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Endocrinology

Cod: T107

SERUM CITRULLINE LEVELS IN PATIENTS WITH DIABETES MELLITUS

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BACKGROUND
Alterations in endothelial function are a common underlying cause for vascular pathologies observed in patients with diabetes mellitus. Around 10% of plasma arginine originates from de novo synthesis from citrulline. Some, but not all, reports have indicated that oral arginine or citrulline supplementation may enhance NO-mediated cardiovascular function. Our aim was to investigate serum citrulline levels in patients with diabetes mellitus.

METHODS
41 control, 35 prediabetic, 40 well-controlled, 44 uncontrolled subjects were enrolled to this study. Participants with known systemic diseases, including cardiovascular disease, renal disease, gastrointestinal disease, pulmonary disease, acute infection, chronic inflammation and cancer were excluded. Serum citrulline levels were analyzed with API 3200 ABSCIEX LC-MS/MS system.

RESULTS
Serum citrulline levels were significantly higher in patients with uncontrolled diabetes [131 (22.9-441 µmol/L)] compared to control [90 (18.8-230 µmol/L)] and well controlled diabetes [97.2 (34.7-285 µmol/L)] ($p=0.002$ and $p=0.019$, respectively). Although serum citrulline levels were higher in prediabetic group [107 (45.2-455 µmol/L)] compared to control group [90 (18.8-230 µmol/L)], the difference was not statistically significant ($p=0.135$).
CONCLUSIONS
It was demonstrated that citrulline, to promote endogenous arginine production, is a more effective way to improve plasma concentration of arginine. Higher citrulline levels in diabetic patients might be due to a compensatory response to the need of nitric oxide production. The size of this contribution must be confirmed in prospective observational and intervention studies.

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Endocrinology

Cod: T108

OBESITY AND METABOLIC SYNDROME IN WOMEN WITH POLYCYSTIC OVARY SYNDROME IN R.MACEDONIA

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Metabolic and endocrine dysfunctions that occur in polycystic ovary syndrome (PCOS) can be associated with future co - morbidities such as diabetes, cardiovascular disease, and endometrial cancer. Generally polycystic ovary syndrome and the metabolic syndrome have many features in common and may share the same pathogenesis. This study was performed to determine the prevalence and predictors of the metabolic syndrome among women with PCOS and different ethnic groups living in R. Macedonia.
Design: The clinical, hormonal, and oral glucose tolerance test results were analyzed in 116 PCOS women. Main Outcome Measures: Waist circumference, fasting glucose, high-density lipoprotein cholesterol and triglyceride concentrations, and blood pressure were the main outcome measures. Results: The prevalence for individual components comprising the metabolic syndrome were: waist circumference greater than 80 cm in 88%, high-density lipoprotein cholesterol less than 1.3mmol/l in 65.5 %, triglycerides greater than or equal to 1.7 mmol/l in 10.4%, blood pressure greater than or equal to 130/85 mm Hg in 7%, and fasting glucose concentrations greater than or equal to 5.6 mmol/l in 7.8%. Mean fasting insulin was 8.6 μIU/ml, and HOMA IR greater than 2,5 in 30%. The prevalence of the metabolic syndrome did not differ significantly between ethnic groups.
Conclusions: The metabolic syndrome and its individual components are common in PCOS, particularly among women with the highest insulin levels and BMI. Hyperinsulinemia is a likely common pathogenetic factor for both PCOS and the metabolic syndrome.

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Endocrinology

Cod: T109

CORELATION BETWEEN THYROID HORMONE LEVELS AND ICU MORTALITY

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BACKGROUND Serum thyroid hormone levels alterations are noticed in patients during critical illness admitted to intensive care units (ICU). The aim of this study was to investigate the prognostic value of the thyroid hormones in ICU patient and correlation with ICU mortality.
METHODS Forty one consecutive patients (23 men and 18 women) without known thyroid disease were included in the study. The patients were divided into two groups: survivors (70.7%) and no survivors (29.3%). We collected the baseline characteristics of each patient as well as Sequential Organ Failure Assessment Score (SOFA Score) and serum levels of thyroid hormones (T4, FT4, T3, FT3, TSH).The primary outcome was ICU mortality.
RESULTS There was significant difference ($P<0.05$) between two group in SOFA Score, T3, T4, FT4. The area under the curve (AUC) for SOFA Score 0.991(95% CI 0.898-1.000, $P<0.0001$), for T3 0.727(95% CI 0.566-0.854, $P=0.0097$), for T4 0.793(95% CI 0.638-0.903, $P=0.0008$), for FT3 0.707(95% CI 0.544-0.8389, $P=0.0299$) and for FT4 0.795(95% CI 0.640-0.904, $P=0.0005$). Multivariate logistic regression analysis showed that significant predictive of ICU mortality was only T4 (OR=0.96; 95% CI 0.93-0.99, $P=0.0106$).
CONCLUSIONS In unselected ICU patients T4 was the most powerful only independent predictor of ICU mortality. It can be hypothesized that T4 level and SOFA Score have the ability to predict ICU mortality.

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Endocrinology

Cod: T110

COMPARISON OF TESTOSTERONE LEVELS MEASURED BY ELECTROCHEMILUMINESCENCE AND LIQUID CHROMATOGRAPHY-MASS SPECTROMETRY IN DIFFERENT AGE AND GENDER GROUPS

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Background: Testosterone (T) is routinely measured by automated immunoassays in large clinical labs. However, this method is prone to analytical interference and, according to several experts, should be replaced by mass spectrometry. To address this question, we compared T levels in different age groups of males and females and evaluated the agreement between these 2 methods on the diagnosis of hypogonadism and hyperandrogenism.
Methods: T was measured with Roche electrochemiluminescent Testosterone II assay (ECLIA) in E170 Modular Analytics (Manheim, Germany) and an in-house liquid chromatography-mass spectrometry assay (LC-MS/MS) in 1910 routine serum samples drawn for androgen profiling. LC-MS/MS was performed with an Agilent Infinity 1290 (Mississauga, Canada) coupled to an AB Sciex QTrap 5500 (Concord, Canada) run in positive mode with atmospheric pressure chemical ionization; transitions were monitored at m/z 289→109 and 289→97. The limit of quantitation (LOQ) and interassay variation were 12 ng/dL and <= 5.1% for ECLIA and 10 ng/dL and <= 5.5% for LC-MS/MS.
Results: T was < LOQ in both assays in all 11 children samples (<= 8 yr). In males, median T (interquartiles) were in ECLIA and LC-MS/MS: 9-17 yr (n=24), 399 (185-622) vs 331 (176-521) ng/dL, r=0.98; 18-49 yr (n=231), 500 (382-632) vs 413 (313-528) ng/dL, r=0.90; >= 50 yr (n=142), 443 (313-612) vs 354 (249-526) ng/dL, r=0.90. In females, results were: 9-17 yr (n=84), 29 (20-43) vs 23 (17-31) ng/dL, r=0.48; 18-49 yr (n=1110), 19 (12-31) vs 19 (13-28) ng/dL, r=0.88; >= 50 yr (n=319), 14 (12-23) vs 16 (12-24) ng/dL, r=0.93. Interassay differences exceeded ±13.6% (total allowable error (TEa) based on biologic variation) in 50-70% male and 50-62% female samples. Taking the reference range for age of each assay, T was low in one assay but not in the other in 11% adult male samples; similarly, T was high in one assay but not in the other in 5.2% adult female samples.
Conclusions: T levels correlated very well (r >= 0.88) in ECLIA and LC-MS/MS in all groups, except girls 9-17 yr. In the latter and all male groups, T was significantly higher in ECLIA. Interassay differences exceeding TEa were seen in 50% or more of specimens; however, interassay disagreement on the diagnosis of hypogonadism in men or hyperandrogenism in women occurred in a much lower proportion of samples (11 and 5.1%, respectively).

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Endocrinology

Cod: T111

IMPROVED URINE LOW CORTISOL ASSESSMENT USING GAS CHROMATOGRAPHY-MASS SPECTROMETRY

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INTRODUCTION
Cortisol is measured in serum for the assessment of adrenal synthesis and secretion to the bloodstream. Due to pulsatility and circadian rhythms, it does not reflect dynamic adrenal-related issues. In contrast, 24-hour urine is a non-invasively collected and stable specimen, which contains at least all metabolites produced in serum. Free cortisol (i.e. glucoronate-unbound) in 24-hour urine is still the best individual biochemical marker for adrenal cortex assessment.
Some mass spectrometry (MS)-based approaches have proven to overcome interferences as well as to improve specificity of traditional immunoassays. With an increasing presence in clinical laboratories, GC-MS postulates as the modern routine methodology for the confirmation of free steroid assays in biofluids. The aim of the study was to compare low urine cortisol values in a commercial extraction-free immunoassay with a reference GC-MS method.

METHODS
Urine samples from 17 patients anonymously referred to our laboratory were included, and cortisol was measured by immunoassay (Architect systems, Abbott), with a detection limit of 0.8 µg/dL. Patients taking medications known to interfere with the immunoassay were excluded. The medical reason for urine cortisol testing was also registered.
Subsequent cortisol quantification by GC-MS was performed and quantified using stigmasterol as internal standard (5977A GC-MS, Agilent). Limit of detection was 0.20 µg/dL (defined as lowest point in the calibration curve).

RESULTS
Of all patients, only five (33.3%) showed undetectable concentrations using GC-MS, whereas up to 12 samples were not quantifiable by immunoassay ($p=0.016$). Some patients yielded a higher cortisol value when analyzed by GC-MS (ie. free cortisol) than the total cortisol value obtained when analyzed by immunoassay. The percentage of discordant results was 23.5%.

CONCLUSION
MS-based assays quantifying free cortisol in 24-hour urine samples provide an accurate approach for the assessment of endogenous cortisol production and, by extension, of the adrenal function. By improving both sensitivity and specificity, GC-MS has been introduced in the clinical laboratories not as substitute, but as a complement to conventional immunoassays, hence allowing a better clinical evaluation.

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Endocrinology

Cod: T112

ASSESSMENT OF SERUM APELIN LEVELS IN PATIENTS WITH SUBCLINICAL HYPOTHYROIDISM

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Subclinical hypothyroidism is the precursor to hypothyroidism because it has a tendency to transform into hypothyroidism. Subclinical hypothyroidism is considered one of the risk factors causing metabolic syndrome. Metabolic syndrome can be characterized by plasma level of apelin released from adipocytes. In the present study, we aimed to measure serum apelin level of patients with subclinical hypothyroidism and compare them with serum apelin level from healthy individuals.
Our study group included 31 patients diagnosed with subclinical hypothyroidism and 23 healthy volunteers. Serum samples were obtained from each participant for the measurement of apelin. These were then stored at -20◦C until the time of analysis. Serum apelin concentrations were determined using an enzyme-linked immunosorbent assay.
The mean serum apelin levels of subclinical hypothyroidism and control groups were 79 ng/L, control group 60 ng/L respectively. There was no statistically significant difference in terms of the mean apelin levels between the groups ($p>0.05$). Apelin levels didn't show significant correlation with BMI ($p>0.05$).
In the present study, no significant difference of serum apelin level was observed between patients with subclinical hypothyroidism and healthy control subjects. However, the apelin levels were higher in the patients with subclinical hypothyroidism than in the control group. The possible relationship between thyroid hormones and apelins is critical to understanding the etiopathogenesis of metabolic disorders.

