ABSTRACTS BOOK

Abstracts of the Fourth Clinical Congress of the Gulf Chapter of the American Association of Clinical Endocrinologists; 3-5 November 2016; Dubai, UAE. I. Lectures, Symposia and Meet the Expert Sessions.

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Abstract

This is the first part of the advance abstracts of the fourth clinical congress of the Gulf Chapter of the American Association of Clinical Endocrinologists to be held on 3-5 November 2016. The declared educational objectives of the congress was to give a "state of the art in endocrine practice". To this end, the organizing committee invited international and regional key opinion leaders to meet the objectives of the congress. We present here abstracts of the congress as submitted by the authors after minimal restyling and editing to suit the publication requirements of the *journal*. Many major issues and topical themes with wide interests in the profession were addressed in plenary lectures. Symposia were organized to suite the specific educational needs of the target audience subgroups. Practical issues were addressed in "Meet the Expert"-type of interactive workshops. We hope that by publishing them in this open access journal we extend the benefit to those who could not make it to the live presentations.

Introduction

These are the advance abstracts of the second clinical congress of the Gulf Chapter of the American Association of Clinical Endocrinologists to be held on 3-5 November 2016. The declared educational objectives of the congress is to give a "state of the art in endocrine practice". To this end, the organizing committee invited international and regional key opinion leaders to meet the objectives of the congress. We present the abstracts of the congress as submitted by the authors after minimal restyling and editing to suit the publication requirements of the *journal*. Many major issues and topical themes with wide interests in the profession were addressed in 8 plenary lectures. More focused issues were included in 7 clinical practice symposia to suite the specific educational needs of the target audience subgroups. Practical issues were addressed in "Meet the Expert"-type of interactive workshops.

The abstracts are presented under their relevant groups; plenary sessions, clinical practice symposia, meet the expert session. The abstracts of the oral and poster free communications are published separately.

I. Plenary Lectures.

L1. Key Note Address: The Year in Thyroid 2016

Hossein Gharib, Mayo Clinic College of Medicine, Minnesota, USA

This presentation will discuss some articles published in 2015-16 with relevance to clinical practice:

- AACE recently released updated guidelines for the management of thyroid nodules. We will review highlights of recommendations for diagnosis and treatment of thyroid nodules.
- Subclinical hypothyroidism is common and controversial. A recent report in the Annals considered treatment with "guidelines and beyond guidelines." The report reviews risks and benefits of treatment.
- Different opinions and recommendations have been suggested for subclinical hypothyroidism in pregnancy, a relatively common condition. This meta-analysis offers a new perspective.
- Is FVPTC benign or malignant? According to a recent study, encapsulated, noninvasive PTC is benign and requires treatment only with partial thyroidectomy. The authors suggest criteria for identifying NIFTP (pronounced nift-P) and favor avoiding the term cancer for a nonlife threatening condition.
- Some highlights of the 2015 ATA Thyroid Cancer Guidelines will be reviewed.
- Recommendations from 2016 guidelines for thyroid cancer management in children will be briefly discussed.

L2. Type 2 Diabetes Management: Consensus and Controversies

Graham McMahon, Northwestern University, Illinois, USA

Whether and when to initiate combination therapy in our patients with diabetes has been hotly debated. In this session we'll review the results of several clinical trials that illustrate the rationale for, and utility of, combination therapy. We'll describe optimal combinations to capitalize on complementary pharmacology, and use some case examples to describe optimal opportunities for combination therapy that balance effectiveness, cost, compliance and tolerability.

L3. Hyponatremia in 2016: Why to Treat? Who to Treat? How to Treat?

Joseph Verbalis, Georgetown University Medical Center, Washington, D.C., USA

Treatment of the hyponatremic patient with the syndrome of inappropriate antidiuretic hormone secretion (SIADH) presents a clinical challenge, particularly in the presence of comorbidities. In contrast to patients with congestive heart failure (CHF), the hyponatremic SIADH patient is clinically euvolemic, without excess sodium retention. This allows therapeutic options that are not feasible in patients with hypervolemia, such as CHF. Currently available treatment options for SIADH include fluid restriction, administration of hypertonic saline, furosemide + NaCl tablets, demeclocycline, mineralocorticoids, urea and vasopressin receptor antagonists. However, all of these treatments have limitations and some may exacerbate comorbid conditions. Deciding among them requires knowledge of these limitations, as well as careful monitoring of the rate of correction of the serum sodium concentration to prevent the osmotic demyelination syndrome. The severity of symptoms and adverse outcomes in hyponatremia is dependent of the acuteness or chronicity of the hyponatremia, since the brain can adapt to low extracellular sodium concentrations via the process of brain volume regulation. Consequently, one can use the neurological symptoms of the patient as a surrogate measure of the chronicity of the hyponatremia. An algorithm will be presented for symptom-based therapy of hyponatremia. Recent data from the Hyponatremia Registry has confirmed poor efficacy for fluid restriction and isotonic saline treatment of hyponatremia compared to hypertonic saline and vasopressin receptor antagonists. Criteria will be presented for predicting failure of fluid restriction based on easily measured parameters to guide appropriate selection of therapy for hyponatremic patients.

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L4. The Year in Adrenal

William Young, Jr., Mayo Clinic College of Medicine, Minnesota, USA

An adrenal-based literature review covering the past 12 months will be completed. The 8 most impactful publications will be selected for presentation. "Year-in" presentations are always very subjective and I apologize in advance for not highlights some of the articles that would also deserve mention in this forum.

L5. Recent Developments in Our Understanding of the Nature and Treatment of Autoimmune Diabetes.

David Leslie, Blizard Institute, University of London, UK.

Diabetes is not a single homogenous disease but composed of many diseases with hyperglycaemia as a common feature. Four factors have, historically, been used to identify this diversity: the age at onset; the severity of the disease, i.e. degree of loss of ß-cell function; the degree of insulin resistance and the presence of diabetes-associated autoantibodies (DAA). Our broad understanding of the distinction between the two major types, type 1 diabetes and type 2 diabetes, are based on these qualities, but it has become apparent that they do not precisely capture the different disease forms. Indeed, both major type of diabetes have common features, encapsulated by adult-onset autoimmune diabetes and maturity onset diabetes of the young. As a result, there has been a repositioning of our understanding of diabetes in the Western world and China. Type 1 diabetes (T1D) is induced by non-genetic events early in life, with variable progression to clinical diabetes reflecting a range of genetic, clinical, immunological and metabolic features. This landscape reveals autoimmune diabetes, similar to other autoimmune diseases, to be predominantly: middle-aged at onset, of varying disease severity, HLA related, with genetic load decreasing with age and with predictive autoantibodies. Gene Risk Scores now show the T1D genetic risk extending into adulthood. Given that autoimmune diabetes has a broad clinical phenotype, there are diverse therapeutic options, while the term, type 2 diabetes, obscures optimal management strategies because it too encompasses substantial heterogeneity. Underlying these developments is a general progression towards precision medicine with the need for individual patient characterisation, currently based on clinical phenotypes but in future augmented by laboratory-based tests.

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L6. How Can We Optimize the Benefits of Metabolic Surgery for Diabetes?

Carel le Roux, Diabetes Complications Research Centre, Conway Institute, University College Dublin, Ireland.

The number of bariatric surgical procedures performed has increased dramatically over the last decade. Even though bariatric surgery has been shown to be superior to medical therapy in terms of glycaemic control and weight reduction, non-surgical therapies are continually improving. The appropriate use of bariatric surgery remains a subject of debate, with many physicians in the field remaining sceptical about it, in view of the risks associated with surgery. Ultimately, surgery can be enhanced by the appropriate use of medication to give patients the best possible outcome as regards their obesity and type 2 diabetes (T2D).

A combination of therapies will be required to optimize the benefits of bariatric surgery, but will certainly be worthwhile in obese patients who are otherwise unable to achieve lasting health benefits. Ongoing head-to-head trials of surgical and surgery enhanced by medication are warranted to determine the best route to obesity management, and to identify the patient populations most likely to benefit from each strategy. Using the currently available treatment options we would suggest that the effect of a gastric bypass on reducing hepatic insulin resistance can be enhanced by adding metformin and the effect on blood pressure and glycaemic control can be enhanced by sodium glucose co-transporter 2 inhibitors. The major benefit of gastric bypass is, however, the weight loss maintenance and this may be enhanced by using high-protein low-glycaemic index (GI) diets more effectively in the future. Thus not only can most of the beneficial effects of bariatric surgery potentially be mimicked, but this may also be enhanced to achieved at a much reduced cost as regards mobidity and mortality.

