become a widely used surrogate for the other more traditional endocrine and ultrasound tests. Women with excessively high AMH almost invariably have one variant or another of polycystic ovary syndrome and are at risk of ovarian hyper-stimulation syndrome should they be treated with gonadotropin's injudicially. Classically, treatment is escalated from oral agents such as clomiphene citrate or letrozole requiring minimal monitoring, possibly through surgical intervention with laparoscopic ovarian diathermy to induction of ovulation with gonadotropin injection. In vitro fertilisation is reserved for complex cases, although the modern trend is towards earlier introduction of ART. With patience on the part of both clinician and patient, and careful attention to detail, ovulation induction can usually be performed safely and effectively in this group of patients with low risk of multiple pregnancy and high rates of fertility, particularly in younger patients. In contrast, the treatment of patients with gonadal failure leading to hypergonadal hypogonadism is unrewarding. It can

be possible to stimulate follicular development in women with absent AMH and low antral follicle number but ovarian response is poor and egg quality frequently also low, particularly in older patients. Although pregnancies and live births have been reported in women as old as 46 after ART, the majority of women over 40 with incipient ovarian failure will experience recurrent implantation failure or miscarriage even if oocytes can be obtained and embryos created. There is now widespread uptake of treatment with donated eggs from younger donors in this group although ethical challenges remain and pregnancy in older women can be problematic. The possibility of regeneration of oogonia from stem cells remains hypothetical in the human.

S3.3 Endocrine Aspects of Male Infertility
Pierre-Marc Bouloux. Centre for Neuroendocrinology, University College Medical School, Royal Free Campus, Hampstead, London NW3 2PF

The hypothalamo-pituitary-testicular axis coordinates two principal functions essential for fertility: production of physiological quantities of sex steroids, and the generation of spermatogenic cells that become mature gametes capable of fertilizing oocytes. The hypothalamic hormone GnRH is the master regulator of these processes, and is released from axon terminals into the portal circulation at the median eminence in discrete pulses, and acts on the gonadotrophs of the pituitary to produce pulsatile LH and FSH release. These gonadotrophins bind to LH and FSH receptors on the Leydig and Sertoli cells respectively, with the production of testosterone, and in the case of FSH the production of several factors,that together with testosterone, induce and maintain spermatogenesis. Both gonadotrophins are required to maintain quantitatively normal spermatogenesis in humans.These processes are totally compromised in hypogonadotrophic hypogonadism, whether congenital (Kallmann syndrome, IHH) or acquired (pituitary tumours, head trauma, CNS infections,haemochromatosis, radiotherapy, vascular disorders). Patients with HH wishing to achieve spermatogenesis can be treated with pulsatile GnRH (4- 20 mcg/pulse) therapy using a subcutaneous delivery system, provided the defect does not reside at the level of the GnRH receptor, and that gonadotrophs are present. The therapeutic dose correlates positively with body weight and negatively with pretreatment testicular size. Serum testosterone unusually normalizes within two months, and spermatoigenesis can take up to 22 months to optimize. An alternative strategy is to employ hCG (LH activity: 1,500 units 2 to 3 times weekly sc) and FSH (Menopur, Puregon, Gonal F: 75 units - 225 units thrice weekly)) preparations, In patients with adult onset HH, spermatogenesis may be initiated with hCG alone. Spermatogenesis can take from 3-20 months to occur. The prognosis for both treatments is suboptimal where orchidopexies have been performed for cryptorchidism. ICSI using TESA, offers fertility potential for men with persistent azoospermia who have failed to respond to a full course of stimulant therapy.

Clinical Practice Symposium D: Cell Replacement Therapy in Diabetes.

S4.1 Whole Pancreatic Transplant Update
Elmahdi Elkhammas, Clinical and Transplant Surgery, The Ohio State University, Ohio, USA.

We all know that diabetes is a prevalent disease worldwide. It results in life threatening complications and is considered a silent killer due to the coronary and vascular complications. Pancreas transplantation has gained momentum in the last 20 years to become an acceptable surgical option for the treatment of diabetes mellitus. Unfortunately it is offered to a smaller number of diabetic patients. In general the transplant community remained more conservative with pancreatic organs in comparison to the liver and renal allografts. This has resulted and more shortage of pancreatic grafts. With large percentage of diabetic patients can do well with aggressive insulin therapy, surgical and medical side effects of transplantation, and unpredictable development of life threatening diabetic complications, it is difficult to offer pancreatic

transplantation at a younger age and prior to the development of diabetic complications. With the increasing number of diabetics with end stage renal disease and other diabetic complications, it becomes obvious that whole organ pancreas transplantation will not be available for the majority of them. More usage of pediatric and older donors is needed. Other means to treat diabetes will continue to be in a major need.

S4.2 Islet Cell Transplantation
Thierry Berney, Divisions of Visceral Surgery and Transplantation, Geneva University Hospitals, Geneva, Switzerland.

Beta-cell replacement is currently the only therapy able to restore euglycemia and physiologic metabolic control in patients with type 1 diabetes. Islet of Langerhans transplantation is a valuable alternative to whole pancreas transplantation because it is a low morbidity, minimally invasive procedure. Islets of Langerhans are isolated for transplantation from organ donors by enzymatic digestion of the procedure, followed by tissue purification on density gradients, in a technically challenging process performed in a dedicated laboratory. Islet transplantation is done intraportally into the liver by percutaneous approach under local anesthesia. Islet transplantation is performed in two different types of patients: in North America, the preferred procedure is islet transplant alone (ITA) in patients with labile type 1 diabetes (severe hypoglycemia) and preserved renal function; in the rest of the world, islet-after-kidney (IAK) or simultaneous islet-kidney (SIK) transplantation are also performed in patients with end-stage type 1 diabetic nephropathy. Functional outcomes of islet transplantation have been constantly improving since the turn of the millennium, and current rates of insulin independence reach 44% at 3 years in the CIT registry and 50% at 5 years in selected centers. However, partial graft function, demonstrated by C-peptide production and requiring reduced exogenous insulin doses, reaches 90% at 5 years and is associated with disappearance of severe hypoglycemia and excellent metabolic control. Two issues are currently being addressed: first, the need for 2-3 donors to achieve these results shows that engraftment is suboptimal; second, attrition of the graft function is observed, with a slow progressive loss of insulin independence over the years. These two phenomena must be understood in order to improve the long-term results of the procedure. Islet transplantation has turned into a successful therapeutic option with considerable potential. This allogeneic cell therapy can be translated to stem cell-derived or xenogeneic tissues, cell lines or other unlimited sources of regulated insulin-producing tissues, to be made available to the large population of patients suffering from type 1 diabetes and hoping for a cure.

S4.3 Stem Cells Therapy in Diabetes: Myths and Realities
Kevin Docherty, Department of Biochemistry, University of Aberdeen, School of Medical Sciences, Aberdeen, Scotland, UK.

Cell therapy in the form of human islet transplantation has been a successful form of treatment for patients with type 1 diabetes for over 10 years, but is significantly limited by lack of suitable donor material. A replenishable supply of insulin-producing cells has the potential to address this problem; however to date success has been limited to a few preclinical studies. Two of the most promising strategies include differentiation of embryonic stem cells and induced pluripotent stem cells towards insulin-producing progenitor cells, and reprogramming/transdifferentiation of acinar, or other closely related cell types, towards functional mature Beta cells. In this talk I will describe progress in both areas with emphasis on our recent work on the ex vivo transdifferentiation of exocrine tissue. When placed in culture the exocrine-enriched material attaches to the dish and grows as a fibroblast-like monolayer that can be repeatedly passaged. These fibroblast-like cells exhibit the characteristic properties of mesenchymal stromal cells (MSCs). In preliminary experiments, using immunocytochemistry and genetic lineage tracing, we demonstrated that the MSCs arose in part through

the epithelial to mesenchymal transition (EMT) of amylase-positive acinar and residual insulin-positive Beta cells. We discovered that the exocrine-enriched material could be efficiently reprogrammed/transdifferentiated towards functional islet cell types. The protocol (10 days) involved: 1. Suppression of EMT using ROCK and TGFBeta signalling inhibitors; 2. Pre-treatment with sodium butyrate and azacytidine to modify the structure of chromatin; 3. Infection with adenoviruses containing the pancreatic transcription factors Pdx1, MafA, Ngn3 and Pax4; and 4. Further treatment with betacellulin, EGF and nicotinamide. The resultant reprogrammed cells were monohormonal; 40% insulin-positive, 4% glucagon-positive, and <2% somatostatin-positive. They secreted C-peptide in response to changes in glucose concentration, and normalized blood glucose levels when grafted into streptozotocin-diabetic NOD/Scid mice. Electron microscopy showed that the morphology of the reprogrammed Beta-like cells was typical of mature Beta-cells, and that they were capable of storing insulin in dense-core granules. The cells produced significant amounts of insulin (33.5±7.3 pg/ug protein) when compared to human islets (226.7±9.5 pg/ug protein). We estimate that the contents of a confluent flask of these fully differentiated cells would have a therapeutic effect following transplantation in humans.

Clinical Practice Symposium E. Clinical Diabetes Update

S5.1 Lifestyle modifications in Diabetes: Do they Work?

Ebaa Al-Ozairi, Department of Diabetes, Endocrinology and Nutrition, Kuwait University, Kuwait City, Kuwait.

Lifestyle intervention is considered the cornerstone of type 2 diabetes management and is the first line treatment option in every single treatment algorithms across all guidelines. But pragmatically, is lifestyle really the cornerstone of diabetes management or something we struggle to cover in consultation? Both nutritional intake and physical activity play a significant role in diabetes preventions and even reversal of diabetes. Physical activity, with or without weight loss improves glycaemia, and controls other risk factors of cardiovascular disease. Despite the evidence, many of our patients and we as health care professional struggle to reach the targets. The lecture will present the latest evidence for the role of lifestyle modifications in diabetes management. The speaker will build on how current evidence can transform into clinical practice to change diabetes outcomes and how developments can transform the outlook for the future.

S5.2 Bariatric Surgery is more effective than intensive medical therapy.

Abdelrahman A. Nimeri, Division of General & Vascular Surgery, Bariatric & Metabolic Institute (BMI) Abu Dhabi, Sheikh Khalifa Medical City, United Arab Emirates.

Introduction: Bariatric surgery is safe & durable long term. It improves weight loss and several comorbid conditions and improves type 2 diabetes mellitus (T2DM). Methods: Review of the literature of bariatric surgery for type 2 DM in morbidly obese patients. Results: Several randomized controlled trials have shown that bariatric surgery is more effective than intensive medical therapy for obese patients with type 2 DM. In addition, a recent 3 year analysis of a RCT showed that Roux en Y gastric bpass (RYGB) is more effective than sleeve gastrectomy (LSG) for T2DM. Furthermore, a long term analysis of the Swedish Obesity Study have shown that bariatric surgery may NOT cure T2DM, but may prevent it. Conclusion: Bariatric surgery is more effective than intensive medical therapy for obese patients with T2DM. It may prevent type 2 DM as well.

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S 5.3 An Overview of Recent Diabetes Trials
Hussein F. Saadi, Department of Medical Subspecialties. Cleveland Clinic Abu Dhabi, Abu Dhabi, UAE.

In this presentation, we will review the results of some of the latest clinical trials on prevention of diabetes (Diabetes Prevention Program Outcomes Study and DaQing Diabetes Prevention Study 23 year follow up), management of diabetes with lifestyle (Look AHEAD) and pharmacologic (GLP-1 Agonist), and safety (Aleglitazar a PPAR α/γ agonist and DPP4 inhibitors). These studies show the following: 1) Intensive lifestyle improves most Cardiovascular Disease risk factors and reduces Cardiovacular and all-cause mortality, 2) Metformin reduces coronary calcium severity in men, 3) Aleglitazar doesn't reduce cardiovascular mortality and morbidity and 4) Some DPP4 inhibitors are associated with increased hospitalizations for heart failure.
Ongoing trials comparing the safety, effectiveness and durability of the many glucose-lowering therapies now available are crucial as they will create a reliable evidence base for clinical care guidelines.

Clinical Practice Symposium F. Pituitary Updates.

S6.1 Pathogenesis & Differential Diagnosis of Hyperprolactinemia
Baha M. Arafah, Division Chief of Molecular Endocrinology, Case Western Reserve University, Cleveland, Ohio, USA

Hyperprolactinemia is a commonly observed clinical entity that could have significant health implications as it often impacts gonadal and reproductive functions as well as bone health. Regulation of prolactin secretion by the pituitary is distinctly different from that of other pituitary hormones. Whereas the dominant hypothalamic regulation on prolactin secretion is inhibitory in nature, it is stimulatory for all other anterior pituitary hormones. Thus, hypothalamic diseases or parasellar mass lesions that impinge on the pituitary stalk often result in a unique clinical presentation consisting of hyperprolactinemia associated with partial or complete loss of other anterior pituitary hormones. Similarly, hyperprolactinemia is a common feature in patients with hypothalamic-pituitary disorders. However, hyperprolactinemia may be caused by a variety of conditions ranging from physiological states such as stress to pathological conditions such as pituitary adenomas.
In most individuals, prolactin circulates predominantly as a 23 kDa monomer, with trace amounts of polymers of the monomeric form as a 60 kDa species, and as a high molecular weight form termed "Big Big prolactin" or macroprolactin. The latter molecular forms of prolactin have minimal biological activity but are measured in the serum assay systems and thus can be confused with mild true hyperprolactinemia. Macroprolactinemia can be identified by gel filtration or precipitation by polyethylene glycol before prolactin measurement is made. As stated above, patients with macroprolactinemia often have minimal of no clinical symptoms related to hyperprolactinemia.
The diagnostic significance of hyperprolactinemia is determined, to a large extent, by the degree of elevation in serum prolactin levels and the associated clinical presentation. While it would be safe to conclude that a serum prolactin level of > 200 ug/L is almost certainly due to a prolactin-secreting pituitary adenoma (prolactinomas) many other potential diagnostic possibilities exist when the level is minimally (25-50 ug/L) or moderately (50-100 ug/L) elevated. Similarly, serum prolactin levels that are >100 ug/L are most often caused by prolactinomas, although other possibilities can be

associated with such levels. It is particularly in situations where the serum prolactin level is <100 ug/L where one needs to integrate all available clinical data to achieve a working diagnosis. In some patients multiple causes of hyperprolactinemia can co-exist. In general, drug-induced hyperprolactinemia (e.g., anti-psychotic dopamine antagonists) are associated with serum prolactin levels of 40-100 ug/L. In such patients, the presence of an additional cause for hyperprolactinemia (e.g., estrogen therapy) might be associated with serum prolactin levels of 100-150 ug/L and thus overlap with the potential possibility of a prolactinomas. The same argument can be made in patients with other diseases or illnesses independently associated with hyperprolactinemia.

A major diagnostic challenge would be patients with mild hyperprolactinemia (25-75 ug/L) who also have additional clinical symptoms such as those that can be associated with partial or complete loss of pituitary function (hypopituitarism). In such patients, two distinct possibilities should be considered, and both would require an MRI scan of the sella turcica. The first possibility includes a non-secreting pituitary tumor or Parasellar mass (e.g., meningioma, pituitary tumor, hypothalamic mass, etc...) that is compressing the pituitary stalk and portal vessels and thus, resulting in hyperprolactinemia and loss of all other pituitary function. The second possibility includes prolactinomas that exhibit the "hook effect". In such patients measurements of prolactin level in serially-diluted (1:10, 1:100) serum sample would address that possibility. On the other hand, an incidentally discovered mild hyperprolactinemia without any obvious known cause and without demonstrating other clinical signs or symptoms (particularly reproductive), would be likely to have the benign entity, macroprolactinemia. The latter entity accounts for 10% of all cases of hyperprolactinemia, and can be followed without any intervention.

Prolactin secreting adenomas represent approximately 50% of pituitary tumors and the vast majority of these are small. In some patients with pituitary tumors prolactin is co-secreted with other hormones such as GH and TSH. In patients with the latter type's features, the clinical manifestations reflect symptoms related to hormones secreted and the mass effect of the tumor. Men often present with large and at times invasive tumors.

S6.2 Management Challenges of the Difficult (Resistant/Giant) Macroprolactinomas
Simon Aylwin, Department of Endocrinology, King's College Hospital, London, UK

In common with other pituitary tumours, prolactin (PRL) macroadenomas may present with: mass effect (visual disturbance or headache), hormone hypersecretion, hypopituitarism, as an incidental finding, during follow up of mainancy or as part of surveillance for inherited or multiple endocrine neoplasia. In most of these patients surgical and other interventions may be required. In contrast, the identification of a PRL macroadenoma is likely to be greeted positively by clinician and patient alike as most of these tumours will respond to dopamine agonist therapy alone. It is important however to avoid over-confidence as 10-20% of PRL macroadenomas may not respond to conventional doses of dopamine agonist (DA), these tumours are frequently referred to as 'resistant'. In addition, truly massive or 'giant' PRL macroadenomas frequently require multimodal therapy even if they are at least partly responsive to the effects of DA.

A working definition of a PRL macroadenoma would be: 1) Failure to achieve size reduction of 50%, and/or 2) Failure to normalize PRL level or at least reduce to levels that permit gonadal function 3) Despite use of maximum conventional doses of dopamine agonist (eg cabergoline 2.0mg/week)

A step-wise approach is recommended for the management of these patients and their tumours:

1. Ensure the diagnosis is correct. Particularly where the initial work-up was undertaken elsewhere before DA began. PRL> 500mcg /L (10,000mU/L) is required for a confident diagnosis of PRL macroadenoma.
2. Use the best DA. There is both evidence and consensus that cabergoline offers superiority in its

action over other dopamine agonists. Patients with difficult PRL macroaenomas should be switched to cabergoline.
3. Increase the dose. Most PRLomas respond to 2mg/week, and higher doses up to 0.5mg daily are often used. However, there is evidence of a further dose-response relationship and some tumours require and respond to escalating doses well beyond this level, with doses up to 12mg/week reported.
4. Trans-sphenoidal surgery may be indicated in DA resistance a) if patients are unable to tolerate escalating doses of DA b) If there is a failure to achieve reduction in size with DA and persisting visual deficit and c) if there is progression of tumour depite therapy.
5. External beam radiotherapy remains a valuable tool to achieve local control of the tumour particularly if there are invasive/aggressive characteristics on histology or radiology.
6. The oral alkylating agent temozolomide is becoming an established part of the treatment algorithm for pituitary tumours and particularly for prolactinoma. Patients who have progressive tumours despite conventional therapy should be offered temozolomide therapy.

S6.3 Body Fluid Balance and Diabetes Insipidus Update

Stephen Ball, The Medical School, Newcastle University, Newcastle Hospitals NHS Trust, Newcastle, UK.

Fluid and electrolyte balance is an essential feature of normal physiology. A neuro-humoral mechanism of exquisite sensitivity serves to match fluid intake and output. The chief components of this mechanism are the ventromedial hypothalamus, the magnocellular neurons of the supra-optic and paraventricular nuclei of the hypothalamus, the posterior pituitary gland and the cells of the renal collecting duct. Together, these function as an integrated sense and response loop, determining renal water loss in relation to water intake and physiological need. The 9 amino-acid peptide hormone vasopressin (AVP) is the principle humeral mediator in this loop. Secreted by the posterior pituitary in response to increased plasma osmolality or reduced circulating volume, AVP increases both the production and expression of specific water channels in the renal collecting duct, facilitating water reabsorption. In the absence of AVP, the sense and response loop is not able to function effectively. This presentation will focus on the physiology and pathophysiology of AVP. It will cover the different forms of diabetes insipidus that result from AVP insufficiency; approaches to the differential diagnosis; and the management of the complex problem of diabetes insipidus associated with adipsia.

Clinical Practice Symposium G: Consensus and Controversies in Diabetes Care

S7.1 The Advantages and Disadvantages of Using HbA1c to Diagnose Diabetes

Eric Kilpatrick, Department of Chemical Pathology, Hull York Medical School, Heslington, York, UK.

HbA1c has now been formally proposed as an alternative to blood glucose as a screening and diagnostic test for type 2 diabetes. It has a number of potential advantages over glucose, such as the lack of need for the patient to fast, as well as indicating glycaemia over several weeks rather than as a spot value. However attractive, there remains concern that factors other than glycaemia may influence the HbA1c result and thereby its means of accurately identifying or excluding an individual as having a high risk of developing microvascular or macrovascular complications. These factors include the presence of an abnormal hemoglobin, hemolytic disease, renal disease and iron deficiency anemia. The magnitude of the effect of these and other disease states on HbA1c values is still not fully elucidated. The future global epidemic of diabetes, which is well established in affluent countries, is now likely to be particularly prevalent in the countries which are least financially able to deal with it. In these areas, the cost of glucose measurement, even for diagnosis, can often be an issue. By comparison, the cost of HbA1c measurement, with

the associated need for rigorous quality assurance of testing, is liable to be completely prohibitive for much of this population.

