ABSTRACT BOOK

The First Clinical Congress of the Gulf Chapter of the American Association of Clinical Endocrinologists, October, 3rd-5th 2013, St Regis Hotel, Abu Dhabi, United Arab Emirates.

Guest Editors: Aly B Khalil[1], Ali S Al Zahrani[2], Salem A Beshyah[3]

[1]Imperial College London Diabetes Center, Abu Dhabi, UAE.
[2]King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia.
[3]Center for Diabetes and Endocrinology, Sheikh Khalifa Medical City, Abu Dhabi, UAE.

Corresponding author: Dr Aly Khalil Email: akhalil77@gmail.com
Published: 20 December 2013
Ibnosina J Med BS 2013,5(6):363-402
Received: 13 December 2013
Accepted: 13 December 2013
This article is available from: http://www.ijmbs.org

Abstract
The first clinical congress of the Gulf Chapter of the American Association of Clinical Endocrinologists was held in October 2013. The declared educational objective 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. In this article, 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. Major issues and topical themes with wide interests in the profession were addressed in 6 plenary lectures. More focused issues were included in several parallel 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 presented as either oral or poster presentations. The abstracts are presented under their relevant groups. We hope that by publishing them in this journal we extend the benefit to those who could not make it to the live presentations.

Introduction
In 2012, members and fellows of The American Association of Clinical Endocrinologists (AACE) practicing in the Arabian Gulf Cooperation Council countries formed an "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 to 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. The announced educational objective

of the congress is to give a "state of the art in endocrine practice". The organizing committee invited international and regional key opinion leaders to meet the objectives of the congress. These are the abstracts of the congress as submitted by the authors after minimal restyling and editing to suit the publication requirements. Major, topical themes with wide interests were addressed in the plenary/state of the art lectures. The Chapter's Board of Directors has created two named lectures. The first is the "Key Note Lecture" on a very hot/topical issue in clinical practice and research and it was delivered this year by the president of the national AACE organization on the AACE strategy on obesity in 2013. The second was the "AACE Gulf Chapter Annual Lecture" which is reserved for a regional member or fellow reflecting on an area of his research interests or extensive clinical practice and was given this year by Professor Hussain Saadi of Cleveland Clinic Abu Dhabi on the vitamin D deficiency in health and disease. More focused issues were included in parallel symposia to suite the educational needs of the target audience subgroups. Finally, practical issues were addressed in "Meet the Expert" type of interactive workshops. The abstracts are presented under their relevant groups. 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

Key Note Lecture: AACE Obesity and Bariatric Surgery Strategies in 2013

Jeffrey I. Mechanick, Metabolic Support, Division of Endocrinology, Diabetes, and Bone Disease, Icahn School of Medicine at Mount Sinai, New York, USA.

The 2013 AACE-TOS-ASMBS bariatric surgery clinical practice guidelines (CPG) serve as an update to the 2008 CPG and include many revised evidence-based recommendations from an expanded database. The major advances include use of sleeve gastrectomy, bariatric procedures for mild obesity (BMI 30-34.9), effects of bariatric surgery on type 2 diabetes, copper nutriture after bariatric surgery, the role of psychological evaluations and alcoholism, as well as important logistical issues, such as informed consent. In addition, the 2013 update contains checklists for preoperative and postoperative evaluation. These guidelines are part of a comprehensive obesity care plan proposed by AACE that also includes a complications-centric risk stratification protocol with an emphasis on lifestyle interventions and pharmacotherapy with newly approved anti-obesity agents.

The First AACE-GC Annual Lecture: Current Perspectives on Vitamin D Deficiency

Hussein F Saadi, Department of Specialist Medicine, Cleveland Clinic Abu Dhabi, Abu Dhabi, UAE.

Vitamin D deficiency results from inadequate synthesis in the skin, decreased dietary intake, impaired vitamin D activation in the liver and kidney, or resistance to vitamin D action. Vitamin D nutritional status is best assessed by measurement of the serum 25 hydroxyvitamin D (25OHD) concentration. Serum concentration <25 nmol/L (10 ng/ml) indicates severe vitamin D deficiency that leads to rickets and osteomalacia. Less severe vitamin D deficiency (25OHD < 50 nmol/L or 20 ng/ml) may be associated with secondary hyperparathyroidism, which can precipitate and exacerbate osteoporosis (hypovitaminosis D osteopathy). Several observational studies have also shown that vitamin D deficiency is associated with increased risk of cardiovascular disease, hypertension, diabetes mellitus (type 1 and type 2), metabolic syndrome, polycystic ovary syndrome, some forms of cancer (breast, ovarian, colon), and autoimmune diseases. A 5-year, randomized, placebo-controlled trial involving 20,000 U.S. men and women (VITamin D and OmegA-3 TriaL or VITAL; ClinicalTrials.gov; number, NCT 01169259) that started in July 2010 will address whether supplementation with vitamin D 2000 IU/day (with or without n-3 fatty acids) will reduce the risk of cancer, cardiovascular disease, and other disorders such as diabetes, hypertension and autoimmune diseases. Several studies have shown that moderately severe vitamin D deficiency is highly prevalent in Middle Eastern countries. This is attributed to insufficient sunlight exposure and low dietary vitamin D intake. In one study of healthy Emirati women volunteers, the mean (± SD) serum 25OHD concentration was 25.3 ± 10.8 nmol/L and almost all had concentrations below 50 nmol/L. In another study from the United Arab Emirates, serum concentrations of 25OHD < 25 nmol/L were found in 82% of 90 un-supplemented healthy term breast-feeding infants and in 61% of their mothers. Adequate vitamin D supplementation is clearly indicated in this high-risk population. Modes of prevention include increased skin exposure to sunlight, increased fortification of food items with vitamin D, and oral vitamin D supplementation. The adequate intake for vitamin D as currently recommended by the Institute of Medicine is 400,

600, and 800 IU of vitamin D for ages below 1 year, 1-70 years, and 71+ years, respectively. However, in the absence of significant exposure to sunlight, there is mounting evidence that 1500-2000 IU of vitamin D is required daily for adults (and 400-1000 IU for infants) to prevent vitamin D deficiency. This presentation will review the scope of the problem of vitamin D deficiency in Middle Eastern countries and recommend strategies for its prevention and management.

Plenary Lectures:

PL1. Can We Revive the Beta Cell Reserve in Type 2 Diabetes?

Faramarz Ismail-Beigi, Chase Western Reserve University School of Medicine, Cleveland, USA.

The pathogenesis of type 2 diabetes (T2DM) includes decreased insulin sensitivity, i.e., resistance to actions of insulin to stimulate glucose transport in peripheral target tissues and to inhibit hepatic glucose production on the one hand, and on the other hand, the deterioration of beta cell function to secrete adequate amount of insulin for the given metabolic state. Based on longitudinal studies, it has become evident that hyperglycemia becomes manifest only when insulin secretion has decreased to less than what is necessary for adequate maintenance of normal glucose homeostasis in any particular individual. Deterioration of beta cell function occurs well before the time of diagnosis of T2DM. The progressive beta-cell malfunction during the prediabetic phase seems to start many years before the diagnosis of T2DM. Furthermore, studies show that the maximal ability of beta-cells to secrete insulin in response to large stimuli is markedly reduced (by as much as 75%) at the time of diagnosis of the disease.

Given the above evidence, an important question is whether any of the available therapeutic agents exhibit beta-cell preservation abilities; or can actually revive the beta cell reserve (if any). The evidence indicates that patients randomized to monotherapy with rosiglitazone compared to metformin or glyburide alone have a longer duration of remaining in the normal glycemic range over the subsequent few years (with metformin being more effective than glyburide). Additional analysis indicates that rosiglitazone and pioglitazone appear to have some beta-cell preservation properties. Other studies show that early intensive treatment with insulin appears to have a beta-cell preserving effect.

A large multicenter randomized controlled trial (GRADE) will examine which of four agents added to basal metformin therapy in early-onset T2DM will prove to be more durable in controlling glycemia over a period of 5 years. The efficacy of basal insulin, a sulfonylurea, a DPP-4 inhibitor, and a GLP-1 receptor agonist added to basal metformin will be evaluated. Beta-cell function will be assessed by estimation of insulin resistance and beta-cell function with yearly oral glucose tests and measurements of glucose, insulin, and c-peptide.

PL2. Newer Therapies in Diabetes

Rayaz Malik, Cardiovascular Research Group School of Clinical & Laboratory Sciences, Manchester University, Manchester, UK.

Optimal management of patients with type 2 diabetes demands a patient-centered treatment approach that advocates weight management, limits the risk of hypoglycemia and adverse events, and addresses the core pathologies of T2DM and obesity. Metformin is the initial agent of choice in the treatment of T2DM in all, national and international recommendations (EASD and ADA). This is based on its efficacy to lower HbA1c, weight and the results of UKPDS, which showed reductions in cardiovascular mortality in patients using metformin. However, patient adherence to therapy is critical and compliance with the standard metformin formulation can be poor, due to multiple daily dosing and GI side effects. Metformin XR can be given once daily and is associated with less GI side effects compared to immediate release metformin (IR); this leads to increased compliance, improved glycemic control. Recent data also suggest that Metformin may have additional benefits with a significant reduction in the risk of cancer and cancer-related mortality. These positive data are in contrast to several large studies using additional glucose lowering therapies, which have shown no improvement (ADVANCE, VADT) or worse CV and mortality outcomes (ACCORD), which have been attributed to hypoglycemia and weight gain. Hence, large CV outcome trials with the newer agents (DPP4i, GLP-1 agonists and SGLT2i) with less risk of hypoglycemia and weight loss are currently underway.

PL3. Hyperlipidemia: EAS/ESC Guidelines and Unmet Needs

Marja-Riitta Taskinen, Department of Medicine, University of Helsinki and Helsinki, University Central Hospital, Helsinki, Finland

The first guidelines on the management of dyslipidemias jointly produced by European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS) was released 2011 to better fight the CVD in the 21st century. The challenge was to summarize the large body of evidence into recommendations that should be simple, straightforward, clear and credible to be implemented in the clinical practice. The guidelines highlight that the causes of CVD are multi-factorial and that successful management of dyslipidemias is fundamental to reduce and prevent CVD risk. The guidelines comprised several new issues. The SCORE model based on European data was used in the assessment of global risk and four different risk categories (very high, high, moderate and low) were introduced as a basis for treatment decisions. A new feature was the inclusion of HDL cholesterol risk charts as HDL chol is a key risk modulator. Impact of other lipid measures such as HDL, triglycerides, apo B and lp(a) are highlighted for the risk assessment. The treatment of dyslipidemias focuses on LDL as a primary target but the targets were revised according to the available evidence for people at moderate, high and very high risk to be <3.0, <2.5 and <1.8 mmol/l (115,100 and 70 mg/ dl) respectively. The guidelines focus on familial dyslipidemias in particular on FH as specific guidance is needed for their appropriate treatment. The guidelines also consider specific populations and their different needs for intervention strategies. CKD is acknowledged as a CAD risk equivalent for the first time.

As relevant evidence on CVD prevention emerges continuously the guidelines always contain some gaps based on lack of sufficient evidence. Despite the widespread use of non-HDL-C and apoB the evidence is not sufficient to recommend their routine use as treatment targets except in specific subgroups like in people with the metabolic syndrome and type 2 diabetes. There is still insufficient evidence to define a therapeutic target level for TG or HDL-C. Likewise strong evidence on the efficacy is missing due to failures of RCTs using drug treatments to lower serum triglycerides or raise HDL cholesterol to further reduce CVD morbidity and mortality. Likewise evidence to prove whether Lp(a) lowering against background statin therapy can reduce the risk for CVD events and mortality is not sufficient to consider treatment of high lp(a) values. This gap prevents the efficient management of the residual risk in high risk subjects who have achieved their LDL goals. In the near future the EAS/ESC guidelines will be revised based on the current evidence to further facilitate the treatment and prevention of CVD.

PL4. Thyroid Nodules and Thyroid Cancer: Case-Based Discussion

Hossein Gharib, Mayo Medical School, Rochester, USA.

There have been many recent advances in thyroid nodule and cancer management. This presentation highlights trends in diagnosis and management, using recommendations from recently published studies as well as guidelines. Most patients with thyroid nodules are asymptomatic. Initial evaluation includes history, physical exam, serum TSH measurement and an US exam. Indeterminate nodules undergo US-guided FNA. FNA-negative nodules require follow up only. T4 suppressive therapy is no longer recommended for benign nodules. FNA-suspicious nodules can be further evaluated by molecular markers whereas malignant nodules warrant surgical excision. Currently, a near-total or total thyroidectomy is optimal surgery for patients with thyroid cancer. The role of prophylactic central neck (level VI) node dissection at initial surgery is a matter of debate. The goals of initial therapy include removal of primary tumor and lymph nodes, minimizing morbidity and cancer recurrence, facilitate ^{131}I treatment, and provide useful information for accurate staging. Postoperative radioiodine remnant ablation (RRA) is used to eliminate post-surgical thyroid remnant. It is reported to reduce local recurrence rates and it also facilitates follow up with serum thyroglobulin (Tg). RRA can be performed following T4 withdrawal or rhTSH stimulation. Generally, low risk papillary thyroid cancer patients do not require RRA; most other tumors should be so treated. The radioiodine doses vary from 30 to 150 mCi, with current recommendations favoring lower, 30-50 mCi doses, for most patients. Suppression of serum TSH with thyroxine (T4) has been an important part of thyroid cancer management for decades. Side-effects of long-term TSH suppression include atrial fibrillation and bone loss, particularly in elderly patients. Current recommendations state TSH 0.3 to 2.0 for low-risk patients, TSH 0.1 to 0.5 for high-risk patients, and TSH < 0.1 for patients with persistent disease. Two useful tests for long-term follow up include serum Tg and neck ultrasound

(US). Serum Tg is an excellent marker for differentiated thyroid cancer and should be measured every 6-12 months, ideally in the same lab and using the same assay, long term. Tg antibodies should be available with each Tg report. Cervical US is highly sensitive for detecting locoregional metastasis, and should be used at 6 and 12 months postop, and yearly thereafter. Rising serum Tg levels always suggest recurrent disease. Local cervical recurrences should be evaluated by US exam and US-guided FNA. Measurement of Tg in the needle washout adds to the accuracy of biopsy, since an unsatisfactory FNA with high Tg is diagnostic of recurrent cancer. Of note, Tg in the needle washout is reliable even when serum TgAb is positive. Additional useful imaging includes WBS (whole body scan), chest-neck CT scan preferably with iodine, and PET, the latter being frequently positive in scan-negative, Tg-positive patients. RAI is used to treat distant metastasis when uptake is documented on WBS; doses often average around 200 mCi. Adverse effects of RAI include sialadenitis, dry eyes, leukopenia, leukemia, pulmonary fibrosis and second primary malignancies. Cumulative doses of > 600-800 mCi are often associated with complications.

Clinical Practice Symposia
Symposium 1: Endocrine Replacement Therapy

S1.1 Growth Hormone Therapy: Classical and Newer Indications and Monitoring

Walid Kaplan, Division of Pediatric Endocrinology, Tawam Hospital, Al Ain, UAE

The use of growth hormone (GH) in humans was started in the mid-1950s, but due to the limited supplies of human pituitary-derived GH back then, its use was limited to the most severely affected patients, and it was later complicated by the development of CJD. After the introduction and abundance of human recombinant GH (hGH), several indications have been approved worldwide, and the list is expected to expand over the years. Beside its main benefits in improving the linear growth, hGH has favorable metabolic effects that resulted in its approve for use in adult patients as well. This lecture will cover the following topics: The list of FDA approved indications of hGH in children and adults, controversial indications and off-label use of hGH, the benefits of using hGH in the common indications, dosing and monitoring of hGH, duration of treatment, Treatment transition from pediatric to adults and safety of hGH.

S1.2 Optimization of Glucocorticoid Replacement Therapy

Baha M. Arafah, Division of Clinical and Molecular Endocrinology, University Hospitals of Cleveland, Cleveland, USA.

Adrenal insufficiency refers to the constellations of clinical features associated with partial or complete loss of secretion of adreno-cortical steroids. Diseases of the adrenal glands themselves (e.g. autoimmune adrenalitis) lead to primary adrenal insufficiency where secretion of all adreno-cortical steroids (aldosterone, cortisol, DHEA, DHEA-S) is impaired. In contrast, central or secondary adrenal insufficiency is caused by loss of ACTH secretion which eventually leads to decreased production of ACTH-dependent steroids (cortisol and DHEA, DHEA-S). The clinical manifestations of glucocorticoid (GC) insufficiency are gradual, often nonspecific but become more apparent at times of increased stress such as an infection or a surgical procedure. On the other hand, mineralocorticoid (MC) insufficiency causes postural hypotension and salt craving. Adrenal androgen deficiency results in clinical symptoms (diminished libido, loss of axillary and pubic hair) primarily in premenopausal women The diagnosis of adrenal insufficiency requires integration of the available clinical and biochemical data and an understanding of the cause of the disease. Such an understanding should address the potential for disease reversibility as is often the case in those with central adrenal insufficiency. The primary goals of therapy are to provide effective hormonal replacement that offer symptomatic relief with minimal if any, adverse events. In an attempt to achieve that, an important concept to emphasize is that there are individual variations in patients' dose-requirements and responses and therefore, there is no single dose that would be appropriate for all patients. Educating patients with adrenal insufficiency about their illness is extremely important not only in minimizing adverse events but also in preventing serious life-threatening events such as adrenal crisis. Patients with primary adrenal insufficiency require at the very least GC and MC replacement whereas those with central disease need GC but no MC therapy.

Glucocorticoid Replacement Therapy: Available GC on the market include hydrocortisone, cortisone acetate, prednisone, prednisolone and dexamethasone. While hydrocortisone and prednisolone are biologically active, both cortisone acetate and prednisone are biologically

inactive and require activation by the 11-β hydroxysteroid dehydrogenase (primarily in the liver). The variable degree of intra-hepatic activation of cortisone or prednisone causes great variability in the biologic activity of these compounds. Although any of the GC can be used, the preferred drug is hydrocortisone. The main advantages of using hydrocortisone include the use of biologically active drug that is identical to the native hormone and the ability to easily fine tune the dose. Hydrocortisone is somewhat more expensive than cortisone acetate or prednisone and has a shorter half-life. Despite these limitations, hydrocortisone is the preferred form of corticosteroid replacement. Most patients with adrenal insufficiency require 15 to 20 mg/day, although some do well with a total of 10-12.5 mg/day. With the known diurnal variation in cortisol secretion, it is hard to provide a practical regimen that can mimic the natural rhythm. Attempts to mimic the natural diurnal rhythm included continuous IV or SC hydrocortisone delivery systems. The latter were obviously impractical for routine use. Promising results are reported from recent studies using newly developed modified slow release preparations of hydrocortisone. Until such preparations become available, one has to rely on multiple doses of hydrocortisone to come close to the natural rhythm.

The daily replacement of hydrocortisone is given in a minimum of two and preferably in three doses. The morning dose (7.5-10 mg, PO) is usually given at 7-8 AM, the mid-day dose (5-2.5 mg) at around 12-1 PM while the evening dose (2.5-5 mg) is scheduled for around 6 PM. Each of the 3 doses should be titrated according to symptoms and adverse events. Occasionally, a rare patient wakes up in the morning with significant withdrawal symptoms and may require an additional dose of hydrocortisone at bedtime. Patients who work different shifts will need to have their schedule change accordingly. Prednisone (3.5-5 mg/day) or prednisolone (3-4 mg/day) divided in two doses are less expensive to use but the dose is harder to carefully titrate. Dexamethasone (0.25-0.5 mg/day) has a long biologic half-life and can be given only once daily as a source of GC replacement but dose titration can be difficult. Patients with potentially reversible forms of adrenal insufficiency should not be treated with long acting GC replacement, especially dexamethasone since its long half-life will suppress endogenous ACTH and therefore impedes potential HPA axis recovery.