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Endocrinology

Cod: T113

THROUGHPUT AND SAMPLE PREPARATION IMPROVEMENTS FOR ENDOCRINE RESEARCH BY MICRO-FLOW LC-MS/MS

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Introduction

Simple and rapid analysis of endocrine samples is necessary in a clinical research laboratory. Additionally, as financial and environmental concerns become more prevalent, heavy use of solvents for high flow LC-MS/MS methods, particularly those involving online extraction, can be an issue. Microflow LC offers a solution to these concerns, whilst greatly enhancing on column sensitivity and chromatography performance, reducing sample consumption and improving system robustness and uptime. As the sample injection volume is minimized, robustness and reproducibility of the entire method is dramatically increased as matrix effects are significantly reduced.

Materials and Methods

Sample Preparation:
Extraction was achieved by protein precipitation/direct injection approach utilizing 20µL of plasma
HPLC Conditions:
Short chromatography was provided by a C8 MicroLC column and a gradient of acidified methanol/water
MS/MS Conditions:
Sciex Triple Quad 4500, operating in Positive MRM

Results

• Microflow LC shows significant performance increases over conventional LC in terms of throughput (3 min vs 6 min) sample requirements (20µL vs 200µL) and mobile phase needs (15µL/min vs 700µL/Min)
• MicroFlow LC has been shown to remove interferences that can cause to misinterpretation of the results
• Sensitivity (based on amount on column) shown to be in some cases 100x vs conventional HPLC
• Results and statistics in plasma show good Accuracy (88 – 105%) Precision (4.4-9.5%)and Linearity (>0.997) with sensitivity of all compounds in plasma significantly below 50pmol/L for most steroids analysed

Conclusions

• We present here a proof-of-concept analysis for the use of micro-flow liquid chromatography for the analysis of steroids in serum.
• The proposed method offers advantages over conventional HPLC in terms of sample requirements, throughput and solvent consumption/disposal.
• In addition, reduction in injection volume and therefore amount of extracted matrix introduced to the system allows improvements in assay robustness and instrument uptime.
• Microflow LC shows good analytical performance across relevant concentration ranges.
• Further research to expand the compounds analysed is ongoing.

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Endocrinology

Cod: T114

ISCHEMIA MODIFIED ALBUMIN LEVELS OF PATIENT WITH HYPERTHYROIDISM

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Thyroid dysfunction such as hyperthyroidism is one of the most common endocrine dysfunction in society. Hyperthyroidism; is a clinical condition that occurs due to exposure to excessive amounts of hormones. In recent years, determining the change in serum albumin structure has allowed the presence of a new serum marker of cardiac ischemia. Hypoxia, acidosis, free-radical damage and membrane disruption reduce albumin binding to the N-terminus of the transition metals. This albumin which changes have occured in the structure is called "ischemia modified albumin (IMA)". Previous studies have shown that strong effects of hyperthyroidism on oxidative stress. In this study, we determined IMA levels of patients with hyperthyroidism and investigated the relationship between these data with thyroid hormone parameters.

A total of 40 patients and 40 healthy subjects aged 21-74 years old who attended Tepecik Training and Research Hospital outpatient clinics were included in this study. Serum fT3, fT4, TSH, TGAb, TPOAb, Albumin and IMA levels were measured.

The hyperthyroidism patients' and healty control groups' mean IMA levels were 0.395±0.008 ABSU and 0.386±0.006 ABSU respectively. There were no significant difference serum IMA levels in the groups($p=0.38$). No significant correlation between IMA levels and fT3, fT4, TSH, TGAb, TPOAb levels was found for patient group.

There were no significant differences between IMA levels in hyperthyroidism patients and healty subjects. There were no significant correlation between IMA levels and thyroid hormone parameters in patients group. In patient group some of them were threated so group was not homogenious. Further studies with large groups are warranted to better define. To confirm our study other studies with largest groups.

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Endocrinology

Cod: T115

SERUM ANTI-MULLERIAN HORMONE AS A SURROGATE BIOMARKER FOR ANTRAL FOLLICLE COUNT IN CONTROLLED OVARIAN STIMULATION

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Background: Diminished ovarian reserve has become a major cause of infertility. The aim of this study was to evaluate the relevance of anti-Mullerian hormone (AMH) additional to Antral Follicle Count (AFC) in assisted reproductive technology (ART) that might affect clinical decision and consequently, ART stimulation protocol.

Methods: The study enrolled 65 females (age range 30-45 years) undergoing assisted reproductive technology. Samples were drawn proceeding AFC that had been determined by transvaginal sonography, measuring follicles of 2-10 mm diameter in size, in early folicular phase. AMH had been determined by electrochemiluminiscence method performed on cobas e411 (Roche Diagnostics).

Results: The following data demonstrate the AFC classification in the four AFC values groups (<4, 5-9, 10-15, >15) in comparison to AMH. In AFC <4 group median of AMH values was 3.38 pmol/L (minimum 0.07, maximum 14.61, n=15), in AFC 5-9 group 7.68 (4.47, 19.25, n=12), in AFC 10-15 group 12.90 (4.29, 30.23, n=17) and in AFC >15 group 27.23 (11.58, 70.13, n=21) respectively.

Conclusions: The introduction of AMH as a standard procedure in assisted reproductive technology in our hospital improved clinical decision and consequently, ART stimulation protocol, providing clinical confidence in reliable assessment of ovarian reserve and response to controlled ovarian stimulation. AMH is useful in the identification of both low and high responders before treatment and may decrease cycle cancellation rate and side-effects such as ovarian hyperstimulation syndrome (OHSS).

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Endocrinology

Cod: T116

SPECIFICATIONS OF A ROUTINE 25OHD MEASUREMENT SYSTEM FOR SERUM/PLASMA 25-HYDROXYVITAMIN D ANALYSIS.

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Abstract

The divergence in analytical quality of serum/plasma 25-hydroxy-vitamin D (25OHD) analysis regardless of the assay used calls for laboratories to anchor their method against an established reference method.
Using DEQAS samples from April 2015 to July 2016, 25OHD was determined using the Roche 25OHD total immunoassay method in use in St. Vincent's University Hospital (SVUH) with the method mean calculated by DEQAS for all Roche users. These were compared to 25OHD results determined by the National Institute of Standards in Technology (NIST) LC-MS/MS reference measurement procedure (n=30). Additionally, estimated recovery of samples containing endogenous 25OHD2 (n=3) using the Roche 25(OH)D total immunoassay was determined.
The overall correlation of the Roche total immunoassay for 25OHD with the NIST reference measurement procedure was good for both SVUH and method mean results (r =0.978 for both). A trend toward under recovery below and over recovery above at a concentration close to 50 nmol/L was identified in both Roche method mean (y=1.298x -14.04) and SVUH submitted results (y= 1.321x -13.58) with a median positive bias of 7.51% and 12.78% determined respectively. The overall laboratory trimmed mean for all 25OHD methods combined (ALTM) compared with the NIST reference method was excellent (r = 0.993), y= 1.033x -0.769 with a median positive bias of 2.29%. In samples containing endogenous 25OHD2 the Roche total 25OHD assay under-recovered by 0.73% for method mean and over-recovered by 4.3% for SVUH submitted results.
The Roche 25OHD total immunoassay demonstrated a good association with NIST in DEQAS external quality assurance samples. The trend toward under and over recovery at approximately 50 nmol/L may be indicative of a calibration misalignment on the Roche total 25OHD immunoassay compared to the NIST LC-MS/MS reference measurement procedure.

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Endocrinology

Cod: T117

TRACEABILITY OF CORTISOL ASSAYS – LC-MS/MS REFERENCE METHOD VALUE COMPARISON

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The preferred method of comparison of returned EQA results, ensuring traceability of results to the SI unit, utilises reference target values where available. This ensures the transfer of accuracy from definitive methods to routine methods. Where available, the use of reference target values is also a requirement of ISO17043.
Individual donations (both males and females) of human serum, all with endogenous steroid alone, encompassing the analytical range for cortisol (150 – 400nmol/L) were analysed by a validated reference method utilising isotope dilution LC-MS/MS methodology. Traceability of analysis was assured by the inclusion of certified reference material within the analytical run.
The prepared pools were circulated to all participants of the Weqas endocrine scheme. Each distribution consisted of 5 samples with reference target values, enabling both linearity and traceability to be assessed. The deviations from the 'true' result (the reference method) for the main analyser groups were plotted in the form of bias plots (Bland–Altman plots). The ID-GCMS traceable group which included Abbott, Beckman and Roche methods showed reasonable agreement with the reference method. However within this group there was still some variability. The Tosoh AIA and Siemens Centaur showed a positive bias.
Peer review of performance against method mean and overall mean data cannot identify true errors in accuracy. This can only be achieved by comparison with traceable reference methods such as isotope dilution LC-MS/MS.

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Endocrinology

Cod: T118

OUR EXPERIENCE ASSESSING GH SECRETION DEFICIENCY APPLYING STIMULATION TESTS

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INTRODUCTION
Short stature is a definition that applies for children 2 standard deviations below the corresponding mean height for a given age, sex, and population group. These situations should be diagnosed and treated early to ensure normal growth.
Among the etiologies of short stature may be mentioned deficiency Growth Hormone (GH), peripheral resistance to GH action, intrauterine growth restriction, hypothyroidism, celiac disease, among others.
Due to the pulsatile secretion of GH, the isolated GH measurement provides little information. To evaluate the GH deficiency, stimulation tests should be performed followed by measurement of GH at different times.
OBJECTIVES
To describe our experience applying dynamic stimulation tests with Arginine and/or Clonidine.
To describe the pediatric population evaluated.
MATERIAL & METHODS
Arginine and Clonidine stimulation tests performed at CEMIC during November 2012- October 2016.
RESULTS
We evaluated 85 children with a median age of 9 years old (Range: 9 months – 16 years). Males to female ratio was 1,9:1. 53% of the patients were below percentile 3 in the growth chart for age and height, 12% where in percentile 3, 8% in percentile 5 and 27% above percentile 10.
We performed 82 arginine and 67 clonidine stimulation test. 46% of the evaluated children showed a positive response to arginine, and 84% to clonidine. However, 84% of the non-responsive for arginine, did show a positive response to clonidine; and 36% of the non-responsive to clonidine, responded to arginine.
Growth hormone was measured at 0, 30, 60, 90 and 120 minutes post stimulus. The maximum GH secretion was detected at 30 minutes in 60,5% of the children for arginine, and at 60 and 90 minutes equally (46,5%) for clonidine.
DISCUSSION
We believe that because of socio-cultural reasons, boys show more concern on stature than women. Nevertheless, the response to stimulus was similar in both groups: 91% boys vs 93% girls.
Apparently, clonidine is a more efficient stimulus, having more kids responding to the stimulus and with higher values of GH. The response is observed latter that arginine (60 vs 30 minutes) possibly because of different administration pathways.