S7.2 The Role of Postprandial Hyperglycemia in Diabetes Control and Complications
John Gerich, Department of Medicine, University of Rochester, School of Medicine, Rochester, New York, USA.

In Type 2 diabetes postprandial hyperglycemia occurs mainly as a result of the failure to suppress endogenous glucose production rather than a reduction in tissue glucose uptake (Woerle et al, Am J Physiol 290: E67, 2006). Thus, after meal ingestion in patients with type 2 diabetes, the absolute rate of tissue glucose uptake is normal but the amount of glucose entering the circulation from the meal and endogenous production is increased. There are at least four reasons why postprandial hyperglycemia (PPH) is important. First of all, PPH increases earlier and at a greater rate than fasting hyperglycemia (FPG) (Woerle et al, Arch Int Med 164:1627, 2004). For individuals with HbA1c levels between 4 and 8%, PPH increases at approximately 4 times the rate of FPG. Secondly, PPH contributes more to HbA1c levels than FPG at HbA1c levels less than 8.5% and more than 70% at HbA1c values below 7.3% (Woerle et al, Diabetes Res Clin Pract 77: 280,2004). Thirdly, PPH is usually the rate limiting factor for obtaining optimal glycemic control (Woerle et al 2007). Using a 'treat the fasting first' approach, Woerle et al showed that the failure to achieve HbA1c levels below 7% was due to failure to control PPH. Finally, epidemiologic data indicate that PPH is associated with increased risk of cardiovascular disease (Coutinho et al, Diabetes Care 22: 233, 1999; Tominago et al, Diabetes Care 22: 920. 1999; EPIC Norfolk Study BMJ 322: 1, 2001). Thus individuals with impaired glucose tolerance are at increased risk for cardiovascular events. Moreover these observations are supported by clinical trials examining the effects of acarbose (an agent which targets almost exclusively PPH by delaying intestinal absorption of dietary carbohydrate) on the risk for myocardial infarction (see meta-analysis of Hanefeld et al, Eur Heart J 25: 10, 2004). The practical implication of these findings is that if a patient's HbA1c is greater than two standard deviations above the normal mean e.g., >6.0% and his/her FPG is less than 6.5 mM, the major problem is PPH and thus additional therapy should emphasize agents directed to PPH.

S7.3 Ethnic Differences in Diabetes Risk: Do We Know Why?
Naveed Sattar, Institute of Cardiovascular and Medical Sciences, Glasgow, Scotland, UK.

This talk will discuss the difference risk levels for diabetes by ethnicity and explain why it is that some ethnic groups develop diabetes at much lower average BMI and younger age. Is it genetics or is it environment? It cannot be environment alone given, for example, the much lower BMI cut-points in South Asians compared to Europeans to (22 vs 30 km/m2) yield the same level of diabetes risk. Emerging evidence suggests that different ethnicities store fat in different ways with higher risk groups having a lower subcutaneous capacity so that weight gain more quickly leads to ectopic fat in organs such as liver. Beta cell function may also be compromised in some ethnic groups where lifestyle factors, in particular lower activity and fitness may further exaggerate diabetes differences. A potential role for fetal programming will also be discussed. This talk will explain these issues and try to draw out clinically relevant and public health messages for Gulf / MENA countries.

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S8.1 Clinical Practice Symposium H. Clinical Diabetes Update
Diabetes in the Elderly
Abdulraof A Almahfouz, Department of Medicine, King Faisal Specialist Hospital, Riyadh,

Saudi Arabia.

As people live longer and become heavier, the prevalence of Type 2 diabetes prevalence increases as well with aging. Throughout the world and specifically our region, the prevalence of diabetes has reached an epidemic proportion. And although the older patient is at risk of micro and macrovascular complications as younger adults, the elderly is at higher risk than the younger adult. Moreover, they are at high risk for polypharmacy, functional disabilities, cognitive impairment, falls and other comorbidities that puts them at high risk of side effects of medication. On the other hand the elderly population are heterogeneous group that ranges from an otherwise healthy and fit individuals to others with multiple morbidities, frailty and functional disabilities. Hence individualizing treatments and goals are key to providing safe and effective management. Unfortunately most trials addressing treatment targets as well as treatment options were performed on younger individuals. However, some of those trials do have older patients included. As such a number of issues related to the elderly need to be addressed in trials specifically designed for the elderly. Since the risk associated with therapy is higher in the elderly, avoiding hypoglycemia with its dangerous sequelae is of paramount importance in this category of patients. Although most pharmaceuticals used in the younger population can be used for the older ones, one should be aware of the different precautions, contraindications, drug-drug interactions and dose adjustment needed in the elderly patients. So it is incumbent on all of us to be aware of these issues and keep abreast of new developments in this field.

S8.2 Diabetes in Patients with Declining Renal Function

Salem A. Beshyah, Center for Diabetes and Endocrinology, Sheikh Khalifa Medical City, Abu Dhabi, United Arab Emirates.

Management of hyperglycemia in patients with declining renal function and in those with end stage renal disease (ESRD) is a challenging task. Uremia itself and both types of dialysis can complicate glycemic control by affecting the secretion, clearance, and peripheral tissue sensitivity of insulin.

Blood glucose levels can fluctuate widely due to various and opposing effects of ESRD and dialysis. The hemoglobin A1c (HbA1c) level can be falsely high in ESRD, but remains a reasonable measure of glycemic control in this population. Glycemic targets needs to be individualized depending on age, comorbid conditions. The kidney contributes by about 25% of circulating plasma glucose in the fasting state and in addition, most diabetes drugs are excreted at least in part by the kidney, so that patients in ESRD are at greater risk of hypoglycemia. Insulin is the cornerstone of treatment, since most oral diabetes drugs are contraindicated or not recommended in this population. Insulin doses should be lowered in those with low glomerular filtration rates.

Management of patients with diabetes mellitus and chronic kidney disease (CKD) poses a major challenging task because multiple factors in each condition may impact the other. Loss of kidney function and dialytic therapies conspire to change glycemic regulation in ways that can both worsen and improve blood glucose control. Despite the unique nature of DM in patients with CKD, there currently are no specific guidelines to direct glycemic therapy in these patients. There is benefit of glycemic therapy in preventing such complications as diabetic kidney disease and mortality in patients with no kidney disease, but such benefits are largely unproven in patients with advanced CKD. By reviewing the relevant literature, we argue that glycemic control can still be beneficial in preventing complications, even in dialysis-dependent patients, but there is need for a much better understanding of the CKD-related characteristics of DM. More research is needed to determine whether uremia-related improvement in glycemic control can have a beneficial impact. Finally, we are at an important crossroads in the development of several novel therapeutic agents against diabetic kidney disease. We provide an

overview of such agents and their stage of development.
Management of diabetes in dialysis patients:
ESRD and dialysis add to the complexity of glycemic management in this population. Abnormal glucoregulation includes reduced insulin sensitivity and renal clearance of the hormone.
Implementation of dialysis affects glucose and insulin levels, while increasing insulin sensitivity. Tight glycemic control carries an increased risk of hypoglycemia in ESRD. Monitoring glycemic control with hemoglobin A(1c) (HbA(1c)) levels may be suboptimal because of analytical and clinical variability of the test. Recent studies on HbA(1c) and clinical outcomes in this population present complementary results on the role of glycemic control in patients with DM with ESRD.

Several practical issues are worth addressing when discussing the management of diabetes in patients with declinic kidney function. These include the safety and risks of metformin at different levels of renal function, use and choice of various sulphonylureas, possible advantages of DDP-IV inhibitors, the preferred insulin regimens during dialysis and the pivotal importance of avoidance of hypoglycemia.

S8.3 Depression in Type 2 Diabetes
Khalida Ismail, Institute of Psychiatry, King's College London, 10 Cutcombe Road, London, UK.

Depression is a common comorbidity in type 2 diabetes and is associated with worse biomedical outcomes, including mortality. The epidemiology of depression in type 2 diabetes will be summarized, followed by an overview of the current theories of the underlying mechanisms. An emerging theme is that depression and type 2 diabetes may share common underlying inflammatory pathway. Finally, a simple approach to the assessment and management of depression will be given.

Clinical Practice Symposium I. Adrenal and MEN Syndromes Updates

S9.1 Management of Persistent Cushing syndrome.
William F. Young, Jr. Mayo Clinic College of Medicine and Division of Endocrinology, Diabetes, Metabolism, & Nutrition, Mayo Clinic, Rochester, Minnesota USA

The initial cure rate for pituitary-dependent Cushing syndrome (CS) is 85% at centers with experienced pituitary neurosurgeons. However, in those with an initial cure, the recurrence rate is 25%. Thus, the long-term durable cure rate for the patient with pituitary-dependent CS is only 65%. Thus, the management of persistent CS is an all too frequent conundrum in endocrinology. The first question the clinician should ask in the patient with persistent CS is whether the initial diagnosis of pituitary-dependent CS correct? Findings to support a pituitary-dependent cause include: positive immunohistochemistry (IHC) for ACTH on pituitary tumor pathology examination; and, a period of remission in the signs and symptoms of CS following trans-sphenoidal surgery (TSS) in these settings, a pituitary-dependent cause can be assured. Patients can only have one cause of Cushing syndrome you just need to be certain that the cause was correct the first time around! In these patients, if the pituitary MRI shows a tumor, treatment options include a second pituitary surgery (associated with a very low cure rate), focused radiation therapy (eg, gamma-knife), or bilateral adrenalectomy. A fear of Nelson syndrome is never a good reason to not cure CS. If the MRI is negative, then treatment options include surgical (bilateral adrenalectomy) or medical. If CS was not cured for a period of time after TSS and IHC for ACTH on pituitary pathology was negative, then the clinician should reassess whether the patient truly had pituitary-dependent disease. Inferior petrosal sinus sampling (IPSS) should be performed if not done prior to the first TSS. If IPSS documents an ectopic source for ACTH, then a search for the source should be initiated.

S9.2 Phaechromocytoma and Paragangliomas: Investigation and Management.

Pierre-Marc Bouloux. Centre for Neuroendocrinology, University College Medical School, Royal Free Campus, Hampstead, London NW3 2PF

Phaeochromocytoma (PCC) is a rare tumour with an incidence of 2–8 cases per million per year. It is an unpredictable lesion that if missed or suboptimally treated, may be associated with potentially lethal cardiovascular complications. The prevalence of catecholamine secreting lesions in patients with hypertension is 0.1-0.6%; 80-85% are adrenal medullary in origin, the remainder (paragangliomas: PGL) being extraadrenal, arising in sympathetic ganglia in the abdomen, less commonly the pelvis and in rare cases from the mediastinum. Head and neck paragangliomas (HNPGL) represent the parasympathetic counterparts of phaeochromocytomas and are rarely catecholamine secreting. About 35% of catecholamine secreting lesions occur as part of a hereditary disorder. In contrast to PCC, familial catecholamine secreting tumours are frequently multicentric, and metachronous. When suspected, biochemical confirmation is mandatory, and assay of fractionated urinary or plasma free metanephrines, and imaging with CT/MRI for localization, supplemented by functional imaging when available. Succinate dehydrogenase (SDH) is a heterotetrameric enzyme (subunits A, B, C and D) attached to the inner mitochondrial wall with key roles in cellular energy production by virtue of its roles in the tricarboxylic acid (TCA, Krebs) cycle and as the complex II component of the electron transport chain. Mutations in genes that encode SDH subunits (SDHA, SDHB, SDHC or SDHD) or an associated protein (SDHAF2/SDH5) are associated with inherited PPGL or head and neck paraganglioma (HNPGL) with most mutations occurring in SDHB and SDHD. Germline mutations in SDHA, SDHB, SDHC, SDHD and SDHAF2 all compromise SDH activity. Mutations in SDHB cause PPGL more frequently than HNPGL, while the reverse is true for mutations in SDHD. SDHB mutations increase the risk of malignant paraganglioma. Thus, although only about 10% of PPGLs are malignant, a germline SDHB mutation may be detected in up to 50% of individuals with a malignant paraganglioma. These genotype–phenotype correlations can be utilised to prioritise gene testing for germline mutations. An increasing trend is to test multiple genes simultaneously rather than individual genes sequentially. Rarer and more recently recognised genes implicated in inherited PPGL and HNPGL include SDHA, SDHC, SDHAF2, TMEM127, MAX, FH and HIF2A. The personal and family history and clinical examination may uncover risk factors for inherited disease. The presence of two or more cases of PPGL or HNPGL in a family most likely results from a familial mutation. In an individual with a phaeochromocytoma, paraganglioma (PPGL) or HNPGL, the presence of a family history of a tumour associated with a syndromic cause of PPGL should prompt genetic testing for the suspected syndrome. Familial PPGL is usually inherited as an autosomal dominant trait, with the children of a mutation carrier having a 50% chance of having inherited the relevant PPGL gene mutation. For SDHD, SDHAF2 and MAX however, the risk of a mutation carrier developing a tumour depends on the parent from which the gene has been inherited, with clinical disease generally seen only when the mutation has been inherited from the father. Hence, if a son were to inherit an SDHD mutation from his mother, his risk of developing a tumour is remote, but if any of his children were to inherit the SDHD mutation from him, they would be at significant risk of developing a tumour. Although currently, germline mutations in 12 genes are known to be associated with inherited PPGL, and it is likely that this number will increase. The three longest recognised genetic causes of predisposition to PPGL are neurofibromatosis type 1 (NF1, von Recklinghausen's disease), multiple endocrine neoplasia 2 syndrome types A and B (MEN2A and MEN2B) and von Hippel–Lindau (VHL) disease. These disorders will be discussed during the presentation.

S9.3 Multiple Endocrine Neoplasia: From Genes to Bedside: MEN1
Simon Aylwin, Department of Endocrinology, King's College Hospital, London, UK

The classic description of MEN1 includes multiple tumors of the endocrine pancreas, pituitary and parathyroid, regarded as the principal MEN1-associated tumors. It is a condition with variable presentation and incomplete penetrance and with the advent of routine genetic testing in patients and family members it is useful to have a modern definition:
• Clinical MEN1: the presence of two or more of the principle MEN1-associated tumors
• Familial MEN1: the presence of one or more MEN1-associated tumors and a first degree relative with MEN1
• Genetic MEN1; an individual with a recognized germ line mutation in the MEN1 gene without evidence of associated tumors.

When to consider MEN1?
MEN1 testing should be considered in an individual with two or more principle tumors, in symptomatic and asymptomatic first degree relatives of a patient with MEN1, and in other atypical situations where there are unusual features such as a young age or multifocal tumors.
How to evaluate the patient with MEN1?
Clinical evaluation is essential particularly for pancreatic endocrine syndromes e.g. hypoglycemia MRI imaging of pancreas and pituitary and biochemical assessment of calcium, pituitary function and gut hormones should be undertaken. In asymptomatic individuals the optimum intervals between screening have not been identified but guidelines suggest every 2-3 years for imaging.

Management of the individual neoplasms - how does this diverge from the sporadic disease:
• Parathyroid tumors are invariably multiple. Localization studies are less helpful and either total or subtotal (3.5 glands) parathyroidectomy should be carried out
• Pituitary tumors can be managed as for the sporadic cases. In many patients, smaller adenomas can be monitored without intervention
• Careful scrutiny is required for pancreatic neoplasms. Multicentric tumors need to be considered for insulinoma and gastrinoma. Gastrinoma can be often be managed medically: Tumors >1-2cm should be considered for resection
Less common tumors in MEN1: Bronchial and thymic carcinoids occur infrequently in MEN1. The adrenal glands frequently become nodular although the majority remain non-functional. They are treated as in sporadic patients.
Support for patients: MEN1 is a highly complex disorder and can be overwhelming for patients. There are excellent resources available from the Association for Multiple Endocrine Neoplasia Disorders

S9.4 Multiple Endocrine Neoplasia: From Genes to Bedside: MEN2
Stephen Ball, The Medical School, Newcastle University, Newcastle Hospitals NHS Trust, Newcastle, UK.

Multiple Endocrine Neoplasia type 2 (MEN2) is an autosomal dominant familial cancer syndrome characterized by the multiple and metachronous development hyperparathyroidism, medullary thyroid cancer and phaeochromocytoma. MEN2 sets a paradigm in molecular and translational medicine. Identification of gain-of-function mutations in the RET proto-oncogene as the genetic basis of the MEN2 has opened the door to an era of tailored management. This presentation will cover the clinical features and presentation of MEN2; the molecular pathophysiology of RET; and describe how genetic testing can enable a tailored approach to intervention based on the correlation of genotype and phenotype.

Clinical Practice Symposium J. Nuclear Medicine in Endocrinology: Diagnostic and Therapeutic

S10.1 High versus Low Dose Radioiodine Therapy in Thyroid Cancer
Aly Bernard Khalil, Imperial College London Diabetes Centre, Abu Dhabi, UAE.

131 radioiodine (RAI, 131-I) administration after thyroidectomy in patients with differentiated thyroid cancer include ablation of residual normal thyroid tissue, adjuvant therapy of subclinical micrometastatic disease, and treatment of clinically apparent residual or metastatic thyroid cancer. The treatment decision for the use of 131RIA should be based on patient risk stratification as follows:

1. In the high risk group with local extensive disease or with distant metastases, there is evidence that RAI 131-I is beneficial for reducing recurrence and death. On that basis, Most guidelines recommend postoperative RIA for all patients with known distant metastases, gross extrathyroidal extension of the tumor regardless of tumor size, or in the absence of other high-risk features.
2. In the intermediate risk group, the use of RIA should be selective based on the combination of age, tumor size or multifocality, lymph node status, and individual histology that predicts an intermediate to high risk of recurrence or death from thyroid cancer.
3. In the absence of a proven benefit on either disease-free survival or recurrence, ATA do not routinely recommend RAI ablation for patients with unifocal cancer <1 cm without other high-risk features.

Until recently, there were controversies on the optimum dose of I^{131} radioactivity to administer. Recent randomized trials suggest the use of low dose radioactivity for low risk patients and to reserve higher doses for intermediate to high risk groups. However, there are no randomized trials that evaluate long-term outcomes of patients treated with low or high radioiodine dose activity.

S10.2 Thyroid: FDG PET CT and Dosimetry in Thyroid Cancer.
Hojjat Ahmedzadehfar, Department of Nuclear Medicine, University Hospital Bonn, Bonn, Germany.

Positron emission tomography (computed tomography (PET/CT) is a highly sensitive, low invasive technology for cancer biology imaging. The role of 18F- FDG PET/CT in differentiated thyroid cancer (DTC) is well established, particularly in patients presenting with elevated Tg levels and negative radioactive iodine whole body scintigraphy. There are also other PET-tracers, which are useful in diagnosis of and treatment planning for DTC, like 68Ga-DOTATOC and 124I, respectively. The diagnosis and therapy of medullary thyroid carcinoma (MTC) is also sometimes challenging and need PET/CT imaging with tracers like 18-FDG, 18F-FDOPA and 68Ga-DOTATOC as well as imaging with 123I-MIBG for evaluation the extend of the disease as well as the possibility of a radionuclide therapy with 131I-MIBG.

S10.3 Use of GA68 DOTA in Neuroendocrine Tumors.
Abdulredha A. Esmail, Department of Nuclear Medicine, Kuwait Cancer Control Center. Kuwait City, Kuwait

Neuroendocrine tumor imaging has developed dramatically in the last decade with the introduction of SPECT/CT and PET/CT instruments. Neuroendocrine tumors are characterized by the expression of variable degree of different somatostatin receptors. These receptors are utilized for imaging purposes by the application of somatostatin analogues. Benefits are gained by the use of PET Ga-68 labeled peptides radiopharmaceutical when compared to the conventional SPECT radiopharmaceuticals. The normal physiological distribution of the Ga 68 peptides is explained and hence abnormal localizations are outlined. The histopathological correlations of the tumors are crucial in interpreting image findings. Illustrations to the clinical and technical points are briefly described and examples from Kuwait Cancer Control Center are demonstrated. The concept of such introduction will be the future of personalized medicine.

S10.4 Role of SPEC CT in the Intraoperative Probe in Management of Primary Hyperparathyroidism.
Hojjat Ahmadzadehfar, Department of Nuclear Medicine, University Hospital Bonn, Germany.

Hyperparathyroidism (HPT) is one of the most common endocrine disorders. Diagnosis is clinical and biochemical. Pre-operative imaging tests are not in themselves a means of diagnosis, but rather facilitate surgical intervention insofar as they assist surgeons in locating the pathological parathyroid gland. The applications of SPECT and SPECT-CT in the field of Nuclear Medicine are constantly increasing. Due to the wide diversity of techniques and protocols used in the management of HPT, it is difficult to perform fair comparisons. Nevertheless, both techniques have been proven to increase the sensitivity of planar imaging and improve the localization of foci visualized in planar images, which is highly beneficial for surgery, especially in unilateral or minimally invasive approaches. Although hybrid imaging does not significantly increase the sensitivity of SPECT, it can improve the localization of pathological glands and offering anatomical information. Furthermore, SPECT-CT can increase the specificity of the scintigraphic technique, specifically in patients with concomitant thyroid nodular pathology and in patients with distorted anatomy because of a previous cervical surgery.