It is important to consider the impact of other drugs and illnesses on GC replacement doses. The major site of GC degradation is the liver where these compounds can be degraded through several enzymatic pathways. The primary mechanism is reduction through the 5-b reductase. Another, less important pathways is the 6 b hydroxylation. The latter becomes more important during states of hypercortisolism. Glucocorticoid metabolism is accelerated in patients with hyperthyroidism. Several drugs such as Phenytoin, Phenobarbital, Carbamazepine and Mitotane accelerate the metabolism of synthetic GC especially the halogenated ones (e.g., dexamethasone, betamethasone) but have minimal impact on hydrocortisone metabolism. Rifampin, an anti-tuberculosis drug increases the metabolism of hydrocortisone and a greater degree that of other synthetic glucocorticoids. Thus, in patients treated with these drug, GC doses might need to be adjusted depending on the drug and the steroid used. An important consideration in the treatment of patients with adrenal insufficiency is patients' education about their own illness and the need for dose adjustments with inter-current illnesses. For a mild illness such as a common cold, the daily dose can be doubled for 2 days or so. For a more moderate stressful event such as same day surgery, three times the daily dose is adequate and for a more severe illness such as open heart surgery, 100 mg of hydrocortisone every day is more than sufficient. Higher doses are not necessary unless one is treating a severe inflammatory process such as septic shock. Once the total dose of GC is over 50 mg of hydrocortisone, there will be sufficient MC activity such that fludrocortisones therapy need not be administered. Patients are advised to carry a medic alert ID indicating their diagnosis, and their dependence on corticosteroids.

The best parameter to monitor replacement therapy is clinical symptoms (e.g., energy level, fatigue) and sign including weight gain and blood pressure. Measurements of plasma ACTH and/or serum cortisol are not routinely necessary, unless poor absorption is suspected. Similarly, measurements of urinary free cortisol provide no benefit in dose adjustments.

Further Reading

1. De Bono M, Ghobadi C, Rostami-Hodjegan A, et al. Modified-Release Hydrocortisone to provide Circadian Cortisol Profiles. J Clin Endocrinol Metab 2009;94:1548-54.
2. Bornstein SR. Predisposing factors for adrenal insufficiency. N Eng J Med 2009; 360:2328-39.
3. Bergthorsdottir R, Leonsson-Zachrisson M, Oden A, Johannsson G. Premature mortality in patients with

Addison's disease: a population-based study. J Clin Endocrinol Metab 2006; 91:4849-53.
4. Al-Aridi R, Abdelmannan D, Arafah BM. Biochemical diagnosis of adrenal insufficiency: The added value of dehydroepiandrosterone sulfate (DHEA-S) measurements. Endocrine Practice 2011,17:261-70.

S1.3 Current Perspectives on Testosterone Replacement Therapy in the Ageing Male

Pierre Bouloux, Department of Neurodocrinology, Royal Free Hospital London, United Kingdom

Although a substantial body of epidemiological evidence supports the notion that free testosterone levels decline in the ageing male, the clinical significance of this age-related change remains unclear. The fall in free T is gradual and affects a relative minority of men. Thus in one study, using an arbitrary testosterone cut-off level of <10.4nmol/l (300ng/dL), the prevalence of symptomatic androgen deficiency was 5.6% (Araujo et al 2007). In a larger population study (EMAS), using testosterone threshold below which symptoms become increasingly prevalent resulted in only 2.1% of middle aged men meeting the criteria for symptomatic hypogonadism, although this number increased with increasing age, obesity and co-morbid illness (Wu et al 2010). The problem is compounded by the fact that many of the symptoms characteristic of classical hypogonadism in young men are not associated with low testosterone levels in middle age and older men. In general, the symptoms most closely associated with lower testosterone levels in this group can be divided into three groups: 1) Sexual (decreased morning erections, frequency of sexual thoughts, erectile dysfunction) 2) Physical (inability to engage in vigorous activity, difficulty walking >1km, inability to bend or stoop. 3) Psychological (loss of energy, sadness, fatigue. Of those, it appears from this large population based study that the presence of 3 sexual symptoms combined with a total testosterone level <11nmol/l (320ng/dL) and a free testosterone level of 220pmol/l. Testosterone replacement therapy (TRT) requires special considerations in the aging male. Thresholds at which improvements in symptoms may be anticipated appears to vary between individuals, possible as a consequence of pharmacogenomic considerations. Furthermore, the prescriber needs to focus on the possibility of adverse effects, especially prostate health, and to avoid excessive rises in hematocrit. Recent evidence suggests that measurement of both DHT and estradiol levels may be helpful in optimizing replacement therapy.

References

1. Araujo AB, Esche GR et al. Orevalence of symptomatic androgen deficiency in men. J Clin Endo Metab. 2007; 92:4241-47.
2. Tajar A et al. Characteristics of secondary, primary, and compensated hypogonadism in aging men: evidence from the European Male ageing study. J Clin Endo Metab 2010;95:1810-8.
3. Wu FW et al. Identification of late-onset hypogonadism in middle aged and elderly men. N Eng J Med 2010;363:123-35.

S1.4 Challenges in Thyroxine Therapy in 2013

Hossein Gharib, Mayo Medical School, Rochester, United States of America

This is a case-based presentation to illustrate important clinical points about thyroxine (T4) therapy in thyroid practice. It includes 1. discussion of practical issues in hypothyroidism with the following objectives 2. Subclinical hypothyroidism: 3. CV risks; 5. risks of overt disease; 6. criteria to select patients for Rx Causes and course of primary hypothyroidism 7. How to select T4 dose 8. a review of why some patients on thyroxine therapy continue to complain of symptoms 9. Thyroid testing in pregnancy and normal TSH levels and 10. Explanation of why serum TSH is abnormal in some patients on apparent adequate T4 doses.

Symposium 2: Cardiovascular Protection in Diabetes.

S2.1 Glycemic Management and Cardiovascular Risk

Faramarz Ismail-Beigi, CWRU School of Medicine, Cleveland, USA.

People with higher than normal blood glucose levels have increased risk of mortality due to cardiovascular disease (CVD). In addition, patients with diabetes have 2- to 4-fold higher risk of death due to CVD. Whether intensive treatment of hyperglycemia in patients with type 2 diabetes reduces the risk for CVD among patients with established was addressed in three large multicenter trials, ACCORD, ADVANCE, and VADT. The ACCORD trial, similar to the other two trials, recruited adult older patients (age ~60) with established type 2 diabetes (duration of ~10 years).

Participants had a history of CVD or had risk factors for the development of CVD. The primary outcome of ACCORD, ADVANCE and VADT trials was fatal and non-fatal CVD events. The results of all three trials suggest that in older adults with established type 2 diabetes with either prior CVD events or 2 or more risk factors for CVD, intensive glycemic control does not reduce total or CVD-related mortality, and was associated with increased all-cause and CVD-related mortality in ACCORD. Results of these trials will be compared to previous trials focused on the same question, including the UKPDS trial. Based on the results of these studies, implications for potential modification of approaches to the management of patients with established type 2 diabetes will be discussed. Taken together, the above findings in addition to recent analysis of data from a large research data-base (Diabetes Care 36:2366-2371, 2013) and an analysis of the VADT study (Diabetes Care 36:2408-2414, 2013), suggest that intensive glycemic treatment of patients with established CVD offers little benefit in the prevention of CVD disease. However, more aggressive glycemic management initiated during earlier stages of the disease appears to have protective benefits.

S2.2 Management of Hypertension in Patients with Diabetes

Rainer Düsing, Department of Internal Medicine, Medizinische Klinik und Poliklinik, Bonn, Germany.

Recent epidemiological studies support the concept that arterial hypertension represents the most aggressive cardiovascular risk factor to date. However, it is important to note that the absolute risk associated with hypertension is largely dependent on comorbidities. In this context, diabetes is a key factor to dramatically increase the risk for cardiovascular and renal events in patients with hypertension. Epidemiological data demonstrate that the prevalence of diabetes in hypertensive patients is approximately twice that in the general population. On the other hand, patients with diabetes exhibit high rates of hypertension ranging between 70–90%. Among the underlying mechanisms of this prevalent comorbidity of hypertension and diabetes, overweight/obesity has been identified to play a crucial role. The mechanisms of both obesity associated hypertension and diabetes have in part been elucidated. After manifestation of diabetes hypertension may also be promoted by renal functional changes due to diabetic nephropathy. Hypertension, on the other hand, may further impair insulin sensitivity by structural changes within the microcirculation. Prevention and therapy of overweight/obesity thus play a key role in cardiovascular and renal prevention.The increased cardiovascular and renal risk of diabetic hypertensive patients is one of the reasons, why previous guidelines have unanimously recommended goal blood pressure on treatment to be lower in hypertensive patients with comorbid diabetes than in the general hypertensive population. However, strong evidence for this recommendation is still lacking. The present review will summarize the ongoing debate on blood pressure goals in hypertension with comorbidities including diabetes and will point to the necessity of individualized strategies in these clinical situations.

S2.3 Evaluation and Management of Hypertriglyceridemia: Why and How?

Marja-Riitta Taskinen, University of Helsinki and Helsinki University Central Hospital, Helsinki, Finland.

Plasma triglyceride concentration is a biomarker of triglyceride rich lipoproteins (TRLs) comprising chylomicrons and VLDL species and their remnants. The evidence that elevated levels of TRLs are strong CVD risk factors has grown rapidly based on data from both general populations and subjects with CVD. Whether triglycerides per se are promoting atherosclerosis has remained a debated issue. It should be recognized that high triglycerides are metabolically linked to small dense LDL cholesterol and low HDL cholesterol. This combination is known as the atherogenic lipid triad. Recently a consensus has emerged that non-fasting triglyceride levels are a better risk marker of CVD than fasting triglycerides. This casual connection is recently supported by using Mendelian randomized approach. In Copenhagen Heart Study 1 mmol/l (39 mg/dl) increase in nonfasting remnant cholesterol was reported to be associated with a 2.8 fold causal risk of ischemic heart disease independently of HDL cholesterol. The data imply that the focus to reduce the residual risk among patients treated with statins should be lowering of plasma TRLs.

ATG level <1.7 mmol/ (<150 mg/dl) is considered a desirable goal for high risk patients in the guidelines. A consensus exists that management of lifestyle and secondary factors is the first step for mild to moderate hypertriglyceridemia. Patients with severe or very severe hypertriglyceridemia request immediate treatment due to the risk of pancreatitis fibrates being the first choice. In contrast the drug treatment of moderate hypertriglyceridemia is a debated issue and a

clinical challenge due to the failure of clinical trials with TG lowering drugs. If in high risk patients LDL chol is at goal but triglycerides remain elevated intensification of statin therapy is recommended. Adding fibrate may be considered as fenofibrate reduced major CVD events in subgroup analyses (FIELD, ACCORD) of subjects with high TG/low HDL chol. Recently the non-HDL cholesterol has emerged as a secondary goal in these patients. Whether the future will provide better tools to reduce TRLs and their remnants remains an open issue.

S2.4. Anti-Platelet Therapy in Diabetes

Salah Abusnana, Sharjah University and Rashid Centre for Diabetes & Research, Ajman, UAE.

Most guidelines were recommending aspirin for the primary prevention of cardiovascular events in people with diabetes, until recently. Those recommendations were based on indirect evidence from large trials. Most of these trial included populations at high risk of cardiovascular (CV) events. The efficacy of aspirin therapy in trials of diabetic subjects supported only by scant evidence. Meta-analysis on the efficacy of antiplatelet therapy in the prevention of major CV events found a clear benefit of aspirin overall, but no statistically significant benefit in the subgroup of people with diabetes. The risk of major CV events in people treated with low dose aspirin compared with placebo was found in three additional trials published after that meta-analysis, no significant reduction seen. Recent meta-analyses incorporating the results of recent trials agree in indicating that the use of aspirin is associated with a 10% reduction in the risk of major CV events, with no significant effect on CV or all-cause mortality. Other factors like, differential sex effect, is also suggested. The evaluation of the risk-benefit balance is very important, particularly after the results showed lower than expected benefit of the antiplatelet therapy. Risk of major bleedings with excess of one or two cases for 1,000 individuals treated with aspirin for 1 year. In the real world setting, such a risk is even higher, is probably increased in the presence of diabetes and exponentially increases with age. It seems reasonable to suggest antiplatelet therapy as primary prevention, only for patients with a 10-year risk >15%, and without contraindications for aspirin.

Symposium 3. Microvascular Diabetic Complications

S3.1 Update on Pathogenesis and Management of Diabetic Nephropathy

Fuad Ziyaedh, Departments of Internal Medicine; Biochemistry & Molecular Genetics, American University of Beirut, Beirut, Lebanon

Diabetic nephropathy is the leading cause of ESRD disease globally. Microalbuminuria is the earliest reliable predictor of nephropathy, and clinically overt disease becomes progressive when heavy proteinuria ensues, associated with significant hypertension and increasing degrees of renal failure. Pathologically, there is diffuse and/or nodular glomerulosclerosis, arteriolar hyalinosis, and tubulointerstitial fibrosis. Susceptibility is determined by genetic predisposition, hemodynamic factors (high systemic and intra-glomerular pressure), and suboptimal hyperglycemic milieu which is aggravated by abnormal glycation reactions, oxidative stress and activation of the intrarenal Angiotensin II system. The glomerulopathy is due to the traditionally-recognized glomerular mesangial cell injury (leading to mesangial matrix expansion and filtration failure) and the recently recognized podocyte injury with detachment or apoptosis (leading to proteinuria). Proteinuria per se is an independent disease-progression factor and is associated with tubulointerstitial fibrosis. Our research using cell culture, animal models, and human studies has identified excess activity of Transforming Growth Factor-beta (TGF-β) as the cause of glomerulosclerosis and that of Vascular Endothelial Growth Factor (VEGF) as probably the cause of albuminuria. Early detection and treatment of diabetic nephropathy (especially optimal control of glycemia, hypertension, and proteinuria) can greatly delay the development and/or progression of diabetic nephropathy. The recommended management guidelines are undergoing continuous refinements but they can be summarized generally by the following: optimal glycemia (HgbA1c <7%), hypertension control (< 130/80 mm Hg, although this target is being revisited), reduction of proteinuria (<1 g/d), low protein diet (<0.8 g/kg/d), and cessation of smoking. Renoprotective therapy with agents that intercept the renin-angiotensin-aldosterone axis, resulting not only in lowering systemic blood pressure but also intraglomerularl pressure, has shown superiority over traditional antihypertensive agents. Other benefits of these agents are their antiproteinuric effect and the inhibition of high levels and activity of intra-renal TGF-β and VEGF systems.

S3.2 Advances in the Management of Diabetic Retinopathy

Ammar Safar, American Hospital, Dubai, United Arab Emirates.

Significant advancements in our understanding of diabetic retinopathy have taken place in the past few years. This lecture will outline the new concepts in the pathogenesis, classification and discuss the latest approach in managing patients with diabetic retinopathy.

S3.3 Diabetic Neuropathy: Evaluation and Management

Rayaz Malik, Cardiovascular Research Group, School of Clinical & Laboratory Sciences, Manchester University, Manchester, UK.

Small fibres constitute 70–90% of peripheral nerve fibres and regulate several key functions such as tissue blood flow, temperature and pain perception as well as sweating, all of which are highly relevant to the clinical presentation and adverse outcomes associated with foot ulceration in patients with diabetes. Recent studies demonstrated significant abnormalities in the small fibres in subjects with impaired glucose tolerance and diabetes, despite normal electrophysiology, suggesting that the earliest nerve fibre damage is to the small fibres. Although skin biopsy has been proposed as a 'gold standard' technique for evaluating small fibre neuropathy, the data in diabetic neuropathy are limited and the technique itself is invasive and requires expert assessment, which is not widely available. Corneal confocal microscopy (CCM) is a relatively new technique which until recently has been used predominantly in clinical research. However, it has emerged as a powerful technique for the study of corneal nerves. It is now increasingly recognized as a powerful, non-invasive and reiterative test to enable early diagnosis, assess progression and the benefits of therapeutic intervention in diabetic and other peripheral neuropathies. There are currently no pathogenetic treatments currently licenced for diabetic neuropathy. Glucose control has been shown to be beneficial in preventing the progression of neuropathy in type 1 but not type 2 diabetes. There are data to suggest that ACEi and Fibrates may benefit neuropathy. For the treatment of symptoms there are only two approved therapies: Pregabalin and Duloxetine. However, there are recent data to suggest that vitamin D deficiency may be important in the development of painful neuropathic symptoms and treatment may be beneficial.

Symposium 4. The Foot in Diabetes

S4.1 Wound Management in the Diabetic Foot Ulcers

Zbigniew Ruszczak, Wound Care Clinic, Sheikh Khalifa Medical City, Abu Dhabi, UAE.

One of the main problems challenging the health care system is the diabetic foot and diabetes-related wound healing complications. Effective wound healing is of special interest of the Dermatology Division at SKMC, the main UAE center operating multidisciplinary Wound Care Clinic. Out of over 3000 patients with "non-healing" wound per year, approx. 65% of are diabetes-related difficult to heal neuropathic/angiopathic foot ulcers. Additional 25% of patients suffer from post-surgical wound infection requiring long-term specialized treatment. Dermal substitution and wound healing are areas of medicine in which there have been many recent advances, but neither the commercially available products nor the products currently described in experimental studies are able to fully substitute for natural living skin. Additionally, geographic (high temperature & moisture), cultural (way of dressing, type of shoes) and religion-related issues are factors influencing wound care and making established, Europe or US-oriented guidelines less applicable. We are presenting own, long-term clinical experience in facing and challenging the problem of diabetic foot and diabetes-related wound care, based on the daily practice of the Wound Care Clinic. The application of region-oriented healing regimens, unconventional approaches and the need of multidisciplinary cooperation are presented.

S4.2 Peripheral Vascular Disease and the Surgical Aspects of Diabetic Foot

Abdullah Al Wahbi, Department of Surgery, King Saud Bin Abdulaziz University for Health Sciences and King Abdulaziz Medical City, Riyadh, Saudi Arabia.

More than 85% of lower limb amputations are proceeded by diabetes foot ulcer. With an epidemic of diabetes in the GCC countries amputation epidemic is inevitable. Peripheral arterial disease associated with diabetes is the determinant factor for diabetic foot ulcers outcome. Vascular assessment should be routine in all patients with diabetic foot ulcers and aggressive vascular diagnostic and interventional approach should be available in all secondary and tertiary care hospitals.

S4.3 Podiatric Aspects of the Diabetic Foot

Sami Tabib, Podiatry Chiropody Center, Dubai and Imperial College London Diabetes Center, Abu Dhabi, UAE.

The pedal manifestations of diabetes are well documented and potentially limb and life threatening. Recognition of risk factors and treatment of diabetic foot disorders require the skill to diagnose, manage, treat, and counsel the patient. All patients with diabetes require a foot inspection whenever they present to any health care practitioner, and they should receive a thorough lower extremity examination at least once annually. Patients with complaints relating to the diabetic foot require more frequent detailed evaluations. Diagnostic procedures, such as laboratory testing, imaging studies, vascular and neurologic evaluation, and plantar foot pressure assessment, may be indicated in the assessment and care of the diabetic foot. Risk Stratification where the patient is classified according to a cumulative risk category is critically important. This enables the physician to design a treatment plan and determine whether the patient is at risk for ulceration or amputation. Diabetic patients at risk for foot lesions must be educated about risk factors and the importance of foot care, including the need for self-inspection and surveillance, monitoring foot temperatures, appropriate daily foot hygiene, use of proper footwear, good diabetes control, and prompt recognition and professional treatment of newly discovered lesions. Integration of knowledge and experience by a multidisciplinary team approach promotes more effective treatment, thereby improving outcomes and limiting the risk of lower extremity amputation.

Symposium 5. Advances in Management of Pituitary Tumors

S5.1 Recent Advances in Management of Cushing's Disease

Pierre Bouloux, Neuroendocrinology, Royal Free Hospital, London, UK.

Cushing's syndrome (CS) is a devastating but uncommon disorder with an incidence of approximately 1:200,000. It results from exposure to (endogenous) chronic inappropriate levels of free circulating cortisol or to prolonged exogenous glucocorticoids, and is associated with glucose intolerance or frank diabetes mellitus, osteoporosis, hypertension, and increased cardiovascular risk, depression, psychosis, infertility and impaired quality of life. Untreated, it is associated with a fivefold excess mortality. On the other hand, with normalization of cortisol levels, mortality rates return to normal. The condition is commoner in women, and is divided into ACTH dependent (80-85% cases: of which pituitary adenomas = 80%, ectopic ACTH 20%), and ACTH independent causes (adrenal adenoma 60%, carcinoma 40%). Very rare adrenal causes are bilateral primary pigmented nodular hyperplasia, (isolated or as part of carney complex), macronodular adrenal hyperplasia, ectopic actions of G-protein coupled receptors (e.g. GIP, beta adrenergic receptor), and the McCune-Albright syndrome.