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Endocrinology

Cod: T119

THE RESEARCH OF THE FREQUENCY OF INTERFERENCE IN THYROID FUNCTION TESTS

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Background: Interference is defined as the effect of substance in the sample which changes the correct value of laboratory results. The frequency of interference in immune techniques is varied. The frequency of interference depends on population of the study, technique for detecting the reaction and researcher's method. Unexpected or inconsistent results with clinical findings should suggest the possibility of interference. In this study It is aimed to investigate the frequency of interference in thyroid function tests (TSH, fT3, fT4) which are the most common requested laboratory tests.
Methods: Thyroid function tests of 47915 patients are analyzed in Ankara Numune Education and Research Hospital in October 2014- May 2015. Five samples which had the incompatible results with clinical findings are re-evaluated just because of the suspicion of interference. The detection of interference included; repetition of test via different immune techniques, serial dilution, polyethylene glycol (PEG) precipitation and incubation with heterophilic blocking tubes (HBT).
Results:The results of two different immune techniques and before/after incubation with HBT showed no significant difference. Linear curves had observed in serial dilution. After PEG precipitation; below 40% of recovery had obtained in one sample, therefore it is interpreted as macro-TSH. The frequency of interference in thyroid function tests for 8-month study period was 0.01%.
Conclusion: No information is found about the best test for defining the cross reaction. It is also aforethought that interference should not be excluded by using any single procedure.

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Cod: T120

DEVELOPMENT OF AN ENHANCED CHEMILUMINESCENT C-PEPTIDE ASSAY* ON VITROS® 5600 INTEGRATED AND VITROS® 3600 IMMUNODIAGNOSTIC AND VITROS® ECI/ECIQ IMMUNODIAGNOSTIC SYSTEMS

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Background: C-peptide is a useful biomarker to assess beta-cell function in the pancreas. Additionally, C-peptide measurements are used as an aid in the diagnosis of hypoglycemia, diabetes mellitus and insulinoma. We have developed a prototype enhanced chemiluminescent assay for the quantitative measurement of c-peptide in serum and plasma for use on the VITROS® 5600 Integrated and VITROS® 3600 and ECi/ECiQ Immunodiagnostic Systems.
Methods: Precision was evaluated per CLSI EP05-A3 by testing a 5 member panel in duplicate 2 times per day for 20 days. Cross reactivity with proinsulin was assessed up to 1000ng/ml; and cross reactivity with insulin was assessed up to 26,396µIU/mL. A total of 110 samples spanning the assay range were tested in the prototype assay and on a commercially available automated c-peptide test. LoB, LoD, LoQ were evaluated per CLSI EP17-A2 by testing 100 replicates of 1 LoB fluid and 5 LoD fluids over 5 days. High dose hook was assessed up to 200ng/mL. Testing was conducted across two reagent lots and three VITROS® systems.
Results: The within lab %CVs ranged from 2.8% to 3.8% on the VITROS® 3600 and 2.1% to 3.6% on the VITROS® ECi for samples ranging in concentration from 0.28 to 12.4ng/mL. At 1000ng/mL, the observed % cross reactivity for proinsulin was 0.5%. At 26,396µIU/mL of insulin, no cross reactivity was detected. For the method comparison, regression analysis yielded slopes ranging from 0.98 to 1.04, intercepts ranging from -0.02 to 0.07, and Correlation Coefficients ranged from 0.98 to 0.99 among the VITROS® systems. The overall mean % bias for the prototype method ranged from 0.56% to 4.25% among the VITROS® systems compared to the commercially available automated comparator method. The LoB was 0.009ng/mL, The LoD was 0.027ng/mL, and the LoQ at 20% CV was 0.045ng/mL. No high dose hook was observed for the assay up to 200ng/mL.
Conclusion: Preliminary performance data demonstrate that the prototype assay has excellent precision, minimal to no cross reactivity with proinsulin and insulin, excellent correlation with a commercially available method, an LoQ consistent with other commercially available methods, and shows no high dose hook up to 200ng/mL.
*Under development

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Endocrinology

Cod: T121

ROLE OF 25(OH)VITAMIN D IN DIFFERENT AGE GROUPS IN AUTO IMMUNE THYROIDITIS IN INDIAN POPULATION

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Aim:Vitamin D deficiency has been associated with several autoimmune diseases and most commonly with autoimmune thyroiditis (AT). The aim of the study was to investigate the association of AT in different age groups with low 25(OH) vitamin D levels in Indian population.
Methods and Materials:Study was conducted in Asian Institute of Gastroenterology Hyderabad on 300 patients visiting op with thyroid disease from April 2016 to Sep 2016,age&sex matched with vitamin D deficiency divided into 3 Groups,GROUP -1 (N = 68cases, 68control) Children0-18 years (34:34 M/F) cases, GROUP-2(N = 126 cases, 126 control) adults, age18-65years (63;63M/F)GROUP -3(N = 106cases,106 control)elderly age 65-85 years(53:53M/F)Fasting sample are collected to estimate 25(OH) vitamin D,FT3, FT4, TSH,TPO-Abs levels using Cobas e 601analyzer(Roche Diagnostics)Electrochemiluminescence(ECLIA)method. Statistical analysis was carried out using SPSS 19.0.
Results: In Study I; Group I Cases vs.Controls:Vitamin-D :(16.8 ± 9.3 and 21.1 ± 9.4 ng/mL) P < 0.01.TSH(-2.1 ± 1.9 vs. 1.8 ± 1.3 mcUI/mL), p = 0.14, FT3 levels(3.7 ± 1.0 vs. 4.1 ± 1.6 pg/mL,) p = 0.16,FT4 levels(15.3± 5.3 vs. 14.7± 3.1 ng/dL,) p = 0.33,TPO Ab.(252.4 ± 180.0 vs. 229.7 ± 193.3 IU/mL)p=0.33;In Study II:Group II Cases vs Controls: Vitamin D(14.8 ± 9.3 vs 23.1 ± 7.4 ng/mL)P < 0.01,TSH:(2.5 ± 0.9 vs.2.0± 1.3)p=0.22,FT3:(4.0 ± 0.8 vs. 3.7 ± 1.0 pg/mL),p = 0.30; FT4(15.2± 3.0 vs. 14.3 ± 3.3 ng/dL), p = 0.31,TPO-Ab:(203.7 ± 213.0 vs. 203.6 ±210.1 IU/mL)p = 0.44,In Study III; Group II Cases vs Controls TSH:(1.6± 0.8 vs.1.7± 1.1 mcUI/mL), p 0.39; FT3:(4.0± 0.8 vs. 3.7± 1.0 pg/mL), p = 0.30; FT4:(15.2 ± 3.0 vs. 14.3 ± 3.3 ng/dL), p = 0.31,TPO-Ab:(293.7 ± 203.0 vs. 303.6 ±210.1 IU/mL), p = 0.44,Vitamin-D:10.8 ± 9.3 and 20.1 ± 7.6ng/mL, P < 0.01. A significant correlation between 25(OH) vitamin D and TPO-Ab (r = -0.22, p = 0.03) FT3 (r = 0.26, p = 0.008) has been found elderly subjects with AT while no correlation between 25(OH) vitamin D levels, TSH (r = -0.012, p = 0.10) and FT4 (r = 0.17, p = 0.32).In Study IV; The prevalence of AT was significantly is high in severe and moderate vitamin D deficiency (28% vs. 13%,) p = 0.002 in elderly.
Conclusions:This study says that elderly patients with vitamin D deficiency had a significantly higher prevalence of AT compared to adults and children with vitamin D deficiency.So screening for AT should be suggested in subjects with vitamin D deficiency in terms of TSH.

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Endocrinology

Cod: T122

DEVELOPMENT OF A HIGH-SENSITIVITY PROTOTYPE ASSAY FOR THYROID STIMULATING HORMONE (TSH) ON THE VITROS® 3600 AND ECI/ECIQ IMMUNODIAGNOSTIC AND 5600 INTEGRATED SYSTEMS

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Background: A new prototype assay for thyroid stimulating hormone (TSH) is under development for the VITROS® 5600, 3600 and ECi/ECiQ Systems. The prototype assay targets a faster time-to-result with reduced sample volume, expanded measuring range and improved sensitivity.

Methods: All testing was conducted on the VITROS® 3600 and ECiQ Immunodiagnostic Systems. LoB/LoD/LoQ and precision were evaluated using modified CLSI protocols. Five precision pools were evaluated, with TSH values ranging from 0.105 to 71 µIU/mL. Precision testing occurred in ten runs on two instruments over a period of five days, with two replicates per run (n=40). Accuracy of the prototype assay was evaluated by testing 120 serum samples ranging from 0.002 to 189 µIU/mL TSH. Samples were tested on the prototype assay and the current VITROS® Immunodiagnostic Products TSH assay with an extended calibration range. Passing-Bablok regression was used to analyze the results.

Results: The prototype assay was determined to have LoB = 0.0005 µIU/mL, LoD = 0.0025 µIU/mL and LoQ (20 %CV) = 0.0031 µIU/mL with a time-to-result of 24 min. Analysis of the method comparison study generated a slope of 1.027 and y-intercept of 0.0019. Testing of the five precision pools (n=40) produced total imprecision ranging from 5.0 to 6.4 %CV.

Conclusion: The results demonstrate that the prototype TSH assay is accurate, precise and sensitive, while delivering assay results 40% faster.

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Endocrinology

Cod: T123

ANTI –TPO AND ANTI-TG ANTIBODIES IN AUTOIMMUNE THYROIDE DISEASES DIAGNOSIS

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Background: Irrespective of the recommendations of the use of serum TSH as a cornerstone of thyroid function testing, the laboratory diagnosis and monitoring of thyroid disease are based on the thyroid panel including anti-TPO and anti-TG, which are essential to manage thyroid diseases especially autoimmune thyroid diseases Graves' disease and Hashimoto's thyroiditis.
Methods: In this clinical study prospective assessment of the morning serum anti-TPO and anti-TG concentrations were performed in 50 subjects with Graves' disease and 50 with Hashimoto's thyroiditis and 40 healthy subjects. Serum concentrations of anti-TPO and anti-TG were determined by chemiluminescence immunoassay of CLIA methods analyzer Immulite 2000.
Results: Patients with Graves' disease and Hashimoto's thyroiditis showed significantly higher concentrations of anti-TPO and anti-TG compared with healthy individuals ($P < 0.001$).
Anti-TPO values in the control group were 3.7± 0.46 IU/ml and anti-TG values were 10±0.05 IU/ml, significantly lower ($P<0.001$) compared to anti-TPO values (238.5 ± 7.95 IU/ml) in Graves' disease and (333.3 ± 8.55 IU/ml) in Hashimoto's thyroiditis.
Anti-TG values in the control group were 10±0.55 IU/ml, significantly lower ($P<0.001$) compared to anti-TG values (42 ± 4.95IU/ml) in Graves' disease and (53.3 ± 0.55Ul/ml) in Hashimoto's thyroiditis.
Conclusion: Serum concentrations of anti-TPO and anti-TG respectively as organ specific autoantibodies are very precious parameters that enable precise and fast Graves' disease and Hashimoto's thyroiditis diagnosis.