L7. AACE-Gulf Chapter Medal Lecture.
Parathyroid Hormone & Its Receptors in Human Physiology and Pathology

Abdul Badi Abou Samra, Hamad Medical Corporation, Doha, Qatar

PTH, an 81 residue peptide secreted by the parathyroid gland and PTHrP, a 139, 141 or 173, residue peptide expressed in various tissues and pathologically secreted by human cancer that cause hypercalcemia, bind and activate a common G protein-coupled receptor, the PTH/PTHrP receptor (PTHR1 or PTH1R), leading to stimulation of several intracellular signaling pathways, which include adenylate cyclase, phospholipase C and ERKs. PTH is the main minute-to-minute physiological regulator of extracellular calcium concentrations and is inversely regulated by calcium level through a negative feedback loop. PTH rapidly increases extracellular calcium concentrations by direct effects on the distal renal tubule to stimulate calcium reabsorption and by increasing calcium release from bone. Other minute-to-minute mineral effects of PTH include its phosphaturic effects in the renal tubules. Long term effects of PTH on calcium include stimulation of 1α hydroxylation of 25 hydroxy-vitamin D leading to increased calcium and phosphorus absorption in the gut. PTHrP is a physiological regulator of multiple cellular functions during embryonic development where PTHrP is released locally in the vicinity of cell layers expressing PTHR1 and during bone development. Animal experiments using universal and localized PTH, PTHrP and PTHR1 knock out, or over expression identified novel roles for PTHR1 in multiple physiological functions in the development, differentiation and/or growth of bone, teeth, skin, hairs, adipose tissues and heart. PTH, PTHrP and/or their common receptor have been implicated in human diseases such as cachexia of chronic kidney diseases, failure of tooth eruption, osteoarthritis, osteoporosis and metabolic bone diseases. PTH and PTHrP are excellent bone forming therapeutic agents and their antagonists may have a role in prevention of cachexia associated with chronic kidney disease and human cancer.

L8. The Cardiovascular Outcome Trials for Anti-diabetes Medication.

John Wilding, University Hospital Aintree, Liverpool, UK.

There has been longstanding controversy about the effect of glucose lowering (and glucose lowering medication) on cardiovascular disease in people with type 2 diabetes. The long term follow up of UKPDS suggested modest benefit, but this was thrown into doubt by meta-analysis of the rosiglitazone trials, that suggested possible harm, and also by the result of the ACCORD study, which found an increase in CV death with intensive control. Although these concerns have largely been resolved, they have led to a regulatory requirement for CV outcomes trials for all new glucose lowering medicines. The results of these trials are now being reported on a regular basis, and have the potential to change the way we treat type 2 diabetes. It is already accepted that multiple risk factor intervention, as used in the STENO 2 study, so it is important to recognise that to test effectiveness of newer glucose lowering drugs this need to be done on a background of optimal control of blood pressure and lipids and access to antiplatelet therapy where appropriate. The trials with DPP-4 inhibitors saxagliptin, aloglitin and sitagliptin were clearly neutral for the primary outcome of cardiovascular events, although concerns were raised about hospitalisation for heart failure. Likewise the ELIXA trial with lixisenatide also showed no benefit or harm. However the EMPA-REG outcomes trial was clearly beneficial, especially in relation of heart failure and this was followed by LEADER (wth liraglutide) [Figure 1) and SUSTAIN 6 (with semaglutide, a weekly GLP-1 RA in development)

that also appeared to show benefits. The next few years will see the results emerging of several new trials, particularly of GLP-1RA and SGLT2i classes. If the effects seen in earlier trials are confirmed with these results it has the potential to revolutionise diabetes treatment.

II. Clinical Practice Symposia:
CS1. Pituitary Update 2016.
CS1.1. Hypopituitarism: Pathogenesis and Management
Paul Stewart
University of Leeds, Leeds, UK.

The prevalence of hypopituitarism is in the order of 5/10,000 and usually arises because of tumours, infiltrative/ infective or other disorders such as trauma or apoplexy affecting the hypothalamus and/or pituitary. Hypophysitis can occur following ipilimumab (a monoclonal Ab to CTLA4) treatment of cancers such as melanoma. Inherited genetic causes for example due to mutations in PROP1, LHX3, LHX4, HESX1 and OTX2 are described.

Hypopituitarism is associated with increased mortality largely due to cardiovascular disease with standardised mortality rates (SMR) of approximately 1.8:1. Confounding pituitary hormone deficiencies such as gonadotropins, ACTH deficiency (with higher doses of hydrocortisone replacement conveying the greatest risk) and growth hormone deficiency have all been postulated to have an aetiological role, but an evidence base on mortality outcomes from replacement regimens are lacking. Pituitary radiotherapy is a confounding factor that appears to convey an additional cerebrovascular mortality risk particularly in younger patients. Although standardized mortality ratios in pituitary disease are falling due to improved treatment, mortality is still elevated above that of the general population; ensuring physiological replacement therapy and treatment of co-morbidities (hypertension, hyperlipidaemia) is essential.

ACTH deficiency occurs in 60-70% of cases of hypopituitarism and is particularly challenging to treat. Historically we have over treated patients with replacement glucocorticoids and have failed to mimic the normal circadian rhythm. Other factors notably concomitant GH deficiency increases glucocorticoid exposure through impaired cortisol metabolism. Paradoxically, despite overtreatment in many cases there is still unacceptable morbidity and mortality from adrenal crises during intercurrent illness. Novel therapies using sustained/ delayed release hydrocortisone compared to current immediate release may improve patient outcomes.

Finally, and as yet un-quantified, is central hypoadrenalism secondary to exogenous use of synthetic corticosteroids. Data indicate that 1% of the UK population (rising to 3% over 70 years) are taking prednisolone in a mean daily dose of ~7mg. Inhaled steroids notably fluticasone are in widespread use, particularly potent and frequently cause suppression of the hypothalamo-pituitary adrenal axis as assessed by a flat cortisol response to the short synacthen test. Whilst such patients taking steroids may have sufficient glucocorticoid for day to day function, the failure to mount an endogenous cortisol response to stress can be life-threatening.

CS1.2. Prolactinoma 2016
Amir H. Hamrahian
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Dopamine agonist (DA) therapy has allowed prolactinomas to become a unique primary brain tumor for which medical management is the primary treatment modality. Doses of cabergoline beyond 3.5 mg/week are rarely required in controlling prolactin (PRL) secretion and reducing tumor size in prolactinomas. Most patients require an average dose of 1 mg per week. Benefits of anti-estrogens or aromatase inhibitors have been occasionally reported. A recent large UK follow-up study does not support a clinically significant association between the use of DA for the treatment of hyperprolactinemia and cardiac valvulopathy. Maximum tumor diameter and baseline PRL levels are among important predictors of recurrence after DA withdrawal in some study.

Prolactinoma is a common cause of infertility in women and treatment with DA allows restoration of fertility in most cases. Data on exposure of the fetus to cabergoline during the first weeks of pregnancy have now been reported in more than 900 cases. Accordingly, there is no convincing reason to change cabergoline to bromocriptine when pregnancy is desired. Follow-up studies of the children for up to 12 years after fetal exposure to cabergoline did not show any physical or developmental

abnormalities. Treatment discontinuation is recommended at the time pregnancy has been confirmed for most patients with a need for close monitoring especially in patients with macroprolactinoma. Breast-feeding has no harmful effect on tumor growth. About 40% of women with a microprolactinoma may not require DA therapy after one or more pregnancies.

Prolactinoma coinciding with psychosis can represent a therapeutic challenge. In contrast to most antipsychotic drugs, aripiprazole may be used in such patients and therefore can be a valuable pharmaceutical tool to treat both prolactinoma and psychosis.

Hyperprolactinemia may be tolerated in some patient populations including postmenopausal women as long as there is no tumor growth. However, there is some evidence that fracture prevalence is increased in patients with untreated hyperprolactinemia compared to those on treatment, independent of gonadal function. In addition, prevalence of obesity and adverse metabolic profile is higher in patients with prolactinomas than in matched controls. While dopamine-agonists are the first-line approach in treating prolactinomas, surgery can be considered in selected cases besides non-responders or patients with dopamine-agonist intolerance. Surgery for prolactinomas can result in prolonged remission in up to 70% of microprolactinomas and 30% of noninvasive macroadenomas. Patient who require DA after surgery, are usually able to reduce their weekly cabergoline dose. Accordingly, surgery may be an alternative effective treatment option particularly for those who are intolerant or resistant to medical therapy.