The diagnosis of Cushing's syndrome is a multi-step process. The initial diagnosis of inappropriate hypercortisolism is established in the presence of a persistently raised 24hr urinary free cortisol, a raised midnight serum or salivary cortisol, or failure of serum cortisol to suppress (to less than 50nmol/l) following an overnight (or conventional low dose Liddle) dexamethasone suppression test. Next come determination of the cause of CS. An ACTH estimation is essential, and a level <5ng/l indicates an adrenal cause, prompting CT scanning of the adrenal glands. On the other hand, levels > 15ng/l can be confidently ascribed to an ACTH dependent cause. Although hypokalemia is commonly seen in ectopic ACTH secretion, it can also occur in 10% patients with a basophil adenoma of the pituitary (CD). In 80% patients with CD, cortisol is reduced to less than 50% of the basal value following a high dose dexamethasone suppression test (2mg 6hrly for 48 hours), but this lower than the pretest probability of CD in women (90%), and this test is not recommended where there is access to bilateral inferior petrosal sinus sampling. In the latter, a basal central:peripheral ACTH gradient exceeding 2.1 or a CRH stimulated gradient of >3:1 is indicative of CD. CD is usually caused by an ACTH secreting microadenoma of the pituitary, which usually given a hypo-intense signal on MRI that fails to enhance with gadolinium. The MRI sensitivity is 60% versus a background incidentalomam rate of 10% or so. A selective pituitary microadenomectomy remains the mainstay of treatment for CD, a good (potentially curative) prognosis indicated by an undetectable cortisol level 24-48 hrs after surgery. Non-curative procedures mandate consideration of pituitary irradiation, and occasional bilateral adrenalectomy; medical therapy with metyrapone/ketoconazole, and pasireotide (low response rate) can also be considered while awaiting a response to radiotherapy.

S5.2 Contemporary Management of Acromegaly

Baha M. Arafah, Division of Clinical and Molecular Endocrinology, University Hospitals of Cleveland, Cleveland, USA

Acromegaly is a chronic disorder resulting from sustained increased growth hormone (GH) secretion and the subsequent elevation in insulin-like growth factor–I (IGF-I) levels, most frequently caused by a pituitary adenoma. Sustained elevation of GH and IGF production is the whole mark of acromegaly as it leads to the characteristic clinical presentation of disfiguring acral enlargement in adults and gigantism in prepubertal children. In addition, elevation of the two hormones leads to substantial morbidity and mortality as a result of associated metabolic alterations that include: high blood pressure, diabetes mellitus, and cardiovascular disease. Acromegalic patients are at increased risk of developing other tumors or lesions of the body such as thyroid cancer and colon polyps. The goals of treating acromegalic patients include complete removal of the tumor causing the disease, providing symptomatic relief, reduction of multisystem complications, and control of local mass effect. While trans-sphenoidal tumor resection is considered first-line treatment of patients in whom a surgical cure can be expected, pharmacological therapy is playing an increased role in the armamentarium against acromegaly in patients unsuitable for or refusing surgery and in those who failed surgical treatment (inadequate resection, cavernous sinus invasion, or transcapsular intraarachnoid invasion).

In some select cases medical therapy could be the primary treatment option. Three broad drug classes are available for the treatment of acromegaly: somatostatin analogs, dopamine agonists, and GH receptor antagonists. Somatostatin analogs (SSAa) are considered the first-line pharmacological treatment of acromegaly, although efficacy varies among the different formulations. Available preparations include Octreotide long-acting release (LAR), Lanreotide sustained release (SR) and Lanreotide Autogel (ATG). Although they have similar efficacies, there are instances where there could be benefit in switching from one to the other in some cases of treatment failure. The novel multi-receptor somatostatin analog Pasireotide, has shown promise in the treatment of acromegaly. On the average, SSAs therapy improve symptoms and signs of acromegaly in nearly 85% of patients and normalizes GH and IGF-1 levels in approximately 50% of those patients. In addition significant reduction in tumor sizes is observed in nearly half of those using these agents especially when it is used as primary therapy. Dopamine agonists have been the earliest and most widely used agents in the treatment of acromegaly but have been found to be less effective than somatostatin analogs. Among the dopamine agonists, cabergoline has shown greater efficacy and tolerability than bromocriptine. Dopamine agonists have the advantage of oral administration, resulting in increased use in select patient groups. Selective GH receptor antagonists, such as pegvisomant, act by blocking the effects of GH, resulting in decreased IGF-I production despite persistent elevation of GH serum levels. Thus far, tumor growth has not been a concern during pegvisomant therapy. Multiple drug therapy is often necessary in some patients with resistant and /or persistent disease.

Selected References

1. Melmed S, Colao A, Barkan A, Molitch M, Grossman AB, Kleinberg D, et al.: Guidelines for acromegaly management: an update. J Clin Endocrinol Metab 2009; 94:1509-17.
2. Sandret L, Maison P, Chanson P. Place of cabergoline in acromegaly: A meta-analysis. J Clin Endocrinol Metab 2011; 96:1327-35.
3. Van der Lely AJ, Biller BMK, Brue T, Buchfield M, et al. Long-term safety of Pegvisomant in patients with acromegaly: Comprehensive review of 1288 subjects in ACROSTUDY. J Clin Endocrinol Metab 2012: 97:1589-97.
4. Buhk JH, Jung S, Psychogios MN, Göricke S, et al.: Tumor volume of growth hormone-secreting pituitary adenomas during treatment with pegvisomant: a prospective multicenter study. J Clin Endocrinol Metab 2010; 95:552–8.
5. Arafah BM, Brodkey JS, Kaufman B, Velasco M, Manni A, Pearson OH. Transsphenoidal microsurgery in the treatment of acromegaly and gigantism. J Clin Endocrinol Metab 1980; 50:578-85.
6. Carlsen SM, Lund-Johansen M, Manjila S, Wu OC, Khan FR, Khan MM, Arafah BM, Selman, WR. Pharmacological management of acromegaly: a current perspective. Neurosurg Focus, 2010; 14:1-9.
7. Schreiner T, Aanderud S, Johannesen Ø, Svartberg J, et al. Preoperative octreotide treatment in newly diagnosed acromegalic patients with macroadenomas increases cure short-term postoperative rates: a

prospective, randomized trial. J Clin Endocrinol Metab 2008; 93:2984–90.
8. Freda PU, Katznelson L, van der Lely AJ, Reyes CM, Zhao S, Rabinowitz D: Long-acting somatostatin analog therapy of acromegaly: a meta-analysis. J Clin Endocrinol Metab 2005; 90:4465–73.

Symposium 6. Endocrine Practice for Primary Care
S6.1 Individualized Diabetes Care

Faramarz Ismail-Beigi. Western Reserve Uuniversity, School of Medicine, Cleveland, USA.

Based on the results of recent large multicenter randomized trials, it is now recommended that therapy for each patient with type 2 diabetes (T2DM) must be individualized. An early step in this process is choosing a glycemic goal that is specific for each particular patient. To accomplish this, first an assessment of the patient's risk of developing hyperglycemia-related complications versus the risks of therapy must be considered. Next, important issues including comorbid conditions, presence or absence of micro- and macro-vascular complications, age, life expectancy, duration of disease, history of severe hypoglycemia, psychological status, capacities for self-care, economic considerations, and family and social support systems should be evaluated. Based on long-term follow-up of participants in the UKPDS trial, a near-normal glycemic target can be suggested in younger patients with relatively recent onset of T2DM and little or no micro- and macrovascular complications; here the aim is prevention of complications over the many years of life. In older individuals with T2DM of many years duration and evidence of CVD (or multiple CVD risk factors), a somewhat higher target can be suggested. Once the target range is identified, then individualization of therapy must be considered. There are now multiple (>11) classes of medications available for the management of glycemia. In choosing medications (or their combinations), safety profile of the agent, risk of producing hypoglycemia, effectiveness in glucose-lowering, side effects, tolerability, cost, ease of use, anticipated degree of adherence, self-care capacity of the patient, home support systems, and potential extra-glycemic effects should be considered. Two newer classes of medications, namely DPP-4 inhibitors and GLP-1 receptor agonists, their action to stimulate insulin secretion, and their safety profile will be discussed. Unlike other classes, these agents (especially the GLP-1 receptor agonists) also decrease circulating levels of glucagon, a hormone whose plasma concentration is often increased in T2DM. Finally, a member of the newest class of glucose-lowering agents, namely inhibitors of SGLT2 sodium-glucose co-transporters, has been approved for use. The utility of this class of agents will also be discussed.

S6.3 Interpretation of "Unusual" Thyroid Function Tests

Nicholas Woodhouse, Department of Endocrinology, Sultan Qaboos University, Muscat, Oman

The evaluation of thyroid function must include a careful clinical as well as biochemical assessment. It is generally recognised that the sensitive thyroid stimulating hormone (TSH) assays are, for the most part, the most reliable way of assessing thyroid function. However spuriously low values may be found in patients with pituitary lesions, after treating thyrotoxicosis and in the sick euthyroid syndrome. Conversely TSH levels may be raised in thyrotoxicosis due to TSH secreting pituitary tumors and in euthyroid patients with thyroid hormone resistant states. Discordant thyroid function tests (TFT'S) are often occur in patients on thyroid hormone replacement therapy. Free thyroid hormone (FT4) levels are often raised when the TSH is normal. And conversely T4 levels are often normal when the TSH is elevated. Increased thyroxine T4 requirements occur in pregnancy, malabsorption states and in patients taking medications that impair thyroid hormone absorption and increased losses of T4 may occur in the nephrotic syndrome and increased metabolism in patients on tyrosine kinase inhibitors. The speaker will discuss the underlying mechanisms of these events.

Symposium 7. Pediatric Endocrinoogy

7.1 The Approach to Short Stature

Ibrahim A. Al Alwan, Department of Pediatric Endocrinology, College of Medicine, King Saud Bin Abdulaziz University for Health Sciences, Riyadh, KSA.

Short Stature is one of the most common presentations seen in pediatric endocrine clinics. This common complaint is challenging even to the experienced pediatric endocrinologist. The differential diagnosis is wide and one or multiple mechanisms can be involved in one patient. The ultimate diagnosis maybe not even is reached after considerable time of follow- up. Childhood growth depends

on complex interaction between several variables such as genetic, hormonal, nutritional, and psychosocial. Short stature is defined as height below -2.0 SDS below the mean "2.3 percentile" for age, sex and population. This definition is purely statistical; it implies that 2.3% of the populations are short. The vast majority of these children have no definable cause. Important points to consider in the history and examination in assessment of short stature will include the birth weight/length, family heights & maturational history, systems review for chronic illness, general development, and psychosocial history, where examination includes specific systems, body proportions (arm span/ segmental ratios); dentition/other midline defects, visual fields/fundi and thyroid examination. To reach diagnosis specific assessment includes full blood examination, erythrocyte sedimentation rate, electrolytes, coeliac screen, calcium and phosphate, thyroid function, bone age, karyotype (females) and maybe provocative growth hormone testing. The treatment for short stature is largely dependent upon the underlying etiology. Reassurance is the only requirement if the patient has a non-pathological cause of short stature. International guidelines for growth hormone therapy will be presented and also cover some potential growth hormone use in non-approved etiologists.

S7.2 Prevalence of Pre-diabetes and Diabetes Among Overweight Emirati Adolescents in Sharjah Government Schools

Elham Al Amiri, Department of Paediatric Endocrinologist, Al Qassimi Hospital, Sharjah, UAE.

The obesity epidemic has resulted in more young people being at risk of development of type 2 diabetes. Based on the latest results, it seems like type 2 is progressing more rapidly in children. Screening to promote earlier diagnosis and treatment of type 2 diabetes is of significant importance, as untreated disease leads to metabolic, microvascular, and macrovascular complications. However, the choice of screening methodology in adolescents is controversial. The UAE is ranked 11th worldwide in prevalence of diabetes in adults according to latest IDF figures 2012. However; there is paucity of data on the prevalence of pre-diabetes and diabetes in Emirati adolescents. A cross sectional study was conducted to estimate the prevalence of pre-diabetes, diabetes among Emirati children aged 11-17 years in Sharjah government schools. 1034 students participated in the study. The study was triangulated by a questionnaire, physical examination and blood testing. A subset of students was assessed for their serum lipid status.

S7.3 Genetic Mutations Causing Neonatal Diabetes in the Community of Abu Dhabi; an Important Message to Health Care Professionals.

Asma Deeb, Department of Pediatric Endocrinology, Mafraq Hospital, Abu Dhabi, UAE.

Introduction: Advances in molecular endocrinology revealed many genetic causes of diabetes in patients misdiagnosed as type 1 diabetes mellitus. Presentation with diabetes before 6 months of life, autoantibody negative status and presence of insulin-dependent diabetes in more than one sibling are major clues to monogenic diabetes. Neonatal diabetes is a form of monogenic diabetes which can as isolated diabetes or as a part of a syndromic multiple system involvement. **Patients:** We report a series of patients with insulin-dependent diabetes from the Emirate of Abu Dhabi. All patients were pancreatic autoantibody negative and some presented with diabetes before 6 months of age. All patients were born at term and were small for gestational age. All were born to first degree relative parents. The diabetes was insulin-dependent in all patients; 2/3 of patients were on multiple daily injections and the rest on insulin pump therapy. Half of the patients had associated liver impairment, a quarter had skeletal dysplasia and one had exocrine pancreatic deficiency due to pancreatic agenesis. 3 patients died at ages 3, 6, 7 years and one had liver failure requiring transplant. **Methods:** Genetic analysis for causative mutations for neonatal diabetes was carried out in all patients. KCNJ11, ABCC8, INS genes were sequenced in all patients while EIF2AK3, GCK, IPF1 and RFX6 genes were sequenced in some patients based on specific clinical features. Written consent was obtained from all families. **Results:** Pathogenic gene mutation was detected in all patients. Half of the patients had genetically confirmed Wolcott Rallison syndrome due to mutation in the EIF2AK3 gene; W430X, G956E and I650T. The latter mutation was novel. All parents of affected children were confirmed to be heterozygous carriers. 4 siblings were homozygous for a novel mutation in insulin gene; INS c-331C>G. One child had a novel heterozygous H410Y ABCC8 variant. One child had a kATP channel mutation and was successfully switched to Sulphonylurea. **Conclusion:** Neonatal diabetes is an important cause of diabetes in a community like Abu Dhabi in which consanguinity is common. Presentation with diabetes before 6 months of age should prompt suspicion of monogenic diabetes.

Children with neonatal diabetes should be monitored for development of other associating conditions particularly kidney and liver failure which are the main cause of death in this condition.

S7.4 Calcium Disorders in Children

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

Calcium levels are tightly regulated across all ages. Calcium is very important for building healthy normal bones with low risk of fractures and deformities. Calcium regulates important functions of many organs, tissues and cells, most importantly, cardiac and skeletal muscles and nervous system. Acute changes in Calcium levels will immediately lead to response from PTH. This will start a cascade of changes to restore Calcium homeostasis. Calcium absorption in the intestine and long term maintenance of calcium stores depends on adequate Vitamin D levels and ability to convert 25 OH Vit D to 1,25 (OH)2 D in addition to normal vitamin D receptor and response elements. Hypocalcaemia is common in neonates' especially premature and sick neonates with inability to take adequate enteral nutrition. PTH response in neonates is usually immature in the first few days. Infants and children may present with severe hypocalcaemia manifested most often by repeated convulsions and tetany. Neonates may also present with apnea.

Hypocalcemia is caused most often by disorders related to PTH and Vitamin D. Other causes include renal impairment, hypomagnesaemia and familial hypercalciuric hypocalcemia. Vitamin D deficiency and metabolic disorders are associated with rickets with or without hypocalcaemia. Management of hypocalcaemia includes providing adequate calcium by intravenous or enteral rout and identifying and treating the underlying condition.
Hypercalcemia is rare in infants and children. Primary hyperparathyroidism may rarely occur in children. Other causes of hypercalcemia include vitamin D toxicity, Williams syndrome, tumors, fat necrosis, immobilization and familial hypocalciuric hypercalcemia.

Symposium 8. Metabolism Update

S8.1 Endocrinology of Iron

Pierre Bouloux, Department of Endocrinology, Royal Free Hospital, London, United Kingdom

Iron is an essential micronutrient, required for adequate erythropoietic function, oxidative metabolism and cellular immune responses. Although absorption of dietary iron (1-2 mg/d) is regulated tightly, it is just balanced with losses. Therefore, internal iron turnover is essential to meet the requirements for erythropoiesis (20-30 mg/d). Hepcidin, made primarily in hepatocytes in response to liver iron levels, inflammation, hypoxia and anemia, is the main iron regulatory hormone and once secreted into the circulation, binds ferroportin on enterocytes and macrophages, triggering its internalization and lysosomal degradation. Thus, in chronic inflammation, the excess of hepcidin decreases iron absorption and prevents iron recycling, resulting in hypoferremia and iron-restricted erythropoiesis, despite normal iron stores (functional ID), and anemia of chronic disease (ACD), which can evolve to ACD plus true ID (ACD + ID). In contrast, low hepcidin expression may lead to iron overload, and vice versa.

Laboratory tests provide evidence of iron depletion in the body, or reflect iron-deficient red cell production. The appropriate combination of these laboratory tests help to establish a correct diagnosis of ID status and anemia. Hemochromatosis type 1 (also HFE hereditary hemochromatosis or HFE-related hereditary hemochromatosis) is a hereditary disease characterized by excessive intestinal absorption of dietary iron resulting in a pathological increase in total body iron stores. Humans, like most animals, have no means of excreting excess iron. Excess iron accumulates in tissues and organs disrupting their normal function. The most susceptible organs include the liver, adrenal glands, heart, skin, gonads, joints, and the pancreas; patients can present with cirrhosis, polyarthropathy, adrenal insufficiency, heart failure or diabetes. The hereditary form of the disease is most common among those of Northern European ancestry, in particular those of Celtic descent. The disease is inherited in an autosomal recessive pattern. Transfusional hemosiderosis occurs in patients who have a life long dependency on blood transfusions, resulting in ferrotoxicity within the pituitary (hypogonadotrophic hypogonadism and GH deficiency), the thyroid, the parathyroids, the pancreas, and

the gonads. Illustrative cases will be used to demonstrate the endocrine pathologies associated with iron toxicity and their management.

S8.2 Nonalcoholic Steatohepatitis

Hussein Elsiesy, Liver Transplant Department, Multi Organ Transplant Centre, King Faisal Specialist Hospital and Research Center, Riyadh, KSA.

Nonalcoholic fatty liver disease (NAFLD) is subdivided into nonalcoholic steatohepatitis (NASH) refer to hepatic steatosis associated with inflammation in absence of significant alcohol use, and nonalcoholic fatty liver (NAFL) refer to steatosis without inflammation. NASH is a growing epidemic that is seen worldwide leading to liver cirrhosis and hepatocellular carcinoma. Risk factors include central obesity, type 2 diabetes mellitus (DM), dyslipidemia and metabolic syndrome. The prevalence of obesity in the gulf countries is 23-48% while the prevalence of DM in UAE is among the highest worldwide. Epidemiologic data on nonalcoholic fatty liver disease (NAFLD) and NASH in the gulf countries are limited, it is estimated that the NAFLD prevalence in Saudi Arabia is 7-10%. The pathogenesis of NASH is not fully understood, insulin resistance is the main mechanism and oxidative stress as a second hit causing the inflammatory component of NASH, hepatic iron, gut bacteria, leptin and antioxidant deficiencies has been implicated as potential oxidative stressors. The most important risk factors for disease progression is histological evidence of disease progression, other risk factors include age greater than 45, high aminotransferases (>2 upper limit of normal), DM, fibrosis on liver biopsy, high BMI and visceral obesity. Coffee appears to have protective effect. NASH can present with hepatomegaly, mild to moderate elevation of AST and ALT together with radiological imaging suggestive of fatty infiltration, liver biopsy is the gold standard to diagnose and differentiate NASH from NAFL using NAFLD activity score, there is no consensus about which patients require liver biopsy. Several therapies have been investigated for treatment of NASH. Weight loss is the therapy with a reasonable evidence of safety and benefits.

S8.3 Bariatric Surgery Update

Abdelrahman A. Nimeri, Bariatric Metabolic Institute, Sheikh Khalifa Medical City, Abu Dhabi, UAE.