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Endocrinology

Cod: T124

CALCULATION OF FREE ANDROGEN INDEX (FAI) USING REAGENTS KITS OFFERED BY DIFFERENT MANUFACTURERS

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BACKGROUND. Measurement of serum total testosterone (TTE) and free testosterone (fTE) in disorders of androgen metabolism of men and women might be useful. In most of laboratories fTE cannot be measured, therefore free androgen index (FAI) has been used instead for approximately 25 years. It is generally accepted that TTE should be measured on the same analytical platform along with SHBG. Under certain circumstances this could not be the case. We have experienced situation when serum level of TTE and SHBG was measured using two different commercial immunoassays: Architect i2000 2nd Generation TTE (Abbott Diagnostics, USA) and Immulite 2000 SHBG (Siemens Healthcare Diagnostics, Germany) for FAI calculation. Our aim was to evaluate possibility of calculation of FAI results in laboratory routine in such circumstances.
METHODS. We analysed 74 patients (55 female and 19 male in the age range 6-44 and 8-59 years respectively) admitted for the laboratory assessment of androgen status. Firstly, serum levels of TTE and SHBG were measured by chemiluminescent microparticle immunoassay (CMIA) on Architect ci8200 using two methods: Architect i2000 SHBG and Architect i2000 2nd Generation TTE. Secondly, serum level of SHBG was measured by chemiluminescent immunoassay (CIA) on Immulite 2000 using Immulite 2000 SHBG method. FAI were calculated in both groups by formula: TTE (nmol/l)/SHBG (nmol/l)x100%. Passing-Bablok regression analysis was used for method comparison.
RESULTS. Concentration ranges of SHBG by Architect i2000 SHBG and Immulite 2000 SHBG were 4.60-347.90 nmol/L (mean 58.57 nmol/L) and 5.28-346.0 nmol/L (mean 58.70 nmol/L) respectively. Passing-Bablok regression analysis between Architect i2000 SHBG and Immulite 2000 SHBG gave slope of 0.977 (95% CI:0.91-1.01) and intercept of 2.010 (95% CI:0.377-4.906), r=0.98. TTE was measured on Architect i2000 only. We calculated FAI-1 for Architect i2000 2nd Generation TTE and Architect i2000 SHBG and FAI-2 for Architect i2000 2nd Generation TTE and Immulite 2000 SHBG. Acceptable agreement between FAI-1 and FAI-2 has been found: regression analysis gave slope of 0.929 (95% CI:0.906-0.971) and intercept of 0.041(95% CI:-0.037-0.114). A statistically significant positive correlation (r=0.99) was found between both FAI groups.
CONCLUSIONS. Findings suggest that FAI can be calculated from results obtained using commercial immunoassays offered by different manufacturers: Architect i2000 2nd Generation TTE and Immulite 2000 SHBG.

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Endocrinology

Cod: T125

OXIDATIVE STRESS AND GLUCOCORTICOID RESISTANCE

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Backround: Glucocorticoids (GCs) are widely used as therapeutics in several diseases such as autoimmune, lung and central nervous system (CNS) diseases as well as in some types of cancer. However, many patients develop glucocorticoid resistance which impedes their response to therapy. Many studies demonstrate oxidative stress (OS) occurrence in the above diseases but its effect on the mechanism of GC-action and on GCs' therapeutic effect remains unknown.
Aim: The aim of this study is to investigate in vitro the effect of hydrogen peroxide (H_2O_2) and antioxidant compound α-tocotrienol (ATT) on the expression of GILZ (glucocorticoid-induced leucine zipper) and FKBP5 (FK506 binding protein 5), which are known primary Glucocorticoid Receptor (GR) target genes, with GR being the main mediator of GC-action.
Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from healthy blood donors and cultured in vitro with dexamethasone (Dex) (0.1, 1μM) in the presence or absence of H_2O_2 (10-200μM). The antioxidant effect of ATT (50-200μM) was studied by pre-incubating PBMCs with this compound for 1 and 2h, followed by the addition of H_2O_2 (100μM) and Dex (1 μM). Total RNA was isolated and cDNA was synthesized. The GILZ and FKBP5 mRNA levels were quantitated by Real-Time PCR. Cell-permeant probe H_2DCF-DA (dichlorofluorescein diacetate) was used to evaluate cellular OS by Flow Cytometry.
Results: The presence of Dex increased the GILZ and FKBP5 mRNA levels, as expected. The presence of H_2O_2 decreased significantly the Dex-induced expression of GILZ and FKBP5 genes in a dose-dependent manner. The presence of ATT inhibited the diminishing effect of H_2O_2 on GILZ and FKBP5 mRNA levels and restored the Dex-induced expression of these genes. Flow Cytometry analysis showed that H_2O_2 increased significantly the cellular OS levels, implicating its suitability as OS inducer, while ATT reduced the OS as expected.
Conclusions: The presence of H_2O_2-induced OS on PBMCs inhibits the expression of GC-dependent genes whereas the addition of antioxidants reverses the H_2O_2-induced inhibition of GC-GR signaling. Our findings support that OS interferes with the mechanism of action of GCs and imply that it may play an important role in the resistance to GCs.

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Endocrinology

Cod: T126

CASE STUDY: MACRO TSH IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background:Immunassay methods are widely used, just because of having good sensitivity and specifities. However, they have also limitations. TSH (Thyroid Stimulating Hormone) is typically measured by a two site-immunassay, and interference from other endogenous antibodies is an ongoing problem. There have been reports of macro-TSH that enables decreasing of clearance leads to accumulation of molecules, falsely increasing the TSH level. RF(Rheumatoid Factor) interference resembles the similar mechanism as interference from other types of antibodies.We report cases with spuriously elevated TSH levels which are discordant with their clinical condition.
Methods:We used the Access DXI (Beckman Coulter) for the measurement of thyroid function tests (TFTs) based on CLIA (Chemiluminescence Immunassay).Measurements of TFTs were repeated in two different analytical platforms, CLIA (Advia Centaur XP, Siemens) and ECLIA (Electrochemiluminescence Immunassay) (Cobas, Roche Diagnostics). We evaluated the RF values of the patients in AU580 Beckman Coulter autoanalyzer.
Results:Patient A, Patient B, Patient C, Patient D applied to the endocrinology clinic of Ankara Numune Training and Research Hospital between March-April 2016. TFTs of the patients are listed; Patient A: high TSH (24.63 μIU/mL; normal reference interval (NRI: 0.5-5.5 μIU/mL), high fT4 (1.63 ng/dl; NRI: 0.61-1.12 ng/dl), , Patient B: high TSH (71.62 μIU/mL) normal fT4(0.66 ng/dl), Patient C: high TSH (54.19 μIU/mL), slightly high fT4 (1.16 ng/dl), Patient D: high TSH (87.97μIU/mL), low fT4(0.37 ng/dl). After the initial evaluation, endocrinologists are suspected of macro-TSH in these patients, than we further evaluated samples by PEG(Polyethilene Glycol) precipitation and repeated the measurement on different anaylzers, normal TFT's were observed. We also retrospectively investigated the medical history of patients and we observed that all of four patients had diagnosed rheumatoid artritis. Following this, we detected the high level of RFs;26,34,53 ,76 IU/ml (0-14 IU/mL). As a conclusion, we believe that high TSH values may due to RFs.
Discussion:: Macro TSH is an interference could lead clinicians to misdiagnose the patient. Spurious elevation of TSH should be considered and further investigated with serial dilution, repeating the measurement of TSH on an alternative platform, heteropgile blocking tube and measure rheumatoid factors, if possible.

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Endocrinology

Cod: T127

CORRELATION OF ENDOCRINE AND EXOCRINE PANCREATIC FUNCTIONS IN DIABETES MELLITUS TYPE 2 PATIENTS: THE EFFECT OF GLP-1 RECEPTOR AGONIST AND DPP-4 INHIBITOR TREATMENT

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Background: A strong positive correlation between pancreatic endocrine and exocrine function has previously been described in chronic pancreatitis. Here, we examined this correlation in diabetes mellitus type 2 patients treated with recently introduced incretin-based therapies including the GLP-1 receptor agonist exenatide and the DPP-4 inhibitor linagliptin.
Methods: The study group included 39 subjects with type 2 diabetes mellitus treated with metformin and randomized to 3 months of treatment with exenatide, linagliptin or the sulphonylurea derivate gliclazid MR as active comparator. Laboratory markers of endocrine (fasting blood glucose, C-peptide, HbA_{1c}) and exocrine function (faecal elastase-1 - FELA and ^{13}C-mixed triglyceride breath test - ^{13}C-MTG) were evaluated before and after 3 months of therapy. The results were statistically analysed by t-tests and paired correlations (and by one-sample Wilcoxon tests or Spearman rank correlations, alternatively) using SPSS software.
Results: In the whole group a significant correlation of ^{13}C-MTG test with C-peptide (Spearman's $r = -0.323$; $p = 0.048$) and HbA_{1c} ($r = -0.397$; $p = 0.008$) was found, while no correlation could be seen for FELA. HbA_{1c} was significantly reduced by all three types of therapy ($p = 0.019$; $p = 0.025$ and $p = 0.003$ for exenatide, linagliptin and gliclazid MR, respectively), whereas no parameter of pancreatic exocrine function was changed by any of the antidiabetic drugs. After treatment, the only endocrine-exocrine correlation to remain preserved was the association between HbA_{1c} and ^{13}C-MTG test ($p=0,014$) in the linagliptin group.
Conclusions: A correlation between endocrine and exocrine pancreatic function as measured by HbA_{1c}, C-peptide and ^{13}C-MTG test was detected in type 2 diabetic subjects on metformin monotherapy. This endocrine-exocrine correlation was preserved only by DPP-4 inhibitor treatment.
Supported By: European Commission Seventh Framework Programme (SAFEGUARD – Safety Evaluation of Adverse Reactions in Diabetes), RVOVFN64165, AZV 15-26854A, AZV 15-27863A, SVV260019/2014.