CS1.3. Acromegaly: New Advances in Medical Therapy

Gregory Kaltsas,
National and Kapodistrian University, Athens, Greece

Long acting somatostatin analogs (SSAs), dopamine agonists (cabergoline) and the growth hormone antagonist pegvisomant have been used for the treatment of acromegalic patients mainly following initial surgery. As it seems unlikely that one single agent may achieve cure in 100% of cases, combination of these medications have been used. SSAs and cabergoline is used in patients with mildly elevated IGF-1. SSA-pegvisomant combination normalizes IGF-1 in the majority of patients albeit there is a higher risk of significant liver enzyme elevation compared to SSA monotherapy. Data on pegvisomant-cabergoline combination is limited, but this may be an option in the setting of SSA intolerance. Pasireotide is a new multireceptor-targeted SSA with superior biochemical efficacy to octreotide, due to higher affinity for SSTR-5, but potentially affecting glucose homeostasis. Newer evolving treatments include oral octreotide that uses a transient permeability enhancer to obtain gut absorption, antisense oligonucleotides that by binding to growth hormone receptor inhibits protein expression and targeted secretion inhibitors using botulinum toxin. Somatopril, a novel enzymatically stable SSa with affinity for human somatostatin receptors SSTR2, SSTR4 and SSTR5, has been shown to cause excessive GH suppression whereas octreotide implants are being developed.Temozolomide used in combination with other medical therapies in patients with aggressive GH-secreting tumors.

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CS1.4. Growth Hormone Deficiency in the Transition Period'

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GH therapy has generally been discontinued after the attainment of adult height, however, GH deficiency became one of the approved indications for GH treatment in adults since 1997. Metabolic disorders along with abnormal body composition and low quality of life are well reported in untreated adults. The transitional period represents the time between the completion of growth and young adulthood, and it is recommended that GH therapy should continue during this period when indicated. Adult candidates for GH therapy should be retested for GHD after holding the treatment for a short period of time; the scope of testing is driven by the nature of the underlying condition or the established diagnosis during childhood. This lecture will summarize the recommendations of the AACE, the Endocrine Society, and the GH Research Society regarding the GH treatment in adults during the transitional period.

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CS2. Diabetes Update

CS2.1. Non-genetic Effects in the Origins of Type 1 Diabetes

David Leslie,
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Genetics cannot fully explain the hereditary patterns of autoimmune disorders. In fact, genome-wide association studies have shown that genetic polymorphisms account for only 20% of the phenotypic variance. In addition, monozygotic (MZ) twins show moderate rates of concordance for autoimmune disorders. Evidence for the role of environmental factors in the development of autoimmune diabetes is provided by population, migration and twin studies. In North America and Europe, and possibly world-wide, population studies have shown that the incidence of childhood type 1 diabetes has been increasing over the past 100 years, particularly in younger age groups. On the other hand, the proportion of diabetic patients with high diabetes-risk genotypes (DR4-DQ8/DR3-DQ2) has decreased, and lower risk genotypes (DR4-DQ8/X and DR3-DQ2/X) has increased, implying an increasing role in environmental factors (acting in genetically susceptible persons) in promoting diabetes. The various hypotheses implicating non-genetic effects resolve around beta cell stress associated with an aggressive immune attack in which the genetic effect and severity of the disease is greatest in the younger onset cases and least in adulthood-onset diabetes. Factors implicated include enteroviral infections, especially in early life, the hygiene hypothesis, body mass index an insulin resistance, low birth weight, breast feeding, age at introduction of complex nutrients and the overload hypothesis whereby a number of environmental factors - in particular, impacting child or fetal priming to increase beta cell stress and autoimmune predisposition - could explain the increased risk of type 1 diabetes in European population.

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CS2.2. Management of Type 2 Diabetes: Sequential or Early Combination.

Graham McMahon,
Northwestern University, Illinois, USA.

Several recent clinical trials have created new opportunities for managing our patients with type 2 diabetes more safely and more effectively. In this session we'll review major recent trials including SU. the implications of their results for appraoches to care. We'll also look at emerging diabetes technologies and how they inform our approach to monitoring of glucose levels, and to managing insulin effectively. finally, we'll explore several new therapeutic approaches that are in clinical trials.

CS2.3. Diabetic Eye Disease: Beyond Laser Therapy!

Selwa Al Hazzaa,
King Faisal Specialist Hospital & Research Center, Riyadh, Saudi Arabia

No Abstract

CS2.4. Diabetic Kidney Disease: What is New?

Dawood Riyami,
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Progressive renal decline precedes the onset of microalbuminuria, and as it continues, it increases the risk

of proteinuria. Therefore alternative models of diabetic nephropathy beyond the albuminuria-centric model have been strongly suggested. Intensive research is under way to find better predictors of progression to ESRD. Application of new high-throughput technologies, such as genetics, genomics, proteomics, and metabolomics platforms, should help us understand the mechanisms of progressive renal decline. Despite the implementation of renoprotective therapies over the past two decades, the risk of end-stage renal disease (ESRD) in type 1 diabetes (T1D) is not decreasing but increasing. Personalized approaches are being developed in other diseases and should be tried for progressive renal decline in diabetic nephropathy.

CS3. Endocrine Disorders during Pregnancy.

CS3.1. Thyroid Dysfunction in Pregnancy

Hossein Gharib,
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Profound physiologic changes in thyroid physiology occur in pregnancy. Some of these include increased iodine requirement, increased thyroid gland size, increased metabolism of thyroid hormones, elevated serum T4, first-trimester TSH suppression, etc. Autoimmune thyroid disease may cause subclinical hypothyroidism, overt hypo- and hyperthyroidism, and post-partum thyroiditis. Sometimes diagnosis are difficult and management controversial.

Recent nomograms for TSH levels in pregnancy help identify those that need be treated or require increased LT4 dose. TSH screening is recommended for those at high risk for thyroid disease. Although debated by some, most agree that pregnant women with SCH and positive TPO should be treated.

When using anti-thyroid drugs in pregnancy, it is good to remember that they pass thru placental and can block thyroid hormone synthesis in the fetus. PTU is the drug of choice for hyperthyroidism in early pregnancy. Women with a history of Graves' disease before pregnancy, even if eu- or hypothyroid now, may still have TSH receptor antibodies that cause hyperthyroidism in the fetus.
Postpartum thyroiditis is more common than recognized, may cause either hypo- or hyperthyroidism postpartum that is often mild and transient, and more likely to recur after subsequent pregnancies. If severe and/or symptomatic, treatment should be given.

CS3.2. Gestational Diabetes Updates

Bashir Salih,
Corniche Hospital, Abu Dhabi, UAE

Gestational diabetes could be pre-gestational discovered for the first time in pregnancy or true gestational diabetes. Studies have shown that hyperglycaemia is associated with significant morbidity to the new born and his mother. Some of those adverse outcomes could have serious implications for both mother and baby in later life. UAE and other Gulf states are among the countries with the highest prevalence of diabetes in the world, universal screening should be used to detect gestational diabetes.

Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) a large observational study and subsequently other studies were aimed to clarify unanswered questions of maternal glycaemia less severe than overt diabetes and pregnancy outcome.
The findings convincingly demonstrate the continuous independent 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 Hyperglycaemia in Pregnancy in March 2010 (Diabetes Care March 2010).
All pregnant women were advised to be tested with Fasting blood Glucose at their first antenatal visit and either the patient is having overt diabetes, gestational or needs further screening at 24-28 weeks gestation.
Since its publication several countries and associations including the ADA, WHO have adopted these recommendations.
More work is required to elucidate how women with diabetes, regardless of type, to improve the outcomes of their pregnancy. This applies in particular to preconception preparation. The best outcomes will be achieved if there is an effective partnership between the woman and the health professionals responsible for her care. The challenge for health professionals is how to empower women with diabetes to fully participate in this partnership.
Diabetes in pregnancy should be managed by multidisciplinary team involving all health professionals responsible for her care in pregnancy

CS3.3. Prolactinomas in Pregnancy

Mussa Al Malki,
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Prolactinomas are the most common functional pituitary tumors and usually appears in women especially between the third and fourth decades of life, with a female: male ratio of 10:1 in that period then being equally distributed among genders after 50 years. Up to 90 percent are small in size, and intrasellar that rarely increase in size 1-3.
The large majorities of patients show symptoms of hypogonadism, infertility and often with symptoms derived from tumor growth such as headache and visual field defects.
Untreated women are usually not able to achieve pregnancy, but treatment with dopamine agonist (DA) usually restores fertility and results in pregnancies.
Women with prolactinaemia are frequently treated with DA with aim to normalize prolactin levels, reversion of hypogonadism and to reduction of tumor mass especially in macroprolactinoma. However, surgery, radiotherapy may be necessary in some cases.
DA such as bromocriptine and cabergoline appear to be effective and safe during early pregnancy. Nevertheless, DA use throughout pregnancy is less common 4,5, but the data in the literature did not show any evidence of any risk of preterm delivery or fetal malformations, comparing to those in the general population

It is advisable to stop DA immediately once pregnancy is confirmed, except for women with invasive macroprolactinomas or in patients with pressure symptoms (visual disturbance and/or headache) as the risk of tumor enlargement in pregnant patients with macroprolactinomas is higher than that in those with microprolactinomas.
Women with macroadenomas need periodic visual fields testing during pregnancy; if visual field defects detected or progressive headaches develop, an MRI should be done, otherwise there is no need for periodical imaging during pregnancy.