Clinical Practice Symposium K. Current Perspectives in Adolescent Endocrinology.

S11.1 The Many Faces of Diabetes in Children and Adolescents.
Asma Jasim, Pediatric Endocrinologist, Dubai Hospital and Dubai Diabetes Centre, Dubai Health Authority, Dubai, UAE.

No abstract received

S11.2 Abnormal Thyroid Function Tests in Children and Adolescents: Treat, Refer or Defer?
Walid Kaplan, Department of Pediatric Endocrinology, Tawam Hospital and Faculty of Medicine, United Arab Emirates University, Al Ain, UAE.

Abnormal thyroid test is one of the common referrals to pediatric endocrinology. While some of those abnormalities indicate underlying diseases and should be treated, several others represent transient changes, or age-related variances that need no intervention. In this lecture, I will review the physiology of thyroid hormone synthesis and will present few cases of abnormal thyroid tests to increase your awareness of the differences in thyroid functions between children and adults, and to help you decide when to treat, refer, or defer your future pediatric cases.

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S11.4 Approach to Delayed Puberty: Diagnosis and Management
Sareea Al Remeithi, Division of Pediatric Endocrinology, Sheikh Khalifa Medical City, Abu Dhabi, UAE.

Puberty leads to sexual maturation and reproductive capability. It requires an intact hypothalamic–pituitary–gonadal (HPG) axis and is heralded by the reemergence of gonadotropin-releasing hormone (GnRH) secretion from its relative quiescence during childhood. The exact trigger that initiates puberty in girls and boys is unknown, but is thought to be influenced by a complex interplay of factors including genetics, nutrition, neurotransmitters, and hormones. Delayed puberty is defined as the absence of testicular enlargement in boys or breast development in girls at an age that is 2 to 2.5 SD later than the population mean (traditionally, the age of 14 years in boys and 13 years in girls). This clinical diagnosis also is made in the absence of menarche by age 16 years or in the absence of menarche within 5 years of pubertal onset. Using these criteria, approximately 2.5% of healthy adolescents will be identified as having pubertal delay.

Constitutional delay of growth and puberty (CDGP) is the single most common cause of delayed puberty in both sexes, but it can be diagnosed only after excluding a wide variety of underlying conditions that are known to lead to delayed or absent puberty. Pathologic causes of delayed puberty can be divided into three main categories including hypergonadotropic hypogonadism, permanent hypogonadotropic hypogonadism, and transient hypogonadotropic hypogonadism (functional hypogonadotropic hypogonadism). The aim of the initial evaluation is to rule out causes of delayed puberty other than CDGP. Diagnostic testing can be extensive and expensive, and not all tests have high discriminatory value. Therefore, testing should be directed by conducting a through history and physical examination. Management of pubertal delay should address the underlying cause if one can be identified. In case of CDGP, expectant observation or a short course therapy with low dose testosterone in boys or estrogen in girls could be considered with goals to induce the appearance of secondary sexual characteristics and or acceleration of growth. Patients with permanent hypogonadism require lifelong replacement with sex steroids. The focus of this session will be to describe the indications for and initial evaluation of pubertal delay and to outline commonly used sex steroid regimen to induce puberty in both sexes.

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S11.4 The Transition Between Pediatric and Adult Care: Turner Syndrome as a Model

Elham Al Amiri, Pediatric Endocrinology, Al Qassimi Hospital, Sharjah, UAE

The transition between pediatric and adult care; Turner syndrome as a model

Turner syndrome affects around one in 2500 female live births, the majority of which carry mosaicism in at least some tissues. Thus, the phenotypic features vary significantly among affected individuals. Consequently, while short stature and gonadal dysgenesis are almost universal in Turner syndrome, many other organ systems are affected to varying degrees and at different stages of life. A multi-

disciplinary approach to management is therefore essential, and should be based on knowledge and awareness of the likely and potential adverse outcomes in each organ system.
The level of medical and neuropsychological complexity throughout the life span of a patient with Turner's syndrome (TS) provides the rationale for a more structured transition from pediatric to adult health care. During late adolescence, the focus of care shifts from maximizing final adult height to completing feminization with estrogen therapy, detecting early antecedents of associated adult conditions, implementing needed therapeutic lifestyle changes, and assessing psychobehavioral risk. An increased prevalence of the dysmetabolic syndrome and osteoporosis is observed in TS. The prevention of obesity and assurance of adequate calcium intake and weight-bearing activities combined with early detection and treatment of specific abnormalities can ameliorate these associated adult morbidities. During the final phase of transition, the pediatric endocrinologist should engage the patient with TS in developing a comprehensive adult care roadmap or 'transition passport', which serves as a powerful educational tool. The aim of refining the transition process is to improve adult outcomes and quality of life for patients with Turner syndrome.

III.. Meet the Expert Sessions (MTE1-MTE18)

MTE 1. Hyperparathyroidism: Diagnosis and Medical Treatment

Ghada El-Hajj Fuleihan, The Calcium Metabolism and Osteoporosis Program and WHO Collaborating Center for Metabolic Bone Disorders, Department of Medicine, American University of Beirut, Beirut, Lebanon.

The most common clinical presentation of primary hyperparathyroidism (PHPT) is asymptomatic hypercalcemia detected by routine biochemical screening. Some patients may be detected through a work-up of low bone density, and few may have nonspecific symptoms, such as fatigue, weakness, anorexia, mild depression, and mild cognitive or neuromuscular dysfunction. In few the presentation may be atypical and include a spectrum of disturbances in calcium homeostasis, ranging from symptomatic severe hypercalcemia (parathyroid crisis) to normocalcemic primary hyperparathyroidism. In countries where hypovitaminosis D is prevalent, such as the Middle East, PHPT may be characterized by overt severe clinical bone and stone disease. Biochemical screening tests with a serum calcium account for the identification of most patients with primary hyperparathyroidism (PHPT), who are usually unaware of their diagnosis, and have mild and sometimes intermittent hypercalcemia. The diagnosis is confirmed with an elevated or inappropriately normal parathyroid hormone levels using a second or third generation PTH immunoassay. An increased calcium/creatinine clearance ratio, or genetic testing, is used to rule out the much rarer form of familial PHPT hypercalcemic hypocalciuria (FHH). Serum 25(OH D but not 1, 25 (OH) 2 D, level should be measured in all subjects. Genetic testing reveals that 10% of subjects harbor mutations associated with familial PHPT, and as the cost of genetic testing continues to decline it is likely to be utilized more frequently, and assist in the management of patients. The management of the symptomatic patient is surgical, by an experienced endocrine surgeon, with removal of the parathyroid adenoma in 80-85% of cases, or 3 1/2 gland parathyroidectomy in the case of hyperplasia. Pre-operative imaging, is used as management aid to guide surgery but not as diagnostic tool, and minimally invasive parathyroidectomy with intra-operative PTH is the procedure of choice. The 2013 International Workshop on the Management of Asymptomatic revised the latest 2008 guidelines on the management of asymptomatic patients. They recommended surgery in patients with: age < 50 years, a serum calcium level, more than one mg/dl above upper limit of normal, a BMD DXA T-score less than -2.5 (Z score is used in young individuals) at any skeletal site, or a compression fracture identified by X-ray, CT scan, MRI or VFA, a

creatinine clearance < 60 ml/min, or an increased stone risk by biochemical analysis, or the identification of nephrocalcinosis. Surgery may be a viable option even in subjects who do not meet above criteria, and is also indicated in subjects in whom medical surveillance is not desirable or possible. Patients who do not meet surgical criteria or those who cannot undergo surgery, can be monitored medically, with annual measurement of serum calcium and eGFR, BMD testing every 2-3 years, with vertebral X-rays or VFA in case of height loss, and additional renal testing if stone disease is suspected. In such cases pharmacologic therapies targeting the hypercalcemia and skeleton can be used, but the benefit of such an approach remains to be proven.

MTE 2. Unusual Pituitary Masses: An Evidence-based Approach

Baha M. Arafah, Division Chief of Molecular Endocrinology, Case Western Reserve University, Cleveland, Ohio, USA

The increasing use of imaging modalities for various unrelated disorders such as headaches or head trauma has resulted in increasing recognition of sellar and parasellar masses in patients with minimal or often, overlooked clinical manifestations. The majority of these lesions are eventually diagnosed to have pituitary adenomas. Many, but not all of the sellar or parasellar masses have clinical manifestations that are related to or caused by mechanical compression of surrounding structures and / or alterations in pituitary hormone secretion. These lesions can be difficult to diagnose easily and would require additional studies and expertise. The latter would include sound awareness of the anatomy of the sella turcica and parasellar region, good understanding of the physiology of pituitary hormone secretion and a reasonable appreciation of the strength and limitations of the imaging modality used. Precise imaging with and without contrast and with high topographic resolution are helpful not only in determining the nature of the lesion but also its relationship to surrounding structures. MRI imaging is the best approach to obtain such detailed data and is obviously superior to CT scanning.

Thus, in approaching a sellar / parasellar mass one would need to integrate clinical history, biochemical data and imaging characteristics. Each one of these parameters provide a clue to the diagnosis. Evaluation of pituitary function and establishing the pattern of hormone loss can often help provide a clue to the cause. The Impact of sellar/ parasellar masses on pituitary function depends on: The pathological process involved, rate of growth of the mass, its size and the involvement of and the anatomic relation of the mass to structures that determine pituitary function such as the hypothalamus, the pituitary stalk and the pituitary gland itself. For example, a patient presenting with a pituitary mass associated with ACTH and prolactin deficiencies but has normal gonadal and thyroidal functions would most likely have an autoimmune hypophysitis. Similarly, the presence of diabetes insipidus at presentation in somebody who did not have prior pituitary surgery is not likely to have an adenoma but could instead have metastatic cancer or perhaps a craniopharyngioma or other inflammatory disease such as neuro-sarcoidosis. In such instances and most others the imaging characteristics would add more information to narrow the differential diagnosis. Important imaging features to address include the epicenter of the mass, its location (intra VS peri-sellar), its signal intensity (T1 VS T2; pre VS post contrast enhancement), size of the sella turcica and the presence of boy erosions. For example, a large sellar / suprasellar enhancing mass associated with a relatively small sella turcica would most likely have metastatic cancer to the sella rather than an intrinsic tumor. The latter scenario would be extremely likely when the clinical presentation includes the onset of diabetes insipidus. On rare occasions, patients may present with more than one pathologic diagnoses involving structures within the sellar and parasellar region. Examples of a few unusual cases of sellar / parasellar masses will be reviewed and the approach to their management will be discussed. It is important to re-emphasize that in approaching a sellar and/ or parasellar mass, one would need to integrate clinical, biochemical and

imaging data to offer a unifying diagnosis and offer selective management options.

MTE 3. Difficult Thyroid Function Test!
Pierre-Marc Bouloux. Centre for Neuroendocrinology, University College Medical School, Royal Free Campus, Hampstead, London NW3 2PF.

Thyroid function tests (TFTs: fT4, fT3 ,TSH)) are amongst the most commonly requested laboratory investigations at both primary and secondary care level, and are generally straightforward to interpret, enabling confirmation of euthyroidism, hypothyroidism or hyperthyroidism in most patients. In a subgroup of patients, TFTs can seem confusing, either by virtue of being disconsonant with the clinical scenario or because of incongruence with each other [e.g. fT4/3 with non-suppressed TSH); raised TSH, but with normal fT4/3]. In such cases, the clinical context becomes important, as is the consideration of potential confounding factors such as alterations in normal physiology (e.g. pregnancy), intercurrent (non-thyroidal) illness, and medication usage (e.g. thyroxine, amiodarone, heparin). Laboratory artefacts generated by commonly used TSH or fT4/3 immunoassays should be screened for, thereby avoiding unnecessary and costly additional investigation and/or treatment, in cases where assay interference exists. In the remainder, consideration should be given to screening for rare genetic and acquired disorders of the hypothalamic–pituitary–thyroid (HPT) axis [e.g. iodine deficiency, resistance to thyroid hormone (RTH), thyrotropinoma (TSHoma), dysalbuminaemic hyperthyroxinaemia, mutations of NIS]. In this presentation, I shall give some examples illustrating the scope of such diagnostic pitfalls in the interpretation of thyroid function tests.

MTE 4. New ATA Guidelines: Cases-Based Discussion
Richard Mack Harrell, Memorial Regional Hospital, Fort Lauderdale, Florida, USA
See Abstract L1 above.

MTE 5. Cushing Syndrome Cases
William F. Young, Jr. Mayo Clinic College of Medicine and Division of Endocrinology, Diabetes, Metabolism, & Nutrition, Mayo Clinic, Rochester, Minnesota USA

Cushing syndrome is a symptom complex that results from prolonged exposure to supraphysiologic concentrations of glucocorticoids. The most common cause of Cushing syndrome is the use of synthetic glucocorticoids to treat an inflammatory condition—termed exogenous or iatrogenic Cushing syndrome. Endogenous or "spontaneous" Cushing syndrome is rare and is caused by hypersecretion of corticotropin (ACTH) (ACTH-dependent Cushing syndrome) or by primary adrenal hypersecretion of glucocorticoids (ACTH-independent Cushing syndrome). Excess ACTH secretion by a pituitary tumor is the cause of endogenous Cushing syndrome in 85% of patients and is termed "Cushing's Disease." Cushing's disease occurs five times more frequently in women than in men, with the peak incidence occurring between 20 to 50 years of age. Ectopic ACTH-secreting neoplasms and the ACTH-independent forms of Cushing syndrome (adrenal adenoma, adrenal carcinomas, and adrenal nodular hyperplasias) are responsible for 15% of the endogenous cases. Although Cushing syndrome is not common, the clinical features of hypercortisolism are common. The clinician's role is to 1) recognize Cushing syndrome, 2) confirm Cushing syndrome with biochemical tests, 3) determine the cause of Cushing syndrome and 4) provide a definitive cure. The focus of this presentation will be on the recognition, confirmation, and subtype evaluation of Cushing syndrome. The clinical and biochemical phenotypes should focus and guide the clinical evaluation and treatment.

MTE 6. Diabetes Pumps and Sensors: Clinical and Technical
Mario Skugor, Cleveland Clinic Lerner College of Medicine of Chase West Reserve University and The Endocrine and Metabolic Institute,

Department of Endocrinology and Metabolism, Cleveland Clinic, Cleveland, Ohio, USA.

Insulin pumps are becoming the more and more accepted devices for delivery of the insulin. The advantages over intermittent injections include the possibilities to deliver several basal rates during the day, temporary increases and decreases in the basal rates, delivery of the bolus without separate injection. Delivery of the bolus in different fashions; true bolus, square bolus, or partial bolus with square bolus after that. These features allow considerable degree in flexibility with different types of physical activity, eating schedules and concurrent medications that affect glycemic control.

Modern pumps also allow maintain the record of the insulin delivery, and concurrent blood glucose levels. These records are easily downloaded to the computer and can be presented in different graphic forms (that can be useful, but also cumbersome at times). However, the main promise of the insulin pumps is not yet realized. That is a possibility to pair the pump with continuous glucose monitoring system that would allow automation of the insulin delivery. The first steps are taken and today there are several systems that allow glucose monitoring every 5 minutes in interstitial fluid and transmitting the information to the pump where these are available for review (allowing discovery of unknown patterns in daily glucose profiles) and could be used to set different forms of alarms that warn of impeding hypoglycemia, running outside the desired glucose range for prolonged time, or need for bolus administration. CGM-s have to be calibrated twice a day using the finger blood glucose determination (calibrations should be done at the time of relatively stable glucose levels to avoid problems with lag between interstitial fluid and blood). These systems are available with sensors that have useful life of 3 or 7 days, and could be used intermittently to uncover problems (professional use) or continuously by patient to guide his therapy. Use of SGM-s allows for improvement in glycemic control (using the HbA1c measurements) without increasing the risk of hypoglycemia. Fully integrated systems (bionic pancreas) are still in development but first success stories are being published. Most recent report achieved fully automated control over 5 days period. Exact technical details of these attempts are kept secret. What is known is that some systems use double sensors some distance from each other (using two different techniques of measurements) and other incorporate the sensor and insulin infusion site in same device (again, some distance apart).

MTE 7. Hyperaldosteronism Cases

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Case Detection. Case detection can be completed by measuring a morning plasma aldosterone concentration to plasma renin activity (PAC-to-PRA) ratio while the patient is taking antihypertensive drugs. Patients with hypertension and hypokalemia, treatment-resistant hypertension (3 antihypertensive drugs and poor control), severe hypertension ($\geq$160 mm Hg systolic or $\geq$100 mm Hg diastolic), hypertension and an incidental adrenal mass, or onset of hypertension at a young age should undergo case detection testing for PA. Two key points: 1) PRA is suppressed to <0.6 ng/mL/hr in almost all patients with PA, regardless of any medications except mineralocorticoid receptor (MR) antagonists; 2) If the patient is hypokalemic or requiring potassium supplements while treated with a MR antagonist, then complete MR blockade is absent and case detection testing and confirmatory testing can be done while the patient is treated with their low-dose MR antagonist (eg, spironolactone 25 mg/d or eplerenone 50 mg/d). Confirmatory Testing. We perform aldosterone suppression testing with orally administered sodium chloride and measurement of 24-h urinary aldosterone and sodium. In the patient with undetectable PRA, and when the 24-h urinary sodium is >200 mEq, a 24-hr urinary aldosterone of >12 mcg confirms PA. The list of drugs and hormones capable of affecting the renin-angiotensin-aldosterone axis is extensive, and in patients with severe hypertension while treated with multiple antihypertensive agents, a "medication

contaminated" evaluation is unavoidable. Finally, confirmatory testing is not needed in the subset of patients with spontaneous hypokalemia and a high PAC (eg >30 ng/dL) and undetectable PRA (eg, <0.6 ng/mL/hr)—there is no other diagnosis except PA to explain these findings! Subtype Studies. Aldosterone producing adenoma (APA) is found in approximately 35% of cases and bilateral idiopathic hyperaldosteronism (IHA) in approximately 60% of cases. Adrenal CT is not accurate in distinguishing between APA and IHA. Therefore, adrenal venous sampling (AVS) is essential to direct appropriate therapy in most patients with PA who seek a potential surgical cure. When a solitary, hypodense, and unilateral macroadenoma (> 1 cm and <2 cm) and normal contralateral adrenal morphology are found on CT in a young pt (eg, <35 yr), unilateral laparoscopic adrenalectomy is a reasonable treatment option. AVS can be omitted in this select patient subset because the development of nonfunctioning adrenocortical adenomas is and age-dependent process. However, most patients with PA are older than 35 years and in others the CT may show normal-appearing adrenals, minimal unilateral adrenal limb thickening, unilateral microadenomas (<1 cm), or bilateral macroadenomas—in these cases, if the patient wants to pursue the surgical option, AVS is needed. At Mayo Clinic, we use continuous cosyntropin infusion during AVS (50 mcg/h started 30 minutes before sampling and continued throughout the procedure) for the following reasons: (a) to minimize stress-induced fluctuations in aldosterone secretion during nonsimultaneous AVS; (b) to maximize the gradient in cortisol from adrenal vein to inferior vena cava (IVC) and thus confirm successful sampling of the adrenal veins; and (c) to maximize the secretion of aldosterone from an APA. Confidence in successful cannulation of both adrenal veins is critical to patient care. When cosyntropin infusion is not used, some centers require only a 10% cortisol gradient between an adrenal vein and the IVC—a change that can be seen in minute-to-minute adrenal cortisol secretion and a change that is within the coefficient of variation of some cortisol assays. Thus, we favor the use of cosyntropin infusion during AVS. Treatment. The cause of the PA helps to determine the appropriate treatment. Excessive secretion of aldosterone is associated with increased risk of cardiovascular disease and morbidity. Therefore, normalization of circulating aldosterone or MR blockade should be part of the management plan for all patients with PA. In experienced hands, laparoscopic adrenalectomy is a straightforward surgical procedure. Medical management should include a MR antagonist. Our typical starting dosages are spironolactone 25 mg once daily or eplerenone 25 mg twice daily. We increase the dose by 25 mg every 2 weeks as needed with a treatment goal of a mid- to high-normal serum potassium concentration without the aid of oral potassium supplements. Unlike all other antihypertensive medications, the treatment goal is not blood pressure driven. If additional agents are needed, we start with a thiazide diuretic.