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Endocrinology

Cod: T128

COMPARISON OF TWO 3RD GENERATION TSH ASSAYS BY BECKMAN COULTER

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BACKGROUND: TSH is produced by the pituitary gland and its main effect is releasing T3 and T4 and by that controlling metabolic functions within the cells. Determination of TSH levels is the first step in assessing the overall thyroid function. Also, TSH is regularly monitored in patients diagnosed with thyroid dysfunction who are using replacement drug therapy. Mainly because of this reason TSH should be measured using comparable assays and methods.
The 3rd generation TSH assays with functional sensitivity 0,01-0,02 µIU/L were first introduced in 2003 (3rd IRP 81/565). In January 2016 Beckman Coulter announced the release of the new Access TSH (3rd) assay to replace Access Hypersensitive hTSH and FastTSH assays. Purpose of this study was to determine if the results obtained with these two assays were comparable.
METHODS: Samples of 39 patients (n=39) were obtained using standard venipuncture procedures and centrifuged at 4000 rpm for 10 minutes. TSH levels were measured simultaneously using Access HYPERsensitive hTSH reagent (Lot 534301) and Access TSH (3rd IS) (Lot 623183) on Beckman Coulter UniCel DxI 600 analyzer.
RESULTS: Results of the two TSH assays were compared using Passing and Bablock regression with significance level alpha=0,05. The computed p-value was p=0,821 which shows that the relationship between the two methods is linear.
CONCLUSION: From the results obtained by this study it is seen that THS levels measured with Access HYPERsensitive hTSH and Access TSH (3rd) are comparable and there is no drawback in interpretation of the patients results obtained using HYPERsensitive hTSH in the past with TSH (3rd) results obtained in the future.

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Endocrinology

Cod: T129

PREANALYTICAL HANDLING IN ACTIVE PLASMA RENIN CONCENTRATION MEASUREMENT

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Background: Renin, a member of Renin-Angiotensin-Aldosterone System, is constitutively produced as an inactive precursor prorenin. It is well known that cryoactivation of prorenin may occur in low temperature range (2–8°C), giving false positive active plasma renin concentration (PRC). Thus, it is recommended to rapidly freeze and thaw samples avoiding low temperature.
The aim of this study was to compare two preanalytical procedures in active PRC measurement in thawed plasma specimens.

Methods: 30 EDTA plasma samples, with PRC ranging from 0.8 to 128 ng/mL were split into two aliquots, rapidly frozen and stored (20 days, -25°C). Split aliquots were processed on the same day by either rapidly thawing (37 °C, water bath) or left to thaw at the room temperature (RT, 25 °C) prior the analysis. PRC was determined on the same microplate with DRG Renin ELISA enzyme immunoassay (intra-assay CV = 4.5%). PRCs obtained by the two preanalytical procedures were compared by Bland and Altman analysis. The concordance between the two storage procedures was checked by inter-rater agreement (kappa).

Results: Bland and Altman plot revealed an average positive bias of 11.9% (95% CI: 7.1-16.7) in RT-thawed aliquots compared to PRC in rapidly thawed aliquots. However, a very good agreement between the two preanalytical procedures in classifying patients as low, normal or high, according to the reference interval was observed (weighted kappa = 0.919).

Conclusion: Despite a mild positive bias, thawing frozen plasma samples at room temperature is not-inferior to water-bath thawing procedure for active plasma renin concentration measurement, in providing clinically reliable information.

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Endocrinology

Cod: T130

LIPASE ASSAY FOR THERMO SCIENTIFIC INDIKO AND INDIKO PLUS CLINICAL CHEMISTRY ANALYZERS

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Background: Determination of lipase is used for investigation of pancreatic disorders. In acute pancreatitis the lipase concentrations rise to 2-50 fold the upper reference limit within 4-8 hours after beginning of abdominal pain peaking at 24 hours and decreasing within 8 to 14 days. Elevated lipase values can also be observed in chronic pancreatitis and obstruction of the pancreatic duct.
Thermo Scientific™ Indiko™ analyzers, Indiko and Indiko Plus, are bench top clinical chemistry analyzers, especially suitable for small and medium sized laboratories or as a back-up for bigger laboratories. They are applicable for colorimetric and turbidimetric assays as well for electrolytes employing ISE technology. The Indiko analyzers are user-friendly complete systems including the instrument, system reagents, calibrators and controls as well the CE marked applications.
Methods: Enzymatic color test. A synthetically produced lipase substrate (1,2-o-dilauryl-rac-glycero-3-glutaric acid-(6-methylresorufin) ester) is added to a micro emulsion which is specifically split by lipase in the presence of colipase and bile acids. The combination of colipase and bile acids makes this specific and reliable for pancreatic lipase without any reaction due to lipolytic enzymes or esterases. The reagent composition has been thoroughly optimised so there are no serum matrix effects. The generated methylresorufin-ester is spontaneously degraded to methylresorufin. The absorbance at 575 nm by this red dye is directly proportional to the lipase activity in the sample.
Results: The assay measuring range is 16-300 U/l extended with automatic dilution up to 1500 U/l. The repeatability (within-run precision) is 1.0-1.3 % (CV; N=84) and the within device (total) precision is 2.4-4.0% (CV; N=84).
A comparison study was performed by the Konelab PRIME 60i Lipase method as a reference. Linear regression was $y = 0.96x + 5.1$ and $r = 0.997$ (N=77).
Conclusion: The results demonstrate that Lipase can be analyzed reliably and easily using Indiko clinical chemistry analyzers.

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Endocrinology

Cod: T131

NEW DIRECT BILIRUBIN ASSAY FOR THERMO SCIENTIFIC INDIKO AND KONELAB CLINICAL CHEMISTRY ANALYZERS

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Background: Total bilirubin in serum is composed of three fractions: unconjugated bilirubin, which is extremely apolar and practically insoluble in water at physiologic pH and body temperature; conjugated bilirubin, bound to sugar, is water soluble and δ-bilirubin, which is covalently bound to albumin.
A number of inherited and acquired diseases affect one or more of the steps involved in the production, uptake, storage, metabolism and excretion of bilirubin. Depending on the disorder, unconjugated bilirubin, conjugated bilirubin or both, are major contributors to hyperbilirubinemia.
Thermo Scientific™ Indiko™ and Konelab™ used in this study are random access, fully automated, clinical chemistry analyzers (Indiko, Indiko Plus, Konelab 20, 20XT PRIME 30, PRIME 60). Colorimetric, turbidimetric and ISE methods are well applied and CE marked. All these analyzers are complete easy-to-use systems including the instrument, system reagents, calibrators and controls.
Methods: Direct Bilirubin is a two part liquid assay applied on Indiko and Konelab clinical chemistry analyzers. Direct bilirubin in presence of diazotized 2,4-dichloroaniline (DCA) forms a red colored azo compound in acidic solution. The absorbance at 540 nm is directly proportional to the direct bilirubin concentration in the sample.
Results: The assay measuring range is 2-170 µmol/l extended with automatic dilution up to 1190 µmol/l. The repeatability (within-run precision) is 0.4–1.2 % (CV; n=80). The within device (total) precision is 2.5–4.6 % (CV; n=80). Open on-board stability is 30 days and calibration interval 14 days.
Conclusion: With this ready-to-use system reagent, direct bilirubin analysis on Indiko and Konelab analyzers is quick and accurate with excellent open on-board stability.

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Endocrinology

Cod: T132

FALSELY ELEVATED SERUM ESTRADIOL LEVELS ASSESSED ON ELECTROCHEMILUMINESCENT ASSAY IN TWO PREPUBERTAL GIRLS

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Introduction: Estradiol (E2) immunoassays ideally require solvent extraction or chromatography to avoid interference from steroid cross-reactivity and matrix effects leading to spurious results and unnecessary additional tests. Direct E2 immunoassays are proned to these interferents.
Aim: to report 2 patients with unexpected high E2 levels measured by Estradiol II electrochemiluminescent immunoassay (Cobas 6000, Roche Diagnostics International Ltd).
Patients: Case1: a 9-yr prepubertal girl evaluated due to mild short stature presented high E2 levels in two distinct serum samples (78 and 62 pg/ml) besides prepubertal gonadotropin levels, normal bone age and normal pelvic ultrasound. Case 2: a 7-yr girl with central precocious puberty under GnRH analogue therapy (Leuprolide acetate) presenting clinical regression of pubertal signs, supressed gonadotropin levels, prepubertal ovarian size with very high E2 levels in distinct serum samples (ranging from 86 to 293 pg/ml).
Methods and results: Samples from these two patients were considered inadequate for their clinical condition when measured on direct estradiol II immunoassay (normal prepubertal range - up to 28 pg/mL). To rule out matrix effects, serum samples were subbmited to a previous extration with ethyl ether followed by E2 remeasurement. Extraction decreased E2 levels to prepubertal range in both patients (E2 < 15 pg/mL). One serum sample from case 1 was also assessed on another direct immunochemiluminometric assay (ICMA, E2 estradiol, VITROS ECi analyzer, Ortho-Clinical Diagnostics). Interestingly, E2 levels obtained on ICMA was concordant with the pos-extraction ECLIA result.
Conclusion: Falsely high E2 levels on direct ECLIA is a uncommon event, but with important clinical implication. Its recognition requires constant surveillance by both laboratory and physician. The detection of interference may require the use of an alternate assay or additional measurements pos ethyl ether extration. Finally, pos extraction E2 ECLIA can represent a simple, practicable and inexpensive method to eliminate interfence.

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Endocrinology

Cod: T133

REFERENCE INTERVAL DETERMINATION FOR SERUM AND URINE ALDOSTERONE FOR HEALTHY BELGIAN POPULATION

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Background: Aldosterone measurement is critical for the screening and diagnosis of primary aldosteronism and other disorders of the renin-angiotensin system. Liquid chromatography coupled to triple quadrupole mass spectrometry (LC-MS/MS) has become an essential tool for small molecule quantitation. We have switched from the RIA to LC-MS/MS. Change the method used in the lab means new reference range. So we present a reference interval study for both urine and plasma aldosterone for a healthy Belgian population determined by LC-MS/MS.

Methods: For the reference interval study, we enrolled 224 healthy Caucasian volunteers (98M: mean age 35 ± 11 y and 126 F: mean age 43 ± 12 y).A subset of 95 healthy volunteers agreed to collect a 24h urine. Exclusion criteria were: prescription of any medications (including oral contraceptives), history of hypertension, abnormal plasma sodium and body mass index (BMI) >30 kg/m². We measured urine sodium concentration on a Cobas c501 (Roche Diagnostic, Manheim, Germany) and calculated daily excretion of NaCl using: the following formula: ExcNaCl = 58×V24h ×[Na], where ExcNaCl is the 24h urine excretion of NaCl in mg/d.
Reference range determination was performed with Medcalc software with the robust method according the CLSI C28-A3.

Results: The distribution was not normal in our reference population for urine, the 95th percentile was 24.6 (90%CI: 21.6-27.6) µg/d. Mean sodium intake was 8.9 ± 3.2 g/24 hours and was not significantly different (p=0.27) in men and women. Plasma aldosterone concentrations were not normally distributed for women but well for men. We found a significant difference between levels according to gender ($p<0.0001$); the 95th percentile was 175(90%CI: 160.2-189.5) ng/L for women and 104(90%CI:92.2-114.5) ng/L for men.