If symptoms of tumor re-growth develop, therapy with DA should be reinitiated. Meanwhile, it is important to inform the patient that bromocriptine remains the drug of choice as it was proven to be safe in more than 6,000 pregnancies as compared to 789 mothers treated with cabergoline 6.

After delivery, prolactin levels usually lower than before conception so that only a proportion of patients need to restart medical therapy7,8.
Lactation may be allowed as it does not increase the recurrence rate of hyperprolactinemia or tumor enlargement. Women who want to breastfeeding shouldn't be discouraged 9, although lactation may be impaired with use of DA.
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CS4. Newer Therapies in Diabetes.
CS4.1. Newer Insulin: What are they and for whom?

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Type 2 diabetes is a complex multifactorial disease that represents a serious challenge to achieve optimal

glycemic control for the prevention of related morbidity and mortality. Whilst there are an increasing number of therapies for the treatment of diabetes the most potent is insulin that is often used as the last therapeutic resort. Basal insulin is often used an adjunct therapy with its escalation to various forms of a basal bolus regimen. Basal insulin therapy with NPH insulin has increasingly been superseded in many practices with insulin glargine U100 that is associated with less hypoglycemia though overall glycemic control does not differ to NPH. There are 2 new long acting basal insulin preparations that have become available, though currently not licensed in all countries to date. Degludec is a modified human insulin preparation with a fatty acid C16 side chain attached that forms multi-hexamer chains following subcutaneous injection. Glargine U300 is the higher concentration form of glargine U100 that leads to larger precipitates on injection that alters its pharmacokinetic profile. Both degludec and glargine U300 have a flat profile lasting a full 24 hours and may be seen to be a further therapeutic advance with fewer hypoglycemic events, particularly nocturnal hypoglycemia, and potentially providing better flexibility and safety of insulin dosing. Therefore, those patients and patient groups vulnerable to hypoglycemia may benefit from these new long acting basal insulin preparations.

CS4.2. GLP1 Agonists: Current Status of Efficacy and Safety
John Wilding
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Glucagon like peptide 1 (GLP1) is a major physiological incretin in humans and also has important effects on appetite and satiety. Reduced GLP-1 secretion may contribute to the pathophysiology of type 2 diabetes. Native GLP-1 is rapidly degraded by the enzyme dipeptidyl peptidase 4 (DPP4); but DPP4 resistant GLP1 agonists have been developed for treatment of diabetes and recently also for obesity. GLP1 agonists are either derivatives of exendin 4 (a peptide with ~ 50-% homology to human GLP1 found in Gila monster saliva) or modified human GLP1 with fatty acid, albumin or immunoglobulin molecules attached to prolong half-life. Duration of action varies so that they are given either twice daily (exenatide), once daily (liraglutide, lixisenatide) or weekly (exenatide QW, dulaglutide, albiglutide). All agents are effective at lowering HbA1c (magnitude of effect depends on baseline HbA1c and trial design but is reported to be between 0.8 and 1.5%). Weight loss is more variable and this may relate to CNS penetration of different compounds. Liraglutide (at the higher dose of 3mg) has recently been approved for treatment of obesity in some countries. CV outcome trials for lixisenatide, liraglutide and the developmental compound, semaglutide have been reported and show no adverse CV effects in high risk patients with lixisenatide, and CV and microvascular benefit with liraglutide. Semaglutide showed CV benefit but an increase in retinopathy that may be due to rapid improvement of glycaemic control. Newer developments include combination treatments with insulin and emerging data on use of GLP1 RA with SGLT2 inhibitors that are likely to lead to further expansion of GLP1 RA to treat type 2 diabetes.

CS4.3. SGLT2 Inhibitors: Latest Developments
Muhammad Abdel Ghani, Hamad Medical Corporation, Doha, Qatar

Sodium-glucose cotransport inhibitors (SGLT2i) are a novel class of antidiabetic agents which lower the plasma glucose concentration by inhibiting renal glucose reuptake and producing glucosuria. In addition to lowering the plasma glucose concentration, SGLT2 inhibitors exert multiple other metabolic benefits in T2DM. Further, most recently, empagliflozin has been shown to lower the 3-point MACE and reduce the risk of nephropathy in T2DM with existing CVD. I will discuss the clinical efficacy of this class of drug in lowering the plasma glucose concentration, and potential adverse events. Lastly, I will discuss possible mechanisms for the improvement in CVD risk and the potential combination of this class of drugs with other antidiabetic agents.

CS5. The Adrenal Disorderders in Focus.
CS5.1. Mineralocorticoid Hypertension
Paul Stewart
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The hallmark of mineralocorticoid hypertension is inappropriate renal sodium retention with suppression of plasma renin activity. Its importance lies in the contribution to “essential hypertension” and premature patient mortality; having been considered a rare cause of hypertension (<1%) it now accounts for between 5-10% of all patients. Understanding the underlying causes and optimal treatment and “ownership” of this aspect of cardiovascular morbidity by endocrinologists is essential to ensure optimal patient outcome. The principal cause is

primary aldosteronism (PA) due to autonomous secretion of aldosterone from the adrenal glands and should be considered in any patient with unexplained hypokalaemia (accepting that the majority of patients with proven PA have normal circulating potassium), family history of stroke/ hypertension <40years of age, resistant hypertension despite triple therapy or in patients with an adrenal incidentaloma. A random plasma aldosterone/ renin ratio is the initial screening test of choice with the caveat that the endocrinologist is aware of the performance of local assays and the potential impact of concomitant medication. Salt suppression studies are usually required to confirm autonomous aldosterone production. Thereafter, the differential diagnosis lies between an aldosterone-producing adenoma (APA) or bilateral/ idiopathic adrenal hyperplasia (BAH), the latter explained by enhanced sensitivity of aldosterone secretion to angiotensin II. Glucocorticoid or dexamethasone suppressible hyperaldosteronism is a rare autosomal dominant cause of hyperaldosteronism caused by a chimaeric CYP11B gene. Adrenal vein sampling maybe required in patients with presumed APA wishing surgery; surgery is ineffective and contraindicated in patients with BAH. Targeted medical therapy with mineralocorticoid receptor antagonists and particularly the selective antagonist eplerenone is effective. Genetic studies have uncovered novel genes that explain the molecular basis for ~ 50% of cases of APA, the majority of which relate to mutations in ion channels that maintain hyperpolarization within the zona glomerulosa. Finally, Syndrome of Apparent Mineralocorticoid Excess, Liddle's syndrome, some forms of congenital adrenal hyperplasia and activating mutations in the MR are examples of monogenic mineralocorticoid excess where aldosterone levels are suppressed.

CS5.2. Update on Pheochromocytoma and Paraganglioma

William Young, Jr., Mayo Clinic College of Medicine, Minnesota, USA

Introduction: Catecholamine-producing tumors that arise from chromaffin cells of the adrenal medulla and sympathetic ganglia are termed "pheochromocytomas" and "paragangliomas", respectively.
Methods: Data will be presented based on extensive clinical experience and literature review.
Results: The diagnostic approach to catecholamine-producing tumors is divided into two series of studies. First, the diagnosis of a catecholamine-producing tumor must be suspected and then confirmed biochemically by the presence of increased urine or plasma concentrations of fractionated metanephrines and catecholamines. Second, the catecholamine-producing tumor needs to be localized to guide the surgical approach. Cross sectional imaging of the abdomen and pelvis with CT or MRI is the first localization test. Approximately 85% of these tumors are found in the adrenals and 95% are in the abdomen or pelvis. If the abdominal imaging is negative—first, pause and make sure that you are not dealing with false-positive biochemical testing— then scintigraphic localization with [123I]-meta-iodobenzylguanidine (123I-MIBG) is indicated. Approximately 40% of patients with catecholamine-secreting tumors have disease-causing germline mutations—the syndromes include multiple endocrine neoplasia types 2A and 2B, von Hippel Lindau disease, neurofibromatosis type 1, and succinate dehydrogenase mutations. The treatment of choice for pheochromocytoma is surgical resection. Most of these tumors are benign and can be totally excised. Some form of preoperative pharmacologic preparation is indicated for all patients with catecholamine-secreting neoplasms.
Conclusion: Pheochromocytoma and paragangliomas are rare, but potentially lethal, cause of hypertension. Biochemical confirmation should precede imaging studies. Careful preoperative pharmacologic preparation is key to a successful surgical outcome. All patients need lifelong annual biochemical follow-up.