MTE 8: Organ and Cell Replacement Theraphy in Diabetes: Panel Discussion

Kevin Docherty, Elmahdi Elkhammas, Thierry Berney. University of Aberdeen, School of Medical Sciences, Aberdeen, Scotland, UK, The Ohio State University, Ohio, USA and Geneva University Hospitals, Geneva, Switzerland.

There are two main alternative sources of islets for transplantation: ES/iPSC-derived progenitors, and fully transdifferentiated Beta cells derived from tissues that are closely related in developmental terms to the pancreas. Both approaches are based on advances in our understanding of the developing mouse pancreas. In the case of ES/iPSC derived islets the aim is to recapitulate the various stages of development in a tissue culture dish. Thus the pluripotent cells are teased along a differentiation pathway that includes formation of definitive endoderm (DE), pancreatic progenitors, islet progenitors, and from there towards fully functional Beta cells. There are a number of published protocols that differ slightly from each other, but which have at their core the sequential addition of the following factors: activin A to induce formation of DE, cyclopamine to induce foregut endoderm and

mimic formation of the pancreatic anlage, retinoic acid and FGF to promote pancreatic morphogenesis, inhibition of activin signalling with SB431542 to block formation of liver lineages, Noggin to inhibit BMP signalling, and a gamma secretase inhibitor to inhibit exocrine and promote endocrine lineages. With these protocols it is possible to reproducibly generate islet progenitors. When grafted in immunocompromised mice these progenitors differentiate over a 12 week period, such that substantial levels of human C-peptide can be detected in the blood, and the grafted cells can at that stage protect the mice from the diabetes-inducing effects of streptozotocin. On the basis of these encouraging results plans are underway to take ES/iPSC-derived islet progenitors into clinical trials. At the same time a number of groups are tackling the problem of obtaining fully functional Beta cells from ES/iPSCs. Trans-differentiation involves transcription factor mediated changes in the phenotype of adult cells. Theoretically it would be less challenging to transdifferentiate cells such as those derived from the exocrine pancreas or liver that are developmentally more closely related to islets than are cells from, for example, skin or bone marrow. The exocrine and endocrine cells of the pancreas arise from a common progenitor cell that expresses the transcription factor NGN3. A logical approach would be to direct exocrine cells back towards this progenitor and then redirect a developmental programme towards islets. This can best be achieved ex vivo using adenoviruses containing NGN3, PDX1, MAFA and PAX4, along with growth factors and DNA modifying molecules. Unlike ESC/iPSC differentiation protocols, direct reprogramming of adults cells generates (as one might expect) fully functional and mature Beta cells for transplantation.

MTE 9. Clinical Perspective on Clinical Imaging for Adrenals

Simon Aylwin, Department of Endocrinology, King's College Hospital, London, UK

With the increasing availability of cross sectional imaging the majority of adrenal lesions are now identified through imaging before an adrenal pathology is suspected. The likelihood of significant pathology depends very much on the clinical context. The clinician and radiologist may wish to determine if the lesion represents a metastasis and alters the staging of a patient with known malignancy. The objective may be to assemble enough evidence to avoid intervention. It may be that the imaging findings are the first diagnostic evidence of hormone hypersecretion or an otherwise important pathology. There are three broad categories where assessment of an adrenal abnormality is required:

1) Where a patient with known malignancy. In many patients with known malignancy, cross sectional imaging identifies adrenal masses. This may be relevant to the initial staging or evolve during surveillance. In this setting the majority of lesions can be correctly assigned to either metastasis or adenoma with the use of a triphasic CT scan with pre-contrast, dynamic (venous) and delayed phase imaging. The enhancement 'washout' characteristics of metastasis differ from adenomas and the distinction can be made with a high degree of accuracy.

2) In otherwise healthy patients who have undergone 'health screens' or who are investigated for unrelated conditions, an adrenal abnormality is likely to be irrelevant and such as liver here the lesion is genuinely incidental and likely to be innocent: the 'incidentaloma'. In these patients the priority is to avoid unnecessary intervention. Again, triphasic CT is essential to categorise the lesion accurately and if the imaging characteristics in relation to both the contrast washout and the morphology of the lesion are reassuring then the chances of malignancy become very low indeed.

3) There are many patients where the clinicians are concerned about non-specific symptoms and cross sectional imaging identifies an adrenal mass that is relevant. In this situation, we prefer to use the term 'unexpected' rather than 'incidental'. Although the presentation with, for example, weight loss may not have suggested adrenal pathology, a large adrenal mass may be the cause. In this situation precise

clinical, biochemical and radiological investigation is evidently appropriate.

The session will evaluate these scenarios through case discussions.

MTE 10. Hyponatremia
Stephen Ball, The Medical School, Newcastle University, Newcastle Hospitals NHS Trust, Newcastle, UK

Hyponatremia (serum Na+ <135 mmol/L) is common in standard clinical practice. Despite this, it remains an area of in which there is significant uncertainty. Hyponatremia is associated with increased mortality and morbidity across a range of clinical contexts. However, whether the relationship is causal, or one of simple linkage through underlying disease severity remains to be determined. There are divergent approaches to the differential diagnosis and management of hyponatremia, reflecting the diverse clinical settings in which the problem is found. The apparent absence of a clear evidence-base, together with speciality-specific differences in perceived clinical priorities have hindered the development of a coherent approach to the problem. This meet the expert session will focus on some key themes. 1) An evidence-based approach to the differential diagnosis of hyponatremia, 2) Finding the balance in management: treating the patient rather than simply treating the serum Na+ concentration 3) When (and when not) to use hypertonic fluid and 4) Approaches to the management of over-correction

MTE 11: Assessment of Ovarian Reserve and Ovarian Ageing
William Ledger, Obstetrics & Gynecology, School of Women's & Children's Health, University of Southwest Australia, Sydney, Australia.

The social trend towards deferral of pregnancy and child birth in the developed world is leading to an increasing number of women presenting with a complaint of infertility due primarily to advanced female age. This phenomenon is experienced less rarely amongst males in whom sperm quality and quantity deteriorate much later in life than do oocyte quantity and quality in women. The assessment of ovarian reserve and ovarian ageing has become an integral part of the work of the reproductive medicine specialist, mainly to identify those women at risk of premature ovarian ageing who should be advised to consider trying earlier for pregnancy, or possibly oocyte freezing. Additionally, measurement of ovarian reserve is useful when planning management of ovarian stimulation for ART, since overstimulation carries risk of ovarian hyperstimulation syndrome and under stimulation results inadequate yield of oocytes and hence lower pregnancy rates. Ovarian reserve has classically been assessed by studying the hypothalamo-pituitary component of the axis, with elevated FSH in the early follicular phase of the cycle being correlated with poor ovarian function. However more recently it has become possible to assess ovarian reserve more directly by measuring serum concentrations of Anti Mullerian Hormone produced from pre antral and small astral ovarian follicles, and also by way of transvaginal ultrasound to measure antral follicle count. These measurements are usually closely correlated, although interesting variants have been reported. In future it may be possible to measure directly the regulators of very early follicle development including GDF9 and BMP15, and improved methods of measurement of ovarian reserve may lead to more rational approaches to the management of the older patient wishing to conceive a child.

MTE 12. Graves Orbitopathy: Evaluation and Management
Pierre-Marc Bouloux, Centre for Neuroendocrinology, University College Medical School, Royal Free Campus, Hampstead, London NW3 2PF

Graves ophthalmopathy (GO) can impair visual function as well as exerting a profound impact on quality of life. Treatment is unsatisfactory, with after 10 years, up to 32% patients stating that their eyes

do not look normal. Only a minority of patients with Graves' disease (GD) develop ophthalmopathy. In a recent Italian series of 348 patients with GD (Tanda et al 2013), seen during an 8 year period, around 74% has no ocular involvement at presentation, 20% had mild and inactive GO, whereas 6% had moderate to severe active GO and 0.3% had sight threatening optic neuropathy. After 18 months, 10% of patients with no GO developed mild active GO and moderate to severe disease developed in 2.6%. Most patients with mild disease will resolve spontaneously with control of hyperthyroidism. The TSHR-Ab titre correlates well with a more severe course of GO. Assessment of severity can be performed using the 'NOSPECS' classification, and disease activity using the clinical activity score (CAS). Orbital imaging by CT/MRI is recommended for unilateral ophthalmopathy, to rule out other disorders such as orbital meningioma, lymphoma, orbital myositis, and idiopathic orbital inflammatory disease. Imaging should also be done in euthyroid or hypothyroid patients, those in whom there is suspicion of dysthyoid optic neuropathy, and prior to surgical decompression.

Optimal management of GO requires a multidisciplinary approach. The chosen modality for treatment of the GD may influence the course of GO, and 131I therapy not recommended in patients with active GO, unless under glucocorticoid cover. Similarly, rehabilitative orbital surgery should be postponed until euthyroidism has been established using carbimazole/probythiouracil and the GO inactive. Smoking cessation is essential. With mild GO, given the tendency for spontaneous recovery, only symptomatic treatment (eg hypromellose eye drops) is necessary, supplemented by sodium selenite (200 mcg daily for 6 months). Immunosuppression with iv pulses of methylprednisolone (500 mg iv weekly for 6 weeks followed by 250 mg weekly for 6 weeks) is appropriate for moderate to severely active GO, and orbital retrobulbar irradiation can improve ocular motility disturbance and diplopia, but should be avoided in patients with diabetic retinopathy, severe hypertension or <35 years. The results of trials using rituximab have yet to be reported, although early reports are encouraging, suggesting superiority to glucocorticoid therapy (Salvi 2013)

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MTE 13. Endocrine responses in critical illness and stress

Stephen Ball, The Medical School, Newcastle University, Newcastle Hospitals NHS Trust, Newcastle, UK.

The body's response to critical illness involves a complex set of neuro-humoural responses. These include predictable and profound changes in the adrenal, thyroid and gonadal axes: driven by both central and peripheral mechanisms. Much research has focused on whether these endocrine responses are adaptive, or indeed may contribute to the pathophysiological cascade of multi-organ failure. This Meet the Expert Session will review these issues in some detail, describing the common issues that arise in the care of patients with critical illness and the evidence-base for and against intervention.

MTE 14. Diabetes Overlap Syndromes: What type of Diabetes is it? Type 1, Type 2 or Something Else?

Sara Suliman, Imperial College London Diabetes Centre, Abu Dhabi, UAE Imperial College London, UK.

Historically, diabetes has been viewed rather simplistically as Type 1 (or young-onset, autoimmune diabetes) and type 2 (adult-onset diabetes associated with obesity, insulin resistance and other chronic disorders such as hyperlipidaemia, hypertension and gout). More recently, due to advances in diagnostic techniques including biochemical assays and molecular biology, it has

been accepted that Diabetes Mellitus is a heterogeneous group of metabolic diseases characterized by hyperglycemia (resulting from defects in insulin secretion, insulin action, or both) with many different pathophysiological sub-types. Correct identification of the type of diabetes has clinical implications both for selection of appropriate therapy and for prognosis, furthermore, identification of genetic forms of diabetes is helpful for identification of affected family members and genetic counselling. The aim of this session is to provide an interactive case-based overview of the sub-types of diabetes and provide a helpful framework to investigate patients with diabetes especially those with confusing intermediate phenotypes. This will focus on sub-types including obese Type 1 DM, childhood/adolescent/slim Type2 DM, latent autoimmune diabetes of adulthood (LADA), secondary diabetes including pancreatic disorders, endocrine disorders and diabetogenic drugs; as well as genetic defects in insulin production or insulin action including: maturity-onset diabetes of the young (MODY), mitochondrial disorders, severe insulin resistance syndromes, lipodystrophies and diabetes associated with chromosomal abnormality syndromes. Time has been allocated to discuss interesting cases presented by the audience at the end of the session.

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MTE 15. Growth disorders; how to approach a child/adolescent with short stature.

Jamal Al Jubeh, Division of Pediatric Endocrinology, Sheikh Khalifa Medical City, Abu Dhabi, UAE.

Short stature is the most common reason for referrals to pediatric endocrinologists. Normal growth occurs in a particular pattern. Infants have a very rapid growth averaging about 25 cm in the first year of life. Growth decelerates over the following 2-3 years. Prepubertal children grow at a rate of about 5-6 cm/year until the time of puberty when they have a growth spurt. Normal variants of growth that result in short stature in children include familial short stature and constitutional growth delay. These children usually have normal growth velocity during childhood. Pathological short stature can be caused by many conditions. It is particularly important to have comprehensive evaluation before doing specific endocrine testing. Thorough history and physical examination can give clues regarding the diagnosis in many children. Short stature can be caused by many syndromes. Examples include Turner syndrome, Noonan syndrome, Prader Willie and Russel Silver. Syndromes usually present with typical dysmorphic features and constellation of abnormal clinical features. However, Turner syndrome may present with isolated Short stature. There are more than 200 skeletal dysplasia types that cause short stature. These condition cause disproportionate short stature. Many systemic diseases are associated with short stature. It is important to diagnose and manage the underlying disease in order to improve growth. Radiologic and Laborartory evaluation includes bone age X-rays, CBC, electrolytes, renal function, thyroid panel, ESR and celiac screening (tissue transglutaminase or endomysial antibodies). Laboratory evaluation for growth hormone deficiency (GHD) starts with serum IGF-1 and IGF-BP3. Growth hormone deficiency is usually associated with Low IGF-1 and IGF-BP3 along with slow growth velocity and delayed bone age with the exclusion of other causes. Growth hormone stimulation tests will help diagnose or exclude GHD. However, these tests are not very accurate or reproducible and should be interpreted with caution. Growth hormone therapy can result in

improvement in linear growth and improved adult height in GHD and several other approved indication. Short term serious adverse effects are rare. However, this treatment is still very expensive and the long term adverse effects are still not adequately known

MTE 16. Multiple Endocrine Neoplasia: Evaluating the patient and Family

Simon Aylwin[1] & Stephen Ball[2]
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The last decade has seen an explosion in the area of clinical genetics in relation to endocrine neoplasms. This session aims to bring new discoveries into a clinically meaningful framework using case illustrations.

The use of routine genetic testing has allowed the focused screening of asymptomatic individuals and also the release of genetically unaffected members from screening programs. Within MEN2, a strong genotype phenotype relationship has allowed definition of the optimum time for prophylactic thyroidectomy. However, these recommendations can give rise to complex issues within a family.
The spectrum of familial phaechromocytoma/paraganglioma has evolved and now includes >12 recognized susceptibility genes. These have differing clinical characteristics, patterns and associations and recognition of the precise genetic syndrome may influence management and surveillance. Furthermore, the genetic background influences the malignant or benign behavior of the se neoplasms.
Within the area of pituitary tumors, there is increasing recognition of the familial occurrence of acromegaly and gigantism due to mutations in the AIP gene within the Familial Isolated Pituitary Adenoma (FIPA) spectrum. However, the majority of families with multiple pituitary adenoma patients do not have an identified mutation. There are an increasing number of genetic conditions that redispose to pituitary tumors although most are low penetrance. Who and how to refer for screening is an evolving area. The co-presenters will discuss these areas in order to stimulate discussion.

MTE 17. Sweating and Flushing: Evaluation and Management.

Pierre-Marc Bouloux. Centre for Neuroendocrinology, University College Medical School, Royal Free Campus, Hampstead, London NW3 2PF

Intrusive flushing and sweating are not uncommon symptoms reported by patients. The key to management is a thorough anamnesis.
Flushing:
The clinical characteristics of flushing are important. Provocative or Relieving Factors. Certain agents that trigger the flush suggest an underlying systemic disease as the cause for the flushing, such as mastocytosis and carcinoid syndrome. Morphology: Is there a constant pattern to the flush? Is the redness patchy or confluent, and what is its colour? Is cyanosis present, and is the flushing preceded or followed by pallor? The morphology of the flushing may suggest not only the cause of the flushing but also, in the case of carcinoids, the anatomic origin of the disorder. Associated Features: These may include respiratory symptoms, gastrointestinal symptoms, headache, urticaria, facial oedema, hypertension, hypotension, palpitations, or sweating. Temporal Characteristics: The frequency of flushing and timing of the specific features during each flushing reaction should be recorded. A 2-3 week diary in which the patient records qualitative and quantitative aspects of the flushing event and lists exposure to all exogenous agents, may be helpful. When the diagnosis remains obscure, the patient may be given an exclusion diet listing foods high in histamine, foods and drugs that affect urinary 5-HIAA tests, and foods and beverages that cause flushing. If the flushing reactions completely disappear, restoring the excluded items individually can identify the causative agent. If the flushing reactions continue unchanged, then further metabolic workup should b be undertaken.

Sweating (hyperhidrosis):
Primary generalized hyperhidrosis is characterized by sweating surplus to the amount appropriate to thermal regulation. Generalized sweating may occur at a lowered threshold with excessive volume loss of body fluids resulting in the potential for dehydration or electrolyte loss. Hyperhidrosis may also be secondary to a number of systemic processes and illnesses, including phaeochromocytoma, thyrotoxicosis, diabetes mellitus, diabetes insipidus, hypopituitarism, anxiety, menopause, carcinoid syndrome, and drug withdrawal. Nocturnal hyperhidrosis, in particular, may point to the diagnosis of tuberculosis, lymphoma, endocarditis, diabetes, and acromegaly. Amelioration of hyperhidrosis in these cases requires treatment of the underlying disease.
In "diencephalic epilepsy" or 'paroxysmal sympathetic storm', there is sweating, flushing, hypertension, lacrimation, shivering, and respiratory changes in a patient with a lesion at the level of the foramen of Monro. Similar episodes can occur in patients following head trauma, neoplasia thalamic lesions and hydrocephalus. Such episodes are not true epilepsy, as EEG is normal and the episodes refractory antiepileptic drugs.

Sweating in response to emotional stimuli and mental effort involves the palms, soles, and axillae, typical of primary focal hyperhidrosis. In palmar hyperhidrosis, sweat may constantly pour from the skin surface and in severe cases patients cannot use a pen without soaking the writing paper, not shake hands. There may be accompanying plantar hyperhidrosis with staining and damage to shoes. Topic antiperspirants containing 6 to 25% aluminum chloride in alcohol are the first line of therapy for axillary hyperhidrosis, but are ineffective in the treatment of palmar or plantar hyperhidrosis because of the much thicker skin. Tap water iontophoresis is a safe and inexpensive therapeutic modality for palmar hyperhidrosis, possibly via poral plugging. The effect is temporary however, requiring iterative treatments. Anxiolytics such as benzodiazepines may be helpful when hyperhidrosis is triggered by specific psychosocial stressors. Anticholinergic medications are occasionally helpful. Intradermal injection of botulinum toxin has been shown to decrease focal hyperhidrosis of the palms and axillae for 2 to 6 months and may be the treatment of choice for these conditions.

MTE 18. Adrenal disorders and genital ambiguity; from a gender assignment dilemma to life threatening situations
Asma Deeb, Division of Pediatric Endocrinology, Mafraq Hospital, Abu Dhabi, UAE.

Adrenal disorders can be the underlying cause of pathology in a wide range of genital abnormalities. Although genital ambiguity can be distressing, it is often an indication for an underlying adrenal life-threatening condition which prompts health care provisional for management. In this regard, genital ambiguity constitutes a major part of pediatric endocrine emergency. The urgency in this condition is two folds. One is the urgent need for proper gender assignment for the newborn and the other is in establishing the diagnosis to prevent or to treat acute adrenal crises. Adrenal steroid biosynthesis is complex and its understanding is crucial for proper diagnosis and management of a wide spectrum of endocrine diseases. There is a major embryology background too to these disorders and understanding the sequence of fetal development of the adrenal gland and its link to gonadal development is important. In this session, I shall go into an introduction of adrenal disorders presenting with genital ambiguity and will throw light on the link to disorders of sexual differentiation. I shall go through the approach to managing such disorders and present some case scenarios in this topic to invite an interactive discussion.

IV. Free Communications
A. Oral Communications (OC1-OC11)
OC1. Automated Sural Nerve Conduction Study, Reliability and Agreement with Traditional Method. F Algreeshah, A Madanat,

D Alqaissi, E Shesha, King Saud Medical City, Prince Salman Hospital, Riyadh, Saudi Arabia.