Conclusions: We have provided reference intervals on a well-characterized population of normotensive healthy young subjects free of interfering medications. Finally, we urge the Clinical Chemistry community to develop an international standard reference material for aldosterone and a candidate reference method for LC-MS/MS. Once this standard is available, new studies for ARR cut-offs will be required in order to better screen the patients at risk of PA.

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Endocrinology

Cod: T134

VALIDATION OF SERUM ANDROSTANEDIOL GLUCURONIDE BY LC-MS/MS

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Background: Plasma androstanediol-glucuronide (ADG) is considered to be a highly marker of peripheral androgenicity. The quantification of steroidal glucuronide conjugates by immunoassays may underestimate some conjugates since hydrolysis is needed in sample processing. To overcome these limitations, we have validated a LC-MS/MS method for ADG determination in plasma and serum and to compare it with our previously employed ELISA.

Methods: We used a HPLC system AD20XR Shimazu connected to triple quadrupole mass spectrometer TQ5500 (SCIEX, Framingham, Massachusetts, USA). 3 water and serum samples depleted in steroids were spiked with a known concentration (0.2, 1 and 5 ng/mL) of ADG; these samples were run on 3 different (n=3) days to evaluate within and between-run CV. With those samples, we evaluated also recovery and matrix effects. Linearity of the calibration curves(0.1, 0.5, 1, 5, 10 ng/mL) for serum was assessed by performing linear regression. The limit of detection (LOD) and limit of quantification (LOQ) were calculated with the lowest concentration that we tested. LOD and LOQ were respectively defined as 3:1 and 10:1 signal/noise ratio respectively. The e-noval software (Arlenda, Belgium) was used to perform the statistical calculations.

Results: The detection mode was MRM in negative mode. The intra-run precision (CV) was 2.5-6.3% and between-run precision (CV) was 4.7-7.4%. Recoveries were: into natural matrix (95%CI: 94.3-107.5) and water (95%CI: 101.2-111).Within the calibration ranges, the linear regression model is fitted ,the equation was: Y=0.03078+0.9867X. The LOD was 0.018 (+/-0.002) µg/L (n = 5) and the LOQ at 0.059(+/-0.006) µg/L (n = 5).For the comparison between LC-MS/MS(X) and ELISA(Y), the Passing-Bablok test gave the following regression equation: Y=1.14+1.31X. The average median was 2.57 µg/L (95% CI: 1.18-6.3) for LC-MS/MS and 4.33 µg/L (95% CI: 2.53-10.3) for ELISA. Between the serum (X) and plasma (Y) in LC-MS/MS, the regression equation was: Y=0.09+0.92X, the median average was 2.57 µg/L (95% CI: 1.18-6.3) in serum compared with a median average of 2.46 µg/L (95%CI:1.21-6.3) in plasma.

Conclusions: We have validated the method by LC-MS/MS. We noted a significant bias between ELISA and LC-MS/MS. Finally, we urge the Clinical Chemistry community to develop an international standard reference material for steroids and a candidate reference method for LC-MS/MS.

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Endocrinology

Cod: T135

VALIDATION OF A 13 STEROIDS PANEL WITH THE CHROMSYSTEM KIT BY LC-MS/MS.

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Background: It is important for clinicians to obtain an accurate and precise dosage of steroid hormones. For this purpose, liquid chromatography triple quadrupole mass spectrometry (LC-MS/MS) has become an essential tool for small molecule quantification due to its high sensitivity, specificity, excellent reproducibility and the ability to perform simultaneous analysis. The aim of our work was the validation of the MassChrom® for Steroids in Serum/Plasma kit by LC-MS/MS (Chromsystems). This method comprises the detection and quantification of aldosterone(ALDO), cortisol(COR), cortisone, cortsicosterone, 11-deoxycortisol(S), androstenedione,(AND), dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate(DHEAS), dihydrotestosterone(DHT), estradiol (E2), 17 α-hydroxyprogesterone (HYP), progesterone and testosterone(TST) as total steroids.

Method : Until now Radio-Immunoassays(RIA) or ELISA were used for the determination of some of the mentioned compounds. Validation of the new methodology has been carried out using an Sciex QTrap6500 MS/MS(Framingham, MA, USA) equipped with LC-30A Nexera UHPLC system (Shimadzu Co., Kyoto, Japan).The 13 steroids were separated in 2 panels.
For sample preparation, to 500 µl serum/QC/calibrator both Internal standard Mix and Extraction buffer were added before performing an extraction in a 96-well solid phase extraction(SPE) plate. The procedure was validated by testing 3 levels in triplicate during 3 different days. Statistical analysis was performed using the Enoval validation software (Arlenda, Mariakerke, Belgium).

Results: The evaluation of the mentioned kit was carried out at the following concentrations (µg/L) for each steroid. Panel 1: ALDO(0.025-3.08), cortisol(10.2-288), cortisone(1.03-38.9),corticosterone (0.52-48.2) and S (0.09-13.9). Panel 2: AND(0.18-14), DHEA(0.97-55.9), DHEAS(105-5975), DHT(0.06-1.34), E2(0.04-4.94), HYP (0.1-15.1),progesterone (0.17-25.6) and TST(0.05-11.8).
The mean recoveries values did not differ significantly from 100% while the precision, as CV%, was below 10% for both the intraday and interday variability except for corticosterone(11%).The developed method was shown to be linear (R2>0.99) for all steroids in serum. The limit of detection(LOD) and limit of quantification(LOQ) were calculated with the lowest concentration tested.

Conclusions: The method based on LC-MS/MS using the MassChrom® Kit has been satisfactory validated and meets the requirements to be applied in routine.

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Endocrinology

Cod: T136

ESTABLISHMENT OF REFERENCE VALUES FOR SIX STEROIDS IN SERUM BY LC-MS/MS

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Background: Steroid hormones play a crucial role in controlling metabolism, immune functions and inflammation. Modifications in steroid profiling reflect disease status and help research into a wide number of health disorders, including congenital adrenal hyperplasia, Cushing's disease and polycystic ovarian disease. However, the quantification of steroids by immunoassays may underestimate some of them. To overcome these limitations, we obtained the new reference range values with an LC-MS/MS method based on the MassChrom® kit . In the present work a reference interval for serum androstenedione, corticosterone, cortisone, cortisol, aldosetrone and 11-desoxycortisol for a healthy Belgian population is presented.

Methods: For the serum reference interval study, recruited participants were normotensive (clinical blood pressure <140/90 mmHg), without antihypertensive or corticosteroid treatment, non-smokers and did not take any oral contraception. All participants gave informed consent and were fasting. We enrolled 55 healthy Caucasian volunteers (36 F: mean age 43.6 ± 11.7 yo and 20 M: mean age 38 ± 13 yo) .Blood samples were centrifuged immediately after the draw (morning) for 10 minutes at 2500 g, aliquoted and stored frozen at -80°C before further analysis. Study was approved by ethic committee of the university in Liege. The analysis was performed with the MassChrom® kit from Chromsystems (Heimburgstrasse, Munich, Germany) using panel 1 for corticosterone, cortisone, cortisol, aldosterone and 11-desoxycortisoland, the panel 2 was used for androstenedione on a QTrap 6500 (Sciex,Framingham, Massachussets, USA). Statistical analysis was performed using Medcalc (Mariakerke, Belgium) software.

Results: No difference for the gender was observed for these 6 steroids. The reference values were obtained with a robust and validated method, being 0.17-1.38 µg/L for androstenedione, <9.85µg/L for corticosterone, 16.5-28.82 µg/L for cortisone, 30.48-230.98 µg/L for the cortisol, <156 ng/L for aldosterone and <0.44 µg/L for 11-desoxycortisol.

Conclusions: We established new reference intervals in LC-MS/MS for 6 steroids in serum. A low number of volunteers limit the validity of our study results. However, we will continue the recruiting to obtain a larger number of reference values to be in line with CLSI recommendations.

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Endocrinology

Cod: T137

ANALYTICAL PERFORMANCE OF LC-MS/MS METHOD FOR SIMULTANEOUS DETERMINATION OF URINARY CORTISOL AND CORTISONE

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Introduction: Free urinary determination is a useful screening test for Cushing´s syndrome diagnosis. Most methods for cortisol measurement are based on immunoassays, which are rapid and easy, but lack specificity. LC–MS/MS is an increasingly common tool in the clinical laboratory and has the potential to overcome the immunoassays limitations. Aim: Our aim was to develop and validated a LC-MS/MS method for simultaneous measurement of cortisol and cortisone in 24h urine sample. Methods: First step consists in addition of 50 uL isotopic internal standards in 200 uL of the urinary sample. Subsequently, the samples were submitted to bi-dimensional liquid chromatography, consisting of trapping column and reverse-phase C18 analytical column with a total run time of 1.8 minutes. A Xevo TQS (Waters) tandem mass spectrometer equipped with atmospheric pressure chemical ionization source was used as detector and was operated in the positive ion mode. We evaluated the sensitivity, the precision, the presence of carry-over, the recovery, the linearity and the accuracy of this method. Results: Analytical sensitivity was 0.16 ug/dL for cortisol and 0.26 ug/dL for cortisone.: Functional sensitivity was 0.50 ug/dL, intra-assay and inter-assay coefficient of variation were less than 15%, carry-over was not detected, recovery ranged from 98% to 117%, linearity ranged from 95% to 119% and high accuracy (97% to 104%) were obtained for both cortisol and cortisone measurements. Conclusion: We standardized a fast and suitable simultaneous method for routine measurement of urinary cortisol and cortisone.

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Endocrinology

Cod: T138

FREE TESTOSTERONE – ULTRAFILTRATION VS CALCULATED RESULTS

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Background
Testosterone circulates in the bloodstream as protein-bound and free form. Only the free testosterone (fT) is thought to be the biologically active component. Several mathematical calculations are routinely used for its assessment, because a reference method is time-consuming and unsuitable for routine. Previously, comparing the two published algorithms for calculating fT, we obtained results disagreement only among men population. The purpose of this study was to compare calculated fT results with those measured using centrifugal ultrafiltration method.
Methods
As a part of the hormonal status evaluation we analyzed fT in 20 males (mean age 35 years). Serum samples were collected according to a standard operating procedure using a blood activator tubes (Becton-Dickinson, Eysins, Switzerland). Testosterone and sex hormone-binding globulin were measured using chemiluminiscent microparticle immunoassay on ARCHITECT i1000SR (Abbott Diagnostics, Lake Forest, IL, USA), while albumin was determined using the Beckman Coulter AU480 (Beckman Coulter Inc., Brea, CA, USA) analyzer. For calculating fT two different published algorithms (Vermeulen eta al. and Ly et al.) were used, whereupon results were compared with concentrations obtained after centrifugal ultrafiltration using Centrifree ultrafiltration devices (EMD Millipore Corporation, Billerica, MA, USA) according to the manufacturer protocol. Statistical analysis was conducted by MedCalc for Windows, version 12.4.0 (MedCalc Software, Mariakerke, Belgium).
Results
There was statistically significant difference in fT median values obtained by different approaches (Kruskal-Wallis test: 0.230 nmol/L after ultrafiltration vs calculated fT 0.740 nmol/L and 0.505 nmol/L; $P<0.001$). However, a very strong correlation between fT values measured after centrifugal ultrafiltration and those obtained by one of the used mathematical algorithm was achieved ($r=0.896$, $P<0.001$).
Conclusion
Results demonstrated that used algorithms are in strong disagreement with the method of centrifugal ultrafiltration for determination of fT. Since centrifugal ultrafiltration procedure is relatively simple and available, it could be a good choice for accurate measurement of fT.