Type 2 diabetes mellitus (T2DM) has traditionally been a medical disease treated by medications for 200 years. In 1995, Walter Pories suggested for the first time that an operation could treat T2DM. Bariatric surgery has long been known to introduce weight loss. However, does it also treat T2DM. Bariatric surgery is safe in experienced hands. However, bariatric surgery is not without risk. In addition, early aggressive treatment-better outcomes (failure to rescue concept). **Methods:** Review of the literature of the current status, outcomes and metabolic effects of bariatric surgery. **Results:** Three recent RCT have shown that bariatric surgery (LAGB, LSG, RYGB and BPD) is superior to intensive medical therapy for the treatment of type 2 DM. In addition, bariatric surgery improves the other components of the metabolic syndrome (HTN, Dyslipidemia, etc...). Long term results of the Swedish Obesity Subject study has shown that the overall mortality rates, the rates of fatal and non-fatal heart attacks, and the prevalence of T2DM is lower in the surgical arm of the study after 20 years. In addition, bariatric surgery leads to more than 80% chance in preventing T2DM in the surgical arm in patients who were obese but did not have T2DM. Mortality after bariatric surgery in centers of excellence is as low as 0.3%. However, age more than 65, history of DVT/PE, history of obstructive sleep apnea, poor functional status and extremes of BMI are predictors of poor outcome. Patients with tachycardia after surgery warrant surgical exploration despite negative radiographic studies. It is important to have a low index of suspicion to diagnose (OSA). LSG is positioned between LRYGB and LAGB in clinical effectiveness and safety. Bariatric surgery at BMI Abu Dhabi is equivalent in outcomes to American College of Surgeons Bariatric Surgery Programs. **Conclusion**: Bariatric surgery is not cosmetic surgery, it can save lives and has significant important metabolic components on type 2 DM, risk of heart attacks and death.

S8.4 Overview of Metabolic Surgery Management: Colouring Outside the Lines

Ebaa Al-Ozairi, Department of Diabetes and Endocrinology, Kuwait Hospital, Kuwait City, Kuwait

The global epidemic of obesity has fuelled an exponential

increase in metabolic surgery. In Kuwait, there is more than 6000 metaoblic surgery done on a yearly basis. People with morbid obesity who undergo metabolic surgery often also have comorbid conditions such as diabetes. Patients with T2DM undergoing bariatric surgical procedures demonstrate substantial and sustained weight loss, reductions in diabetes medications in 84%, and remission of hyperglycemia in 77%. Surgical intervention in patients with more recent onset of T2DM appears to result in higher rates of resolution than in patients with longer known duration of disease. These findings suggest bariatric surgery may represent a potential first-line therapeutic management strategy for T2DM, particularly in those with lesser degrees of obesity or shorter duration of disease. Although this has generated substantial interest in the scientific community, minimal level 1 data is available to guide such an approach. There is what can only be described as a cultural disconnect when bariatric surgery was being promoted for the treatment of T2DM. Diabetologists were interested in the percentage reduction in body weight, HbA1c, lipid profiles and blood pressure, where surgeons rather reported reduction in excess body weight and "cure" rates for T2DM, dyslipidemia and hypertension. This talk will highlight the current evidence of various metabolic surgery and will focus mainly on T2DM from various metabolic and nutritional aspects and the management required by physicians.

Meet The Experts Sessions

MTE1. The Controversial Role of Sweetners in Diabetes

Jeffrey I. Mechanick, Metabolic Support, Division of Endocrinology, Diabetes, and Bone Disease, Icahn School of Medicine at Mount Sinai, New York, USA

There are emerging mechanisms linking the use of sweeteners with adverse outcomes in patients with type-2 diabetes Mellitus (T2DM), beyond the obvious effect of excess calories. Potential culprits, still plagued by controversy and knowledge gaps, include artificial sweeteners, high fructose corn syrup, and sucrose. Attractive mechanisms and areas of future research involve intestinal taste receptors and beta cell function, as well as food-seeking behavioral changes with artificial sweeteners. The downstream effects of these mechanisms are represented by weight gain and obesity, worsening glycemic control, and the appearance of metabolic syndrome and cardiovascular disease. A working model of nutritive and non-nutritive sweeteners in the nutritional management of T2DM is presented within a framework of comprehensive lifestyle medicine.

MTE2. Insulin Pump Therapy: A Case Based Discussion

Asma Deeb, Mafraq Hospital, Abu Dhabi, UAE.

Insulin pump therapy has gone a long way as a modality of treating diabetes. The advanced technology of insulin delivery is proven to be closest in mimicking the pancreatic physiological secretion. Insulin pumps are smart devices, however, to achieve the optimal results of their use, comprehensive training by a multidisciplinary team is required. As with many other electronic devices, the more use and training, the better utilization of the various functions offered by the pumps. Choice of a patient as a pump candidate needs to be carefully done by a team with expertise in the technology. Many criteria need to be fulfilled prior to embarking in this complex expensive therapy. Insulin pump therapy utilizes various software either to retrieve downloadable information or to adjust pump settings. Understanding of the various software by the health care providers is an essential part of the therapy. In this interactive session, various case scenarios will be presented for discussion. Special clinical features in some interesting and common cases will be a focus to initiate a discussion on how to best utilize insulin pumps to control diabetes. In addition, software of commonly-used pumps will be demonstrated.

MTE3. Management of the Male Infertility

Pierre Bouloux, Department of Endocrinology, Royal Free Hospital, London, UK.

About one in six couples are subfertile, and of those, a dominant male factor is responsible for about 30% of causes. The outcome of treatment for the infertile male has been transformed by technological advances over the past two decades, and epitomized by the rapidly changing fertility prognosis in Klinefelter's syndrome. Men with Klinefelter syndrome were considered infertile until 1996. Over the last decade, developments in microsurgical techniques and advances in artificial reproductive technologies (ART) allowed more than 50% of patients with Klinefelter syndrome to have their own children through the combination of microsurgical testicular sperm extraction (TESE) and the use of freshly retrieved sperm for in-vitro fertilization (IVF).The fact that sperm can be found in the testes of men with Klinefelter syndrome has challenged the

previous assumption that men with Klinefelter syndrome are always sterile. Viable spermatozoa can now be extracted from the testes via surgical biopsy, and a spermatozoon can be directly injected into an ovum.

More than 60 children have been born worldwide after successful intracytoplasmic sperm injection (ICSI) in couples in which the male partner has Klinefelter syndrome. A minority of men with Klinefelter syndrome have viable sperm in their ejaculate and are able to provide sperm for cryopreservation for future pregnancies. Microdissection testicular sperm extraction is an effective sperm retrieval technique in men with Klinefelter syndrome.Men with hypogonadism who respond to medical therapy (hCG, aromatase inhibitors) may have a better chance of sperm retrieval.

References

1. Schiff JD, Palermo GD, Veeck LL, et al. Success of testicular sperm injection and intracytoplasmic sperm injection in men with Klinefelter syndrome. J Clin Endocrinol Metab. Nov 2005;90(11):6263-7.
2. Damani MN, Mittal R, Oates RD. Testicular tissue extraction in a young male with 47,XXY Klinefelter's syndrome: potential strategy for preservation of fertility. Fertil Steril. Nov 2001;76(5):1054-6.
3. Wikstrom AM, Painter JN, Raivio T, Aittomaki K, Dunkel L. Genetic features of the X chromosome affect pubertal development and testicular degeneration in adolescent boys with Klinefelter syndrome. Clin Endocrinol (Oxf). Jul 2006;65(1):92-7
4. Ramasamy R, Ricci JA, Palermo GD, Gosden LV, Rosenwaks Z, Schlegel PN. Successful fertility treatment for Klinefelter's syndrome. J Urol. Sep 2009;182(3):1108-13.

MTE4. Management of Hyperprolactinemia and Prolactinomas

Baha M. Arafah, Division of Clinical and Molecular Endocrinology, University Hospitals of Cleveland, Cleveland, 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. It 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 small or larger 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.

Patients with no signs and symptoms related to hyperprolactinemia may not require treatment even when the cause is a microprolactinoma. These microadenomas rarely grow in size and, thus, in the absence of symptoms, no treatment would be indicated, but continued follow up would be warranted. The ultimate goal of therapy is to restore gonadal function and fertility. In patients with pituitary adenomas an additional goal of therapy would be to eliminate the mechanical effects of the tumor on surrounding tissue. Eliminating or treating the underlying cause of hyperprolactinemia would be the primary approach in managing patients with this biochemical abnormality. Prolactinomas represent around 50% of pituitary tumors and the vast majority are small. Men often present with large invasive tumors. Treatment of microprolactinomas aims at reversing related symptoms and at restoring normal gonadal function and fertility, while treatment of macroprolactinomas aims at both tumor shrinkage and hormonal control. Among available dopamine agonists, cabergoline is the treatment of choice in both cases, with a response rate of nearly 90%. Long term treatment (>5 years) with a high dose (>2mg/week) might raise some concern for the possibility of increased risk for the development of fibrotic thickening of the leaflets of the cardiac valves. Discontinuation of cabergoline may be considered after 2-3 years of treatment, provided normal prolactin level is maintained and is associated with significant reduction in tumor size. Surgical treatment can be used in patients unable to tolerate medical therapy and in others with aggressive tumors. Since estrogens normally stimulate lactotrophs, it was initially thought that prolactinomas might increase in size during pregnancy. This, however, was not found to be a clinically relevant issue in most patients with microadenomas. It is estimated that less than 5% of microadenomas might slightly increase in size during pregnancy. The risk is somewhat higher in patients with macroadenomas, especially with suprasellar extension, and is estimated to be 15 %. Measurement of serum prolactin during pregnancy in these patients is not helpful in identifying those with potential tumor growth. Should a patient presenting with a microadenoma becomes pregnant, cabergoline must be stopped because the risk of tumor enlargement is low, although a fetal exposure has not been shown to induce neonatal malformations. Careful follow-up is however advised in pregnant women with macroprolactinomas. Surprisingly, pregnancy may lead to a prolonged remission of hyperprolactinemia. In women who had a minimal to moderate decrease in tumor size with initial medical therapy, some authorities utilize a surgical debulking procedure prior to pregnancy, in order to decrease the chance of tumor expansion during pregnancy. If compressive symptoms develop during pregnancy, and surgery is not recommended, bromocriptine would be an effective agent in such instances.

Selected References

1. Melmed S, Casanueva A, Hoffman R, et al. Diagnosis and treatment of hyperprolactinemia: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2011; 96:273-88.
2. Deckers OM, Lagro J, Burman P, et al. Recurrence of hyperprolactinemia after withdrawal of dopamine agonists: Systematic Review and Meta-Analysis. J Clin Endocrinol Metab 2010; 95:43-51.
3. Velassi E, Klibanski A, Biller BMK. Potential cardiac valve effects of dopamine agonists in hyperprolactinemia. J Clin Endocrinol Metab 2010; 95:1025-33.
4. Gibney, J, Smith, TP, McKenna, TJ. Clinical relevance of macroprolactin. Clin Endocrinol (Oxf) 2005; 62:633.
5. Arafah B and Nasrallah M. Pituitary tumors: pathophysiology, clinical manifestations and management. Endocrine Related Cancer 2001;8:287-305.

MTE5. Primary Aldosteronism

Rainer Düsing, Internal Medicine, Medizinische Klinik und Poliklinik, Bonn, Germany

The epidemiology of primary aldosteronism is still unclear. In all of the available data sets, referral bias may have markedly inflated the estimates of that particular condition. Actually, the rates of adrenalectomy in unselected populations remain very low. Specific testing for primary

aldosteronism should be restricted to hypertensive patients with otherwise unexplained hypokalemia or an adrenal mass (incidentaloma), and to patients with unspecific clinical findings suggesting secondary hypertension (resistant hypertension, stage 2 hypertension in young patients, fast development of stage 2 hypertension, non-dipping in ABPM etc.). Diagnostic procedures can be separated into screening, confirmatory test and localization procedures. Even within this simple step-by-step approach, many problems remain unresolved. Thus, the most suitable cut-off for aldosterone-renin ratio values is still unknown. Also, there is a continuing debate whether plasma renin concentration can be utilized instead of plasma renin activity. Finally, the choice of confirmatory test in suspected primary aldosteronism is still under debate and what cut-off values for plasma aldosterone should be employed e.g. following saline infusion. Once the diagnosis is established, all patients with primary aldosteronism should undergo adrenal computed tomography as the initial study in subtype testing and to exclude adrenocortical carcinoma. The presence of a unilateral form of primary aldosteronism should be established/excluded by bilateral adrenal venous sampling and, when present, optimally treated by laparoscopic adrenalectomy. Patients with bilateral adrenal hyperplasia or those unsuitable for surgery should receive a mineralocorticoid receptor antagonist. In the future, aldosterone synthase inhibitors will be available. It will be interesting to establish whether such agents will have a role in patients with primary aldosteronism.

MTE6. Management of Phaeochromocytoma

Rainer Düsing, Internal Medicine, Medizinische Klinik und Poliklinik, Bonn, Germany

Pheochromocytomas are catecholamine-producing tumors that arise from chromaffin cells. Most pheochromocytomas are located in the adrenal gland, but some may occur at extra adrenal sites, referred to as paragangliomas. Excessive catecholamine secretion causes the classic triad of symptoms including hypertension with headaches, palpitations and sweating. The prevalence of pheochromocytomas and paragangliomas is not precisely known. Available data point to 0.05–0.2% of hypertensive patients but referral bias may have exaggerated available estimates. The diagnosis of pheochromocytoma depends upon the demonstration of catecholamine excess by measuring catecholamines and metanephrines in timed (24 h) urine samples or metanephrines in plasma. Recent studies have shown that measurement of fractionated metanephrines in urine or plasma provides superior sensitivity to measurements of the parent catecholamines and that determination of plasma fractionated metanephrines may be the screening approach of choice. If elevated plasma metanephrines are not markedly elevated above reference values (less than 4-fold), clonidine suppression should be performed. After establishing the diagnosis, localization by CT or MRI of the adrenal glands and abdomen is recommended. Both methods, however, are characterized by low specificity and, therefore, complementary ^{123}I-metaiodobenzylguanidine scintigraphy should be performed. Improved sensitivity has been achieved with newer compounds such as [18F]-flurodopamine ([18F]-FDA), [18F]-fluorodihydroxyphenylalanine ([18F]-FDOPA), and [18F]-fluoro-2-deoxy-D-glucose ([18F]-FDG). Since recent studies have demonstrated that most pheochromocytomas show uptake of [18F]-FDG, positron emission tomography (PET) using this agent may be the method of choice. Because approximately one third of the pheochromocytomas turn out to be hereditary entities, genetic testing is recommended. This is especially true in the presence of a family history of pheochromocytoma, in young patients (<50 years) or in case of multiple, malignant, or bilateral tumors. Laparoscopic or surgical removal (often adrenal sparing) of the tumor following preoperative α- and ß-blockade is the treatment of choice and usually curative.

MTE7 Controversies on Statin Therapy

Ibrahim Salti, Division of Endocrinology and Metabolism, American University of Beirut Beirut, Lebanon.

It is generally agreed that statin therapy in all patients with high or moderate cardiovascular risk is considered non-controversial. Moreover, the guidelines emphasize the importance of achieving very low LDL-cholesterol especially in high risk patients. Equally important is the recommendation for early initiation of statin therapy especially in acute coronary syndrome. The use of statin therapy in low risk patients remains to be controversial although recent studies have favoured this trend. However, in recent years the following concerns have been raised concerning the safety of statin therapy. These are 1) Diabetogenic effects: In some but not all statin trials, a modest increase in new onset diabetes was observed. In a recent meta-analysis of 13 large statin trials, the estimated incidence of new onset diabetes was 9%. It is generally agreed that this minor risk is outweighed by the overall CV benefit

from statin therapy. 2) Effect on Cancer incidence: Some of the earlier statin trials (e.g. the PROSPER and LIPID trials) have shown a slight increased risk of cancer particularly in the elderly. However more recent systematic reviews and large meta-analysis, showed no increased incidence of cancer with statin therapy. In fact, in some trials, a decrease in cancer incidence and or improved survival have been observed. 3) Effects on strokes and cerebral bleeds: Studies aggressing this point, have consistently shown that statin therapy reduces the incidence of ischemic strokes but has a neutral effect on haemorrhagic strokes. In the SPARKLE trial, there was a 33% reduction in strokes but no change in haemorrhagic strokes. Moreover, there was no link of low LDL-cholesterol and cerebral haemorrhage. 4) Effects on cognitive function: The majority of studies showed no effect of use of statins on cognitive function, while fewer studies showed some benefit and fewer others showed a deterioration. Thus there is no evidence to conclude that statins have detrimental (or beneficial) effects on cognitive function. The following potentially favourable effects of statins have been pointed and will be briefly discussed: anti-arrhythmic effects, effects on bone metabolism, use in chronic kidney disease decreased risk of pancreatitis and effect on non-alcoholic fatty liver disease (NAFLD)

MTE8. Multiple Endocrine Neoplasia

Nicholas Woodhouse, Department of Endocrinology, Sultan Qaboos University, Muscat, Oman.

Multiple Endocrine Neoplasia (MEN) describes the occurrence of tumors in two or more endocrine organs in the same patient. There are two main types depending on the glands involved, MEN 1 (associated with mutations in chromosome 11q13) and MEN 2, the latter being divided into three subgroups, MEN 2a and 2b and Medullary Thyroid Cancer (MTC) only. The gene causing the MEN 2 syndromes is mapped to chromosome 10cen-10q11. MEN syndromes may be familial or sporadic although care should be taken in describing disease as sporadic– the family member with the disease may have died before it was diagnosed. Clinical features are: MEN 1: Tumors of the parathyroid, pancreas and pituitary, rarely adrenal cortex, carcinomas and lipomas. MEN 2a: MTC, phaeochromocytomas, parathyroid hyperplasia/ tumors. MEN 2b: As MEN 2a with additional associated abnormalities such as mucosal neuromas, Marfanoid features. The speaker will illustrate will his talk with cases he has observed during his career.

MTE9. Diabetes in Pregnancy

Bashir Taha Salih, Department of Obstetric Medicine, Corniche Hospital, Abu Dhabi, UAE.

Diabetes prevalence is on rise globally. Recent statistics show that UAE and other gulf countries are among the leading countries with the highest prevalence in the world. Gestational diabetes could be pre-gestational but discovered for the first time in pregnancy or true gestational diabetes. Studies have shown that hyperglycemia is associated with poor outcome in pregnancy. Studies like Hyperglycemia and Adverse Pregnancy Outcome (HAPO) and others were aimed to clarify unanswered questions of maternal glycemia less severe than overt diabetes and pregnancy outcome. The results indicated strong association of maternal glucose level below those diagnostic for diabetes with adverse pregnancy outcome. International Associations of Diabetes and Pregnancy Study Groups (IADPSG) have published their recommendations on the Diagnosis and Classification of Hyperglycemia in Pregnancy in March 2010 (Diabetes Care March 2010). The IADPSG was formed in1998 as an umbrella organization to facilitate collaboration between the various regional and national groups that have a primary or significant focus on Diabetes and Pregnancy. Since its publication several countries and associations including the ADA have adopted these recommendations. They recommend universal screening for all patients at their first antenatal visit and either the patient is having overt diabetes, gestational or needs further screening at 24-28 weeks gestation. Diabetes in pregnancy should be managed by multidisciplinary team involving all health care professionals responsible for her care in pregnancy including the patient and her family.

MTE10. Management of Hypogonadotrophic Hypogonadism

Pierre Bouloux, Department of Endocrinology, Royal Free Hospital, London, UK.