OBJECTIVE: To evaluate the agreement between Automated Sural NCS (ASNS) and Traditional Sural NCS (TSNCS) in Diabetic patient with Diabetes polyneuropathy. METHODS: 100 patients who were followed at Prince Salman Hospital Diabetic center, Riyadh were assessed using both ASNS and NCS. We compare amplitude and conduction velocity in both .each method were done independently with no access to the result of the other test.study performed from May-2013 to January 2014. RESULTS: 49 females and 51 males (49% and 51% consecutively) with total 200 nerves were studied by each method. Mean age of 45.3/+-9.2 years .Using conventional methods the median amplitude was 11 mV and 9mV, mean 11.2/+-6.3 and 15.5/+-10 mV (right and left respectively).Amplitude using automated method, median was 8mV and 9 mV, mean of 9/+-4.3 mV and 10.6/+-5.8 mV (right and left respectively).Conduction Velocity (CV) were as follow: median using conventional method was 45 m/s in each side, 59 m/s in each side by automated method. Mean was 38.6/+-16.2 m/s and 39.7/+-15.7 m/s for right and left .Using conventional NCS and 54.6/+-11.1 m/s and 55.8/11.9 m/s using automated NCS. The correlation coefficient for 2oo nerves tested by TSNCS was 0.5,and for ASNCS 0.25. CONCLUSIONS Our patient data suggest that the automated Sural nerve conduction study (ASNCS), is reliable diagnostic tool for Sural nerve study.

OC2. Non-Islet-Cell Tumor Inducing Hypoglycemia in Diabetic Patient: Case Report and Clinical Review. R Braham, M Aldawish, R Ahmed, M A Musallem, A Alsaeed, F Alsabaan, Prince Sultan Military Medical City, Riyadh, Saudi Arabia.

Hypoglycemia is a common medical emergency, mostly as a result of a complication of therapy with oral hypoglycemic agents or insulin in patients with diabetes mellitus (DM). Nonislet-cell tumor hypoglycemia (NICTH) is a rare but serious paraneoplastic syndrome which is uncommon in diabetic patient. We report an illustrative case of diabetic patient suffering from NICTH. A 94-year-old man was admitted to the hospital with hypoglycemia (1.6 mmol/L). He has type 2 DM since 20 years on Mixtard. Recurrent episodes of hypoglycemia occurred regularly since 6 months. Since then, the patient stopped the insulin therapy but he continued to have hypoglycemic attacks. The renal function, the liver panel and the synacthen test were normal. Sulphonylurea derivatives were not detected in the patient's urine. The other laboratory investigations showed a diminished C peptide, proinsulin, insulin-like growth factor 1 (IGF-I) and IGF binding protein 3 levels. Based on these findings, an IGF-II secreting tumour was suspected. Molar ratio between total IGF-II and IGF-I was 25. Computed tomography demonstrated a large pelvic tumor mass. Pathological report revealed fibrosarcoma with in situ hybridisation showing high expression level of IGF-II mRNA. There was no hypoglycemic episode in the days following the surgery and the insulin therapy was restarted one month later. We present this case to insist that NICTH should not be ignored when unusual clinical presentation of recurrent episodes of hypoglycemia occurs in diabetic patients. Low serum insulin, C peptide and IGF-1 levels indirectly implied the diagnosis of this rare disease.

OC3. Well-Differentiated Thyroid Cancer: The Philippine General Hospital Experience. T Edward Lo, A Uy, P D Maningat, University of the Philippine, Philippine General Hospital, Philippines.

BACKGROUND: Differentiated thyroid carcinoma is the most common thyroid malignancy. Asian women in particular were observed to have the highest incidence rates for well-differentiated thyroid cancer (WDTC). Although WDTC is associated with a good prognosis, it may have a highly recurrent state and fatal outcome in a few selected group of patients. Filipinos in particular were reported to be the ethnic group with the highest incidence of thyroid cancer in studies done in Hawaii

and Los Angeles. Thyroid cancer among Filipinos were also observed to be more aggressive and recurrent in nature. This paper aims to describe the clinical experience of a tertiary care hospital center in the Philippines (Philippine General Hospital) in managing patients with differentiated thyroid cancer. METHODS: This is a retrospective cohort study of 723 patients diagnosed with WDTC (649 Papillary and 79 Follicular) seen at the Philippine General Hospital between January 1990 and June 2014. We evaluated clinic-pathologic profile, ultrasound features, management received, clinical course, tumor recurrence and eventual outcome during a mean follow-up period of 5 years. RESULTS: Mean age at presentation was 43 ± 13 for papillary thyroid cancer (PTC) and 44 ± 13 for follicular thyroid cancer (FTC). Majority of both PTC (63.2%) and FTC (54.4%) presented initially as stage 1. A greater proportion of FTC cases (12.7% vs 3.7%) presented with distant metastases with lung and bone being the most common. Nodal metastases at presentation were observed more frequently among PTC (29.9% vs. 7.6%). Fine-needle aspiration biopsy (FNAB) was less reliable in diagnosing FTC with only 32% diagnosed preoperatively. Majority of cases received complete thyroidectomy, subsequent radioactive iodine therapy and TSH suppression therapy which led to a disease free state in most cases. Excluding patients with distant metastases at presentation, recurrence rates for papillary and follicular thyroid cancer were 30.1% and 18.8% respectively. Recurrences for PTC and FTC frequently occurred within 15-16 months from the initial post-surgical radioactive iodine therapy. FTC had a higher mortality rate (2.5% vs. 0.3%). CONCLUSIONS: PTC among Filipinos presents at a younger age, larger tumor size, higher distant metastases at presentation and a higher recurrence rate suggesting a more aggressive and recurrent behaviour for this type of thyroid malignancy. FTC among Filipinos also presents at a younger age and a higher recurrence rate but appears to behave similarly with other racial groups. Nodal metastases at presentation was more commonly observed in PTC while distant metastases at presentation affected more FTC patients. Most Filipinos with WDTC will be categorized as stage I upon presentation. Majority will achieve disease free state after complete thyroidectomy, radioactive iodine (RAI) therapy and adequate TSH suppression therapy. Overall prognosis and survival rates remained to be excellent among Filipinos with WDTC although a higher morbidity from disease recurrence was commonly seen.

OC4. Parathyroidectomy for Primary Hyperparathyroidism a Review of 140 Cases in a Single Institution Over 10 Years. R Skelly, C Backhouse, Taiba hospital Kuwait, Colchester University Hospital UK, Kuwait.

There are as yet, few compelling arguments for parathyroidectomy in patients with mild hyperparathyroidism .Isolated studies have pointed to an increased mortality. The most cogent arguments have been to slow the rate of increased bone loss prevalent in the disorder and hopefully reverse it . We examined the appropriateness of preoperative diagnostic tests and imaging with the view that all patients contemplating surgery should have calcium, PTH, urine calcium/creatinine ratio, 25OHvit D, DEXA done prior. It also sought to assess validity of preoperative imaging with sestamibi and thyroid ultrasound . There were 80 females and 60 males with an average age of 73.5. The average preoperative calcium was 2.77 and for PTH 6.4. In all 35% of cases were symptomatic with main symtoms being tiredness , lack of energy and non-discrete aches and pains. There was an improvement in symptoms that was immediate in the majority (80%). There was no correlation between degree of hypercalcaemia and symptoms . VIT D levels were measured in only 20% of patients and of these 95% had low VIT D levels average 30 mmol/l. DEXA was performed in only 22% of patients and 5% were osteoporotic, 12% had osteopenia. Preoperative imaging was effective in localizing adenoma with combined imaging being successful in correctly identifying site in 80%, thyroid U/S being more sensitive. The rate of multiple adenomata was 5% .

OC5. ACTH Dependent Cushing's Syndrome: The Use of an Octreotide Trial to Distinguish Between a Pituitary or Ectopic Source. O Elshafie, A Sajwani, N Woodhouse, Sultan Qaboos University Hospital, Oman

OBJECTIVES: Adrenocorticotropic hormone (ACTH) overproduction is usually due to a pituitary tumour which is often not visible on magnetic resonance imaging (MRI). In some patients, ACTH overproduction is due to an ectopic source. Our objective was to develop a simple non-invasive technique to differentiate one from the other. METHODS: Serum cortisol levels were measured in 9 patients with ACTH-dependent Cushing's syndrome before and during a 72 hour therapeutic trial of octreotide. Computed tomography (CT) scans of the neck, chest and abdomen was normal in 6 patients and abnormal in the 3 patients with ectopic ACTH production. RESULTS: Serum cortisol levels returned to normal in the 3 patients with confirmed ectopic ACTH production. No response occurred in the other 6 patients, 3 of whom had a pituitary microadenoma. The MRI was normal in the others. CONCLUSION: We recommend a 72 hour trial of octreotide in all patients with ACTH-dependent Cushing's syndrome and a normal pituitary MRI. This will identify those patients with ectopic ACTH-producing tumours, and will be a useful alternative to inferior petrosal sinus sampling in centres where this procedure is not available.

OC6. Whether Adiposity Indices That Predict Insulin Resistance and Metabolic Syndrome in Women with Polycystic Ovary Syndrome (PCOS) are Different with Those Ones in Normo-Ovulatory Non Hirsute Women? F R Tehrani, S Minooee, F Azizi, Reproductive Endocrinology Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

OBJECTIVE: Insulin resistance (IR) and metabolic disorders are common in polycystic ovary syndrome (PCOS). However it is not still clear, which adiposity marker could precisely predict metabolic syndrome (MetS) and IR in PCOS women and whether these indices are different in normo-ovulatory non hirsute women. Given the lack of population based studies and the lack of consensus on the best predictor of cardio metabolic risks in PCOS women in comparison to normal populations, the present study aimed to compare the validity of various available indicators on data derived from a geographically diverse group of women with PCOS, participants of a large population based study. MATERIAL&METHODS: The subjects of the present study selected from Iranian PCOS prevalence study including 1772 reproductive aged women. Waist circumference (WC), body mass index (BMI), waist-hip ratio (WHR), lipid accumulation product index (LAP), and visceral adiposity index (VAI) were examined and homeostasis model assessment (HOMA) index was calculated. Mets was defined according to the Joint Interim Statement. Receiver operating curves were used to evaluate the extent to which measures of adiposity can predict IR and Mets risk.RESULTS: LAP and VAI indexes were two indicators (sensitivity and PPV of 70%, 80% and 60%, 83%, respectively) that best predict IR in PCOS women. Among healthy women the LAP and WC were better markers (sensitivity and PPV of 78%, 75% and 82%, 81%). The two most reliable indicators for prediction of MetS among PCOS and normal women were WC and VAI (sensitivity and PPV of 83%, 81% and 97%, 95%) and VAI and LAP (sensitivity and PPV of 88%, 83% and 98%,98%). CONCLUSIONS: While the appropriate adiposity indicators and their optimum cut off values vary in PCOS women, compare to the normal controls, LAP is an easily obtainable index that might be useful for screening of cardio-metabolic complications among both groups.

OC7. Comparison between the International Association of the Diabetes and Pregnancy Study Group Criteria for Diagnosing Gestational Diabetes and the Former American Diabetes Association Criteria: A Prospective Study Among Saudi Women. E Alfadhli, Saudi Arabia.

OBJECTIVE: To compare between the International Association of the Diabetes and Pregnancy Study Group (IADPSG) criteria for diagnosing gestational diabetes (GDM) and the former ADA criteria. METHODS: A total of 277 Saudi pregnant women underwent a 2-h 75 g oral glucose tolerance test at 24-28 weeks of gestation. Both IADPSG and the former ADA criteria were used for GDM diagnosis. The women were divided into three groups; group 1; GDM diagnosed by both criteria, group 2; GDM diagnosed by IADPSG only, and group 3 those whom considered normal by both criteria. IADPSG criteria were used to handle the GDM cases during the study. RESULTS: Forty seven (16.9%) and 115 (41.5%) women were diagnosed with GDM by the former ADA and the IADPSG criteria, respectively. Group 2 had the same clinical characteristics as group 1 except for lower blood pressure (P= 0.001), and less frequent glycosuria (P= 0.01). On the other hand, they were older (P = 0.004), heavier (P = 0.000) and had higher frequencies of past GDM (P = 0.000) and history of recurrent abortions (P = 0.003) than group 3. In addition, they had significantly more cesarean deliveries (P = 0.040), longer hospital admissions (P = 0.001), neonatal hypoglycemia (P = 0.000), and low Apgar score (P = 0.024) than group 3. CONCLUSIONS: The IADPSG criteria increased GDM prevalence. The additional GDM cases identified by IADPSG have the same clinical characteristics and adverse pregnancy outcomes as GDM identified by the older criteria and differ from non GDM cases.

OC8. Factors Associated With Diabetes Mellitus Prediction Among Pregnant Arab Subjects with Gestational Diabetes. N A Johani, A AlSerehi, B A Mahmoud, King Fahad Medical City, King Saud Bin Abdulaziz university For Health Sciences, King Faisal Specialist Hospital, Saudi Arabia.

There is scarcity of available information on the possible significant risk factors related to diabetes mellitus (DM) prediction among expectant Saudi mothers with or without gestational diabetes mellitus (GDM). The present study is the first to identify such risk factors in the Arab cohort. A total of 300 pregnant subjects (mean age 33.45 ± 6.5 years) were randomly selected from all the deliveries registered at the Obstetrics Department of King Fahad Medical City, Riyadh Saudi Arabia from April 2011 to March 2013. Demographic and baseline glycemic information were collected. A total of 7 highly significant and independent risk factors were identified: age, obesity, family history of DM, GDM < 20 weeks, macrosomia, insulin therapy and recurrent GDM. Among these factors, subjects who had insulin therapy use are 5 times more likely to develop DMT2 (p-value 3.94 x 10-14) followed by recurrent GDM [odds-ratio 4.69 (Confidence Interval 2.34-4.84); p=1.24 x 10-13). The identification of the risk factors mentioned with their respective predictive powers in the detection of DMT2 needs to be taken seriously in the post-partum assessment of Saudi pregnant patients at highest risk.

OC9. Assessing the Impact of Adopting the New AHA/ACC Lipid Guidelines on Diabetic Patients Attending Secondary Care Facility. FHA Hammadi, AAA Nuaimi, JSA Dhuhouri, SA Alshaikh, S Beula, TM Fiad, Sheikh Khalifa Medical City, Abu Dhabi, UAE.

The American Heart Association (AHA) and the American College of Cardiologists (ACC) in their new guidelines eliminated titration of lipid lowering therapy to a specific LDL-C target and introduced a risk-based decision making for which moderate- or high-intensity statin therapy is recommended1. The AHA/ACC guidelines represent a move away from the conventional practice whereby titrating therapy is based on driving the prevailing LDL-C level to a defined target, a practice currently been recommended by the American Diabetes Association (ADA). The purpose of this study is to assess the impact of adopting the AHA/ACC guidelines on an unselected cohort of subjects with diabetes currently been treated in accordance with the ADA guidelines2. We analysis a diabetic cohort attending a secondary care clinic which included 445 patients aged 40 to 75 years without cardiovascular

disease (CVD) and all adults with history of CVD, number = 129 patients. In the context of primary CVD prevention and based on the ADA guidelines. The number of diabetic patients aged between 40-75 years who fulfilled the requirement for primary prevention with statin therapy was 386 out of 445 patients (86.7%) with a mean on treatment LDL-C of 2.1 mmol/L. The impact of adopting the new AHA/ACC guidelines is: a) 59% will be considered for high-intensity statin therapy on grounds of 10-year ASCVD risk > 7.5% (up from 25%); and b) 41% being treated with moderate-intensity statin therapy on grounds of 10-year ASCVD risk < 7.5% (down from 61%). Among subjects with history of CVD, when treatment was based on the ADA guidelines, the mean on treatment LDL-C was 2.04 mmol/L. Those received moderate- and high dose-statins were 62 (48% with mean LDL-C 2.04 mmol/L) and 59 (46% with mean LDL-C 2.03 mmol/L) patients respectively. Adopting the new AHA/ACC guidelines mandates that all the 129 patients (100%) being considered for high intensity statin therapy (up from 46%). In conclusion, applying the new AHA/ACC guidelines will lead to doubling in the number of patients being considered for high- rather than moderate-intensity statin therapy in the setting of both primary and secondary prevention of CVD.

OC10. Predictability of Gestational Diabetes Mellitus (GDM) Using Glycosylated Hemoglobin in First Trimester – A Prospective Study at a Secondary Care Hospital in South India. S Bhat, J Bali, A Kamath, P Bhat, S Umakanth, Melaka Manipal Medical College & Kasturba Medical College, Manipal University, India.

BACKGROUND: Gestational Diabetes Mellitus (GDM) is a common medical disorder in pregnancy seen in 10-15% of pregnant women in India. Universal screening of GDM is done using a 50-g glucose challenge test at 24-28wks gestation and if positive, a diagnostic oral glucose tolerance test is done. Glycosylated hemoglobin (HbA1c), the weighted average of glucose concentration, helps to assess long-term control over the preceding 2-3 months. This study was done to know predictability of GDM using HbA1c in first trimester. DESIGN AND METHODS: A prospective observational study was conducted in antenatal women booked in our hospital from first trimester. HbA1c was done in first trimester followed by universal screening at 24-28wks gestation. 70 cases of GDM and 100 controls were identified and computation was done using crosstabs of study variables and outcomes. Analysis was done by ROC to know sensitivity and specificity of HbA1c and prediction of GDM. RESULTS: The mean first-trimester HbA1c was 5.2% (+0.5%) in controls and 5.7% (+0.8%) in GDM cases. Among GDM cases, mean HbA1c in those requiring insulin was 5.9% and in those controlled only by diet was 5.5%. The area under the curve for HbA1c was 65.8%. A sensitivity of 55.7% and specificity of 72% was found with a cut off of 5.5 for HbA1c. CONCLUSIONS: Development of GDM correlated with marginally higher first trimester HbA1c. Larger studies are required to confirm these findings so that women at high risk of developing GDM are detected earlier in course of pregnancy itself, thereby reducing maternal and perinatal complications.

OC11. Distinct Metabolic Abnormalities Underlie the Transition From NGT to IFG and IGT in Arab Individuals. S Hassoun, M Abdul-Ghani, M Alkasem, Z Dabbous, A B Bener, A Jayyousi, ABA Samra, M Zirie, Hamad Medical Corporation, Doha, University of Texas Health Science Center at San Antonio, San Antonio, Texas, USA.

Insulin resistance and beta cell dysfunction are core defects in type 2 diabetes (T2DM). Impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) are intermediate states in the transition in glucose tolerance from normal to T2DM, both of which are associated with increased conversion rate to T2DM. Understanding the metabolic abnormalities that lead to the development of IFG and IGT will help develop strategies to prevent the development of T2DM. In the present study, we have examined the metabolic abnormalities responsible for the development of IFG and IGT in Arab individuals. 43 subjects with

NGT (n=17), isolated IFG (N=17) and isolated IGT (n=9) received 75-gram OGTT and plasma glucose, insulin and C-peptide concentrations were measured at baseline and every 15 minutes for 3 hours after the glucose drink. Insulin secretion was measured with the incremental area under the plasma insulin and C-peptide concentration curves and insulin sensitivity was measured with the Matsuda Index. Beta cell function was measured with the Disposition Index as the product of insulin secretion and insulin sensitivity indices. IGT subjects manifested severe insulin resistance compared to IFG and NGT subjects. The Matsuda Index was 3.7±0.4, 7.2±1.0 and 8.4±1.1, respectively.

B. Poster Communications (P1-P38)

P1. Prevalence of Metabolic Syndrome in Poly Cystic Ovary Syndrome and the Use of Neck Circumference in Defining Metabolic Syndrome.
BP Pillai, AT Prabha, V Krishna, H Kumar, International medical center, Muscat, Oman and Amrita Institute Of Medical Sciences, Kochi, India.

INTRODUCTION: Poly cystic ovary syndrome (PCOS) is a common endocrine disorder with a high prevalence of metabolic syndrome. Neck circumference has been proposed as a surrogate marker of metabloc syndrome which is simple and easy to perform in the outpatient setting compared to waist circumference. Aim of the study was to evaluate the use of neck circumference in defining metabolic syndrome. MATERIALS AND METHODS: This was a prospective observational study involving 121 PCOS patients over a period of two years. The prevalence of metabolic syndrome was estimated using the modified ATPIII criteria as well as IDF criteria. Neck circumference was measured at a point just below the thyroid cartilage with the subject looking straight ahead with shoulders down. RESULTS: The prevalence of metabolic syndrome was found to be 30.6% by modified ATPIII and 52% by IDF criteria. There was a statistically significant positive correlation between neck circumference and waist circumference ($p < 0.001$). The mean neck circumference was higher in patients with metabolic syndrome by both criteria. CONCLUSION: The prevalence of MetS in this south Indian study population of PCOS was 30.6% by ATP 111 criteria and 52% by IDF criteria. The prevalence of metabolic syndrome will differ based on the definition criteria. The usefulness of different definition criteria of Metabolic syndrome in predicting cardiovascular and metabolic outcome is yet to be determined. NC correlated well with WC and MetS. Neck circumference could replace waist circumference in defining metabolic syndrome which is simpler and easier to measure in a busy outpatient setting as well as in community screening.

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P2. Vitamin D Deficiency and Cardiometabolic Risks in Arab Adolescents: The "Veiled" Female Advantage.
Y Al-Saleh, N Al-Daghri, A Al-Othman, M Alokail, O Al-Attas, A Alnaami, M Al-Harbi, H Alfawaz, G Chrousos, King Saud bin Abdulaziz University of Health Sciences, King

Saud University, Saudi Arabia and Athens University, Greece.