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Endocrinology

Cod: T139

SOYBEAN ISOFLAVONES ELEVATE SERUM ESTRADIOL BUT DO NOT AFFECT CHOLESTEROL CONCENTRATION IN ACYCLIC FEMALE RATS

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BACKGROUND: Soybean isoflavones genistein (G) and daidzein (D) are natural selective modulators of estrogen receptors, which may exert estrogenic or antiestrogenic biological actions, depending on their concentration and the concentration of endogenous estrogen within the targeted tissue. Isoflavones may improve menopausal symptoms, such as hot flashes. In this study we tested if isoflavones may affect weight gain, concentration of estradiol and cholesterol in serum of middle-aged acyclic female rats.
METHODS: Middle-aged (MA; 12-13-month-old) female rats in constant diestrus were used for this study. Two weeks prior the experiments the animals were put on a semi-purified soy-free diet. First group was subcutaneously injected with 35 mg/kg b.w. of genistein (MA+G) and the second with 35 mg/kg b.w. of daidzein (MA+D), every day for 4 weeks. The control group (MA+V) received vehicle only (mixture of sterile olive oil and absolute ethanol, ratio 9:1) under the same regime. After decapitation, blood was collected from the trunk of each animal and allowed to clot by leaving it at room temperature in glass tubes (without any coagulant) for at least 30 minutes. The clot was removed by centrifuging, and the supernatant further used. Serum estradiol and cholesterol were determined from each animal (n=6 for each group) by ECLIA in case of estradiol, and CHOD- PAP colorimetric assay, in case of total cholesterol measurment.
RESULTS: The average body mass of MA female rats was 311 ± 26g, and soflavone treatments did not affect this parameter. However, serum estradiol concentrations were elevated after isoflavone treatments: in comparison with the value obtained for control group (147 ± 36pM), estradiol was 32% ($p<0.05$) and 98% ($p<0.05$) higher in MA+G and MA+D group, respectively. Mean serum total cholesterol concentration was 96.2 ± 11.6mg/dl for MA+V group, and this value was not changed significantly in isoflavone -treated animals.
CONCLUSIONS: Genistein and daidzein elevated serum estradiol concentration in middle-aged acyclic female rats, D being being more effective than G. However, the isoflavone treatments did not induce weight loss, or cholesterol-lowering effect in our model.

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Endocrinology

Cod: T140

RELATION BETWEEN OSTEOCALCIN AND THE ENERGY METABOLISM

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BACKGROUND: Numerous previous findings have indicated the potential relation between the osteocalcin, well known as the traditional parameter of bone turnover, and the regulation of energy metabolism. The aim of this study was to identify the intensity of the relationship between osteocalcin levels and calculated indexes, which evaluate insulin sensitivity, insulin resistance and/or secretory capacity of the pancreas, in euglycemic, obese subjects.
METHODS: The study included 57 (11 men and 46 women) euglycemic, obese patients (BMI=41.03±6.61 kg/m²). The control group consisted of 48 healthy individulals, age and sex matched (BMI=23,15 ± 2,04 kg/m²). Blood was drawn to all subjects in order to determine glucose and insulin levels (0 and 120. minute of OGT testing) and calculate HOMA indexes (HOMA-IR, HOMA-B%, HOMA-S%), as well as EISI (estimated insulin sensitivity index), EFP (estimated first phase) and ESP (estimated second phase). The level of osteocalcin was measured on system Cobas e 411. The results were analyzed by statistical package of Data Analysis.
RESULTS: Compared to control, the obese do not differ in the glucose levels (0. and 120. minute of OGTT) (p=0.238;p=0.172). Statistically lower osteocalcin levels were found in examined group (24.72±9.8 vs 33.31±10.89 ng/mL;p<0.01). There was a statistically significant degree of positive correlation between osteocalcin and EISI (r=0,340;p<0,01). The inverse correlation was found between the levels of osteocalcin and HOMA-IR (r=-0.276; p<0.01), as well as HOMA-B% (r=-0.337;p <0.01), EFP (r = -0.332; p <0.01) and ESP (r=-0.266;p <0.01). Multiple regression analysis showed that both, obesity (BMI) and osteocalcin have a significant inverse prediction with EISI and HOMA-IR, but the level of prediction of BMI is substantially higher compared to the osteocalcin.
CONCLUSIONS: The effect of osteocalcin in the glycolregulation is evident, but its contribution is significantly smaller in relation to primarily considerable factors associated with the obesity. Therefore, when assessing the position and the role of osteocalcin in glycemic control, must always bear in mind that osteocalcin represents only one of the many contributing factors, some of which often exhibit more dominant influence then osteocalcin itself.

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Endocrinology

Cod: T141

PERFORMANCE EVALUATION OF THE ADVIA CENTAUR ANDROSTENEDIONE ASSAY*

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BACKGROUND
Androstenedione is a 19-carbon steroid that serves as a precursor for testosterone and estrone. It is most commonly used in conjunction with other steroid assays to evaluate the function of the adrenal glands and ovaries or testes and to determine the cause of symptoms of androgen excess.

A new ADVIA Centaur® Androstenedione (ANDRO) assay for the measurement of androstenedione in human serum and plasma is being developed by Siemens Healthineers. The studies below describe preliminary performance of the assay on the ADVIA Centaur® Immunoassay System.

METHODS
The ADVIA Centaur ANDRO assay is a fully automated competitive immunoassay using direct chemiluminescent technology. Reagents include a biotinylated sheep monoclonal antibody coupled to streptavidin-coated paramagnetic particles in the solid phase and a newly developed acridinium ester in the Lite reagent. The assay requires 20 µL of patient sample or calibrator, which is incubated with solid phase and Lite reagent. Competition for solid phase binding occurs between androstenedione in the sample and the Lite reagent. Separation follows, and the amount of signal generated is inversely proportional to the concentration of androstenedione in the sample. The time to first result is 18 minutes.

RESULTS
LoQ studies and linearity evaluation of the ADVIA Centaur ANDRO assay demonstrated an assay range of 0.30 to 10.00 ng/mL; with automated dilution, the measuring interval was extended to 50.00 ng/mL. The assay correlated well with LC-MS/MS, and equivalent performance was obtained using serum, lithium heparin, and EDTA plasma tube types. The assay showed <10% interference for all interferents tested and <1% cross-reactivity for all endogenous and most exogenous cross-reactants evaluated. Within-lab precision was <9% CV (with 95% confidence) across the assay range. Stability data demonstrated a calibration interval and onboard stability of 20 days and 16 days, respectively.

CONCLUSIONS
The ADVIA Centaur ANDRO assay demonstrates good precision and close correlation to LC-MS/MS.

*Information about this device is preliminary. Safety and effectiveness for the uses discussed have not been established. The device is under development and not commercially available. Future availability cannot be ensured.

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Endocrinology

Cod: T142

IS NAFLD A GOOD PREDICTOR OF CARDIOVASCULAR RISK IN WOMEN WITH PCOS?

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Introduction: Dyslipidemia, obesity and diabetes are potent cardiovascular risk factors that tend to cluster in women with PCOS. Non-alcoholic fatty liver disease (NAFLD) is one of the additional risks for cardiovascular disease development in PCOS women. The aim of this study was to estimate that additional cardiovascular risk (CVR) using several NAFLD indexes (APRI, LAP and HIS) and the index of central obesity (ICO) and to compare these indexes ability to predict CVR in women with PCOS.

Methods: Study included 54 women, aged 18 to 40 years, with proven PCOS (32 lean, BMI <25 kg/m², 22 overweight or obese, BMI >25 kg/m²) and 46 healthy control. Cardiovascular Risk Score (CVRS) was calculated by adding the points for each risk factor (BMI, low HDL-c, high non-HDL-c, smoking, blood pressure and fasting glycemia). We have calculated several NAFLD indexes: the aspartat aminotransferase (AST)/platelet ratio (APRI) index, lipid accumulation product (LAP) and hepatic steatosis index (HIS) and ICO. In order to compare the ability of these indexes to predict CVR in women with PCOS, we performed ROC analysis.

Results: We found significantly higher CVRS values in obese PCOS compared to both lean groups (PCOS and control, $p<0.05$ respectively). HIS and LAP indexes were significantly higher in obese PCOS women compared to other subgroups, and at the same time lean PCOS and lean control didn't differ regarding these two NAFLD indexes. Study subgroups didn't differ regarding the APRI index. All NAFLD related parameters showed significant positive correlation with CVRS (HIS 0.427($P<0.001$), APRI 0,278 ($P<0.01$), LAP 0.566 ($P<0.001$)). ROC curve showed a satisfactory ability of NAFLD indexes and ICO to predict CVR (AUC LAP= 0.776; HIS, APRI =0.757; ICO=0.751). Model 1 (consisting of integrated LAP, HIS, APRI and ICO values) presented the best diagostic accuracy in discriminating patients with high CVRS (AUC > 0.8 which is excellent diagnostic accuracy).

Conclusions: Results of this investigation showed that CVR in PCOS women is related to their obesity status. NAFLD is real, additional CVR factor in this population and combination of NAFLD indexes and ICO showed satisfactory ability to predict that risk.