Male hypogonadotrophic hypogonadism (HH) is not a final diagnosis, since several disorders, such as hyperprolactinaemia, hypothalamo-pituitary disorders, or systemic illness can result in HH. On the other hand, micropenis and /or bilateral cryptorchidism in an infant may be a strong pointer to an underlying diagnosis of HH and prompt a referral to a paediatric endocrinologist. HH may represent one of a spectrum of pubertal disorders,

from constitutional pubertal delay to permanent congenital HH. HH is one of the few readily treatable causes of male infertility, and recent evidence suggests that up to 10% of congenital IHH may demonstrate a reversible phenotype. Congenital isolated hypogonadotrophic hypogonadism (IHH) may be associated with anosmia (Kallmann syndrome : KS) or euosmia. Causes of KS include those caused by loss of function in several genes including KAL1, NELF, FGFR1, FGF8, PROK2, PROKR2. Causes of euosmic IHH include genetic lesions in GNRHR, GPR54, FGFR1, FGF8, PROK2, PROKR2, TAC3, TACR3, GNRH1, CHD7. Other congenital syndromes associated with HH include adrenohypoplasia congenital (DAX1), HH associated with childhood onset obesity (leptin, leptin receptor, PC1), and HH associated with mental retardation and obesity (Prader Willi), Bardet Biedl syndrome, and the CHARGE syndrome. HH can also occur in association with combined pituitary hormone deficiency, including that due to lesions in PROP1, LHX3,HESX1,SOX3,and SOX2. Treatment options vary for those wanting fertility and those not interested in fertility. Testosterone is the primary treatment used to induce secondary sexual development and sexual function in hypogonadal males, and is available in a variety of formulations including injections, patches, and gel. In boys with delayed puberty, the starting dose is usually 50 mg of a long acting ester IM monthly, which induces virilization without compromising height. The dose is gradually built up over 2-4 years to the full replacement dose of 100-200 mg of enanthate every 2-3 weeks. For those desirous of fertility, gonadotrophin replacement is necessary. For those with immature testes, treatment with sc hCG is given at a dose of 1000U every 3 days, and FSH 75U alternate days. The dose of hCG is titrated to obtain a trough T level of about 10nmol/l. Factors predictive of a better outcome include larger initial testicular volume (>4ml), absence of cryptorchidism, and higher levels of inhibin B.

MTE 11. Assessment of Fracture Risk

Yousef Al Saleh, Department of Medicine and Endocrinology, King Saud University for Health Sciences, Riyadh, KSA.

The diagnosis of osteoporosis centers on the assessment of bone mineral density (BMD). Osteoporosis is defined as a BMD 2.5 SD or more below the average value for premenopausal women (T score < -2.5 SD). Severe osteoporosis denotes osteoporosis in the presence of one or more fragility fractures. The same absolute value for BMD used in women can be used in men. The recommended site for diagnosis is the proximal femur with dual energy X-ray absorptiometry (DXA). Other sites and validated techniques, however, can be used for fracture prediction. The predictive value of BMD can be enhanced by use of other factors, such as biochemical indices of bone resorption and clinical risk factors. In the absence of validated population screening strategies, a case finding strategy is recommended based on the finding of risk factors. Treatment should be considered in individuals subsequently shown to have a high fracture risk. Because of the many techniques available for fracture risk assessment, the 10-year probability of fracture is the desirable measurement to determine intervention thresholds. The practical web-based tool, named FRAX®, predicts the ten-year risk of osteoporosis fracture in men and women it will be of considerable use to health care professionals and policy makers throughout the world, particularly in places where there are few DXA machines. An individual's parameters such as age, sex, weight, height, and femoral neck BMD if available, are entered into the website tool, followed by clinical risk factors which include a prior fragility fracture, parental history of hip fracture, current tobacco smoking, long-term use of glucocorticoids, rheumatoid arthritis, other causes of secondary osteoporosis and daily alcohol consumption. The FRAX® algorithm then provides a figure indicating a ten-year fracture probability as a percentage, which provides guidance for determining access to treatment in healthcare systems. The algorithm is intended as a platform technology to aid in the quantification of risk. The decision on whether or not to treat will depend upon local factors that may or may not include cost-effectiveness analysis. At the end of the day, treatment will depend upon the costs of intervention, the wealth of the individual or the nation and the proportion of that wealth devoted to healthcare.

MTE12. Ultrasound of Thyroid Nodules

Aly B. Khalil, Imperial College London Diabetes Center, Abu Dhabi, United Arab Emirates

It is estimated that by palpation, the prevalence of thyroid nodules in the general population is 4-7%; it increases by US to reach 45-50%. Of note, benign adenomas or cysts account for approximately 90% of those detected thyroid nodules. In the work up of a patient with a thyroid nodule, attention should be given to some worrying symptoms and signs such as: family history of thyroid cancer; history of previous

irradiation or exposure to high environmental radiation; child with a thyroid nodule; unexplained hoarseness or stridor associated with a goiter; painless thyroid mass enlarging rapidly over a period of few weeks; palpable cervical lymphadenopathy; insidious or persistent pain lasting for several weeks. Thyroid sonography (US) should be performed in all patients with known or suspected thyroid nodules (Revised ATA guidelines 2009) or if planning for fine needle aspiration under ultrasound guidance (FNA US) or for the identification of non-dominant thyroid nodules (British Guidelines). US features suggestive of thyroid malignancy include by order of magnitude (low to high): coarse calcifications, comet tail sign, hypoechogenicity, absent halo or indistinct margin, intranodular blood flow on color Doppler, and microcalcifications. US by itself has low specificity. The combination of US and FNA US adds more sensitivity and specificity. Indications for thyroid biopsy include: difficult to palpate nodules or nonpalpable ('other") nodules found on US that meet US FNA criteria; posterior nodules; predominantly cystic nodules (with a solid component); nodules with non-diagnostic cytology from prior FNA that have grown.

MTE12. Management of Thyroid Cancer

Ali S. Alzahrani, King Faisal Specialist Hospital and Research Center, Riyadh, KSA.

The incidence of thyroid cancer has dramatically increased over the last 3 decades. Its management has also witnessed significant progress. Fine needle aspiration biopsy (FNA) remains the standard approach for diagnosis of thyroid nodules, the most common presentation of thyroid cancer. The reporting of this procedure is now commonly following the Bethesda System which represents a significant progress in terms of linking the cyopathological diagnosis with risk of malignancy and offering practical management recommendations for the different cytopatholgical categories. Molecular diagnosis utilizing single or a panel of gene mutations or using expression profile of a large number of genes is gaining significant popularity and has become a helpful tool in cases of indeterminate cytology. Not only that these genetic aberrations are taking their position in the diagnostic work up of thyroid cancer but some of them such as the common $BARF^{V600E}$ mutation, the classical genetic mutation in papillary thyroid cancer are also gaining interest in prognostication and decision making in DTC management.

Total or near-total thyroidectomy is the recommended surgery for most cases of DTC. Exceptions are small classical DTC without features of invasions or spread to local lymph nodes or distant sites. Radioactive iodine ablation is recommended for high risk cases (TNM stage III & IV) and for many cases with lower risk (TNM stage I & II) but with large tumors, atypical cytological features or evidence of invasion or local/distant spread. The level of thyroid hormone suppressive therapy should be tailored to the status of the disease and risk of recurrence with more degree of suppression in the high risk patients or those with persistent /recurrent disease and lesser degree of suppression in patients in remission with low risk of recurrence. Long term surveillance depends mostly on measurement of stimulated serum thyroglobulin and neck ultrasonography. Other imaging techniques, especially the use of computed tomography/positron emission tomography are indicated in cases of biochemical evidence of disease (elevated serum thyroglobulin) while the use of repeated radioiodine (RAI) whole body scans is fading away since it has low sensitivity for detection of recurrence.

Major advances in our understanding of the molecular pathogenesis of DTC over the last decade have been effectively utilized for development of novel therapies for patients with progressive/metastatic DTC that is non-responsive to RAI. A large number of tyrosine kinase inhibitors blocking the MAPK kinase pathway and the cell surface growth factor receptors are undergoing phase II and III trials and some of them such as Sorafenib are widely used off label but are likely to be approved in the near future for treatment of advanced cases of radioiodine refractory DTC. These aspects of the management of DTC will be discussed during the session.

MTE13. Thyrotoxic Emergencies

Feryal Al Saber, Bahrain Defence Forces Hospital, Manama, Bahrain.

In the United States , the prevalence of hyperthyroidism is approximately 1.2% (0.5% overt and 0.7% preclinical); the most common causes include Graves' disease toxic multinodular goiter , and toxic adenoma. Guidelines for the diagnosis management of patients with hyperthyroidism have been published by both the American Thyroid Association and American Association of Clinical Endocrinologist both associations determined that thyrotoxicosis represents a priority area in need of updated

evidence-based practice guidelines.

It's not only the diagnosis and management of the disease is I important, the diagnosis of the emergencies is as important as the diagnosis of the disease itself, not only that but the emergencies of the complications of the treatment modalities occupies a higher priority in diagnosing them and managing them in a proper and immediate manners to prevent mortality especially in the presence of comorbidities.

MTE14. Thyroid Disorder in Pregnancy

Bashir T. Salih, Department of Obstetric Medicine, Corniche Hospital, Abu Dhabi, UAE.

Thyroid disorder is one of the commonest pre-existing endocrine complaints during pregnancy. The overlap between common symptoms and signs of normal pregnancy and thyroid disease renders clinical assessment of thyroid function even more difficult than normal. However, the physiology of the thyroid gland changes considerably during pregnancy, such that careful selection of investigations and appropriate interpretation of their results using pregnancy-specific reference ranges is essential to avoid misdiagnoses. Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease in pregnancy and postpartum should be implemented (ATA published in 2011). The fetal thyroid functions autonomously from early in the second trimester of pregnancy, the placenta is mostly impermeable to maternal thyroid hormone, and maternal thyroid status does not directly affect fetal thyroid function although maternal iodine deficiency may. Hyperthyroidism should be managed with minimal doses of antithyroid medication, rarely by surgery, and radioactive iodine is absolutely contraindicated. The disease is often quiescent in second and third trimesters and treatment sometimes may be stopped. Neonatal thyroid function should be monitored. Well treated hypothyroidism rarely causes problems in pregnancy and thyroxin doses may require alteration in some cases. Postpartum thyroiditis is caused by destructive autoimmune lymphocytic thyroiditis and is associated with TPO antibodies. The initial thyrotoxic phase might be followed by euthyroid and hypothyroid phases. Most patient recover spontaneously. Thyroid disorders, if diagnosed and treated adequately, are associated with good pregnancy outcome.

MTE15. Asympotomatic/Mild Hyperparathyroidism

Abdul-Badi Abou Samra, Department of Medicine Chairman, Hamad Medical Corporation, Doha, Qatar.

Primary hyperparathyroidism witnessed dramatic changes in its clinical presentation and a continuing debate on its diagnostic approach and management. With the introduction of automated blood chemistry, the clinical picture of primary hyperparathyroidism shifted from painful kidney stones and debilitating osteoporotic fractures to asymptomatic hypercalcemia discovered on routine laboratory tests; this raised debates regarding the benefit of parathyroid surgery versus conservative management in asymptomatic patients. The debate has settled by the development of guidelines based on the natural history of the disease where asymptomatic patients are sorted for surgery by age (less than 50) and by degree of hypercalcemia (more than 1 mg/dL above the upper normal range of calcium). The role of localization studies in the surgical decision and which localization study to use continue to be the subject of debate. More recently, the development of sensitive assays for parathyroid hormone, a new entity of normocalcemic hyperparathyroidism, has been recognized and has become the subject of a more serious debate regarding diagnostic approach and management. Some investigators argue that the normocalcemic hyperparathyroidism is an early point in the natural history of the disease and if discovered should be addressed and treated, particularly if associated with osteoporosis. Others rightly argue that surgical intervention in the absence of hypercalcemia places the patients at the risk of complications without evidence of benefit. The topic of normocalcemic hyperparathyroidism will remain a challenge for the endocrinologist until randomized clinical trials are developed to show the evidence for the aggressive versus the conservative approach.

MTE16. Genetics of Diabetes: What Does it Mean to the Clinician?

Sara Suliman, Imperial College London Diabetes Center, Abu Dhabi, United Arab Emirates

Diabetes mellitus (DM) is a heterogeneous group of disorders characterized by hyperglycemia resulting from defective insulin secretion, insulin resistance or both. Genetics has long been known to play a role in DM due to the heritability of the disease. For example the odds of the offspring of a father with type 1 DM developing the disease

is 1 in 17 (1), whereas, for a mother the risk is 1 in 25 – 100 (1) with the risk reducing with increasing maternal age. If both parents have type 1 DM the risk of an offspring developing Type 1 DM is 1 in 4-10 (1). The majority of the genes accounting for heritability in T1DM have been identified and key genes appear to be associated with the HLA system. Similarly, the offspring of a parent with type 2 DM has a 1 in 7-13 (1) chance of developing DM depending on whether the parent was diagnosed before or after the age of 50 years. An offspring born to two parents with Type 2 DM has a 1 in 2 (1) chance of developing type 2 DM. Recent advances including, genome wide association studies, have identified diverse loci associated with type 2 DM (n=65) (2). Unfortunately the genes known to contribute to type 2 DM (to date) only account for a minority of the heritability of type 2 DM (3). Genetic evidence has also highlighted the mechanisms underlying the development of DM. A sizeable minority of individuals with DM, have a genetic (monogenic) form of DM, whereby a defect in a single gene results in disease and therefore these are inherited diseases (dominant or recessive). This includes diseases such as MODY (maturity onset diabetes of the young), neonatal DM, insulin receptoropathies and the lipodystrophy syndromes amongst others. Although rare, monogenic DM syndromes have a great impact leading to DM at a very young age. Identifying the affected genes has helped elucidate the aetiology of DM and related features in other organ systems (e.g. HNF4A and renal disease). For clinicians, specifying a diagnosis has led to improved genetic counselling, prediction of clinical course and changes in treatment, e.g. stopping insulin and injections with no alternative treatment necessary [GCK (glucokinase) mutations], insulin injections being replaced by tablets (e.g. Sulphonylureas in low dose in HNFA or high dose in potassium channel defects - Kir6.2 and SUR1 mutations) (4) or with tablets in addition to insulin (e.g. metformin and insulin in insulin resistant syndromes). This lecture will briefly touch on the genetics of Type 1 and 2 DM, monogenic DM and on more recent advances in genetic screening tools and research methods.

References

1. ADA. Genetics of diabetes. [Internet Document, available at http://www.diabetes.org/diabetesbasics, accessed on 10.8.2013].
2. Yaghootkar H, and Frayling TM. "Recent progress in the use of genetics to understand links between type 2 diabetes and related metabolic traits." Genome biology 14.3 (2013):1-7.
3. Groop L, Pociot F. Genetics of diabetes - Are we missing the genes or the disease? Mol Cell Endocrinol. 2014;25;382(1):726-39.
4. Hattersley A, et al. The diagnosis and management of monogenic diabetes in children and adolescents. Pediatric Diabetes 2009; 10 (Suppl 12):33-42.

Free Communications

Oral Communications

OC1: Cervical Lymph Node Thyroglobulin elevation from Fine Needle Aspirates is a Reliable Marker of Papillary Thyroid Cancer Nodal Metastasis

Samer El-Kaissi, Suphia Sherbeeni, Saudi Arabia.

Objective: To evaluate the utility of thyroglobulin measurement from fine needle aspirates (FNA) of cervical lymph node (CLN) in patients with a history of papillary thyroid cancer (PTC). **Methods:** In a retrospective analysis, we evaluated 32 patients (24 F) with enlarged CLN on neck ultrasound post-total thyroidectomy and radioiodine ablation for PTC. FNA biopsies were performed on the CLN and thyroglobulin measured from needle washouts in 1-ml normal saline (FNA-Tg). **Results:** The mean age of the patients was 37.9 years (range 18.4-80.6). There were 9/32 patients (5 F) with an elevated FNA-Tg, mean Tg 7786.3 μg/L (range 10.4-17844.0), and 23/32 patients (19 F) with FNA-Tg < 10 μg/L, mean Tg 3.6 μg/L (1.0-6.4). FNA cytology was reported as malignant or suspicious for malignancy in 8/9 cases with elevated FNA-Tg, and as inadequate in one case, but all 9 CLN were confirmed as malignant after surgical excision. There was no evidence of malignancy in any of the 23 CLN FNA cytology in patients with normal FNA-Tg. On ultrasound, the respective number of cuboidal CLN, hypoechoic CLN and those with abnormal vascularity on Doppler were 5 (56%), 8 (89%) and 5 (56%), compared to 11 (48%), 14 (61%) and 3 (13%) in patients with normal FNA-Tg. **Conclusions:** An elevated FNA-Tg appears to be at least as reliable as the identification of malignant cells on FNA biopsies of cervical lymph nodes in post-surgical PTC patients.

OC2. 17-Beta-hydroxysteroid Dehydrogenase Type 3 deficiency: A Challenging Diagnosis

Fawziya Alkhalaf, Tawfeg M. Ben Omran, Qatar

Background: 17-β-hydroxysteroid dehydrogenase type 3 deficiency is a rare autosomal recessive form of 46, XY disorder of sex development. 17-β-HSD 3 is an important enzyme converting androstenedione to testosterone, and it is essential for normal fetal development of male genitalia. Affected individuals exhibiting different phenotypes at birth and virilization at puberty, sometimes in association with gynecomastia. **Design:** Here we report two phenotypically female siblings (18 and 16 years old) from a consanguineous Palestinian family presented with signs and symptoms of virilization. Both siblings presented with deep voice, facial acne, increased muscle mass and a male pattern of body hair. Genital exam revealed thickened labia majora with clitoris enlargement. **Results:** Karyotype analysis showed a male genotype (46, XY). Hormonal evaluation showed decreased Testerone (7.5 nmol/L). Abdominal and pelvic MRI revealed testicles in inguinal regions bilaterally and nonvisualization of the uterus. These evidences were suggestive of a 46, XY DSD due to 17βHSD3 deficiency. Molecular study of the younger patient showed homozygous missense mutation (c.239G>A p.Arg80Gln) in exon 3 of the HSD17B3 gene. Psychological evaluation showed a well determined male gender identity. It was decided to proceed with male assignment. **Conclusion:** DSD is considered a medical and psychosocial emergency and management requires a multidisciplinary team approach. Reaching a precise diagnosis is often difficult and can be delayed for many years.

OC3. Prevalence and Correlates of Metabolic Syndrome in a Group of Obese School Children Evaluated In the Obesity Clinic in Al Ain, UAE.

Abdelazim Mohamed Mabrouk, Valsamma Eapen, Saeed Yousef, FMHS, Al Ain, United Arab Emirates

Objective: Obesity is a major risk factor for the overall burden of disease globally, and is associated with a constellation of metabolic derangements starting early in life. Since obesity and type 2 diabetes are highly prevalent in the UAE, we hypothesized that the rate of MS among the obese young population of the UAE would also be high. **Patients and Methods:** This study was conducted to ascertain the prevalence and correlates of Metabolic Syndrome among the school children seen in the obesity clinic of the School Health centre in Al Ain, UAE. 260 students were seen in the Obesity clinic at the School Health centre in Al Ain, after being identified through the School Health Screening Program. There were 153 boys and 107 girls. Majority were UAE nationals (70%), while the remaining was from the neighboring Gulf and Arab countries. Evaluation was carried out as part of the clinical assessment. In addition, risk assessment questionnaire and Beck Depression Inventory were filled. We used the adolescent criteria (Cook et al 2003) modified from NCEP - National Cholesterol Education Program Adult Treatment Panel III. **Results:** The mean age of the sample was 14.5 (SD = 2.6) and the mean BMI was 35.3 (SD =6.1). The rate of MS was significantly more among boys than girls (P = 0.001). M: F = 2:1. There was a statistically significant association between the occurrence of MS and increasing BMI (P = 0.048), Family history of obesity (P =0.017), Diabetes (P = 0.038), Hypertension (P = 0.013). Male gender is associated with three of the MS criteria namely HDL, Triglyceride and fasting blood glucose. 94.5% of those with a diagnosis of MS revealed subjective psychological distress as compared to only 5.5% of those who did not receive a diagnosis of MS (P = 0.033). On the Beck depression rating scale three quarters (76.9%) of those with MS scored above a score of 10 indicating the presence of significant depressive symptoms, as compared to 43.4% of those without MS (P = 0.021). **Conclusion:** MS is highly prevalent among UAE adolescents who showed high score of depression symptoms and it is strongly linked to obesity and sedentary life style. More efforts should be directed to increase skills and knowledge among Pediatricians and GPs to identify this syndrome early in order to influence its components and to decrease the risk of morbidity and mortality.

OC4. Quantative Assessment of Diabetic Sudomotor Dysfunction using Electrochemical Sweat Conductance, a Simple Noninvasive Method.

Shesha Eman, Amal Madanat, Mohamad Al-Harbi, Dalal Al-Qaisi, Abdulaziz Al-Ghamdi, Aqeel Al-Ghamdi, Saudi Arabia.