OBJECTIVE: The recent exponential surge in vitamin D research reflects the global epidemic of vitamin D deficiency and its potential impact on several chronic diseases in both children and adults. Several subpopulations, including Arab adolescent boys and girls, remain understudied. This study aims to fill this gap. STUDY DESIGN: A total of 848 apparently healthy adolescent Saudis (334 boys and 514 girls, aged 13-17 years old) were recruited from different public schools within Riyadh, Saudi Arabia. Anthropometrics were taken and fasting blood samples withdrawn to examine serum glucose and lipid profile by routine analysis and 25-hydroxyvitamin D by ELISA. RESULTS: Almost half of the girls (256/514 or 49.7%) had vitamin D deficiency as compared to only 22.2% (74/334) of the boys ($p<0.001$). In contrast, there was a significantly higher prevalence of prediabetes in boys than girls (20.8% versus 14.6%;$p<0.001$). Skin color ($R=-0.12$;$p< 0.001$) was strongly inversely associated with vitamin D status in girls, but not in boys. In boys, the significant predictors of 25(OH) vitamin D include waist circumference, LDL- and HDL-cholesterol, predicting 7% of variance perceived. No significant predictors were elicited in girls. In neither group was fasting blood sugar associated with vitamin D status. CONCLUSION: Vitamin D deficiency is mostly associated with cardiometabolic risk factors in adolescent Arab boys than girls. This reaffirms the innate cardioprotective hormonal and gender-specific advantage of adolescent females in the region although it is masked by the higher prevalence of a known cardiovascular risk factor, vitamin D deficiency, in girls than boys.

P3. Correlation of ALT/AST Ratio with Insulin Resistance in Metabolic Syndrome - A Hospital Based Observational Cross Sectional Study. Ramaya S G, Mishra S K, R Singh, Lady Hardinge Medical College, New Delhi, India.

BACKGROUND: In recent years, non-alcoholic fatty liver disease is considered as a novel component of insulin resistance and metabolic syndrome, which is associated with long-standing elevation of liver enzymes .The aim of this study was to correlate the ALT/AST ratio with insulin resistance calculated by HOMA-IR method among patients found to have metabolic syndrome. DESIGN AND METHODOLOGY: This is a hospital based observational cross sectional study which included 60 subjects of metabolic syndrome defined by International Diabetes Federation criteria.The relevant clinical examination and basic investigations were done. Fasting insulin levels were analysed by chemiluminescence method .Liver function tests were done by fully automated Analyzer Synchron CX-9. Data was processed and analyzed by SPSS version 17.0 software. The Correlation between ALT/AST ratio and HOMA-IR was assessed using The Pearson's correlation test. RESULTS: About 83.3% of patients were observed to have ALT/AST RATIO$\geq$1. On considering patients whose HOMA IR$\geq$2 as insulin resistant and HOMA<2 as non insulin resistant, it was found that about 81.7% patients among the study group were insulin resistant. The ALT/AST Ratio was found to have positive correlation with HOMA-IR (Pearson's correlation coefficient is +0.742 and the significance was <0.001). The ROC curve of ALT/AST Ratio was plotted in relation to HOMA-IR and the area under the curve was 0.862 and the cut off of about 1.06 has the sensitivity of 93.9% and the specificity of 81.8 %. CONCLUSION: This study shows that ALT/AST ratio can be used as screening tool of metabolic syndrome in the community. Further studies are needed on liver enzymes in subjects with metabolic syndrome in comparison with normal population and definite cut off of HOMA- IR to identify metabolic syndrome should be derived among different population.

P4. Hypochondroplasia, Acanthosis Nigricans and Insulin Resistance in a Child with FGFR3 Mutation: Is it Just an Association? M Mustafa, B B Abbas, N Moghrabi, Latifa Hospital, Dubai

, UAE and King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia.

Fibroblast growth factor receptor 3 (FGFR3) gene mutations are well-known causes of skeletal dysplasia syndromes which encompass a wide spectrum of disorders that range from mild hypochondroplasia (the most common type of short-limbed dwarfism in children) to severe thanatophoric dysplasia. Acanthosis nigricans (AN) is associated with severe skeletal dysplasias due to activating mutations in FGFR3, including thanatophoric dysplasia and SADDAN syndrome, however, it is uncommonly seen in Hypochondroplasia patients. We aim to describe the association of Hypochondroplasia, Acanthosis Nigricans and Insulin Resistance in a Child harboring FGFR3 Mutation as few case reports described it. To our knowledge, this is the first case report associating the p.N540 with acanthosis nigricans. We report a Saudi child with short stature due to hypochondroplasia with a heterozygous c.1620C>A; p.N540K mutation in FGFR3 gene, who developed acanthosis nigricans and hyperinsulinemia while on growth hormone treatment. He had high fasting serum insulin 111 pmol/l (15.8 μU/l), high homeostasis assessment index for insulin resistance (HOMA-IR = 3.69 (0.36–2.41. It is not clear whether hyperinsulinism seen in our patient is associated with the FGFR3 mutation or is a potential long-term side-effect of growth hormone treatment. Given the complexity of FGFR3 downstream signaling, the mechanism involved in the development of AN in hypochondroplasia patients is still unclear. Our findings suggest that it might be due to insulin insensitivity either related to skeletal dysplasia itself or secondary to treatment with recombinant human Growth hormone or may represent a new association that should be established by further studies.

P5. A Rare Case of Pycnodyostosis-Toulose Lautrec Syndrome. D Manoharan, S A Harthi, N A Busaidi, P Shanmugam, National Diabetes and Endocrine Center, Royal Hospital, Muscat, Oman.

BACKGROUND: Pycnodysostosis is a rare clinical entity, first described in 1962. It is an autosomal recessive osteochondrodysplasia, diagnosed at an early age. The bones of such individuals are abnormally dense and brittle as a result of insufficient re-absorption process (1). CASE REPORT: An 18 year young Omani girl born to second degree consanguineous parents with no similar family history presented with short stature. She gave history of fracture twice, following trivial trauma .She was 125.5cm tall and had a proptosed eye with blue sclera. She had frontal and parietal bossing and her anterior and posterior fontanels were open. Scoliosis was present. Her digits were short stubby with dystrophic nails. Laboratory investigations were normal. Radiologically diffuse skeletal hyperostosis was seen. Skull shows open sutures with evidence of wormian bones and an obtuse mandibular angle. Acro-osteolysis was seen. She had a normal hearing and fundoscopy. DISCUSSION: Pycnodysostosis is a lysosomal storage disease of the bone caused by CTSK gene mutation that codes the enzyme cathepsin K (3). Life expectancy is normal in this syndrome. There is no specific treatment available for this condition. Fracture should be minimized by taking extra care in handling such child as even a trivial trauma can result in fractures, which is a primary threat. Analysis of the CTCK gene mutation in the patient might be confirmatory, but such syndromes can be diagnosed clinically and radiologically. Therefore even at a primary health centre, such syndromes can be diagnosed provided the physicians are aware of the condition.

P6. Not Using Universal Thyroid Screening Test during Early Pregnancy Will Overlook Three Out of Four Pregnant Women with Thyroid Diorders.

F R Tehrani, S Nazarpour, M Simbar, F Azizi, Reproductive Endocrinology Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran Iran.

BACKGROUND: Thyroid disorders are common in pregnancy and in nonpregnant reproductive aged women. It can be neglected because of physiological changes happened in thyroid gland during pregnancy or common nonspecific thyroid's symptoms observed in pregnant women. The prevalence of overt hyperthyroidism complicating pregnancy has been reported to range between 0.2% and 1.5%, and an estimated 2% to 7% of women are hypothyroid during pregnancy. Maternal thyroid dysfunction during pregnancy has been associated with adverse obstetric and neonatal outcomes as a result it is important to identify thyroid disorders before pregnancy or early in pregnancy. OBJECTIVE: This prospective population based study was conducted among 1st trimester pregnant women to estimate the prevalence of thyroid disorders and thyroid autoimmunity using universal screening. Methods: A total number of 1164 pregnant women were selected using the multi stage, stratified probability sampling procedure. Data were collected through interviews and physical obstetrical examinations. Serum TSH and free T4 (FT4), T3 uptake and thyroid peroxidase antibody (TPOAb) were measured. RESULTS: The mean (SD) of age and BMI of participants were 27.1(5.1) years and 25.3(6.6) kg/m2, respectively. The prevalence of subclinical hypothyroidism was 28.7% (23.4% TPOab positive and 5.3% TPOab negative). On overall positive thyroid peroxidase antibodies (TPOAb) were identified in 10% of participants; 2.7% of euthyroid pregnant women were TPOab positive. Three out of four women with thyroid dysfunction were unaware about their thyroid dysfunctions. CONCLUSION: Clinical and subclinical thyroid diseases are common in pregnancy; they may be overlooked if universal thyroid screening tests are not taken into account.

P7. Glisodin® a Melon Super Oxide Dismutase Extract Attenuates Cardiac Cell Death Cell Via Supression of Oxidative Stress in Heart of Streptozotocin-Induced Diabetes in Wistar.
T Fouzia, O Kheireddine, University of Badji Mokhtar Annaba, Algeria.

We aimed to test whether attenuation of cardiac cell death can prevent diabetic cardiomyopathy. Our study showed that cardiac apoptosis as a major cellular response to diabetes is induced by hyperglycemia-derived oxidative stress. Glisodin as a potent antioxidant prevents the development of diabetic cardiomyopathy. Eight weeks after STZ treatment, cardiac apoptosis was examined by terminal deoxynucleotidyl transferase-mediated dUTP labeling (TUNEL) assay. Oxidative stress in heart tissue was evaluated by measuring GSH content, LPO level and Catalase, SOD activities. Cardiomyopathy was evaluated by measuring LDH and CPK activities. Our results show a significant reduction in diabetes-induced increases in TUNEL-positive cells was observed in a glisodin treatment group. A significant decrease of reduced glutathione content, superoxide dismutase and catalase activities in heart of diabetic rats in heart accompanied by increased of LPO plasma levels, but not in glisodin treatment rats. LDH and CPK activities as biomarkers of cardiomyopathy were decreased in glisodin diabetic rats compared to diabetic control. In conclusion, our results suggest that attenuation of cardiac cell death by glisodin treatment results in a significant prevention of the development of diabetic cardiomyopathy. This process is mediated by the antioxidant effect of glisodin to suppress of oxidative stress in heart.

P8. Effects of Exogenous Insulin Therapy on Thyroid Nodule Size in Patients With Type 2 Diabetes Mellitus. S El-Kaissi, King Fahad Medical City, Saudi Arabia.

OBJECTIVES: Recent evidence suggests that metformin therapyreduces thyroid nodule size by 30%, possibly by moderatingendogenous insulin production. The objectives of this study are to investigate the effects of exogenous insulin on thyroid nodule size in diabetic patients. METHODS: retrospective analysis of patients with nodular thyroid disease and type 2 diabetes mellitus receiving metformin alone or insulin-and-metformin. Thyroid ultrasonography was used to monitor changes in nodule size: ≥2 mm and ≥20%

being statistically significant. RESULTS: 34 insulin-treated (73 nodules) and 53 metformin-only (135 nodules) patients were followed for 5.9-67.9 months (mean 24.5±1.8). Nodule size ranged from 0.17-5.25 cm (mean 1.29±0.08). There were no significant differences in serum TSH, free-T4 or Vitamin D between the two groups, but haemoglobin A1C was higher in insulin-treated patients at baseline and during follow-up (8.75±0.12% vs. 6.48±0.08%; P-value <0.001). In insulin-treated patients, the number of nodules with no change, increase or decrease in size were 49/73 (67.12%), 13/73 (17.81%) and 11/73 (15.07%) at the end of follow-up. The respective number of nodules in the metformin-only group were 105/135 (77.78%), 20/135 (14.81%) and 10/135 (7.41%). Chi-square test for type of treatment and changes in nodule size was not significant (P-value 0.15). 111 nodules underwent fine needle aspiration.4/77 (5.2%) and 3/138 (2.2%) nodules were malignant andexcluded from the analysis. CONCLUSIONS: Compared to metformin alone, there was no association between insulin-and-metformin therapy andchanges in nodule size in diabetic patients. The rates of thyroid malignancy in patients with diabetes mellitus warrant further evaluation.

P9. Radioactive I131 Therapy in the Management Ectopic Thyroid Tissue.
O Elshafie, S Hussein, D Sankhla, N Woodhouse, Sultan Qaboos University Hospital, Muscat, Oman.

Ectopic lingual thyroid tissue was first reported more than 100 years ago, we report an unusual presentation of ectopic thyroid tissue occurring in the patient's submental area. The 8x6 cm mass caused difficulty in talking and a feeling of heaviness in the jaw. The 27 year old female was clinically and biochemically euthyroid at presentation. The clinical diagnosis was confirmed by a Technetium 99m thyroid scan, Magnetic resonance imaging (MRI) and fine needle aspiration. A single therapy dose of Radioactive Iodine ^{131}I (976 MBq) resulted in hypothyroidism after 3 months and complete disappearance of the swelling and her associated symptoms. After 2 years she remains well on lifelong thyroxine replacement.

P10. Distal Renal Tubular Acidosis in Primary Hyperparathyroidism.
T E Lo, I ThieleIsip-Tan, University of the Philippines, Philippine General Hospital, Philippines.

INTRODUCTION: Primary hyperparathyroidism manifests biochemically as a disturbance in serum calcium homeostasis. The kidney appears to be the central organ that sets serum calcium level. Several observed biochemical features of primary hyperparathyroidism are induced by the kidney which include hypercalcemia, hypophosphatemia and increased serum 1,25-dihydroxyvitamin D. Hypercalciuria is an expected feature caused by combined effects of increased calcium reabsorption and bone resorption. Hyperchloremia, defective urinary acidification and renal tubular acidosis have been reported to be associated with primary hyperparathyroidism. Distal renal tubular acidosis due to primary hyperparathyroidism is rarely reported. Renal tubular dysfunction due to significant hypercalciuria appears to be one of the proposed mechanism. CASE PRESENTATION: We present a case of a 26-year old Filipino male presenting with a 3-year history of recurrent episodes of urinary tract infection associated with nephrolithiases. An incidental hypercalcemia noted led to the diagnosis of primary hyperparathyroidism from a hyperfunctioning parathyroid adenoma on further work-ups. Concomitant findings of severe hypokalemia and hypomagnesemia associated with recurrent proximal muscle weakness led to the consideration of an associated distal renal tubular acidosis. Patient underwent minimally invasive selective parathyroidectomy that resulted in full reversal of hypercalcemia and hyperparathyroidism together with the features of distal renal tubular acidosis. He is currently on frequent follow-up for monitoring of electrolyte abnormalities and gradual resolution of nephrocalcinosis. CONCLUSION: Primary hyperparathyroidism can cause distal renal tubular acidosis accompanied by medullary

nephrocalcinosis. Early treatment via parathyroidectomy can help cure secondary distal renal tubular acidosis before development of irreversible renal tubular changes occurs.

P11. The Prevalence and Characteristics of Painful Diabetic Neuropathy in Saudi Patients With Type 2 Diabetes Mellitus.
E Sheshah, A Madanat, R Aman, A dh, Basha, D Al-Qaisi, A A Bakheet, Diabetes Care Center, Prince Salman Hospital, Riyadh Saudi Arabia.

OBJECTIVES: To study the prevalence of painful neuropathic symptoms, its relationship to the severity of clinical neuropathy, age, gender and type of treatment in Saudi patients with type 2 diabetes mellitus. RESEARCH DESIGN AND METHODS: A cross-sectional study was conducted on 366 out of 544 Saudi patients referred from primary health care centers according to inclusion exclusion criteria. Informed consent obtained. Painful neuropathic symptoms were assessed using neuropathy symptom-score. Diabetic peripheral polyneuropathy was determined using neuropathy disability-score. Clinically significant painful diabetic neuropathy defined as moderate painful neuropathic symptoms-score ≥ 5 and mild neuropathy disability-score ≥ 3.SPSS-17 used for statistical analysis. RESULTS: The prevalence of painful neuropathic symptoms was 54.1%. Painful diabetic neuropathy was present in 19.7%. Mean neuropathy symptom-score $\geq 5$was significantly higher in patients with clinical neuropathy than patients without (3.75-6.31).

P12. Effects and Side Effects of DPP 4 Inhibitors – A Literature Review. J Pallivathukkal, Atlas Medical Centre, Oman.

Diabetes mellitus is the only disease in the last 2000 yrs contributing to the mortality and morbidity of the world population, the numbers rising every year, According to W.H.O estimates, by 2025 total 300 million of the worldwide population will be affected by diabetes. For every 21 seconds, someone is diagnosed with diabetes Worldwide. DPP4 inhibitors are a new class of molecules from 2005 which ,from the initial days of launch faced many criticism on its safety and potential benefits and adverse effects .Dpp4 inhibitors blocks the Dpp4 enzyme action which inactivates the GLP 1 and the so the GLP1 acts by either inhibiting the glucagon release and thereby lowering the blood glucose levels or act by stimulating the insulin release and thus reducing the blood glucose level .Dpp4 are proven to be efficient in the management of diabetes and plenty of studies have been conducted and also on going to establish the various aspects of the efficacy and safety profile of the DPP4 inhibitors. I have reviewed the effects and adverse effects of the Dpp4 inhibitors based on the studies conducted. A critical review of head-to-head trials by A.J. Scheen, which is published in Diabetes and metabolism journal in 2012 is a classic work in this subject. Expertise comes from repetition of any work or use and also it will come with time so we expect to get better data and new clinical outcomes in the coming days.

P13. Pakistani Women's Need for Information About Their Diabetic Medication: A Study From Oslo, Norway Where There is a Large Pakistani Population.
W Abuelmagd, K Mahmood, N Tagizadeh, H Håkonsen, E L Toverud, School of Pharmacy-University of Oslo, Oslo, Norway.

BACKGROUND/OBJECTIVES: The Pakistanis represent one of the largest non-western immigrant groups in Norway. The prevalence of Type 2 diabetes among Pakistani women in Oslo is as high as 28%. Former studies show that diabetic Pakistani women have poor drug adherence due to various challenges regarding drug intake. However, no studies have been performed in Norway that investigates the need for information among Pakistani women to achieve a better diabetic control. MATERIAL/METHOD: One hundred and twenty-five diabetic Pakistani women (mean age: 56 years) living in Oslo were personally interviewed using a structured questionnaire. A letter of informed

consent was signed before each interview.The study is approved by The Norwegian Social Science Data Services. RESULTS: All the participants were first generation immigrants. Fifty-two percent didn't know which diabetes type they suffered from. Seventy percent were treated with tablets, 4% with insulin and 24% with both medication forms. More than one third reported poor/ very poor health status. Macrovascular diseases were widely spread among the participants. One in four altered their medication under Ramadan. Illiteracy rate was 27%. The majority said that they could only benefit from oral information and in Urdu. Most of the participants reported satisfaction with the information provided. However, the illiterates were the most satisfied with the information. One-third wished for information about antidiabetic medications, primarily side effects. CONCLUSION: There are major challenges in terms of the need for information regarding diabetes treatment among Pakistani women in Oslo. It is alarming to see their poor self-reported health condition and their uncontrolled diabetes. The low education level and religious aspects are also barriers.

P14. Validation of Self-Reported Oral Health Measures for Predicting Periodontitis Among Adult Filipinos With Type 2 Diabetes Mellitus.
T E Lo, M C Lagaya-Estrada, C Jimeno, G Jasul, University of the Philippines, Philippine General Hospital, Philippines.