CS5.3. Special Features of Adrenal Disorders from the Local Experience

Asma Deeb, Mafraq Hospital, Abu Dhabi, UAE.

Introduction: Adrenal Diseases comprise a wide spectrum of disorders. They include congenital and acquired diseases in various category of enzyme defects, malignancy, genetic disorders and autoimmune diseases. The defect can arise in the cortex, medulla or both. Congenital adrenal hyperplasia is the commonest disorder with deficiency of 21 hydroxylase enzyme being the commonest cause.

Aim: We aim to look at the distribution of adrenal disorders in our endocrine center over 6 years period and highlight special features in our cohort compared to other populations. Considering the high consanguinity rate in our community, we anticipate predominance of genetic adrenal disease.

Patients & Method: Clinic database was examined and patients with adrenal disorders identified. Various underlying diagnoses were classified into disease categories.

Results: We have identified a total of 115 patients under the age of 18 years with confirmed adrenal disease. 52 with congenital adrenal hyperplasia (CAH), 49 premature adrenarche, 4 with familial glucocorticoid deficiency (FGD), 3 with pseudohypoaldosteronism, 2 with autoimmune polyendocrinopathy syndrome (APS), 2 with 5 alpha reductase deficiency, one with mineralocorticoid deficiency and 2 with adrenal-related oncology. Of the 51 CAH patients, 22 had a confirmed genetic diagnosis. Of those, 18 had 21 hydroxylase deficiency and 4 had 17 lyase 21 hydroxylase deficiency. Phenotype-genotype correlation was studied and compared to other population characteristics reported in the literature. The 4 patients with FGD and 2 clinically confirmed CAH tested negative to commonly-known mutations.

Conclusion: Adrenal disease in childhood has a wide spectrum of underlying diagnoses in our cohort and its genetic cause appears to be unique. Establishing the genetic diagnosis in these families will enable better understanding of disease etiology and genetic counselling. We suggest using advanced genetic diagnostic method in highly suspected cases when targeted molecular genetic testing concludes negative results.

CS6. Thyroid Update

CS6.1. Clinical Applications of Molecular Genetics in Thyroid Cancer.

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Thyroid cancer is the most common endocrine malignancy. Exciting progress has occurred in the area of molecular-based management of thyroid cancer. This discussion will specifically focused on genetic marker-based risk stratification of thyroid cancer. In this context, several oncogenic mutations are particularly promising, which is best exemplified by BRAF B600E and TERT promoter mutations. The association of BRAF B600E with aggressive clinicopathological outcomes of thyroid cancer and hence its prognostic value for poor prognosis of thyroid cancer has been extensively studied. Its synergism with conventional aggressive clinicopathological factors and mutations in the promoter of the gene for telomerase reverse transcriptase (TERT) in affecting clinical outcomes of thyroid cancer has become particularly recognized in recent years. TERT plays a critical role in maintaining and protecting the length of chromosomes by adding telomers to their ends, hence promoting cell survival. TERT is now known to also play an important role in several other fundamental biological functions, such as cell proliferation, cell division, and tumor growth. In recent years, two somatic mutations, chr5:1,295,228C>T and chr5:1,295,250C>T (termed here as C228T and C250T, respectively), have been discovered in the TERT promoter in many human cancers, including thyroid cancer. These mutations confer TERT promoter increased transcriptional activities and up-regulate the expression of the TERT gene, thus promoting tumorigenesis. In thyroid cancer, TERT promoter mutations occur progressively more commonly from low-grade to high-grade tumors, being about 10-12% in differentiated thyroid cancer and about 40-50% in poorly and undifferentiated thyroid cancers. Many recent studies demonstrated that TERT promoter mutations were highly associated with aggressive pathological characteristics and poor clinical outcomes, including thyroid cancer recurrence and patient mortality. TERT promoter mutations are significantly associated with BRAF V600E mutation. Coexisting BRAF V600E and TERT promoter mutations are particularly associated with aggressive behaviors of thyroid cancer and sharply increased cancer recurrence and patient mortality. Thus, following this past one decade of remarkable achievements in the BRAF research on thyroid cancer, we are now entering a new exciting era of TERT in thyroid cancer research, which, like BRAF, will likely have an important impact on the management thyroid cancer.

CS6.2. Thyroid Cancer in Children

Ali Alzahrani,
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The incidence of differentiated thyroid cancer (DTC) has been remarkably increasing over the last four decades. The reasons for this increase in incidence are not fully understood but improved diagnostic methods played a major part. Some data also suggest a real increase in the incidence of DTC, especially the papillary type (PTC). Although DTC is predominantly a disease of the 40-50 years of age and affects females more frequently than

males, its incidence in children and adolescents has similarly increased especially in the age group 11-15 years and in adolescent girls. DTC in children and adolescents is unique in its histopathological features, disease course and outcome. Compared to DTC in adults, DTC in children is more likely to be bilateral, larger in size, multifocal and associated with lymph node and distant metastases. Recurrence rate is also higher but mortality is exceedingly rare. Not only that the clinical and histopathological features are different from those in adults but the molecular signatures are also significantly different. $BRAF^{V600E}$ mutation occurs in about 20% of pediatric DTC compared to adult DTC (45%). By contrast, RET/PTC gene rearrangements occur at higher rates than in adult DTC. Other mutations including RAS, PIK3CA, PTEN and TERT occur at much lower rates in pediatric DTC compared to adult DTC. These clinical, histopathological and molecular differences suggest that pediatric DTC is distinct from adult DTC and warrants special consideration in its diagnosis and management. Extrapolating from adult DTC guidelines seem inappropriate in many aspects of the pediatric DTC management. This was the basis for the development of the recently released guidelines for pediatric DTC by the American Thyroid Association (ATA). In my talk, I will review the changing epidemiology of pediatric DTC; the clinical, histopathological and molecular differences from adult DTC; and important recommendations from the recent ATA Guidelines on the management of pediatric DTC.

CS6.3. Subclinical Hypothyroidism
Hossein Gharib,
Mayo Clinic College of Medicine, Minnesota, USA

Subclinical hypothyroidism (SCH) is defined when serum TSH is above normal with normal FT4 levels. "Normal" TSH seems variable, ranging from 0.5-5.0 mIU/L in reference labs; 0.3-4.1 in guidelines; <2.5 in pregnancy and >5 in those >60 years of age. Serum TSH has a stable and narrow range in each euthyroid person.
Consequences of SCH include appearance of symptoms; progression to overt hypothyroidism; possibility of cardiac morbidity & mortality; dyslipidemia and poor QOL. The risk of progression to overt hypothyroidism significantly increases with positive TPO antibodies. Data show that while there is a trend for CHD events and mortality, this is significant for only TSH > 10.
Treatment of choice for hypothyroidism, either primary, secondary or subclinical, is LT4 monotherapy. Combination therapy, including desiccated thyroid extract, is not generally recommended, although it is becoming increasingly popular. Therapeutic target TSH is considered to be 1-3 mIU/L. We will discuss some commonly used drugs that influence T4 absorption and metabolism.