Background: Early recognition and management of sudomotor dysfunction, as an important component of diabetic distal polyneuropathy is vital to prevent foot ulcerations and amputations. The aim was to assess sudomotor dysfunction using electrochemical sweat conductance method and

explore its relationship to the presence, severity of diabetic distal polyneuropathy, and the risk of ulceration. **Design and Methods:** A cross-sectional study was conducted on a sample of 216 diabetic patients. Informed consent was obtained. Patients underwent clinical evaluation, detailed feet assessment: appearance, ankle reflexes, vibration, pressure, pain and temperature preception, Diabetic polyneuropathy, severity and risk of ulcer were determined using neuropathy disability scores. Vibration perception threshold was assessed using neurostesiometer, sudomotor dysfunction was measured using electrochemical sweat conductance by sudoscan. SPSS17 was used for statistical analysis. **Results:** All were Saudi nationals. Mean age was 46.6±11.7. 90.7% had type 2 diabetes. Duration of diabetes was7.2±7.2years. Hypertension was present in 37.0%. HbA1c9.7%±2.4. Diabetic polyneuropathy and risk of foot ulceration accounted for 24.5%, 18.5% respectively. Analysis showed negative correlations between neuropathy disability scores, vibration perception threshold and feet electrochemical sweat conductance 0.476; P<0.0001, 0.462; P<0.0001respectively. Positive correlations were demonstrated between risk of peripheral autonomic neuropathy determined by sudoscan, and both the severity of distal polyneuropathy and the risk of foot ulceration determined by neuropathy disability scores 0.441P<0.0001, 0.386 P<0.0001respectively. Similar positive correlations were observed with tests reflecting small nerve fiber dysfunction: temperature perception 0.365; P<0.0001, and pain sensation scores 0.443; P<0.0001. **Conclusions:** Our study demonstrates that quantitative assessment of sudomotor dysfunction by electrochemical sweat conductance method may be reliably used to assess the presence and severity of peripheral autonomic neuropathy.

OC5. The Effect of Vildagliptin Relative to Sulphonylurea as Dual Therapy with Metformin (or as Monotherapy) in Muslim Patients with Type 2 Diabetes Fasting During Ramadan in the Middle East: The VIRTUE study.

Ahmed Hassoun, Monira Al-Arouj, Mohamed Ibrahim, Dubai Diabetes Center, Dubai, United Arab Emirates.

Objectives: To assess the effect of vildagliptin relative to sulphonylurea on hypoglycemic events, in type 2 diabetic Muslim patients who fast during Ramadan. Primary endpoint was proportion of patients with at least one hypoglycemic event during the fasting period. Secondary endpoints included change in weight, HbA1c levels, treatment adherence and overall safety. **Design and Methods:** This multicentre, prospective, observational cohort study enrolled patients from the Middle East into two cohorts: vildagliptin (n=308) and sulphonylurea (n=265), administered either as dual therapy with metformin or monotherapy. **Results:** Vildagliptin cohort had a significantly fewer patients reporting at least one hypoglycemic event (11, 3.7%) compared to sulphonylurea cohort (66, 25.5%) (p<0.001). The mean change in HbA1c levels from baseline at the end of study was –0.26% in the vildagliptin (Baseline:Mean=7.2%;SD=0.86) group compared to -0.08% in the sulphonylurea (Baseline:Mean=7.4%;SD=1.00) group(–0.18% between treatment difference; p=0.001). The mean body weight change at the end of study from baseline was -0.97 kg in the vildagliptin group compared to -0.29 kg in the sulphonylurea group (–0.68 kg between treatment difference; p<0.001). Treatment exposure and adherence was high and similar in both cohorts. The proportion of patients reporting adverse events was higher in the sulphonylurea cohort (4.3% in Vildagliptin compared to 25.3 % in the sulphonylurea cohort) with hypoglycemia being the most experienced event in both cohorts. **Conclusion:** Anti-hyperglycemic treatment with vildagliptin led to favorable outcomes in comparison to sulphonylurea treatment among diabetic patients who fast during Ramadan. Good glycemic control, weight control and safety results supported this outcome.

OC6. In hospital Hyperglycemia Prevalence, Management, Level of control, Associated Complications and Mortality

Metib Alotaibi, Ali Alzahrani, KFSHRC, Riyadh, Saudi Arabia.

Background: Recently, a major focus has been directed towards inpatient hyperglycemia. There is no available data on the prevalence, management and outcome of diabetes and in-hospital hyperglycemia in Saudi Arabia and Gulf countries. For this reason, we undertook a study to assess the prevalence of in hospital hyperglycemia, the therapeutic approaches used and level of control, the rate of hypoglycemia and the impact of hyperglycemia on the outcome **Patients and Methods**: This is a cross-sectional observational study over a 4-week period in which all non-ICU hospitalized adult patients (≥14 years) admitted in the previous 2 weeks over the next 2 weeks from the start of the study were included. Those with known diabetes or who develop hyperglycemia while in the hospital were the study group. The rest of the patients (Non-hyperglycemic)

served as control (observation group). **Results**: A total of 399 patients (177 Males, 222 females, Median age 46.6, range 14-94 years) were admitted during the 4-week study period. One hundred seven (27%), were known diabetics (52 on insulin and 57 on oral medications) before admission while 30 cases (7.5%) developed hyperglycemia during hospitalization. So the total cases of inpatient hyperglycemia were 137 cases (34.5%) and 262 cases (65.5%) were non diabetic and remained euglycemic. The in hospital management of hyperglycemia consisted of modified home regimen in 39 cases, sliding scale only in 10 cases, Insulin BID in addition to sliding scale in 26 cases, no treatment in 17 cases and OHA in 20 cases. In the study group, the median highest BS was 11.80 (range 4-32) and the median lowest BS was 4.9 mmol/l (range 3-19). The mean ± SD BS was 8.3±3.6 mmol/L. The median percentage of time in which BS >10 mmol/L was 36.4% (range 8-100) and >15 mmol/l 18% of the time (range 4-100%). **Conclusions:** Comparing the outcome of patients with those without hyperglycemia, the risk of infection was much higher (38% vs. 18%, p <0.0001). Although mortality was not statistically

Poster Presentations

P1. Screening and Evaluation of Cardiovascular Risks among Patients with Type 2 Diabetes in Primary Health Care

Almoutaz Alkhier Ahmed, Kingdom of Saudi Arabia

Background: Cardiovascular disease is currently the primary cause of morbidity and mortality in patients with diabetes. For each risk factor present, the risk of cardiovascular death is about three times greater in people with diabetes than people without diabetes. **Objectives:** To determine the risk factors for cardiovascular disease among patients with type 2 diabetes. To stratify the patients into risk categories to develop coronary arteries disease (CAD) based on the British Joint Societies risk chart. To assess the awareness and implementation of the risk assessment charts by primary care physicians. **Subject and methods:** Cross sectional study was designed .Sixty six (66 patients) diabetic patients were selected randomly by simple selection, from them 29 were males and 37 were females. Patients' Medical records were reviewed. The following parameters were detected; blood pressure, lipid profile, weight, height, smoking and degree of glycemic control. A questionnaire was designed and distributed to randomly selected physicians working in primary health care assessed their awareness and implementation of risk assessment charts was done. **Results:** Uncontrolled diabetes was found to be the common risk factor followed by uncontrolled lipid profile, obesity, uncontrolled systolic blood pressure and smoking. Seven percent (7%) of male group felled in highest risk group in compare with 1% in female group (P < 0.05) ,while 31% in male group felled in mild risk group in comparison with 90% in female group (P <0.05) . Sixty two percent (62%) in male group felled in high risk group in comparison with 9% in female group (P <0.05). Criteria for ranking in risk class differed between male and female group. Forty one physicians were contacted and received the questionnaire. Twenty nine (70.7%) physicians were responded to the questionnaire. Twenty two (22) informed that they were aware about risk assessment score systems. Fourteen (14) physicians informed that they were aware about the BJSs charts but only two informed that they had used it to assess their patients. **Conclusion:** Clustering of multi risk factors is a serious event which may raise the risk category of diabetic patients. For each risk category the risk factors may differed between male and female patients. More studies are recommended to study distribution of risk factors between male and female diabetic patients. Attention should be directed towards raising the awareness about the risk assessment scoring system and encouraging physicians to use it.

P2. Awareness of Foot Self-care Among Saudi Diabetic Patients Referred to a Specialized Diabetes Care Center.

Eman Shesha, Amal Madanat, Eman Al-Zahrani, Reem El-Asmari, Adwa Al-Ahmad, Saudi Arabia.

Background/ Objectives: Providing foot self-care education is an important component of the standards of care for all diabetics, which aim at preventing limb loss. The aim of the study was to evaluate the rate of foot self-care counseling, the level of foot self-care knowledge, and the ability to identify & apply appropriate foot-care practices among diabetics referred from primary health care centers to a specialized diabetes care center. **Methods:** A cross-sectional study was conducted at the Center on a sample of 350patients with diabetes. After obtaining an informed consent, patients were interviewed by a trained team. The study questionnaire contained variables about diabetes, foot self-care counseling, knowledge and the ability to identify& apply appropriate foot care practices. SPSS17 was used for statistical analysis. The level of knowledge

was evaluated using a modified Likert scale. **Results:** All were Saudi nationals. age (Mean±SD) 47.6±10.7 years. 20.6% were illiterate. 92.9% had type 2 diabetes. Duration of diabetes was 7.3±7.4years. 74.3% were on oral hypoglycemic agents, 37.1% had hypertension, and 56.3% had dyslipidemia. Only 30.9%received foot self-care counseling. 42.6% had excellent levels of knowledge about the effect of diabetes on foot health. However, only 17.7% had good ability to identify & apply appropriate foot care knowledge, while 42% had absent or weak ability .8.6%of the patients self-managed a previous foot lesion. 3.1% had cautery treatment. 47.4%regarded their foot care practices as inadequate. **Conclusions:** The majority of diabetics at the primary health care centers doesn't receive foot self-care counseling and are unable to identify & apply appropriate foot self-care practices. Development, implementation and monitoring of foot self-care counseling program are urgently needed.

P3. Elevated HbA1C is Significantly Associated with Decreased Post-Exercise Heart Rate Recovery in Patients with Diabetes.

Hareem Hasan, Alawi Alsheikh- Ali, Hamed Hassoun, M. Hamed Farooqi, Ahmed Jebawi, Bruno Blanchon, Dubai Diabetes Center, Dubai, United Arab Emirates

Background: Heart rate recovery is an independent predictor of cardiovascular and all-cause mortality in healthy subjects and those with diabetes. We examined the association between HbA1C and post-exercise heart rate recovery in patients with diabetes. **Design and Methods**: All participants were free from known cardiac disease or severe orthopedic problems. They were referred to exercise specialist for fitness assessment and underwent a graded exercise test using standard Balke-Ware protocol. Heart rate recovery was defined as the decrease in heart rate from peak exercise after one minute of cool down walk at 2 mph speed and 0% inclination. The most recent HbA1C was recorded for each patient. **Results:** We included 411 subjects with diabetes [age 45 ± 10, 269 (65%) males, 375 (91%) with type 2 diabetes, BMI 31 ± 6, 49% with BMI >30 kg/m2]. The mean hemoglobin A1C was 7.3 ± 1.6. The subjects were divided into 4 equal cohorts based on the quartiles of heart rate recovery. Using multiple logistic regression, adjusting for age, gender, BMI, beta blocker usage, metabolic equivalent, hypertension, and duration of diabetes, there was significant association between hemoglobin A1C and odds of having heart rate recovery in lowest quartile, such that for every unit increase in A1C, there was 13% increase in odds of being in the lowest heart rate recovery quartile (adjusted odds ratio 1.125 [1.002, 1.264]). **Conclusion:** Among diabetic patients without known cardiac disease, poor glycemic control as measured by elevated hemoglobin A1C is significantly associated with decreased post-exercise heart rate recovery.

P4. Detrended Fluctuation Analysis May Identify Early Asymptomatic Cardiac Autonomic Neuropathy in Diabetics

Herbert F. Jelinek, Bill Jideh, Ahsan H. Khandoker, Dubai, United Arab Emirates

Background/Objectives: Cardiovascular autonomic neuropathy is a severe and widespread complication of diabetes, which affects cardiac rhythm and can lead to arrhythmia and sudden cardiac death. It is associated with a poor prognosis and a number of clinically significant manifestations. These include exercise intolerance, postural hypotension, asymptomatic ischemia, painless myocardial infarction and increased risk of mortality. Early identification of cardiac autonomic neuropathy will improve subsequent health care intervention, the quality of life of diabetics and reduce the tremendous health and financial burdens associated with neuropathy in diabetes patients. **Design and methods:** In our study, diabetics where separated into cardiac autonomic neuropathy positive subjects (n=11) and those without cardiac autonomic neuropathy (n=11) based conducting five autonomic nervous system function tests. Heart rate variability was also determined using detrended fluctuation analysis values computed from 20-minute ECG recordings. Accuracy was determined by using the area under the curve statistic. **Results:** There was a statistical significance between controls and diabetes subjects with and without cardiac autonomic neuropathy ($p<0.05$). Detrended Fluctuation Analysis recognizes autonomic nervous system dysfunction associated with diabetes. Detrended Fluctuation Analysis showed an accuracy of 73% in identifying cardiac autonomic neuropathy compared to the traditional time domain measure (high frequency power) being 55%. **Conclusions:** Our data indicates that DFA can potentially be used to differentiate subjects based on their disease statue, perhaps identify subjects in the early, asymptomatic stages of a disease, which would contribute to successful therapeutic interventions.

P5. Prevalence of Hypovitaminosis D in Multiethnic Population of UAE

Satedndra Kumar Multani, Sathvik B.S, Padma G.M Rao, Dubai and RAK, United Arab Emirates

Introduction: Vitamin D deficiency or Hypovitaminosis D is newly recognized as a common condition of increasing prevalence worldwide. United Arab Emirates (UAE) has high prevalence of Hypovitaminosis-D, in spite of abundant sunlight. **Objectives:** The objectives of our study was to determine the prevalence of hypovitaminosis D in multiethnic UAE population & to compare the Vitamin D status in Arab & Non-Arab population & to identify the demographic parameters associated with vitamin D deficiency. **Methodology**: It was retrospective study conducted in the Al Zahrawi hospital of Ras Al Khaimah, UAE. The case records of all the subjects who visited the outpatient department of Al Zahrawi hospital during the past 30 months from October 2012 were screened for hypovitaminosis D. **Results:** 425 subjects satisfying inclusion criteria were included. Out of total 425 patients 243 (57.2%) were males &182 (42.8%) were female. 97.4% subjects had hypovitaminosis D & 33.1% had severe Vitamin D deficiency (25OH D3<10ng/ml).The mean age of the study population was 44.8+10.2 years. Majority of our study subjects were Indians 228(53.6%) followed by Arabs 130 (30.6%). The mean & standard deviation of vitamin D level of the study subjects was 14.0+8.13 ng/ml.154 (30.83%) & 247 (58.1%) subjects were having backache & muscle pain respectively as presenting feature. Higher number of study patients 249 (58.6%) had hypertension as the co-morbidity, followed by dyslipidemia 246 (57.9%) & diabetes mellitus in 208 (48.9%). **Conclusion:** Higher prevalence of hypovitaminosis D was observed in multiethnic population. Hypertension was the most commonly observed co-morbidity in the study subjects.

P6. Dumping Syndrome After Gastric Bypass: A Case Report

Asma Al Jaberi, Walid Kaplan, Bachar Afandi, Tawam Hospital, Al Ain, United Arab Emirates

Introduction: Dumping syndrome post gastric bypass surgery has been reported in more than 50 % of the cases. Most patients can be treated effectively with dietary modifications. Less than 5% of do not respond to diet changes. We herein report a case of late dumping syndrome that responded rapidly to a small dose of acarbose. **Case Resport:** A 46 year old woman with T2 DM, hypothyroidism, hypertension, and history of bariatric surgery 4 years ago, started to have symptomatic postprandial hypoglycemia. Strict dietary modifications over three months failed to control her symptoms. CGM at baseline confirmed recurrent episodes of prolonged hypoglycemia. Acarbose 25mg TID was started, and CGM repeated after 10 days. **Results:** Patient reported a dramatic improvement of her symptoms. CGM comparison of baseline versus post therapy showed: average BG 90±30 versus 94±17mg/dL, respectively, P<0.001. Incidence of BG <80mg/dL was 51% versus 11%, BG <60mg/dL was 19% versus 1%, and BG >140mg/dL was 8% versus <1%, respectively. **Discussion:** Efficacy of acarbose in late dumping is related to delayed carbohydrate digestion and therefore blunting the postprandial rise of serum glucose and insulin. A complete disappearance of late dumping symptoms has been reported with acarbose (50/100 mg t.i.d) in patients with dumping and non-insulin dependent diabetes mellitus.

Our case is unusual as our patient developed the dumping syndrome 4 years after surgery. Also her disabling symptoms not responding to strict dietary modifications, improved immediately after initiation of a small dose of acarbose.

P7. The Relationship between Ischemia Modified Albumin and Lipids in Egyptian Type 2 Diabetic Patients

Safa Refaat Abdel Moniem, Internal Medicine, Institute of Ophthalmology, Cairo, Egypt

Background: The most important reason for risk increase in diabetic patients is endothelial dysfunction and subclinical low grade systemic inflammation. Ischemia modified albumin is produced as a result of serum albumin flowing through ischemic tissues, and is a marker of oxidative stress and ischemia. **Patients and Methods:** We evaluate the relationship between serum ischemia modified albumin and lipid profile in Egyptian type 2 diabetic patients. 30 subjects with type 2 diabetes and normal lipid profile; 30 patients with type 2 diabetes and dyslipidemia; and 20 subjects as a control group, participated in this study. **Results:** The study revealed a significant correlation between serum ischemia modified albumin and glycosylated hemoglobin in type 2 diabetic patients without dyslipidemia, and a non-

significant correlation between serum ischemia modified albumin and all lipids of the patients of the same group. The study revealed also a significant correlation of serum ischemia modified albumin to serum triglycerides, total cholesterol and low density lipoprotein cholesterol and very low density cholesterol of type 2 diabetic patients with dyslipidemia, and highly significant correlation of serum ischemia modified albumin to glycolysated hemoglobin, low density lipoprotein and high density lipoprotein of the patients of the same group. **Conclusions:** The present study indicates that measuring serum ischemia modified albumin in diabetic patients with dyslipidemia would provide an index of ischemia due to structural modification of circulating albumin in serum which will aid in better prognosis and management of diabetes mellitus.

P8. Interest Assays of Oxidative Stress Parameters in Type 2 Diabetes Mellitus

Aouacheri Ouassila, Saka Saad, Algeria

Background/objectives: Oxidative stress has been implicated in the pathogenesis of type 2 diabetes mellitus (T2DM) and its complications. The diabetes mellitus is characterized by hyperglycemia together with biochemical alterations of glucose and lipid peroxidation. This study was conducted to investigate the variation in oxidative stress related parameters in T2DM. Design and methods Blood serum samples were collected from the 59 diabetic patients and 48 non-diabetic healthy controls. All the subjects were randomly selected, according to criteria of inclusion and exclusion. Approval was obtained from the Institutional Review Board. Glucose concentration, level of HbA1c and oxidative stress markers (G6PDH, MDA, GSH, GR, GPx and SOD) were estimated. All values were expressed as the mean ± standard error obtained from the number of experiments. Student's t-test was used for the comparing diabetic patients with normal subjects and correlation coefficients were determined by Pearson's simple linear regression analysis. **Results:** Fasting serum glucose concentration in T2DM patients was increased significantly as compared with controls. HbA1c was greater than standards. A significant elevation in MDA and depletion in GSH were observed in diabetic patients in comparison to controls. The diminution in G6PDH activity is accompanied in part with a decrease in the anti-oxidative enzymes activities (GPx and GR); and in other part with an increase in SOD activity in all diabetic patients. Conclusion The present study shows that there is an oxidative stress state in T2DM patients compared with healthy subjects. The intensity of diabetes can be evaluated via the status of oxidative stress.

P9. A Survey of Current Practice of Hyperglycemia Management in Surgical Patients.

Hawa El-Sharef, Tripoli Medical Center, Tripoli, Libya.

Background: Sliding scale insulin (SSI) is associated with a large number of medication errors and adverse events including major swings in blood glucose with increased incidence of both hypoglycemia and hyperglycemia. Despite this, many clinicians still use sliding scale insulin (SSI) regimens. Aim of the study: - was to determine what methods are used for management of in-patient hyperglycemia in current practice in patients for surgery. **Methods:** During the period 1st to 12th of February 2010, the file records of ninety diabetic patients admitted to surgical departments in three teaching hospitals in Tripoli were reviewed. Data extracted included hyperglycemia management regimen used at home, on admission, and in the pre and post-surgical periods. **Results:** During their pre-operative hospitalisation, period 48.9% of patients were shifted to sliding scale, and 22.2% shifted to multiple daily insulin regimen (MDI). During surgery and in post-operative period sliding scale were the method of controlling hyperglycemia in 83.3% and 54.4% respectively. Conclusion:-SSI is commonly prescribed for hospitalized patients with diabetes mellitus in surgical wards. This call for develop educational programs aimed at changing this practice in favor of more physiologic insulin regimens.