INTRODUCTION: Diabetes mellitus is currently being recognized as a global health problem. The likelihood of having periodontal disease among people with diabetes is about 3 times greater and progresses rapidly when uncontrolled. Adults with diabetes were less likely to have been seen or consulted a dentist than to seek consult with a health care provider for diabetes care. This provides an opportunity for health care providers to screen and educate patients regarding the possible oral complications that might develop. A cheap and easy way of clinical assessment via self-reported oral health questionnaire would be of great use especially in a developing country like the Philippines where there's limited resources for health care access. This study aims to validate self-reported oral health measures, socio-demographic and medical variables in predicting the presence and severity of periodontitis in Filipino adults with type 2 diabetes mellitus. METHODS: The validated self-reported oral health questionnaires created by the CDC Periodontal Disease Surveillance Project was translated into Filipino and used in this study. A cross-sectional study of 180 adult diabetic participants was conducted in a single institution. Socio-demographic and medical variables were obtained. Participants were given the self-reported oral health questionnaire and finally underwent a formal periodontal evaluation. Data analysis was done using the software Stata SE version 12. Multivariable logistic regression analyses was used to determine significant predictors that predicted the prevalence of total periodontitis and serious periodontitis. The predictive power of each variable was calculated and expressed using odds ratio. RESULTS: In totality, 93.9% of the study participants had clinically defined periodontitis: 29.4% had mild periodontitis, 37.8% had moderate periodontitis and 26.7% had severe periodontitis. In general, understanding and responses to all oral health questions were very high and consistent. Socio-demographic and medical variables considered to be significantly predictive of serious periodontits were male sex [OR =2.17], low educational status [OR =2.98], poor glycemic control [OR =2.58], less frequent dental visits [OR =2.77] and teeth loss > 6 [OR =5.02]. Self-reported oral health variables shown to be significantly predictive of serious periodontitis included gum disease –Q1 [OR =8.33], state of gum health –Q2 [OR =0.39], loose teeth –Q3 [OR =63.0], brushing of teeth –Q4 [OR =0.65], use of mouthwash –Q4 [OR = 0.69] and poor tooth appearance –Q5 [OR = 48.42]. A recommended set of questions and proposed scoring system based on the logistic regression analysis of each predictors' strength was then formulated. CONCLUSIONS: The use self-reported oral health questions appears to be a potentially useful screening tool for predicting the presence of serious periodontitis among type 2

diabetic patients in a local setting where resources are limited and routine clinical oral examinations are not feasible. This will provide a cost-effective and rapid method of identifying patients who are in need of immediate dental evaluation and would benefit most to a dental referral.

P15. Efficacy and Safety of Once-Weekly Dulaglutide Versus Once-Daily Liraglutide in Type 2 Diabetes (Award 6). T Forst, K M Dungan, S T Povedano, J G González, G Atisso, W Sealls, J L Fahrbach, Profil Mainz GmbH & Co. KG, Mainz, The Ohio State University, Columbus, OH, Hospital Universitario Son Espases, Palma de Mallorca, Universidad Aut'noma de Nuevo Le'n, Monterrey, N.L. México, Lilly Diabetes, Eli Lilly and Company, Indianapolis, IN, Germany, USA, Spain.

BACKGROUND/OBJECTIVES: Dulaglutide, a long-acting glucagon-like peptide-1 receptor agonist, was compared to liraglutide for efficacy and safety in metformin-treated (≥1500mg) type 2 diabetes patients. The primary objective was HbA1C change from baseline at 26 weeks. DESIGN AND METHODS: 599 patients entered a Phase 3, randomized, open-label, parallel-arm study which tested for non-inferiority (margin 0.4%) of once-weekly dulaglutide 1.5mg to once-daily liraglutide 1.8mg. RESULTS: Patients had mean baseline age of 57 years, HbA1C of 8.1%, and weight of 94.1kg. Dulaglutide 1.5mg was non-inferior to liraglutide 1.8mg at 26 weeks (HbA1C change: 0.06%; 95% confidence interval, 0.19, 0.07). Liraglutide-treated patients demonstrated a 0.71kg greater weight reduction than dulaglutide-treated patients. The most common treatment-emergent gastrointestinal adverse events for dulaglutide and liraglutide, respectively, were nausea (20.4%, 18.0%), diarrhea (12.0%, 12.0%), dyspepsia (8.0%, 6.0%), and vomiting (7.0%, 8.3%). Patients who discontinued study and/or study drug due to gastrointestinal adverse events were similar in both groups (dulaglutide 3.0%, liraglutide 4.3%). Hypoglycemia rate was 0.34 (dulaglutide) and 0.52 (liraglutide) events/patient/year. No severe hypoglycemia was reported. Efficacy measures. (26 weeks, Intention-to-treat). Dulaglutide 1.5mg. (N=299) Liraglutide 1.8mg. (N=300). HbA1C change, %, Least squares mean (Standard Error) a -1.42(0.05)‡-1.36(0.05). Percentage patients, HbA1C. CONCLUSIONS: Once-weekly dulaglutide 1.5mg demonstrated non-inferior glycemic control versus once-daily liraglutide 1.8mg, with a comparable safety and tolerability profile.

P16. Efficacy and Safety of Once-Weekly DulaglutideVersus Insulin Glargine in Combination with Metformin and Glimepiride in Type 2 Diabetes Patients (Award-2). V Pechtner, F Giorgino, M Benroubi, J H Sun, A G Zimmermann, Eli Lilly and Company, Neuilly-Sur-Seine, University of Bari Aldo Moro & University Hospital Policlinico, Bari, Evangelismos-Polyclinic, Athens General Hospital, Athens, Chang Gung Memorial Hospital, Taoyuan Hsien, France, Italy, Greece, Taiwan, USA.

BACKGROUND/OBJECTIVES: The once-weekly glucagon-like peptide-1 receptor agonist dulaglutide was compared to insulin glargine in combination with metformin and glimepiride in type 2 diabetes patients. The primary objective was to show non-inferiority of dulaglutide 1.5mg to glargine in HbA1C change from baseline at 52 weeks. DESIGN AND METHODS: Phase 3, parallel-arm, open-label, 78-week study of 807 patients randomized 1:1:1 to dulaglutide 1.5mg (n=273), dulaglutide 0.75mg (n=272), or glargine (n=262). RESULTS: On average, patients were aged 57 years, with HbA1C 8.1% and weight 86.34kg at baseline. Dulaglutide 1.5mg was superior to glargine in HbA1C change from baseline at 52 (1.08% versus -0.63%) and 78 weeks (-0.90% versus -0.59%) (both $p<0.001$); dulaglutide 0.75mg was non-inferior to glargine at 52 and 78 weeks (0.76% and -0.62%; both $p<0.001$). More patients receiving dulaglutide 1.5mg had a HbA1C <7% at 52 and 78 weeks, respectively (53.2%, 49.0%; both $p<0.05$) versus dulaglutide 0.75mg (37.1%, 34.1%) or glargine (30.9%, 30.5%). At 52 and 78 weeks, respectively,

weight decreased with dulaglutide 1.5mg (1.87kg, 1.96kg) and dulaglutide 0.75mg (1.33kg, -1.54kg) and increased with glargine (1.44kg, 1.28kg). At 78 weeks, mean documented symptomatic hypoglycemia rates (≤3.9mmol/L) were lower with dulaglutide 1.5mg and dulaglutide 0.75mg versus glargine (1.7, 1.7, and 3.0 events/patient/year, respectively) (both p≤0.002); severe hypoglycemia was minimal with dulaglutide and glargine. Nausea and diarrhea were more common with dulaglutide 1.5mg (15.4%, 10.6%) and dulaglutide 0.75mg (7.7%, 9.2%) versus glargine (1.5%, 5.7%), respectively. CONCLUSIONS: Dulaglutide 1.5mg demonstrated superior, and dulaglutide 0.75mg non-inferior, glycemic control versus glargine, with an acceptable safety profile.

P17. Effectiveness of Liraglutide in Type 2 Diabetes Mellitus Management: Experience at Zayed Military Hospital, Abu Dhabi.
N Ghuman, D Shaheen, M A Najjar, M A Ali, S Brahim, L Muhammad, Zayed Military Hospital, Abu Dhabi, UAE.

BACKGROUND: In clinical studies human glucagon like peptide-1 analog Liraglutide was effective in reducing HbA1c, weight, and systolic BP, with low risk of hypoglycemia. Objective of this retrospective study was to find out the effectiveness of Liraglutide in reducing HbA1c and weight in clinical practice, as well as tolerability of the drug. STUDY DESIGN: Retrospective cohort. METHODS: Data was collected retrospectively from the pharmacy provided list of all the patients on Liraglutide, from 21ST Sept 2012, to 5th May 2014 and followed up in Zayed Military Hospital (ZMH) DM/Endocrinology Clinic, by reviewing the health records. Adherence to local policy for starting the Liraglutide was also assessed in this cohort (BMI>30kg/m2 + T2DM after the failure of Metformin). RESULTS: Total of 152 patients were issued Liraglutide from the pharmacy. One hundred patients followed up in ZMH and 98 patients had al least two clinic visits. All the patients were either over weight or obese. Mean age was 47.94 years (SD 11.7). Mean paired HbA1c was reduced by 0.9% from the mean baseline HbA1c of 8.42% at 1st follow up, which persisted in available later follow up visits but were smaller than 1st follow up visit. Mean weight was reduced by 1.32 kg from the mean base weight of 99.85kg. Reduction in systolic BP, ALT and LDL was negligible. Only three patients discontinued the treatment due to side effects. One developed acute pancreatitis. Adherence to the criteria to the start the therapy was 96%. CONCLUSIONS: Liraglutide is quite effective in real clinical practice in reducing HbA1c and weight without significant side effects. Adherence to the therapy is excellent. As this therapy results in reduction in weight as compared to Sulphonylurea (SU), and Insulins, hence stops the vicious cycle of obesity and resultant insulin resistance. This study support that Liraglutide is a good agent to treat Type 2 Diabetic patients based on basic pathogenetic mechanistic approach. The criteria to start the therapy was well adhered to.

P18. Glycemic, Blood Pressure and Cholesterol Control in Diabetic Patients Attending Secondary Care Facility.
A A Nuaimi, F H A Hammadi, S A Alshaikh, J S Dhuhouri, S Beula, T M Fiad, Sheikh Khalifa Medical City, Abu Dhabi, UAE.

OBJECTIVE: the aim of this study is to evaluate combined glycaemic, hypertension and hypercholesterolaemia control, in diabetic patients attending secondary care facility. Data was derived from 697 unselected patients with T1DM 9% and T2DM 91% aged ≥ 20 years who attended a secondary care diabetes clinic. Diabetes was defined according to ADA diagnostic criteria[1]; HBA1 <7% defined control. Hypertension was defined by blood pressure ≥140/≥90 mmHg, current use of antihypertensive therapies and established hypertension diagnosis; blood pressure <140/<90 defined control. Dyslipidaemia was defined as an LDL-C level which necessitate the initiation of statin therapy in accordance with the ADA guidelines[1]; LDL-C values below 1.8 mmol/L and 2.6 mmol/L defined control in patients with and without history of CVD respectively. RESULTS**:** 69 % and 85% of

diabetic patients had hypertension and dyslipidaemia respectively. Patients achieved HBA1c, blood pressure and LDL-C goals were 40%, 75% and 74% respectively. In patients with and without history of CVD, concomitant control of diabetes, hypertension and LDL-C<100 mg/dL was achieved in 12% & 24% of patients respectively. When non-HDL-C control of <130 mg/dL was included, percentage of patients reaching all goals concomitantly remained at 24%. Patients received aspirin therapy according to the ADA guidelines[1] represented 76% from the entire cohort. CONCLUSION**:** Our results are consistent with the recently published nationwide surveys[2, 3]. Novel approaches that ensure better BP control, adoption of new strategies to lipid management[4] and the use of safer glucose lowering therapies should facilitate the attainment therapeutic goals and anticipated reduction in CVD.

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P19. Questionnaire Survey on Hypoglycemia and Driving for Individuals with Diabetes in U.A.E. R Tahhan, Al-Zahra Hospital, UAE.

The purpose is to examine the behavior and the knowledge of individuals with diabetes while driving in U.A.E as anti-hyperglycemic medications could lead to hypoglycemia resulting in motor and cognitive dysfunction promoting road accidents. Limited data is available about the subject. METHOD: This is a cross sectional study survey performed on patients with diabetes attending outpatient specialty clinics in one center. Patients were requested to answers three questions related to driving (do you check blood glucose before driving, how low B.G need to go before stop driving, frequency of hypoglycemia on the road in the last 3 and 6 months).The answer to question one was stratified to; yes always, yes sometimes or no. A self-reported hypoglycemia episodes classified to mild, moderate and severe as per ADA recommendation complemented the survey. RESULTS: 104 patients completed the survey after giving verbal consent. 92.3% (96) have type 2 diabetes and 7.7% (8) type1. Male 59.6% (62/104) and female 40.4% (42/104). Mean (SD) age, BMI, diabetes duration and HbA1c; 45.88Â±9.6, 30.88Â±6.04, 7.68Â±5.89, and 7.60Â±1.33 respectively. 86 patients reported driving .31.7% and 6.1%of questionnaire responders are checking their B.G sometimes and always before going on the road. In the sample 50% of insulin users are not doing so at all and 44.4% and 5.6% reported performing B.G checking sometimes and always before their journey. 44.1% (41) did not know the safe B.G level for driving. But when stratified to subgroups according to self-report of hypo in the last one year the experience of hypoglycemia increase the percentage of knowing the safe B.G level ;55.6% and 44.4%(18) in severe hypo group reporting knowing and not knowing compared to 35% and 64.7% in no hypo group p=0.012 respectively. Mean (SD) of B.G level at which should not drive is 71.92Â±11.76 .Mean (SD) hypoglycemia episodes while driving is 0.64Â±2.41 in the last one year .15.1% reported at least one hypoglycemia event. The frequency of hypoglycemia varied ;5.8% one,3.5% two,2.3% three ,1.2% ten and 2.3 14 hypoglycemia events .

P20. Diabetic Ketoacidosis; The Rashid Hospital Experience.

K Hafidh, Z Nazir, Dubai Health Authority, UAE.

OBJECTIVE: To describe the precipitating factors, length of hospital stay and antibody status in patients presenting with diabetic ketoacidosis (DKA) at Rashid hospital over a one year period. DESIGN: Retrospective cross-sectional study involving patients aged 12 years and above with known or previously unknown diabetes presenting with the ADA (American Diabetes Association) diagnostic criteria for diabetic ketoacidosis. BACKGROUND: Diabetic ketoacidosis (DKA) is the most serious diabetic emergency in patients with type 1 and type 2 diabetes and is the leading cause of mortality in children and young adults with type 1 diabetes, accounting for ~50% of deaths in diabetic individuals aged.

P21. Voglibose in Type 1 Diabetes Mellitus – Two Case Studies.

S Umakanth, S Shetty, A PM, P Dhunputh, Melaka Manipal Medical College, Manipal University, India.

BACKGROUND: Voglibose is a competitive alpha glucosidase inhibitor that is used in the management of type 2 diabetes mellitus. Reversible inhibition of this enzyme delays the digestion and absorption of dietary polysaccharides resulting in reduction of postprandial blood glucose excursions. This mechanism is also useful in patients with type 1 diabetes mellitus as shown with acarbose, another alpha glucosidase inhibitor. There are no studies with voglibose in type 1 diabetes mellitus. METHOD: Two patients with uncontrolled type 1 diabetes mellitus were managed by initially increasing the insulin dose until they reached their target HbA1c. After 2-weeks of maintaining good control, voglibose 0.2 mg three times per day was added with each meal along with their usual dose of insulin. They were monitored closely for glycemic control and hypoglycemic episodes for 3 months. RESULTS: Both patients tolerated voglibose very well without significant gastrointestinal symptoms or hypoglycemia. Glycemic control was well maintained over a period of 3 months in both patients. Patient 1 had a reduction in short-acting insulin requirement by 12 units (14%) per day and patient 2 had reduced requirement by 17 (12%) units. In spite of these reductions, HbA1c improved by 0.6% and 0.4% respectively. There was no change in the requirement of basal insulin. CONCLUSION: Voglibose is a safe and effective oral anti-diabetic agent that is also promising in patients with T1DM when used in combination with insulin and dietary advice. Larger studies are required to validate these findings.

P22. Variant Haemoglobins Interfere With HbA1c.

N Hussain, UAE University, UAE.

BACKGROUND: As the American Diabetes Association moves to accept HbA1c as a diabetic diagnostic tool, there is heavy debate about the pros and cons of such a decision. One of the issues is the presence of Hb variants and how these affect HbA1c values. This paper examines current research and practice about Hb variants and how the methods used to analyze it are affected by these variants. METHODS: Firstly, we outline Hb variants and the frequencies with which these occur in different ethnic populations. Secondly, we assess the laboratory methods used to analyze HbA1c and how the methods are, individually, affected by the various types of Hb found worldwide. Thirdly, we highlight the importance of selecting the right analysis method when patients are known to have Hb variants present. RESULTS: Worldwide clinical endocrinologists and laboratorians assume that HbA1c will soon be the gold standard of diagnosing diabetes. Even if this is not yet in wide acceptance, HbA1c is used to monitor for complications, check glycemic control and for decision making about interventions to use. Yet the presence of Hb variants is much stronger than previously acknowledged and it changes the readings of HbA1c drastically. CONCLUSION: In conclusion, we point towards the advantages and disadvantages of each method for HbA1c analysis and highlight how the measurements are altered by Hb variants. This can help the physician recommend the analysis method to be used for known patients and also to treat

HbA1c values with caution in patients who might have Hb variants.

P23. Giant Prolactinoma as Initial Presentation of MEN Syndrome: Case Report and Literature Review.
M Al Ameri, A Al Nuaimi, Sheikh Khalifa Medical City, Abu Dhabi, UAE.

Invasive giant prolactinoma defined as prolactinoma (>4 cm in dimension) with serum prolactin levels of >1000 ng/dL and mass associated clinical symptoms including headache, visual field impairment, and sexual dysfunction. Here, we report a case of invasive giant prolactinoma in a 45-year-old Emirati female with partial initial response to cabergoline treatment, which required later surgical resection as the patient remained with supra sellar extension, visual field impairment despite initial pharmacological treatment. The patient was treated for the Invasive giant prolactinoma, After 48 months, patient presented with parathyroid tumor, multiple pancreatic insulinomas and was subsequently diagnosed with multiple endocrine neoplasia (MEN) syndrome.

P24. Is Wrist Circumference a Clinical Marker for Identifying Diabetes Risk.
S Epuru, S Bano, S Banu, B S Fatima, E Alshammari, University of Hail, Saudi Arabia.

BACKGROUND: Recent studies indicate big wrist size could be a clinical marker for insulin resistance in obese individuals. AIM: The aim of the current study was to find whether wrist size can be a possible clinical marker for high RCBG values in young females which may increase their future diabetes risk. RESEARCH DESIGN: The study included 514 females from University of Hail, Saudi Arabia who were tested for RCBG with One touch Ultra (Lifescan Johnson &Johnson, Milpitas, USA) and body composition analysis with Inbody 720 (Biospace, Korea) and wrist measurements. Those with menstruation cycle on the day of testing were excluded along with pregnant and lactating mothers. Statistical differences were investigated with stepwise linear regression. RESULTS: Around 21% were identified with RCBG > 110 mg/dl. Mean differences for all anthropometric variables considered was significantly high for RCBG group >110 mg/dl as compared to low RCBG group. Regression model included wrist measurement, BMI, percent body fat, body fat mass, visceral fat, waist circumference and waist hip ratio as continuous independent variables and RCBG as dependent discrete variable. Regression model excluded all variables except wrist measurement which explained a significant proportion of variance in RCBG values ($R2 = 0.026$, $F = 14.461$, $p < 0.001$). ROC Curve Analysis suggests wrist measurement of 13 cm and above can be used as a clinical marker to go for definitive testing for diabetes risk. CONCLUSION: Our findings suggest a close relationship for wrist circumference and RCBG in general population opening new perspectives in the prediction of future diabetes risk.

P25. Immune Markers and C-Peptide Levels in Type 1 Diabetes - A Study From a Tertiary Care Hospital in Oman.
F B Kunjumohamed, S R Ratnam, N B Busaidi, R Aktar, M Al Lamki, H A Musalhi, Royal Hospital, National Diabetes and Endocrine Center, Oman.

BACKGROUND: Autoimmune destruction of B cells accounts for more than 90% of type 1 diabetes. The degree of antibody titer and progression of diabetes has been well described. OBJECTIVE: The aim of this study is to assess the auto immune status and C-peptide levels in type 1 diabetes patients who come to our center. Patients and methods. STUDY DESIGN: This is a retrospective study from 1995 – 2013. The data of 67 patients with type 1 diabetes seen at the National Diabetes and Endocrine center was reviewed. The mean age at the time of diagnosis was 16.15(5-34years). Inclusion Criteria. Patients 13 years or older with type 1 diabetes. Exclusion Criteria. Patients with type 2 diabetes or diabetes due to other causes were excluded. Fourteen patients with inadequate clinical details were also excluded. RESULTS: Thirty nine of the 53 patients studied

(73.5%) carried positive immune markers. Twenty eight of them (71.7%) were positive for both GAD (Glutamic Acid Decarboxylase) and ICA (Islet cell) antibodies, twenty three of these patients had low C-peptide levels, and five patients (12%) were with normal C-peptide levels. Eleven patients (20.7%) without antibodies had low c-peptide levels. Twelve out of 23 (52.1%) who had both auto antibodies and low c-peptide levels were diagnosed with ketoacidosis. Twenty four patients had 1st degree relatives with diabetes. Eleven of 17 patients had positive thyroid antibodies and 6 of them were hypothyroid. CONCLUSIONS: More than 70% of study population had both GAD and ICA auto antibodies along with low c-peptide levels. A significant number (>50%) of them presented with ketoacidosis.