CS6.4. Interventional Thyroidology
Enrico Papini,
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Learning objectives 1) To become familiar with the modalities of minimally invasive treatments (MIT), .2) To consider their use as a cost-and risk- effective alternative to surgery for selected benign thyroid nodules and 3) To consider their use, as a palliative option, for local recurrences of thyroid malignancy in patients at high surgical risk. Abbreviations: FNA: Fine-needle aspiration biopsy; 131-I: Radioiodine; LAT: Laser ablation treatment; MIT: Minimally-invasive treatment; PEIT: Percutaneous ethanol Injection treatment; PTC: Papillary thyroid carcinoma; RFA: Radiofrequency ablation; US: Ultrasound. Background: Benign nodules. The majority of cytologically benign thyroid nodules remain stable over time and may be controlled without therapy. However, about 10-15% of them increase in size and result in pressure symptoms or cosmetic concern. Surgery is the traditional treatment for symptomatic thyroid lesions but is an expensive inpatient procedure, requires general anesthesia and carries the probability of neck scarring and surgical complications. Malignant lesions. Some differentiated thyroid cancers show local recurrence of disease during follow-up. Non radioiodine-avid metastases in critical sites require surgery but the surgical option for repeat, clinically occult, neck recurrences of PTC is less definite. When small-size cervical recurrences are revealed in patients who have already undergone neck dissection their resection may be technically difficult and exposes the patient at risk of complications.
Minimally-invasive treatments (MIT). On the basis of these considerations, various modalities for non surgical ablation directed at the destruction of the target lesion with minimal damage to the surrounding tissues have been proposed. Percutaneous ethanol injection (PEI) and thermal ablation with laser (LA) or radiofrequency (RFA)

are now thoroughly assessed and may be reliably used in clinical practice.

Techniques

Percutaneous Ethanol Injection (PEI). After local anaesthesia, a 23-gauge needle is placed under US guidance into the target lesion. In thyroid cysts, after the nearly complete drainage of the fluid collection, ethanol is injected into the cavity and then the needle is withdrawn without alcohol aspiration. Cyst treatment is rapid, inexpensive and nearly painless. The procedure is performed on outpatients that can return to their activities after treatment.

In cervical recurrences of PTC, a 25- to 27-gauge needle is inserted into the target lesion and a small amount of ethanol (from 0.1 to 0.5 mL) is injected into the metastatic lymph node. The needle is then repositioned, performing additional injections until a nearly complete treatment is achieved. Chemical injury induces protein coagulation and small vessel thrombosis which are followed by progressive fibrosis and shrinkage. Limits are the need of multiple sessions and the risk of severe cervical pain and local fibrosis due to alcohol seepage.

Laser ablation (LA). LA is performed inserting, after local anesthesia of the skin, prethyroid muscles and thyroid capsule, from one to two 21-gauge spinal needle(s) into the target lesion. After the US assessment of the correct positioning of the needle(s), a 300 μm-diameter plane-cut quartz optical fiber is introduced through the sheath of each needle until the fiber tip is in contact with the tissue. Illuminations, performed with an output power from 2 to 5 watts for 5 to 10 minutes cause a tissue damage characterized by a cavitation zone encircled by an area of coagulative necrosis up to 2 cm in diameter.

Radiofrequency ablation (RFA). The RFA system is based on an alternating electrical circuit that includes a generator, electrodes and the patient tissue. The electric flow causes frictional ionic agitation with rapid heating of tissues close to the electrode, while peripheral areas receive heat by thermal conduction. The currently available 18-gauge electrode-needles are moderately invasive and permit the destruction of the lesion with the use of the "moving-shot" technique.

Microwaves and high-intensity focused ultrasound are potentially useful MIT procedures that still need a more complete assessment for the treatment of thyroid lesions.

Indications for clinical practice

The safety and long-term outcome of US-guided MIT for benign thyroid nodules have been assessed during the last 20 years in several non controlled and a few randomized trials. Percutaneous ethanol injection and thermal ablation are currently thoroughly evaluated procedures and are accessible in referral centers.

Relapsing thyroid cysts may be managed with US-guided aspiration followed by PEI as the first line treatment, after the risk of malignancy has been ruled-out.

In solid nonfunctioning symptomatic thyroid nodules, LA and RFA result, in a single session, in a nearly 50% volume decrease and the improvement of pressure symptoms. These outcomes persist for several years and are only occasionally followed by thyroid function or autoimmunity changes. Thermal ablation procedures are fairly well tolerated in the majority of cases and the risk of major complications is very low for experienced operators.

Hyperfunctioning thyroid nodules are best treated with radioactive iodine, which provides a safe and effective long-term control of hyperthyroidism. A preliminary treatment with thermal ablation may be considered in large hyperfunctioning nodules to decrease the radioiodine activity and to induce a rapid volume decrease.

Several non-controlled and a few prospective studies demonstrated that PEI, LA and RFA treatment result in a protracted volume decrease, or the disappearance, of small cervical metastasis at Gray-scale and contrast-enhanced US examination. These changes were associated with a decrease of serum thyroglobulin levels and of the uptake of 18-FDG at PET-CT scan. MIT may be considered for the local control of small size, non radioiodine-avid, neck recurrences of PTC in patients who are not candidates for a repeat cervical lymph node dissection.

MIT was proposed, in a few feasibility studies, for the ablation of papillary thyroid microcarcinoma without evidence of multifocality or extrathyroidal spreading in patients at high surgical risk. The palliative results were reported as satisfactory.

Head to head prospective studies of thermal ablation versus surgery comparing long-term efficacy, side-effects, overall expense and impact on quality of life are needed to better define the role of MIT in benign thyroid lesions.

CS7. Endocrinology and Metabolism

CS7.1 PCSK9 Inhibitors in Management of Hyperlipidemia

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Statins have revolutionised the treatment of patients with lipid disorders and of others also known to be a high risk

of cardiovascular disease. However, there are patients who are unable to achieve their lipid targets with these drugs or who are intolerant of them. Until recently, alternative or additional options to statins have been few, with some now not recommended for routine use. Those that are still recommended tend to have a more modest effect on LDL cholesterol than high-intensity statins.

PCSK9 inhibitors are a new class of lipid lowering drugs with a novel mechanism of action which is able to lower LDL cholesterol at least as well as statins and can be used as either monotherapy or in addition to statin treatment. There is accumulating clinical evidence that this lipid reduction translates into reduced cardiovascular risk. However, the requirement for subcutaneous injection as well as the high acquisition cost of these drugs is likely to limit their initial use.

CS7.2. Mechanisms of Bariatric Surgery

Carel le Roux,
Diabetes Complications Research Centre, Conway Institute, University College Dublin, Ireland

Bariatric surgery is a good model to investigate appetite reduction in humans and rodents with associated major weight loss. Gastric bypass, but not gastric banding cause increased postprandial PYY and GLP-1 favouring enhanced satiety. An early and exaggerated insulin response mediates improved glycaemic control. The rodent model of bypass show elevated PYY, GLP-1 and gut hypertrophy compared with sham-operated rats. Moreover, exogenous PYY reduced food intake while blockade of endogenous PYY increased food intake. A prospective follow-up human study of gastric bypass showed progressively increasing PYY, enteroglucagon, and GLP-1 responses associated with enhanced satiety. Blocking these responses in animal and human models leads to increased food intake. A paradoxical increase in energy expenditure after gastric bypass secondary to the enhanced postprandial energy expenditure is evident in both humans and rodents.

Changes occur in the sensory, reward and physiological domains of taste that may mechanistically contribute to the alterations in food preferences after gastric bypass. The sustained nature of weight loss, reduced appetite and shifts in food preferences may be explained by gut adaptation and chronic hormone elevation.

Glycaemic control improves rapidly and is a result of several mechanisms including reduction in calorie intake, weight, hepatic and peripheral insulin resistance as well as an enhanced insulin secretion. Significantly altered gut hormones and bile acid metabolism have been implicated. Finally the improved metabolic milieu results in end organ damage reversal in some patients.

Following gastric bypass, a pleiotrophic endocrine response may contribute to improved appetite reduction, long-term lowering of body weight, glycaemic control and improvements in end organ damage.

CS7.3. The Fatty Liver Epidemic in the Diabetic Clinic!

Ahmed Hassoun,
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Non-alcoholic fatty liver disease (NAFLD) is extremely common especially in people with type 2 diabetes mellitus (T2DM). Unfortunately, the lack of a reliable non-invasive diagnostic blood test or imaging technique for its diagnosis has led to underestimation of the true prevalence of this condition.

The pathophysiology of NAFLD and T2DM are directly interrelated, and people with T2DM are at the highest risk for the development of non-alcoholic steatohepatitis (NASH) even in the setting of normal plasma aminotransferase levels. NASH is characterized by hepatocyte necrosis and inflammation with no or different level of fibrosis. Fibrosis indicates a more aggressive course in patients with NASH and put them at high-risk of cirrhosis, premature mortality, and at increased risk of hepatocellular carcinoma (HCC).