P10. Prevalence of Abnormal Glucose Regulation in Libyan Patients Presenting for Elective Coronary Angiography.

Hawa El-Shrief, Khaled Alwaleed, Tripoli Medical Center, Tripoli, Libya.

Background: Patients with coronary artery disease (CAD) frequently have multiple risk factors. Diabetes and impaired glucose tolerance (IGT) has been associated with cardiovascular events and cardiovascular disease mortality. Aim of the study to determine the prevalence of abnormal glucose regulation among Libyan patients, presenting for elective coronary angiography. **Methods and materials:** All patients referred for diagnostic coronary angiogram at the Catheterization Laboratory of National Heart Centre,

Tajora, Tripoli over a period of one year from April 2007, and March 2008, were included after consent. Patients with history of diabetes were excluded. Diagnostic coronary angiogram was performed for all included patients as well as a standard oral glucose tolerance test (OGTT) with 75 gm glucose. **Results:** 99 patients were included in our study, with mean age of 54.6±11.2 years. 48 (48.5%) of the enrolled patients showed either impaired or diabetic fasting or 2-hour OGTT results. 23 (23.2%) patients were diabetic based on FBG or 2-hour OGGT result, and 19 (19.2%) have IGT. Of 18 (18.2%) with impaired fasting (IFG), 1 (5.6%) patient showed diabetic glucose tolerance (DGT), and 17 (94.4%) patients have IGT. Among patients with abnormal glucose metabolism, coronary angiogram showed significant coronary artery disease in 36 (75%), compared to 28 (55%) of patients with normal fasting and 2-hour OGTT results. **Conclusion:** Abnormal glucose regulation was high among Libyan patients presented for elective angiography. OGTT should be part of the evaluation in this high risk population.

P11. Linagliptin vs Placebo Followed by Glimepiride in Type 2 Diabetes Patients with Moderate to Severe Renal Impairment

Markku Laakso, Julio Rosenstock, Per-Henrik Groop, Uwe Hehnke, Ilkka Tamminen, Sanjay Patel, Maximilian von Eynatten, Hans-Juergen Woerle. United Arab Emirates

Background: Renal impairment (RI) is a serious T2DM complication that restricts options for managing hyperglycemia and associated increased cardiovascular risk. **Method:** This randomized double blind trial evaluated the efficacy and tolerability of the dipeptidyl peptidase 4 inhibitor linagliptin (LINA) in T2DM pts (HbA1c 7-10%) with moderate to severe RI (estimated glomerular filtration rate [eGFR] <60 mL/min/1.73m2; not on dialysis). Pts received LINA 5 mg qd (n=113) or placebo (PBO) (n=122) for 12 wks, then PBO pts were switched to glimepiride 1-4 mg qd (GLIM) and treatment continued to wk 52. Primary endpoint was HbA1c change from baseline at wk 12. At baseline, 63.4% were male; mean age 67±9 y, HbA1c 8.1±0.9% and eGFR 37±13 mL/min/1.73 m2. **Results:** Most had T2DM for >10 y (76.4%) and were on insulin (85.8%). At wk 12, adjusted mean±SE HbA1c change with LINA was -0.50±0.06% (change with PBO - 0.08±0.07%: difference -0.42%, 95% CI -0.60 to -0.24; p<0.0001). In the 40 wk extension, HbA1c was lower with LINA than GLIM. Incidence of drug-related adverse events was similar in the first 12 wks (LINA 23.9%, PBO 24.6%), and lower with LINA in the extension (LINA 38.3%, GLIM 46.5%). Hypoglycemia was less frequent with LINA (LINA 57.9%, GLIM 69.3%). Mean adjusted weight increase after 52 wks was 0.06 kg (LINA) and 1.74 kg (PBO/GLIM). In conclusion, LINA was efficacious and well tolerated in T2DM pts with moderate to severe RI, with less hypoglycemia and relative weight loss vs GLIM. NCT01087502

P12. The Dipeptidyl Peptidase-4 Inhibitor Linagliptin Lowers Postprandial Glucose and Improves Measures of β-cell Function in Type 2 Diabetes

Sanjay Patel, Tim Heise, Martin Larbig, Sonja Weber-Born, Thomas Seck, Uwe Hehnke, Hans-Juergen Woerle, Klaus Dugi, Ahmed Ouda, Dubai, United Arab Emirates

Background: In patients with T2D, progressive deterioration of β-cell function contributes to the development of hyperglycemia. Treatment with incretin-based therapies may potentially improve β-cell function and delay this progressive deterioration. **Method & Design:** Here we investigated the effect of the DPP-4 inhibitor linagliptin on β-cell function, as assessed by changes in Homeostasis Assessment Model (HOMA)-%β index and incremental 2-hour postprandial glucose (PPG) levels after a meal tolerance test. Data from six randomized, 24-week, placebo-controlled, Phase 3 trials of linagliptin 5 mg qd were pooled for this analysis. In total, 2960 patients were available: linagliptin, n=2077; placebo, n=883. Subgroup analyses were conducted in patients who had baseline and week-24 data for HOMA-%β (n=1770) and PPG (n=224) assessments. **Results:** After 24 weeks' treatment, the adjusted mean ± SE change from baseline in HOMA-%β with linagliptin vs placebo was 16.7 ± 4.3 vs 0.2 ± 5.1 (mU/L)/(mmol/L); the placebo-adjusted mean change for linagliptin was 16.5 ± 4.6 (mU/L)/(mmol/L) (p=0.0003). Similarly, after 24 weeks' treatment, the adjusted mean ± SE change from baseline in PPG with linagliptin vs placebo was -44.6 ± 6.0 vs 9.1 ± 7.9 mg/dL; the placebo-adjusted mean change for linagliptin was -53.7 ± 8.6 mg/dL (p<0.0001). **Conclusion:** In summary, this pooled analysis from a large, global Phase III program shows that once-daily linagliptin improves measures of β-cell function relative to placebo. The effect of long-term treatment with linagliptin on β-cell function remains to be determined.

P13. Renal Safety and Outcomes with Linagliptin: Meta-Analysis of Individual Data for 5466 Patients with Type 2 Diabetes

Maximilian von Eynatten, Angela Emser, Mark Cooper, Vlado Perkovic, Julio Rosenstock, Robert Toto, Christoph Wanner, Hans-Juergen Woerle, Ahmed Ouda, Dubai, United Arab Emirates

Background: Long-term glycemic control in diabetes is associated with reduced risk of renal microvascular complications. Linagliptin significantly reduced albuminuria in type 2 diabetes (T2D)-associated nephropathy, and As these effects do not appear to be directly related to short-term glycemic improvements. The aim of these analyses was to evaluate renal outcomes with linagliptin in completed Phase 3, randomized, double-blind, placebo-controlled trials (≥12 wks). **Methods:** Predefined events from 13 trials were analyzed using a composite primary endpoint: new onset of a) micro- or b) macroalbuminuria, c) CKD (serum creatinine increase ≥2.83 mg/dL), d) worsening of CKD (loss in eGFR >50% vs baseline), e) acute renal failure (standardized MedDRA query), and f) death (any cause). **Results:** Of 5466 participants (mean baseline HbA1c: 8.2% and eGFR: 91 mL/min/1.73m2), 3505 received linagliptin 5mg qd and 1961 placebo; cumulative exposure (person yrs) was 1756 and 1057, respectively. Events occurred in 448 (12.8%) patients receiving linagliptin vs 306 (15.6%) for placebo. The hazard ratio (HR) of 0.84 (95% CI: 0.72-0.97, P<.05), was not significantly altered by race, but tended to be stronger in patients <65 vs >65 yrs (HR: 0.77 vs 1.04). The descriptive RRs for individual renal endpoints were: micro- (0.85) and macroalbuminuria (0.88), new onset (0.44) or worsening of CKD (0.76), ARF (0.93), and death (0.77). **Conclusions:** In this large meta-analysis, renal safety and outcomes were significantly improved in patients with T2D treated with linagliptin. These data support a potential direct nephroprotective effect of linagliptin that warrants future long-term controlled trials designed to confirm these findings.

P14. Linagliptin is an Effective Therapeutic for Non-alcoholic Fatty Liver Disease (NAFLD) and Non-alcoholic Steatohepatitis (NASH)

Thomas Klein, Michael Mark, Dubai, United Arab Emirates

Background: Dipeptidyl peptidase (DPP)-4 inhibitors are an established treatment option for type 2 diabetes and have recently demonstrated insulin sensitizing, anti-inflammatory, and anti-oxidative effects. NASH is gaining importance as the hepatic manifestation of the metabolic syndrome and as a primary cause of cirrhosis and hepatocellular carcinoma. Method: We investigated the effects of the DPP-4 inhibitor linagliptin in streptozotocin/high-fat diet (STZ/HFD) neonatal mice, a novel model for NASH. Two-day-old males were injected with STZ (200 μg/mouse, i.p.) and fed a HFD for 4 weeks. Treatment with linagliptin (1, 10, or 30 mg/kg/d) was either for 2 or 4 weeks. Histologic NAFLD scoring (fat deposition, lobular inflammation, hepatocellular ballooning), Sirius red collagen staining, and mRNA analysis for inflammation-related transcripts and fibrosis markers were performed (all data are mean ± SEM). **Results:** In the first study (treatment for 2 weeks), linagliptin significantly reduced NAFLD scores (1 mg/kg: 2.9±0.7, p<0.05; 10 mg/kg: 2.4±1.0, p<0.01) versus untreated controls (4.1±1.1). In addition, linagliptin significantly reduced hepatic tumor necrosis factor- expression (1 mg/kg: 1.4±0.2, p<0.001; 10 mg/kg: 2.1±0.7, p<0.001) versus untreated controls (5.7±1.4). In the second study (treatment for 4 weeks), linagliptin also significantly reduced NAFLD scores (10 mg/kg: 3.7±0.4, p<0.05; 30 mg/kg: 3.6±0.3, p<0.01) versus untreated controls (4.6±0.6). Furthermore, linagliptin significantly reduced collagen formation (10 mg/kg: 0.64±0.02, p<0.05; 30 mg/kg: 0.59±0.05, p<0.01) versus untreated controls (0.96±0.09). In conclusion, the results of this study suggest that linagliptin may be a novel therapeutic approach for the treatment of NAFLD and NASH.

P15. Clinical Experience with Pancreatitis due to DPP4 Inhibitors in Northern Emirates

Mahir Khalil Ibrahim Jallo, Gulf Medical University, United Arab Emirates.

A two case series of DPP4 inhibitors related acute pancreatitis admitted to Gulf Medical University Hospital & Research Center, a 150 bed secondary care hospital in

Northern Emirates in 2012. The first patient was a 38 year old diabetic male on Vildagliptin and the second patient a 60 year old diabetic male on Sitagliptin. Both patients recovered from their acute pancreatitis by withdrawal of the offending drugs respectively and also did not have any alternate explanation as to the cause of the pancreatitis apart from being diabetics making them both a probable DPP4 inhibitors related cases. Acute pancreatitis with Sitagliptin is a known serious adverse event from the studies done during post marketing surveillance, whereas its association with Vildagliptin is limited to case reports. The purpose of highlighting these cases is to draw attention to this serious adverse DPP4 inhibitors side effect and recommending the need for a national online registry for documentation of the possibly related new diabetic medications serious adverse events specially UAE being among the first countries in the region which register and introduce these medications.

P16. Sitagliptin Attenuates Ovariectomy Induced Osteoporosis in Rats

Amina Unis, Manal Hamza, Kingdom of Saudi Arabia

Background and purpose: Osteoporosis is one of the most prevalent metabolic bone disorders especially among postmenauposal women. Diabetes mellitus may be associated with development osteoporosis. Hence, the purpose of the current study was to investigate the effect of Sitagliptin (dipeptidyl peptidase inhibitor IV) on ovariectomy induced osteoporosis in rats. Design and method The study was conducted on 40 female rats that were divided into four groups each composed of 10 rats: Group 1 sham operated group, group 2 ovarectomized (OVX) group, while group 3 and group 4 were OVX rats treated with estrogen replacement therapy (ERT) and sitagliptin respectively for eight weeks. Blood samples were collected at the end of eight weeks for measurement of serum alkaline phosphate (ALP), calcium, phosphorus, osteocalcin and malondialdehyde (MDA). Urine samples were collected for measurement of urinary deoxypyridoline (DPY)/ creatinine. **Results:** The OVX-rats showed a significant decrease in serum calcium, a significant increase in serum ALP, osteocalcin, MDA and urinary DPY)/creatinine levels when compared to the sham operated group. Such biochemical alterations induced by ovariectomy were significantly ameliorated by administration of EHT and sitagliptin respectively. **Conclusions:** Sitagliptin was found to be effective in decreasing bone resorption, increasing bone formation and hence reducing ovariectomy induced osteoporotic changes. Thus, the use of sitagliptin, as anti-diabetic agent, in postmenauposal women should be encouraged.

P17. ECG Assessment by Community Nurses in Rural and Remote Regions

Kinda Khalaf, Ahsan H. Khandoker, Dubai, United Arab Emirates

Background/objectives: Increasing public health costs associated with hospitalization, an increasing aged population with a greater prevalence of chronic disease and a shortage of specialists in rural and remote areas requires more economic ways of identifying individuals at risk of an adverse cardiac event. Targeted population screening such as those with chronic illness may provide better specificity and sensitivity for cardiovascular disease using an ECG assessment. **Design and methods:** Our data compared ECG recorded for a standard 5 minutes on a Welsh-Allyn ECG 12-lead recording device. The automated assessment provided by the Welsh-Allyn device was checked by a cardiology specialist and recorded. All results were compared between people with and without diabetes. **Results:** Of 85 people with diabetes and 70 without diabetes, 8.6% versus 26% were aware of any previous or existing cardiac pathology. The ECG assessment detected 44% of non-diabetics and 53% of diabetics with an ECG anomaly in the current screening. Of those participants with an ECG anomaly 42% were considered serious and warranted further investigation in the non-diabetic group compared to 91% in the diabetic group. **Conclusions:** These findings argue for a strong role for community health nurses in routine assessment and intervention such as nursing care and ensuring compliance with healthy lifestyles. Earlier identification of cardiac problems lead to better treatment prognosis and reduction in hospitalizations. In addition ECG data can be used in nursing research and assessing nursing treatment validation and outcomes.

P18. Insulin Resistance and Psoriasis

Amira El Tawdy, Cairo University, Egypt

Purpose: Psoriatic patients have an increased prevalence of the core components of metabolic syndrome including; obesity, dyslipidemia, insulin resistance, diabetes mellitus and cardiovascular disease. Detection of insulin resistance in psoriatic patients could prevent DM and its complications. In our study, we tried to detect the relation between impaired glucose tolerance (IGT), insulin resistance (IR)

and psoriasis and their possible correlations to clinical variant, duration and severity of the disease. **Methods:** We measured serum blood glucose levels both fasting and 2-h postprandial and ELISA technique was applied in order to measure the fasting serum insulin levels. Based on fasting and 2-h postprandial blood glucose levels, impaired glucose tolerance (IGT) was estimated. Detection of insulin resistance was achieved by evaluation of insulin sensitivity and beta cell function indices, which were applied on 30 psoriatic patients as well as 30 healthy controls. Both Patients and controls lacked any family history of DM. **Results:** The results showed that both fasting and 2-h postprandial blood glucose levels were higher in psoriatic patients than controls with statistical significant difference. **Conclusion:** significant increase rates of both impaired glucose tolerance and insulin resistance in psoriasis suggest that psoriatic patients may carry high diabetogenic risk. Thus the detection of IR has an important value in reducing the risk of DM and preventing its complications, and reducing the risk of other components of insulin resistant syndrome (IRS).

P19. Impaired Redox Status in Prediabetes

Herbert F. Jelinek, Hayder Al-Aubaidy, Sarah Meidinger, Laura Maschirow, Dubai, UAE

Background/Objectives: This study aimed to determine whether there is an association between redox status and prediabetes. **Design and Methods:** The research was a retrospective study of patients attending an Australian rural diabetes screening clinic. Forty six control patients' ad 51 prediabetes patients were enrolled in the study after exclusion criteria were applied. Prediabetes was defined as a blood glucose level greater than 5.6mmol/L and less than 7mmol/L. Demographics data was recorded as well as blood biochemistry including erythrocyte glutathione: glutathione disulfide ratio. **Results:** Clinical variables and medication use were not significantly different between the two groups except for beta blockers in the prediabetes group ($p<0.05$). The erythrocyte glutathione: glutathione disulfide (GSH/GSSG) ratio was significantly reduced in the prediabetes (7.1 ± 3.7 vs 9.9 ± 6.4, $p<0.05$) but cholesterol levels were similar between the two groups. **Conclusions:** The results indicate an imbalance in the redox state in prediabetes with substantially more of the oxidized product present with normal cholesterol levels. The GSH/GSSG ratio presents therefore as a possible early cardiovascular risk factor. Importantly in this study anti-hypertensive medication was non-protective for oxidative stress.

P20. Hypercalcemia due to Hyperthyroidism: a Case Report & Literature Review

Fathimabeebi PK, Mohamed Al Lamki, Noor Busaidi, Hilal Musalhi, Muscat, Oman

Objective: To report a case of thyrotoxicosis presented with symptoms of hypercalcemia and to review literature with similar clinical picture. **Case Report:** 61 year old male, a chronic smoker with past history of peripheral vascular disease, presented to our emergency department with 2 month history of weight loss (10kg), poor appetite, and depression. There was no history of fever, hemoptysis, heat intolerance, and palpitation. On examination he was emaciated. There was no palpable lymphadenopathy, goiter, and associated eye sign. His pulse rate was 78/minute BP-132/72 mmHg. Systemic examination was unremarkable. His blood investigation showed normal complete blood count, ESR, C-reactive protein, glucose, renal and liver function. His calcium level was 3.04mmol, PO4-1.6, ALP190, Parathyroid hormone (PTH) level0.7pmol (1.6-6), TSH<0.003, FT4-74pmol, FT3-32pmol. Thyroid US-diffuse small goiter, Tec-99uptakescan 14%global uptake. CXR was normal His care was transferred under endocrine team .Treated with-IV hydration, palmidronate 60 mg iv, carbimazole 15 mg twice daily. His calcium dropped to 2.4mmol on 5th day of admission. After 6 weeks, he gained 3 kg, and improved symptomatically. **Discussion: H**ypercalcemia due to hyperthyroidism is infrequent. High levels of interleukin (IL-6) seen in hyperthyroidism stimulate osteoclast activity and alter osteoblast -osteoclast coupling. Triiodothyronine (T3) increase the sensitivity bone to IL-6 and leads to accelerated bone turnover. The resulted hypercalcemia suppress Parathyroid hormone release. Thyrotoxicosis can be overlooked by predominant hypercalcemic symptoms. Our patient had an apathic presentation, and his hypercalcemia was merely due to thyrotoxicosis. **Conclusion:** Clinicians should be aware of the association of hypercalcemia with thyrotoxicosis for early detection and management.

P21. Normal Circulating PTH in Saudi Healthy Individuals with Hypovitaminosis D

Yousef Al-Saleh, Nasser Al-Daghri, Khalid Alkharfy, Omar Al-Attas, Majed Alokail, Abdulaziz Al-Othman, Shaun Sabico, George Chrousos. Riyadh, Saudi Arabia.

Background: Recent studies in the Middle East have

shown an increased incidence of vitamin D deficiency across this region of year-round sunlight. There is scarcity of information, however, as to the levels of 1, 25-dihydroxyvitamin D [1,25(OH)2D], the active form of vitamin D, and its associations with cardiometabolic parameters in an Arab cohort and this study aims to fill this gap. **Patients and Methods:** In a cross-sectional study, 33 male and 43 female [22 children and 54 adults, total 76] Saudis with previously established low levels of serum 25-hydroxyvitamin D [25(OH)D] (< 50 ng/ml or 20nmol/l) were recruited. Anthropometrics were obtained and fasting blood samples were taken for a routine measurement of glucose, lipid profile, calcium and albumin, while serum 25(OH)D, 1,25-(OH)2D and intact PTH were quantified using specific ELISAs. **Results:** Serum calcium, intact PTH and 1,25(OH)2D were all within the normal range in both children and adults in both genders. In all subjects, serum 1,25(OH)2D was not associated with intact PTH, while circulating 1,25(OH)D inversely correlated with systolic blood pressure ($p = 0.01$) and waist circumference ($p = 0.04$). Thus, vitamin D deficient Saudi children and adults with normal levels of 1,25-(OH)2D also had normal circulating calcium and PTH. **Conclusions:** This study suggests that local cut-offs should be set that will be of clinical significance in the identification of those at true risk for harder end-points, such as secondary hyperparathyroidism and bone-related diseases.