P26. Prognostic Role of Oxidative Stress and Inflammation in Patients With Acute Myocardial Infarction and Abnormal Glucose Tolerance. L David, A Grosu, Institute of Cardiology, Chisinau Moldova.

Acute myocardial infarction patients with abnormal glucose tolerance have a poor prognosis. We aimed to examine the role of oxidative stress and inflammation in the long-term prognosis of these patients. METHODS: In 83 acute myocardial infarction patients who underwent an oral glucose tolerance test (30 with normal glucose tolerance, group I; 37 with impaired glucose tolerance, group II; 25 with diabetes, group III) we assessed (day 10 after admission) plasma levels of malondialdehyde (MDA), advanced oxidation protein products (AOPP), S-nitrosothiol (S-NT), superoxid dismutase (SOD), total plasma antioxidant activity (TAA), by spectrophotometry and C reactive protein (hs-CRP) by ELIZA. Post-infarction mortality was evaluated during two year followed-up. By multivariate Cox regression analyses were studied prognostic factors for mortality. RESULTS: No difference in baseline clinical characteristics, AMI size and location were observed between groups. Plasma levels of MDA, PPOA, S- NT were significantly higher in groups II.

P27. Characteristics and Achievement of Metabolic Targets in Patients With Type 2 Diabetes Enrolled in the Aboriginal Chronic Care Program at Budyari Community Health Centre Based at Miller, NSW. M Hasan, V Mackay, P Sutton, N. Richards, R Jarman, T Furlong, S Mwangi, H Russell, Bankstown-Lidcombe Hospital, Budyari Community Health Centre, Miller, NSW, Liverpool Hospital, Liverpool, St. Vincent's Hospital, Darlinghurst, Australia.

BACKGROUND: Budyari Community Health Centre at Miller offers a comprehensive program for the local Aboriginal population with or at risk of chronic disease. The health care team consists of Aboriginal health care workers, Diabetes Educator, Dietitian, Renal Nurse, Endocrinologist, Nephrologist, Optometrist and Podiatrist. DESIGN and METHODS: 39 patients with type 2 diabetes mellitus (T2DM) included in this study. First patient enrolled in 1999. T2DM treatment, complications, body mass index (BMI), blood pressure (BP) and metabolic parameters were assessed at enrollment and recent review. RESULTS: Mean age 60.5 years, 26 females and 13 males. 31 (79%) patients are Aboriginal. Average duration of diabetes is 13 years. Mean duration of follow up 4.2 years. 26 (66.7%) patients are on oral hypoglycemic agents (OHA), 11 (28%) on OHA and insulin. 22 (56%) patients have macrovascular complications (IHD 64%, PVD 22%, strokes 14%) whereas 29 (74%) patients have microvascular complications (nephropathy 57%, peripheral neuropathy 29%, retinopathy 14%). Mean BMI remained stable from 37.5 kg/m2 to 37.7 kg/m2. HbA1c decreased from 9.1%, to 8.6%, lipid profile improved from cholesterol 4.9, triglycerides 2.4mmol/l to cholesterol 4.4, and triglycerides 2.1mmol/l. Percentage of patients achieving target BP increased from 59% to 67%. 26.3% of patients continued smoking. Urine albumin creatinine ratio remained elevated around 23 mg/mmol and creatinine increased from 77.6 to 94.4umol/L.CONCLUSIONS: Aboriginal individuals with T2DM receiving multidisciplinary care can achieve improvements in HbA1c and lipid

profile. The planned peer-led education program will focus on weight loss, stabilization of renal function and smoking cessation.

P28. Lipid Profile in Obese and Non-Obese Women with Polycystic Ovary Syndrome: A Community Based Study in Southwest of Iran.
F R Tehrani, H Rashidi, M Bahri, F Azizi, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Polycystic ovary syndrome (PCOS) is one of the most common and heterogeneous endocrinopathy among women of fertile age. It is associated with metabolic abnormalities such as obesity, lipid, glucose and immune profile disorders all of which are related to cardiovascular diseases; so the aim of present study was evaluation of lipid profile of women suffering from PCOS and comparing them between obese and non-obese patients. Out of 646 reproductive-aged women who were randomly selected using the stratified, multistage probability cluster sampling method, 85 ones met the Rotterdam criteria. The subjects were divided into two groups according to their body mass index (BMI), obese (BMI>25 kg/m2) and non-obese (BMI<25 kg/m2). Lipid profile was compared using ANCOVA adjusted for age among these groups. Among PCOS women, 50 (58.8%) ones were obese and 35 (41.2%) were non-obese. Obese PCOS women showed significantly higher serum levels of triglycerides (111.2±45.6 mg/dl versus 83.5±36.8 mg/dl; P=0.003) and lower serum levels of high density lipoprotein (HDL) (42.2±11.0 mg/dl versus 51.7±11.2 mg/dl; P=0.05). Although non-significant, cholesterol (168.9 ±29.4 mg/dl versus 155.1±41.7 mg/dl; P=0.20)1 and low density lipoprotein (LDL) (100.5 ±25.0 mg/dl versus 86.79±41.9 mg/dl; P=0.21) were higher in obese women compared to their non-obese counterparts. In conclusion, our results show that PCOS women who are obese have the worst lipid profile indicating that metabolic especially lipid profile screening of obese PCOS women may be necessary to prevent long term complications of PCOS among this group of patients.

P29. Fluoxymesterone-Induced Gynecomastia in a Patient with Childhood Aplastic Anemia.
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INTRODUCTION: Gynecomastia is a benign condition characterized by enlargement of the male breast, which is attributable to proliferation of the glandular tissue and local fat deposition. Drug-induced gynecomastia merits deep consideration as it may account for 25% of gynecomastia in adults. Although the mechanism is not fully clear, some mechanisms include estrogen-like activities, stimulation of testicular production of estrogens, inhibition of testosterone synthesis or blockade of androgen action. Anabolic steroids in particular when used during the pubertal stage may cause significant irreversible gynecomastia. CASE PRESENTATION: This is a case of a 28 year-old Filipino male who presented with persistent pubertal gynecomastia. During childhood, he was diagnosed with aplastic anemia and treated with prednisone (20 mg/day), human anti-thymocyte globulin and fluoxymesterone (25 mg/day). Fluoxymesterone was continued until puberty leading to irreversible gynecomastia. On physical examination, the patient had a normal male body habitus and genitalia. What was striking was the presence of a grade 3 gynecomastia and the absence of discharge on breast nipple expression. Biochemical and hormonal tests to rule out pathologic causes of gynecomastia were normal. A planned breast reconstruction surgery was temporarily postponed because of residual thrombocytopenia from the aplastic anemia. As of the last visit, he lives a happy life as a fisherman and a father of 2 children. CONCLUSION: Use of Fluoxymesterone especially during puberty can lead to irreversible and persistent gynecomastia. Its' use should always outweigh probable harm as certain associated adverse effects can lead to permanent physical abnormalities brought about by hormonal disruptions.

P30. Cushing's Disease and Cabergoline Monotherapy: Rapid Clinical Improvement, Reversal of Diabetes, Hypertension and Secondary Infertility with a Successful Pregnancy During 4 Years Treatment.
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Cushing's disease describes a state of chronic cortisol excess due to increased ACTH production from a pituitary adenoma. It results in a significant morbidity and carries a high mortality rate if not managed optimally. Surgical removal of the tumor constitutes the ideal treatment modality and provides the best chance for cure. However in many cases this is either not possible or it fails to produce or sustain the desired response. This provides support to advocate cabergoline as a promising option in a specific subset of Cushing disease patients as 80% of functioning adenomas have dopamine D2 receptors ( ). We report a 32 years old female, with florid Cushing's disease who was severely diabetic and hypertensive with recurrent infections and secondary infertility for 10 years. She was successfully treated with cabergoline monotherapy. Her ACTH and cortisol levels were grossly elevated but her pituitary MRI was normal. Any interventions including inferior petrosal sinus sampling measurement for ACTH (IPSS) and Laparoscopic adrenalectomy were refused, but the patient consented to a trial of cabergoline. Her response was dramatic: on 1 mg daily, her serum cortisol levels returned to normal after one week, and by 4 months her blood sugar and BP were normal off all medications. The HBA1C had fallen from 10.7% to 5.4%. Shortly afterwards she became pregnant and on a reduced dose of cabergoline (1.5 mg/week), she delivered a healthy full term baby. Cabergoline was stopped after delivery but was restarted after 6 months as her disease relapsed. She has now been in complete remission for 4 years on cabergoline 1.5 mg/week without any side effects.

P31. Predictive Risk Factors for Fear of Hypoglycemia and Anxiety Related Disorders Among Adolescents With Type 1 Diabetes in Saudi Arabia.
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OBJECTIVE: To find out the Fear of Hypoglycemia (FOH) and anxiety related disorders and their risk factors among Saudi adolescent with type 1 diabetes mellitus (T1DM). METHODS: A cross-sectional study was conducted among 186 adolescents (13–18 years) with T1DM at Diabetes Treatment Center, Prince Sultan Military Medical City, Saudi Arabia from June 2013 to February 2014. Respondents were selected by their availability during routine visits to outpatient clinics and interviewed by research team using FOH survey and Screen for Child Anxiety Related Emotional Disorders (SCARED) scale independently. RESULTS: Female had significantly higher score of FOH and SCARD in all sub domains compared to their counterpart. The mean score of majority of FOH and SCARD domains were higher in older age group (16-18 years), MDI treatment type (compared to Insulin treatment) and higher duration of diabetes mellitus (>7 years). Similarly, multivariate linear analysis also reported that higher age, female gender, MDI treatment type, higher duration of T1DM were the independent risk factor for majority of the FOH and SCARD domains. CONCLUSION: Female gender, age, treatment type and duration of T1DM are strongest determinants for higher risk for majority of the FOH and SCARD subscales.

P32. Barriers to Physical Activity among Saudi Obese Women.
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OBJECTIVES: The prevalence of obesity is increasing worldwide including Saudi Arabia, especially among women. Physical inactivity is an important modifiable risk factor. The aim of the study was to explore barriers to physical activity

among Saudi obese women attending a body-weight reduction program at diabetes care center. RESEARCH, DESIGN AND METHODS: A cross sectional study was conducted between March and May2014, on sample of 129Saudi women attendees of the gymnasium at the diabetes center. Informed consent was obtained. Patients were interviewed by a trained team. The study questionnaire contained variables on demographic, clinical characteristics of participants, and barriers to physical activity: personal (lack of will, awareness, time, fear of injury and age), social (restrictions on women's participation in outdoor activity, the need for accompanying male-person and low value of physical activity), environmental factors (lack of places to be active, weather conditions) and limited income. SPSS-17 used for statistical analysis. RESULTS: All were Saudis, Mean age41.1±12.3years. The majority were house wives 80.6%.76.0% had diabetes mellitus. Mean body mass index was35.1±7.2kg/m².Family history for obesity was present in48.1% of participants. 79.8%of the participants started to gain weight during adulthood in the post delivery period while 17.1% during puberty and 3.1% during childhood. The most common barrier to being physically active was the personal factor55.1 %. Social factor represented 21.7%. Environmental factors 20.2%.limited income represented 3.1%. CONCLUSION: Personal factor is the most common barrier to physical activity, followed by social and environmental factors. Identified barriers should be addressed when planning strategies aiming at prevention of obesity.

P33. Comparing the Association Between Birth Weight and Body Fat Mass in Reproductive Women With Poly Cystic Ovary Syndrome and Their Age-BMI Matched Eumenorrheic Non-Hirsute Controls.

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BACKGROUND: Fetal programming has been introduced as possible pathogen in polycystic ovary syndrome (PCOS) and the association between early-life factors such as fetal adipose tissue and birth weight (BW) leading to development of adulthood obesity and body fat mass (BFM) was reported. We aimed to compare the association between birth weight and body composition in PCOS and their age-BMI matched normal controls. Their birth weights were registered and their body composition was assessed using Body stat ® Body manager. METHODS: A total number of 70 reproductive aged women referred to Reproductive Endocrinology Research Center with PCOS diagnosis and the same number of age-BMI matched healthy women with no polycystic ovaries by ultrasonography and also without hirsutism and/or ovulatory dysfunction, refereed for annual gynecologic, were recruited for the purpose of the present study. Their birth weights were registered and their body composition was assessed using Body stat ® Body manager. RESULTS: Our study demonstrated that BFM and body lean mass (BLM) are significantly increased in adult PCOS women born underweight compared to their normal counterparts. However this positive association BFM and BLM was not observed in PCOS women who were born overweight. Those women who are now affected with PCOS but had normal weight at birth may have higher fat mass during adulthood. CONCLUSION: The impacts of fetal adipose tissue and birth weight on the development of adulthood obesity, BFM and BLM vary in PCOS and eumenorrheic non-hirsute healthy controls. INTRODUCTION: The etiology of Polycystic Ovary Syndrome (PCOS), common but complex endocrine disorder of reproductive-aged women (1), is not clear, but genetic and environmental factors known to play an important role (2). Among the various suggested pathogeneses, much attention has currently been attracted to “fetal programming” (3).

P34. Waist Cut-Off Values to Predict Diabetes Mellitus Type 2 and Hypertension Risk in Arab Adults.

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BACKGRUND: Obesity is considered a major risk factor for diabetes mellitus (DM) and hypertension. Identifying people at highest risk through ethnically appropriate waist circumference (WC) cut-off points was the main target of this study. METHODS: Data were randomly collected nationwide and analyzed from a cross-sectional study of 4350 Saudi adults aged 15- 64 years using a stratified, multi-stage, cluster random sampling technique. DM subjects were either known cases or subjects with fasting blood glucose ≥7.0 mmol/L. Hypertension was determined as having systolic blood pressure ≥ 140 mmHg. Waist circumference (WC) in cm was measured midway between the lower costal margin and iliac crest during the end-expiratory phase. RESULTS: Mean age for the study subjects was: 36.55+12.99 years (37.5±13.9 years for males; 35.6±11.96 for females). The mean waist circumference for all subjects was 92.75+13.65 cm (95.2+14.01cm for males versus 89.9+12.6cm for females.

P35. Hurdles to Laborers' Access to the Right Treatment.

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Introduction: The hurdles to Laborers' access to the right diabetic therapy is exemplified by 2 case histories and discussed:

Case Histories: Case 1. A 28 year old male, laborer, who is 60 kg in weight; non-smoker, non-alcoholic presented with abdominal pain with loss of appetite and burning of urine. HbA1c was 20 and random blood glucose was 43 mmol/l and urinary ketones were ++. Diagnosis was acute pancreatitis, urinary tract infection, hyponatremia, hypertension, type 2 diabetes. On discharge, his medications: Candesartan 8 mg QD, Human Actrapid 12-8-12 Units sc (TID before meals); Metformin 500 mg BID.

Case 2. 29 male, 57 kg, with generalized body ache, extreme weakness, tiredness, polyuria and polydipsia. He was managed previously in a company clinic and was not on regular medications. His random blood glucose was 55.8 mmol/l; HbA1c was 18.7%; Serum Na was 120. He was receiving Metformin 2 gm QD with Glibenclamide 5 mg BID. He was admitted for 4 days and was discharged On Human Actrapid 10 Units SC TID before meals, Amaryl M BID. Insulin Glargline 30 Units HS and was advised to attend for regular follow up.

Discussion:

Reasons: Poor access to the right medical care for low income group/laborers in Middle East are due to several factors 1) most companies do not provide adequate medical care for their laborers. 2. As per the rules most are treated by the company or factory nurses. 3. Some of the superego company doctors do not allow patients to go to see specialist 4. Patients lack of knowledge about the diabetes and its complications. 5. Ignorance and laziness for regular visits to the specialist. 6. Some of the companies provide better increment to doctors who does not refer their patients _ as the extra cost is saved.

Possible solutions: 1) good diabetic education among the masses including patients, caretakers, doctors, nurses and company representatives. 2) Motivate patients to do self-monitoring of blood glucose. 3) To follow up the regular visits.

P36. Effects of a Supervised Combined Exercise Training Program on Glycemic Control, Body Weight, Body Composition, Fitness Level, and Lipid Profile of a Group of Females with Type 2 Diabetes. H Hasan, D Albdelmannan, A Hassoun, H Farooqi, Dubai Diabetes Center, Dubai, UAE.

OBJECTIVE: The objective of this study was to determine the impact of a supervised exercise training program on the glycemic control, lipid profile, body composition, and fitness level of a group of females with type 2 diabetes. RESEARCH, DESIGN AND METHODS: All participants were females with type 2 diabetes, joined a supervised exercise program, twice weekly for six months in

Dubai Diabetes Center. They were free of cardiac disease and referred by their physician. The exercise class was supervised by exercise specialist and was comprised of 45 minutes of aerobic exercise, 10 minutes of resistance exercises, and 5 minutes of flexibility exercises. Body weight, body mass index, body fat percentage, visceral fat level, muscle mass, fitness level, heart rate recovery, lipid profile, and A1c were measured at baseline and at the end of exercise intervention. P values of less than 0.05 were considered significant. Analysis was performed using MS Office Excel 2003 and Stata 13 software. RESULTS: After 6 months, 13 females out of 47 completed the exercise program. Body weight, body mass index, body fat percentage, visceral fat level, muscle mass, total cholesterol, fitness level and heart rate recovery decreased significantly (P value < 0.05). Although, there was improvement in A1c, LDL, HDL, and triglycerides but it did not reach the statistical significance. CONCLUSION: A supervised exercise program significantly improved body weight, body composition, and fitness level of a group of females with type 2 diabetes.

P37. Incidence and Pattern of Thyroid Dysfunction in Patients on Chronic Amiodarone Therapy: Experience at a Tertiary Care Centre in Oman.

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BACKGROUND: One of the potentially serious side effects of amiodarone is thyroid dysfunction (TD). The patient might exhibit amiodarone-induced hypothyroidism (AIH) or amiodarone-induced thyrotoxicosis (AIT). To date, the data about the incidence and pattern of TD in Oman or the Arabian Gulf region are scant. AIM: To determine the incidence and pattern of (TD) in patients on chronic amiodarone therapy. METHODS: A retrospective study which evaluated 59 patients who received amiodarone therapy regularly for at least 12 months from a period of 3 years from October 2007 to October 2010. The patients were followed up at the cardiac clinic at SQUH. RESULTS: The mean age of the cohort was 63 ± 13 years. 51% (n=30) of the patients were female. There were 11 (19%) cases of (TD). Seven (12%) patients were hypothyroid, 3 (5%) had hyperthyroidism and 1 (2%) patient had sub-clinical hypothyroidism. Female gender and presence of anti-thyroid peroxidase antibodies were significantly associated with (AIH) ($p = 0.001$) while age, amiodarone dose and duration of therapy were not correlated with the development of TD (all p – values > 0.05). CONCLUSION: (AIH) was prevalent in our study. Hypothyroidism was more frequent and seen more in female patients and those who had positive anti-thyroid peroxidase antibodies. Initial screening and periodic monitoring of thyroid function is mandatory for all patients on amiodarone therapy.

P38. Neonatal Graves' Disease With Unusual Metabolic Associations From Presentation Till Resolution.

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Neonatal Graves 'disease is a rare disorder seen in 1 in 25,000 births, and in 1-3% of the offspring of mothers with either an active or a previously treated Graves' disease. The disease is usually due to transplacental passage of TSH receptor-stimulating antibody (TRSAb) from a mother with active or inactive Graves' disease. In spite of its rarity, the serious nature of this condition (if not treated) and its association with multisystem abnormalities justifies careful clinical screening and management. We report a preterm 30 weeks neonate with neonatal thyrotoxicosis secondary to untreated maternal Graves' disease, who had in addition to the typical hyperthyroidism symptoms, unusual metabolic associations of neonatal cholestasis and hyperammonemia. Her thyroid function test after birth showed Cord TSH < 0.01 mIU/L (0.35-30), serum TSH < 0.01 mIU/l (0.35-4.9), FT4: 70.6 pmol/l (9.0-19.0), FT3: 13.58 pmol/l (2.6-5.7), high TRSAb (> 36.0 +++ IU/L (< 1.8), elevated serum ammonia 129 µmol/L (18-72), high GTP 831 U/L (9-36), total serum bilirubin peak 123.5 µmol/L (3.4-20.5) and direct serum bilirubin peak 41.4

μmol/L (1.7-8.6), normal metabolic workup.She was started on Lugol's solution, Propranolol, Methimazol and showed good response. Her clinical condition, thyroid functions, metabolic derangement all normalized. At age of 4 months, she was euthyroid clinically and biochemically, TRSAb level was negative, so Methimazol was stopped. Our case report supports previous reports of unusual association of neonatal Graves' disease with hyperammonemia and cholestatic jaundice. Further studies are required to delineate the exact mechanism of this unusual association.