Recent guidelines have reviewed the evidence and came with guidance and recommendations addressing the diagnosis and management of NAFLD. Lifestyle modifications to include diet, exercise, and weight loss remain the most effective therapy for NAFLD. Depending on the degree of weight reduction, individuals may experience improved steatosis, decreased inflammation, and even remission and regression of fibrosis.

As the rate of obesity, and diabetes continue to increase, NAFLD and NASH will bring a tremendous impact on health care in the upcoming years with increasing burden of end stage liver disease, and HCC. It is a health care priority to increase awareness about NAFLD.

Early diagnosis of NAFLD/NASH in type 2 diabetes, should be encouraged since timely intervention is likely to

modify the natural history of the disease and halt the growing epidemic of NASH and its complications.

CS7.4. Male Hypogonadism in Adults: Overview and Update

Rabih Hijazi,
Cleveland Clinic Abu Dhabi, Abu Dhabi, UAE.

Male hypogonadism in adults is a common condition seen in clinical practice. There is little public data about its prevalence in the United Arab Emirates (UAE) but it is more common in aging men and men with certain conditions like diabetes, renal disease, or those receiving chronic glucocorticoid or opiate therapy.

The purpose of this presentation is to provide an overview of male hypogonadism and to shed the light of a growing and parallel health problem using a case study. It also aims to alert clinicians of potential pitfalls in the evaluation and management of male hypogonadism.

MTE1. Challenging Cases in Type 1 Diabetes

David Leslie,
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Diabetes was broadly seen as either severe diabetes, prevalent in children while diabetes developing in adults was usually mild. These two characteristics, namely the age at diagnosis and the obligatory need for insulin therapy, have dominated our views of the major diabetes types to this day. However, it is clear, that what you see (clinically) is neither what you get (in terms of pathogenesis), nor what you should do (therapeutically). Diseases, like diabetes, gain their identity from their clinical phenotype, historical precedent, genotype and specific environmental causes. This approach has lead to classification of diabetes as type 1 diabetes, type 2 diabetes, monogenic diabetes, gestational diabetes and other specific disease forms. Ideally, that identity should be found in categorical features specific (exclusive) for diabetes. But common chronic diseases, like type 1 diabetes, tend to have a complex aetiology, which cannot be encapsulated in a single feature. Three cases are presented with young-onset diabetes. All three cases were started on insulin on the assumption that they had type 1 diabetes. In reality only one of them does. Which one? The three cases highlight the need to define the mode of onset and presentation of forms of diabetes in order to better characterize it and to better treat it. Of the three cases, none requires insulin and only one has type 1 diabetes. The identity of disease and the need to define disease will be discussed.

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MTE2. Diagnosis and Management of Diabetes Insipidus

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Diabetes insipidus (DI) is defined as an uncontrolled solute-free water diuresis ("aquaresis") due to an inability to maximally concentrate the urine. The clinical hallmark of DI is the excretion of a large volume of hypotonic, insipid (tasteless) urine, usually manifested by polyuria and polydipsia. Consequently, patients diagnosed with DI must have hypotonic polyuria: the 24-hour urine volume exceeds 50 mL/kg body weight and the urine is inappropriately dilute (i.e., specific gravity <1.010 and urine osmolality <300 mOsm/kg H2O), in the absence of a solute diuresis such as glucosuria.

DI can result from impaired secretion of the antidiuretic hormone arginine vasopressin (AVP), impairments of AVP biological activity in the kidney, or increased destruction of circulating AVP. These account for the major subtypes of DI: central DI (CDI), nephrogenic DI (NDI) and gestational DI (GDI). True DI must be distinguished from other causes of polyuria-polydipsia, namely solute diuresis (usually from glucosuria), urinary frequency from lower urinary tract symptoms, and primary polydipsia. The diagnosis of DI will be reviewed in the context of a clinical case, including symptoms,

baseline laboratory characteristics, pituitary MRI, and water deprivation testing (both overnight and formal). Benefits and drawbacks of the "indirect" water deprivation test (administration of AVP or desmopressin at the end of the period of water deprivation) and the "direct" water deprivation test (measurement of AVP or copeptin at the end of the period of water deprivation) will be discussed.

Appropriate management of DI depends on both the type of DI as well as the clinical presentation of the patient. In CDI and GDI treatment with desmopressin is generally indicated, but patients with osmoreceptor dysfunction also require prescribed fluid intake to prevent hyperosmolality. In NDI desmopressin rarely has much clinical effect, and strategies to decrease polyuria must be employed.

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MTE3. Neuroendocrine Tumors: Recognition and Management

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Neuroendocrine tumours (NETs) of the gastrointestinal (GI) system (carcinoids and pancreatic NETs, pNETs) although relatively rare are increasingly being recognized. Although the majority of these tumours are slow growing neoplasms (G1 and G2 tumours), a subset may follow a more aggressive course (G3 tumours). NETs can secrete a variety of bioactive substances leading to a secretory syndrome (functioning NETs) and can be diagnosed on the basis of related symptoms; non-functioning NETs are diagnosed either incidentally or due to the development of metastatic disease. Specific and universal neuroendocrine biochemical markers, such as chromogranin A, along with conventinal and functional imaging modalities are used to localize GI NETs, identify the extend of the disease and monitor response to treatment. However, there are limitations in currently available tools in measuring intrinsically indolent disease, whereas some exhibit resolution inadequacies, and/or inter/intra-facility device variability. Recent, advances in tumour spatial and functional imaging along with circulating transcripts (mRNA) may represent the future strategy for real-time monitoring of disease progress and therapeutic efficacy. Surgery represents the best option for treating patients with GI NETs but can not be widely applied in those with extensive disease. However, surgery can be used in combination with medical treatment to ameliorate symptoms of secretory syndromes and decrease tumour load. Long acting somatostatin analogs (SSAs) are used for the management of fucntional syndromes and have ben shown to exert an antiproliferative effect in G1 and G2 GI NETs. Treatment with molecular targeted agents has been shown to prolong progression free survival in progressive G1/G2 pNETs (sunitinib and everolimus) and carcinoids (everolimus), whereas recent studies have demonstarted that treatment with radiopeptides (PRRT) exerts a significant impact in GI NETs and particulalry carcinoid tumours. Chemotherapy with various agents, but more recently temozolomide based chemotherapy, has been shown to be efficacious mainly in progressive G1/G2 pNETs, whereas cis-platin based chemotherapy has traditionally been used for G3 GI NETs. A number of cytoreductive techniques can also be applied, along with surgical or medical treatments, to control the secretory component of functioning NETs or overall tumour load. However, the exact timing of treatment initiation, selection of appropriate therapeutic modality, sequence of different treatments or combination of treatments applied, still need to be defined from prospective controlled studies.

MTE4. Hypoglycemia: Evaluation and Management

Graham McMahon,
Northwestern University, Illinois, USA

Investigating and diagnosing hypoglycemia can be challenging. In this session we'll review the common and unusual causes of hypoglycemia in patients, how the disorders present, what tests are typically useful at the outset, and how to use a 72-hour fast effectively. We'll

also explore the optimal use of radiology (CT, MRI, and endoscopic ultrasound) as well as infusion studies to diagnose insulinoma. The session will cover the treatment and management of several common hypoglycemic disorders. We'll then review several real cases to see the utility of this investigation and management approach.

MTE5. The Adrenal Incidentiloma
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The widespread use of abdominal CT/ MRI has resulted in a new and common diagnosis for the clinical endocrinologist – the management of patients with adrenal incidentalomas. Defined as an adrenal mass discovered incidentally in the work-up or treatment of clinical conditions not related to suspicion of adrenal disease, incidentalomas cover a spectrum of underlying adrenal pathologies with a common pathway of discovery. Because of the risk of malignancy, they raise uncertainty, confusion and concern in doctors and patients alike and consume significant resource. We will define the scale of the problem, discuss diagnostic challenges as they relate to hormone hypersecretion and the ascertainment of benign versus malignant. The natural history and suggested follow-up and treatment of patients based on published clinical guidelines will be addressed; such guidelines perhaps over-inflate the real risk of malignancy and a more "risk-averse" approach to management is now required. One particular area of contention is the term "sub-clinical" Cushing's reported in up to 15% of all cases; the suggestion being that this may account for underlying obesity, low BMD and cardiovascular morbidity. However diagnostic criteria vary considerably with false positive results generating considerable uncertainty. In the absence of any test with 100% sensitivity and specificity, the issue is likely to be one of diagnosing mild Cushing's syndrome where there is a limited evidence base that reversal of the condition significantly alters clinical features. Finally, new biomarker research based on analyzing the urinary steroid metabolome may improve the diagnosis and follow-up of adrenal incidentalomas.