P22. Genetic Pheochromocytoma/Paragaglioma

Fathima Beebi Pambinezhuth, Mohamed Al Lamki, Hilal Musalhi, Noor Busaidi, Muscat, Oman.

Context: The prevalence of Pheochromocytomas in hypertensive patients is less than 1%.Most PHEOs are sporadic ,but a significant percentage (30%) may be associated with germ line mutations of genes predisposing to the development of familial syndromes-Multiple Endocrine Neoplasia (MEN2),von Hippel Lindau disease (VHL),Neurofibromatosis 1(NF-1) and Paraganglioma/ Pheochromocytoma (PGL/PHEOs) related to succinate dehydrogenase (SDH-D,B and C).This review will summarize the important data related to this fascinating clinical syndromes. **Methodology:** We reviewed our PHEO patients and their associated genetic mutations. **Result:** We have a total of 11 PHEOs/PGLs cases. 6 out of 11 showed an associated germ line mutation.5 patients were carriers of SDHB mutation and 1 case of VHL mutation was identified. All of the cases, presented with hypertension at a young age <30 years).Among patients with SDHB mutations-2 patients had malignant extra adrenal PHEOs. Direct sequencing of Exon6 showed SDHB c771dup A mutation in 2 patients (cousins), SDHBc708 T>c in another 2 patients and SDHB c859 G>A in 1 patient. Screening for associated tumors were negative in these patients. Their family screening is awaited. VHL patient has stable benign pancreatic cysts and renal cyst. **Discussion:** Pheochromocytomas are tumors arising from chromaffin cells of adrenal medulla.However, 9-23% of tumors develop from extra adrenal chromaffin tissue, referred as PGLs (Bravo & Tagle 2003, Sibal et al.2006 Most PHEOs occur sporadically. With the advent of genetic testing, it is clear that about 20-30% patients with PHEOs/PGLs carry a germ line mutation associated with a familial syndrome .Genetic testing is strongly recommended for: 1-Patients with extra adrenal PHEOs, multifocal and malignant tumor. 2- Family history of such tumors, 3-Presence of other manifestations of genetic syndrome 4-If onset of symptoms at a young age (<50). The carriers of these mutations are predisposed to the development of multiple endocrine neoplasia (mainly MEN2), Von Hippel, Lindau (VHL), neurofibromatosis 1(NF1) and the PHEO/PGL syndromes. The mutations occur on the genes for succinate dehydrogenase subunit D, B and C (Baysal et al.2000, Neumann et al 2002, Amar et al 2005). Familial PHEOs/ PGLs syndromes are inherited in an autosomal- dominant manner. Pheochromocytomas in MEN-2 & VHL disease are mainly adrenal, bilateral and less malignant. MEN PHEOs secrete epinephrine disproportionately in large amount. VHL PHEOs exclusively secrete normetanephrine.NF1 PHEOs are similar to sporadic cases, mostly (90%) single benign adrenal tumour, 10% bilateral, 6% with PGLs, and 12 % with metastasis. Familial PHEOs/PGLs are caused by mutations in 3 of the 4 genes coding the mitochondrial complex II- SDH subunit B (SDHB -PGL 4), D (SDHD-PGL1), C (SDHC –PGL-3). PGL-SDHD is characterized by head and neck parasympathetic PGLs (glomus tumours), less commonly with sympathetic PGLs and PHEOs. Malignancy is uncommon. Individual with SDHD mutation develop PGL only if mutated gene is inherited from father "maternal genomic imprinting" (Baysal etal 2002). PGL-SDHB is an autosomal- dominant syndrome characterized by sympathetic PGLs, with or without adrenal PHEOs and malignant disease (35%) (Brouwers et al.2006) and secrete mainly norepinephrine /dopamine. They are prone to develop papillary thyroid & renal cell cancer. PGL-SDHC – mainly cause extra adrenal benign parasympathetic PGLs. Patients with these familial syndromes should have lifelong

surveillance for detecting recurrence or the development of associated diseases. Conclusion: It is widely seen that a substantial group of patients with sporadic PHEOs and functional PGL may have germ line mutations predisposing to the development of more generalized diseases. Clinical features such as young age at onset, bilateral, multifocal, malignant and extra adrenal tumor should be seen as indications for genetic screening a lifelong follow up is required for patients with these familial syndromes. The challenge is to have a tangible genetic testing, affordable and linked with appropriate imaging to confirm the presence of the lesion and its secretory profile. To date genetic testing is expensive, and there may be ethnic variation in the context of the same disease. **Preventive Medicine Approach:** Involving clinical geneticist, nuclear medicine, interventional radiologist, endocrine/oncology surgeon, oncologist and the endocrinologist to form a multidisciplinary team for effective management of such cases is needed.

P23. Serum Selenium Status in Thyroid Disorders

D. Sultan Sheriff, Benghazi, Libya

Introduction: The thyroid is the organ with the highest selenium content Up to 80% of circulating T3 is produced by the activity of the selenoenzyme iodothyronine deiodinase(ID-I). Thus, thyroid hormone metabolism may be affected by deficiencies of both selenium and iodine. The selenoprotein glutathione peroxidase (GPx) is one of the key enzymes that protects thyroid gland from oxidative damage caused by excess hydrogen peroxide (H2O2) produced during thyroid hormone synthesis. **Aim:** In the present study, the selenium level and its role in the incidence of thyroid disease among the population aged between18 - 70 years were studied and correlated with serum thyroid hormone levels and Gpx activity. Materials and **Methods:** A total of 183 study subjects, (91 males and 93 females) with diabetics, cardiovascular and thyroid complications referred to Jayadeva Institute of Cardiology, Banglore, India were included in this study. The serum fasting blood glucose (FBG), lipid profile, T3, T4 and Thyroid stimulating hormone (TSH) were measured by automated routine methods by electro chemiluminescence. Selenium was measured by using Graphite furnace Atomic absorption spectrophotometer, Shimadzu. GPx was determined by Enzyme linked immune-assay. **Results:** The present study shows that plasma selenium status had definite correlation between serum selenium status and thyroid function with low levels of selenium being associated with thyroid hormone deficiency and therefore normal thyroid function may need to have a balance between selenium and iodine levels. **Conclusion:** Selenium dependent enzyme glutathione peroxidase shows a positive correlation between selenium status in hypothyroid patients.

P24. The Role of Thyroid Scintigraphy with Tc99m Pertechnetate in Defining the Spectrum of Thyroid Disorders in Young Omanis

S. Hussein, M. Shukaily, Omayma Elshafie, D. Sankhla, Nicholas Woodhouse. Department of Endocrinology, Sultan Qaboos University, Mascat, Oman.

Background: Thyroid disorders are the commonest endocrinopathies in children and adolescence and early diagnoses and treatment is essential to prevent irreversible nervous system damage and developmental delay. It is important to enable the clinician to further provide 1) Genetic counseling and routine sibling examination, 2) Understanding the underlying disease which results in better medical care, 3) Patient care and parental expectations of long term/ temporary therapy, 4) Avoiding long term therapy if it is not indicated. The screening program of congenital hypothyroidism has started on the 1/1/05 in Oman using umbilical cord blood sampling. The incidence of CH is 1 in 2700 live births, however there are no other statistics available regarding the other thyroid. Thyroid Scintigraphy is safe method of imaging and useful for characterization of different thyroid abnormalities. **Objective:** The aim of this study is to determine the role of Thyroid Scintigraphy in diagnosing the different thyroid abnormalities in young Omanis. **Methodology:** This is a cross sectional study performed in patients from birth to 16 years with thyroid abnormalities who have undergone Thyroid Scintigraphy during 2005-2009. A total of 1780 patients have underwent Thyroid Scintigraphy from 2005 to 2009. We analyzed data of 94 young patients. The thyroid scans were reviewed for visual uptake, homogeneity, position, % total uptake and nodules. Ultrasound findings were also reviewed for site, size, echo-texture, nodules and cysts. **Results:** Thyroid disease was commoner in females 62 patients with 2:1 ratio to males. The reasons for performing thyroid scintigraphy were thyrotoxic 37%, hypothyroidism 33% and neck swelling 30%. The commonest thyroid diasease was Hashimotos thyroiditis. Fine needle aspiration of the 9 solitary cold nodules confirmed neoplasm in 3 and 6 benign lesions **Conclusion:** Thyroid scintigraphy is recommended

for differential diagnosis of thyroid diseases, especially in congenital hypothyroidism. Ultrasound appears to be complementary to thyroid scans especially in patients with Hashimotos thyroiditis to exclude thyroid nodules. Thyroid abnormalities are twice as common in females compared to males. Dysgenesis is commoner than dyshormogenesis in patients who presented with congenital hypothyroidism. There was a positive family history with 4 siblings having dyshormogenesis confirmed by thyroid scintigraphy and 2 patients had associated hearing loss since it is an autosomal recessive condition. Most of the patients had Hashimotos thyroiditis. One third of the solitary cold thyroid nodules were malignant.

P25. Tumour-Induced Hypophosphataemic Osteomalacia Response to Treatment with Octreotide and Surgery.

Omayma Elshafie, S. Hussein, M. Norman, Q. Asim, N. Woodhouse, Sultan Qaboos University, Muscat, Oman

Introduction: In humans 2 renal 11 sodium dependent transports are found in the proximal renal tubule and their activity is controlled by PTH, oral phosphate loading and fibroblast growth factor (FGF) 23. The latter is produced by osteocytes and increased circulating levels result in renal phosphate wasting. Tumors of mesenchymal origin may secrete excessive amounts of FGF 23 and cause severe hypophosphataemic o'malacia. These tumours are often small and difficult to find but may be localized by functional imaging with octreotide. We describe a patient with tumoural hypophophataemia who responded clinically to a short trial of octreotide and cured by surgical excision of his tumor. **Case Presentation:** A 38 year old male, presented with slowly progressive bone pains and weakness over 6 years. Hypophosphatemia had been documented 5 years previously and since then he had received treatment with 1 alpha Vitamin D and phosphate supplements without obvious benefit. Scanning initially with PET revealed a hot spot in his R groin thought to have been inflammatory in origin. When seen a year later in SQUH, the serum phosphate was severely reduced 0.5 mmol/L with a markedly increased urine phosphate of 44 mmol/L. The serum calcium and PTH levels were normal and ALP increased. An MRI scan revealed a 3x2, 5 cm lesion in the R sartorious muscle which was positive on octreotide scanning, A therapeutic trial of octreotide 100 mcg 8 hourly was given for 2 weeks .His bone pains improved substantionaly during this period and although there was no significant change in serum phosphate levels which range from 0.42-0.52 mmo/L, His 24 hour urine phosphate fell from 44 to 32 mmol/L. Shortly afterwards his 3x2.5 cm encapsulated tumour was localized using US and completely resected. Histology revealed myositis ossificans. Following surgery there was progressive increase in the serum phosphate levels which were mid normal after 26 days.

P26. Osteoporosis and Osteopenia are Overdiagnosed in Oman. Our Therapeutic Strategies Must Be Changed

S. Hussein, S. Al Hadhrami, J. Al Sulaimi, D. Al Kindi,O. Elshafie, Dr. A. Al Zakwani, N. Woodhouse, Sultan Qaboos University, Muscat, Oman

Introduction: Osteoporosis is a major public concern and characterized by low bone mass with micro architectural deterioration resulting in increased bone fragility and increased susceptibility to fracture. It is estimated that 1 in 2 women and 1 in 5 men over 50 years of age will succumb to fracture during their life time The WHO definition of osteoporosis relates to the peak bone mass (T-Score), and they define osteoporosis as a T-score more than or equals -2.5 SD from values obtained in the local population.
However bone mineral density (BMD) measurements vary considerably between ethnic groups; black Africans having the highest and Asians the lowest BMD. In Oman we are using the Caucasian BMD values as a reference range, thus in the absence of a normal reference range for BMD in Oman the question remains" Are we over diagnosing osteoporosis in Omanis and are we treating people unnecessarily. **Objectives:** To establish 1) Whether Caucasian PBMD reference values are suitable for use in the diagnosis of osteopenia and osteoporosis in Omanis. 2) Normal PBMD reference values in a cohort of healthy young Omanis. **Methodology:** 1) Target population 2) Healthy Omani individuals aged between 25-34 years old. 3)100 subjects are selected randomly from workers in SQU, 50 males and 50 females. Fully informed consent was obtained**.** Exclusion criteria included **s**econdary causes, Medication affecting Ca or Vitamin D metabolism, Pregnancy, Lactation, Chronic diseases, Family history of pathological fractures, Alcoholism. **Results:** All blood samples were normal Using Caucasian BMD reference (Figures 1a and 2a): Most Females and Males are Osteopenic and significant numbers are osteoporotic. Using locally calculated BMD reference (Figures 1b and 2b): Most of the candidates are within normal, few are osteopenic and none are osteoporotic. The normal Omani PBMD measurements are 23.8% Males,

26.5% Females lower than Caucasian values. **Discussion:** Our study clearly demonstrates that normal Omani PBMD levels are substantially lower than those of Caucasians. Indeed a large proportion of our normal population would have been diagnosed as having osteopenia and 10 percent osteoporosis using the normal Caucasian data supplied by the DXA Manufacturer. These diagnoses cannot be correct as there is nothing in their family history or biochemistry to suggest any associated inherited or metabolic bone disease. Vitamin D deficiency although widespread in the Middle East is unlikely to be significant in this study population having normal bone profiles and PTH levels. If an Omani has a lower BMD than a Caucasian or Black individual, is he more likely to fracture? The answer is definitely not; our normal Omani population has BMD values similar to those of Asians and Asians are no more likely to fracture than Caucasians. **Conclusion:** Our findings indicate that we are over diagnosing these disorders and that some patients might be receiving inappropriate antiresorptive and/or bone forming medications. Our findings highlight the need to use data from a normal local population. At the moment we suggest using normal reference Asian values in Omanis

P27. Juvenile Paget's Disease Without Mutation of TNFRSF11B (OPG) or TNFRSF11A (RANK).

Steven Mumm, Omayma El-Shafie, Xiafang Zhang, Samir Hussein, Deborah V. Novack, Nicholas Woodhouse, Michael P. Whyte, Sultan Qaboos University, Oman

Introduction: Juvenile Paget's Disease (JPD) is the extremely rare heritable disorder that features the greatest rates of skeletal turnover documented in humans. In 2002, homozygous loss-of-function mutations in the TNFRSF11B gene that encodes osteoprotegenin (OPG) were discovered in JPD. Most JPD patients have autosomal recessive JPD that reflects remote "founders" in different geographic locations worldwide. Additionally, in 2008, we reported the JPD phenotype in a preliminary report of a Bolivian girl with sporadic, heterozygous, 15-bp tandem duplication in exton 1 of the TNFRSF11A gene that encodes RANK (JBMR 23:S134, 2008). The remaining JPD patients are not understood at the molecular level. Here, we describe this type of extremely rare patient. **Case Report:** A 16-year-old non-consanguineous boy from Oman had progressive skeletal deformities first noted at age 3 years. Physical examination showed macrocranium, severe and painful bony deformities, and bilateral deafness. Retinal examination showed no angioid streaks. He had 8 unaffected siblings. Radiographs and bone scintigraphy were in keeping with JPD, and showed in his skull striking expansion and sclerosis of the diploic space, basilar impression, expanded maxilla, and deformed teeth. Ribs, scapulas, and clavicles were wide and sclerotic. Severe deformities affected the femur and pelvis with loss of cortical differentiation. Fractured ribs and flattened vertebrae were also in keeping with JPD. Serum alkaline phosphatase (ALP=3,900 u/l) and other bone turnover markers (BTMs) were markedly elevated. Despite serum 25OHD=12 nmol/L (deficient), serum parameters of mineral homeostasis were unremarkable. He also had hyperthyroidism. Iliac crest histology (after tetracycline (TCN) labeling) revealed an irregular arrangement of trabeculae, increased osteoid, hypocellular fibrotic stroma, numerous osteoclasts in some areas, large amounts of woven bone, diffuse TCN labeling, and a very high rate of bone turnover, but without the parallel trabecular pattern identified in the OPG deficiency form of JPD (JBMR 19:695, 2004). Despite 4 mg zolendronate i.v. every month x40, BTMs did not achieve ~½ peak levels. The coding exons and adjacent mRNA splice sites of TNFRSF11B (OPG) and TNFRSF11A (RANK) were sequenced without identification of a mutation that would explain his JPD. Similarly, TNFSF11 (RANKL), SQSTM1, TGFB1, SFRP1 and exons 2-4 of LRP5 were negative. Hence, there is additional genetic heterogeneity for JPD.

P28. Catecholamine-Secreting Carotid Body Paraganglionoma: Successful Longterm Preoperative Control of the Hypertension and Clinical Symptoms Using High Dose Octreotide LA.

Omayma Elshafie, Y. Al Baddi, F. Al Azri, S. Hussain, K. Al Wahabi, A. Qureshi, A. Al Mamari, Nicholas Woodhouse, Sulan Qaboos University, Mascat, Oman

Background: Paranganglionomas (PGs) are found distributed throughout the autonomic nervous system. They consist of chief cells, of neural crest origin, which are capable of forming and secreting catecholamines. This occurs in tumours arising predominantly from the sympathetic rather than the parasympathetic nervous system. Adrenal paraganglionomas, usually referred to phaeochromocytomas, account for 90% of all such tumours only 10% being found outside the adrenal and no more than 3-4% of these being in the head and neck. Less than 5% head and neck PGs secrete catecholamines and as in all extraadrenal catecholamine secreting paraganglionomas

(CSPs) they produce predominantly norepinephrine and little epinephrine. Their aetiology is unknown in most cases but about 25% have mutations involving RET, VHL, TVF1, SDHB, SDHC or SDHD genes. The majority of these tumours can be localized by scanning with I-131 labelled MIBG, III Inoctreotide or 18F-dopa positron emission tomography. **Case Report:** Below, we report a patient with a single carotid body catecholamine secreting paraganglionoma (CSP) in whom high dose octreotide produced a complete clinical and near complete biochemical remission. A 48-year-old hypertensive and diabetic patient presented with a 10-year history of progressive right facial pain, tinnitus, hearing loss, sweating and palpitations. Investigations revealed a 5.6 cm vascular tumour at the carotid bifurcation. Her BP was 170/110, on large doses of ACE inhibitors and calcium channel blockers, and she required 100 U insulin daily. A catecholamine secreting paraganglionoma (CSP) was suspected and the diagnosis confirmed biochemically by finding a norepinephrine level of 89,000 pmol/L (N 659-2400) and chromogranin A (Cg-A) of 279 ug/L (n 27-94). MIBG and octreotide scanning confirmed a single tumour in the neck only. After stopping all antihypertensive medications, the patient was given a therapeutic trial of octreotide 100 mcg 8 hourly and after one week the norepinephrine level had fallen progressively from 50,000 to 25,000 pmol/L and Cg-A from 279 to 150 ug/L. Treatment was therefore continued with long acting octreotide- LA initially using 10 mg/week and later increasing to 20 mg/week. Labetalol was given concurrently in a dose of 200 mg twice daily initially and later 100 mg twice daily with the increased dose of octreotide. On this dose her BP was maintained at 130/70 and her symptoms resolved completely. There was a sustained fall in serum chromogranin A levels throughout and the day before successful tumour embolization was carried out the plasma norepinephrine was slightly elevated at 5000 pmol/L, the labetalol having being stopped 3 days before. The following day the tumour was resected completely with minimal BP fluctuations during the 10 hour procedure.

Acknowledgements

On behalf of the Board of Directors, Gulf Chapter of the American Association of Clinical Endocrinologists, the guest editors would like to extend their gratitude to all the speakers, chairs and moderators for the professional conduct of the congress. We would like to express our thanks to abstract review committee (Drs. Ebaa Al-Ozairi, Jumaa Al Kaabi, Hussein Saadi and Mohamed Lamki).