MTE6. Thyroid nodules: A Case Based Discussion
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This session will use specific cases of patients to discuss the contemporary diagnosis and management of benign and malignant thyroid nodules with an emphasis on the use of molecular makers and reference to the recent ATA guidelines. The discussion will be conducted in a question-answer style using interesting stimulating cases. To achieve the best effect of the discussion and learning, the discussion contents will not be disclosed before the discussion starts.

MTE7. Thyroid Emergencies
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This presentation will review four common and complicated thyroid emergencies:
1. Thyroid storm- A severe, uncontrolled state of thyrotoxicosis, usually due to Graves' disease. Needs immediate attention and aggressive intervention with supportive care, 5-Bs and treatment of infection. Mortality may be as high as 35%.
2. Myxedema coma- Life-threatening severe hypothyroidism. Presents with hypothermia, hypoventilation, bradycardia, hyponatremia, often precipitated by infection, drugs or trauma. Treatment includes hydration, ventilation, antibiotics, & thyroid hormone therapy. Mortality remains high.
3. Thyrotoxic periodic paralysis- Endocrine emergency characterized by sudden onset flaccid paralysis, hypokalemia and hyperthyroidism. Most are male and Asian descent. Treatment is aimed at hypokalemia, hyperthyroidism, and hydration. Recovery is full and fast.
4. Amiodarone-induced thyrotoxicosis- Amio, an antiarrhythmic drug with high iodine content, can cause two types of thyrotoxicosis: Type 1 and Type 2. The two must be distinguished because etiologies are different and is treatment. Type 1 is hyperthyroidism with a goiter, some RAIU, increased gland vascularity, with no remission. Type 2 is destructive thyroiditis, a more severe hyperthyroidism, no RAIU, and normal vascularity on US. Treatment for each type is different but thyroidectomy may be necessary.

MTE8. Post-operative Management of Disorders of Water Balance.
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In a patient with onset of polyuria or polydipsia immediately after surgery in the hypothalamic/pituitary area or after head trauma (especially with skull fracture and loss of consciousness), the diagnosis of central diabetes insipidus (CDI) is highly likely since such patients rarely are able to drink excessive amounts of fluids. However, some patients may simply be excreting an intraoperative fluid load via an appropriate post-operative diuresis. Therefore it is best to confirm a diagnosis of CDI before beginning therapy. This is most easily done by withholding intravenous and oral fluids until the serum [Na+] increases to >145 mmol/L, which usually only take a few hours in the setting of true DI.

Postoperative disorders of water balance can follow several distinct patterns: 1) transient DI; 2) permanent DI; 3) triphasic response; 4) hyponatremia without DI ("isolated second phase"); or 5) osmoreceptor dysfunction ("adipsic DI"). The pathophysiology underlying each of these patterns, and their relative incidences and temporal characteristics will be discussed. Representative cases will be presented.

Sometimes the duration of DI is quite transient and the surgeon may prefer to treat only with fluid replacement parenterally or orally (if the patient is awake and able to respond to thirst). To treat post-operative DI, desmopressin can be given parenterally 0.5-2.0 μg subcutaneously, intramuscularly or intravenously. The intravenous route is preferable because there is no question about the degree of drug absorption. Urine output will be reduced in 1-2 hours and the duration of effect is 6-24 hours. If the patient is alert, thirst is a good guide to fluid replacement. Care should be taken that intravenous fluids (especially hypotonic) are not given excessively after administering desmopressin as this can lead to profound hyponatremia. Since the DI may be transient and some of these patients may develop the triphasic pattern, it is desirable to allow polyuria to return before administering subsequent doses of desmopressin.

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MTE9. Multiple Endocrine Neoplasia

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MEN1 is an autosomal dominant disorder that is due to mutations in the tumor suppressor gene MEN1, which encodes a 610-amino acid protein, menin. MEN1 mainly involves the development of parathyroid, pancreatic neuroendocrine and anterior pituitary tumours. Adrenocortical tumours are also increasingly been identified whereas foregut carcinoid tumours (mainly lung and thymic) may also develop. Non-endocrine tumour involvement includes the development of meningiomas, facial angiofibromas, collagenomas and lipomas. The diagnosis of MEN1 in a patient has important implications for family members because first-degree relatives have a 50% risk of developing the disease and can often be identified by MEN1 mutational analysis. Patients with MEN1 have a decreased life expectancy, and the outcomes of current treatments, which are generally similar to those for the respective tumors occurring in non-MEN1 patients, are not as successful because of multiple tumors, which may be larger, more aggressive, and resistant to treatment, and the concurrence of metastases. This is mainly related to the fact that all cells of involved organs carry the triggering mutation and are proned to develop multiple tumours. The prognosis for MEN1 patients is related to the early identification of mainly pacreatic tumours that can metastasize and currently consist the major cause of mortality in MEN 1 patients. Prognosis is expected to be improved by presymptomatic tumor detection and undertaking treatment specific for MEN1 tumors. Thus, it is recommended that MEN1 patients and their families should be cared for by multidisciplinary teams comprising relevant specialists with experience in the diagnosis and treatment of patients with endocrine tumors.

MTE10. Highlights of Thyroid Cancer ATA Guidelines

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Thyroid nodules are a common clinical problem, and differentiated thyroid cancer is becoming increasingly prevalent. Since the American Thyroid Association's (ATA's) guidelines for the management of these disorders were revised in 2009, significant scientific advances have occurred in the field. The aim of these guidelines is to inform clinicians, patients, researchers, and health policy makers on published evidence relating to the diagnosis and management of thyroid nodules and differentiated thyroid cancer. We will review some pertinent recommendations regarding initial evaluation, clinical and ultrasound criteria for fine-needle aspiration biopsy, interpretation of fine-needle aspiration biopsy results, and use of molecular markers. We will also highlight some recommendations relating to staging and risk assessment of patients with thyroid cancer and their follow up as well indications for I131 RX.

MTE11. Cushing Syndrome: Case Discussions

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Introduction: Endogenous Cushing syndrome (CS) is rare. One of the most difficult roles for the endocrinologist is to distinguish between mild CS and pseudo-CS. Methods: Data will be presented based on extensive clinical experience and literature review.
Guidance: The physical examination findings that should double your clinical suspicion for CS include: central obesity and thin extremities; facial rounding and plethora; supraclavicular fat pads; fine "cigarette paper thin" skin; wide (>1-cm) purple-red striae; and, proximal muscle weakness. Serial photographs over time can be very helpful. There are 4 case detection tests: 24-hr urinary free cortisol (UFC), midnight salivary cortisol, 1-mg overnight dexamethasone suppression test (DST), and diurnal serum cortisols. Dependent upon your degree of suspicion, use 1 or all 4.
In the patient with obvious and severe CS, don't waste time with 1-mg DST or salivary cortisol—get 24-hr UFC, a.m./p.m. serum cortisols, and serum ACTH. The "biochemical phenotype" guides the urgency to resolve the diagnosis and treat for a cure. For example, if the 24-hr UFC is >1000 mcg, pursue subtype testing as soon as possible—these patients do die from hypercortisolism. In the patient with severe ACTH-dependent CS and source of ACTH is not evident, don't waste time—send them to bilateral laparoscopic adrenalectomy and save their life! Whereas, if the case detection tests for CS or borderline or normal, re-evaluate if strong clinical suspicion for CS—consider monthly 24-hr UFC. Take your time—these patients will NOT die from CS!!! If the symptoms are mild and biochemical tests borderline—the goal is NOT to correct laboratory values, but rather to treat signs and symptoms of CS—if you are having trouble confirming CS, there is no RUSH! If clinical picture fits with pituitary-dependent CS (eg, female, slow onset, mild to moderate CS, UFC <600 mcg) and there is a definite pituitary tumor on head MRI, then inferior petrosal sinus sampling (IPSS) usually not needed. Conclusions: There is no "one" algorithm for the diagnosis or the subtype evaluation. The clinical features dictate the tests for confirmatory and subtype evaluation. No biochemical test should over-rule clinical intuition! When you have a man with ACTH-dependent CS – think ectopic. Whereas, if your patient is a woman with slowly developing and mild to moderate ACTH-dependent CS – the patient almost certainly pituitary tumor. IPSS is needed in a minority of patients with pituitary-dependent disease (when pituitary MRI does not disclose a tumor or in the patient with severe CS and a pituitary microadenoma is seen on MRI).

MTE12. Meet the Expert Sessions: Management of Osteoporosis.

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No Abstract.

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