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Endocrinology

Cod: T143

EVALUATION OF STEROID SEX HORMONES IN LOW CONCENTRATION SERUM SAMPLES BY LUMIPULSE G IMMUNOASSAY: COMPARISON WITH IMMULITE AND REPRODUCIBILITY

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Background: The assessment of Estradiol (E2), testosterone (T) and progesterone (P4) in low concentrations is not easily available, primarily because the widespread used technique in the clinical laboratory are immunoassay-based methods, which are insufficiently accurate, specific, sensitive, or reproducible[1,2]. However, accurate low serum concentration sex steroid measurement can improve quality of life of post-menopausal women and geriatric men which constitute worldwide two growing populations [3] and are helpful for pediatric diagnosis and therapy in abnormalities of pubertal maturation[1]. In this study, we compared the results obtained from the measurement of low concentration E2, P4 and T serum samples tested with the automated chemiluminescent enzyme immuno-assays Immulite 2000 (Siemens) and Lumipulse G (Fujirebio).
Methods: Samples from patients of different Divisions of the University Hospital "Federico II" were collected within 2 months and stored a -20°C until hormones concentrations were determined. Subjects with endocrine disease and cancers were excluded from the study. We analyzed 47 low E2 concentration samples (values ranging from 17 to 25 pg / mL), 72 low T concentration samples (values between 0.005-2 ng /mL) and 48 low P4 concentration samples (values ranging from 0.2 - 5 ng /mL).
Results: We observed differences in quantitation between the Lumipulse G Fujirebio and Immulite E2 and T assays. In particular, the Lumipulse G method was able to detect T in all 72 serum samples, whereas Immulite measured in 53 samples above the limit of quantitation (LOH) which corresponds to 0.2 ng/ml. Similarly, the Lumipulse G method was able to detect E2 in all 47 serum samples, whereas Immulite quantitate <20 pg/ml in 9 samples. Conversely, we did not observe differences in P4 quantitation between the two methods. Furthermore, we evaluated the reproducibility of Lumipulse G method. The three analytes had good CVs, with all mean values <10% (T 6%, E2 8%, P4 6%).
Conclusions: Lumipulse G Fujirebio assay is able to accurately and reproducibly quantitate T and E2 in low concentration samples in which Immulite cannot. These results may have important clinical implications for improved diagnostic accuracy and patient care.

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Endocrinology

Cod: T144

THE EFFECT OF AQUATIC EXTRACT OF STEVIA ON THE LEVEL OF SERA IL-6 IN DIABETIC RATS INDUCED BY SREPTOZOTOCIN-NICOTINAMIDE(STZ-NA)

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Background: Diabetes is a common chronic disorder that leading to death and morbidity. It can be divided into two types: Diabetic Mellitus Type1 (T1DM) and Diabetic Mellitus Type2 (T2DM). Uncontrolled T2DM is associated with the innate immune system which appears to form chronic inflammation and people with diabetes are very sensitive to infectious diseases. Today, because of side effects of oral medications, traditional treatments have found many applications for diabetes. One of plants with anti-diabetic effects is Stevia Rebaudina Bertoni (Asteraceae). Stevia Rebaudina Bertoni is one of 154 genus Stevia members that produce sweet steviol glycoside. Due to lack of information about the effects of anti-inflammatory and immunomodulatory of the aqueous extract of stevia on diabetic rats, we decided to investigate the effects of stevia upon IL-6 levels in rats induced by streptozotocin-Nicotinamide.
Methods: Wistar rats were divided into five groups including normoglycemic, diabetic, two diabetic groups treated with aquatic extract of stevia (400 mg/kg) and metformin (500 mg/kg) and a healthy group that treated with aquatic extract of stevia (400 mg/kg) for the period of 28 days. On the final day, blood samples were collected from heart for detecting biochemical changes of FBS and IL-6 levels in serum.
Results: Aquatic extract of stevia significantly reduced FBS ($P<0.001$) and IL-6 in treated rats compared with diabetic ones ($P=0.001$).
Conclusion: It is concluded that stevia due to the anti-diabetic and anti-inflammatory effects, decreased the IL-6 level as well as glucose content.

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Endocrinology

Cod: T145

SIMULTANEOUS MEASUREMENT OF SIX STEROID HORMONES BY LIQUID CHROMATOGRAPHY-TANDEM MASS SPECTROMETRY IN CHILDREN WITH ADRENAL DISEASE

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Background: Steroid biochemistry plays an essential role in the diagnosis and monitoring of children with adrenal disease. Those assays require high specificity, reproducibility and sensitivity with a low detection limit. However, current immunoassays can not meet all requirements with standardization problems in particular testosterone, estradiol and androstenedion assays. In recentyears, liquid chromatography- tandem mass spectrometry (LC MS/MS) method has been developed to measure single hormone or steroid hormone panels. The aim of this study was to implement a protocol for simultaneous measurement of six steroid hormones by LC MS/MS in children with adrenal disease and to determine analytical performance of the method.
Methods: A panel was created comprising estradiol, testosterone, androstenedion, dehydroepiandrostenedion sulfate (DHEAS), 17hydroxyprogesteron (17OHP), and 11-deoxycortisol. To evaluate analytical performance precision, limit of quantification, carry over, stability, accuracy and method comparison studies were performed.
Results: The within-run precision was lower than 13% whereas between-run precision was lower than 14.2%. Limit of quantification ranged between 2.32 – 5,92. Carry over was lower than 20% of the LoQ. Accuracy was good, bias was lower than 12%. The method comparison was adequate, however the correlation coefficient was found to be low for DHEAS. Samples were stable for 48 hours at 2-8 0C after precipitation, however 17OHP values significantly decreased at 48 hours.
Conclusion: LC MS/MS showed good analytical performance for simultaneous six steroid hormone assay panel. Therefore it is suitable to use in the diagnosis and monitoring of steroid hormones in children with adrenal disease in daily routine.

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Endocrinology

Cod: T146

UNUSUAL THYROID FUNCTION TESTS: 4 CASE STUDIES

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Background
In a subgroup of patients thyroid function tests (TFT) can be confusing either by being discordant with each other or by being discordant with the clinical picture. We present 4 cases of patients with discordant thyroid function tests
Case 1
Fifty eight year old male with the following TFT: FT4 24.9 (RR12-22) pmol/L, TSH 0.25 (RR 0.3-4.3mIU/L) on 08/01/2015. TFT were measured on the Roche platform. FT4 51 pmol/L, TSH 0.20 on 08/12/2015. He presented with sweating,hand tremor, loose stools and small tender goitre. He was treated with carbimazole. On 29/03/2016 : FT4 25.3 pmol/L, FT3 10.4 (RR 4-6.8pmol/L) and TSH 2.2 mIU/L. The TFT were measured by the Delfia method on 29/03/2016: FT4 11.4 (9-20 pmol/L), FT3 6.9 (3-7.5 pmol/L), TSH 5.6 (0.4-4.4 mIU/L), suggesting assay interference in the Roche method.
Case 2
Twenty six year old female with the following TFT as measured by the Roche assay: FT4 >100 pmol/L, FT3 15.8 pmol/L, TSH 0.2 mIU/L. By the Delfia method: FT4 17.8 pmol/L, FT3 6.4 pmol/L, TSH 0.41. Screening tests suggested heterophilic antibody interference in the Roche assay. Further tests for familial dysalbuminemic hyperthyroxinemia, and antibody to T4 and T3 were negative.
Case 3.
Eighty year old male with FT4 23 pmol/L and TSH 22.1 mIU/L by the Roche assay. The patient was clinically euthyroid. Linear dilution studies showed assay interference in the Roche TSH assay. The TRH test showed a suppressed response. The common alpha subunit levels were within the reference range. Follow up showed that 6 years following diagnosis the patient was treated with thyroxine
Case 4
Fourteen year old male with FT4 26.4 pmol/L , FT3 7.5 pmol/L, TSH 2.4 mIU/L. The patient was clinically euthyroid. Similar increased FT4 values were recorded in a sibling and parent. Screening test for familial dysalbuminemic hyperthyroxinemia was positive and the common Arg242His mutation responsible for this condition was identified.
Conclusions
A small but important subset of patients exhibit TFT results that are discordant with each other. In such patients a structured approach is required to prevent unneccesary/inappropriate investigation and treatment.

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Endocrinology

Cod: T147

MACROPROLACTINEMIA OR HYPERPROLACTINEMIA?

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INTRODUCTION
Prolactin (PRL) is secreted solely by the lactotroph cells of the pituitary gland. As a result, hyperprolactinemia results almost exclusively from diseases that cause hypersecretion of PRL by lactotroph cells. Some of these causes are physiologic and others pathologic.
Two causes of hyperprolactinemia due to decreased clearance of PRL include chronic renal failure and macroprolactinemia. The most common form of PRL in serum is 23 kD in size. Macroprolactin (MPR) is an umbrella term used to describe aggregates of PRL and antibodies, some autoantibodies, to PRL that range in size from about 150 to 170 kD. These complexes are immunologically detectable but not biologically active, so they appear to cause no clinical abnormality. Although these entities are not of clinical significance directly, they are of clinical significance indirectly because they can be misdiagnosed and treated as ordinary hyperprolactinemia. Misdiagnosis can be avoided by asking the laboratory to pretreat the serum with polyethylene glycol (PEG) to precipitate the MPR before the immunoassay for prolactin.
The prevalence of macroprolactinemia screened by PEG-precipitation method is controversial and it varies a lot according to the PRL assay systems. In this sense, we have studied the prevalence of MPR.

MATERIAL AND METHODS
The serum samples were obtained from 50 healthy patients and from 372 patients with hyperprolactinemia. The PEG precipitation has been used for the screening of macroprolactinemia because of its simplicity. To determine free PRL concentrations, serum samples (50μL) are mixed vigorously with 50 μL of cold PEG (molecular weight 6000, 25% in water) and centrifuged at 9,100×g for 10min to remove MPR. The PEG-precipitable PRL (%), which represents the amount of MPR, is calculated as follows: (total PRL-free PRL)/total PRL × 100. Serum PRL levels were measured using Architect immunoassay (Abbott Diagnostics) in treated and non-treated samples.

RESULTS
We have accepted that PRL recovery of 40% of its initial value, after PEG treatment, indicates the presence of macroprolactin in patient's serum. With this in mind, macroprolactinemia is present in 8% in general population. The prevalence is not different between women and men, and it tends to increase in erderly people. In patients with hyperprolactinemia, the prevalence of MPR is of 29%.

CONCLUSIONS
Screening of macroprolactinemia is important for the differential diagnosis of hyperprolactinemia to avoid unnecessary examinations and treatments.

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Endocrinology

Cod: T148

TO STUDY THE ASSOCIATION BETWEEN ENDOGENOUS CORTISOL LEVELS AND DEVELOPMENT OF CENTRAL SEROUS CHORIORETINOPATHY.

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ABSTRACT
Introduction:Central serous chorioretinopathy (CSCR) is characterized by an exudative neurosensory layer detachment of retina. Male gender, type-A personality, emotional stress, pregnancy, infections, hormonal regulatory factors and several immunological reactions have all been implicated in causing CSCR. Although several hypotheses have tried to establish a link between endocrinal abnormalities and CSCR, still none is able to explain the true etiopathogenesis of CSCR.
Aim & Objectives:This study was designed to estimate serum cortisol levels in patients of CSCR and study their potential role in etiopathogenesis of the disease.
Material & Methods :In this study, 25 patients of CSCR satisfying the inclusion and exclusion criteria were enrolled as cases and 25 age and sex matched patients with an acute unilateral rhegmatogenous retinal detachment (RD) were enrolled as controls. Levels of serum cortisol was estimated by chemilumiscence in both groups. Serum cortisol measurement was done twice, due to diurnal variation in its levels.
Results & Observations: Data analysis was done by Pearson's correlation analysis and independent student t-test. The 8:00 AM mean serum cortisol value in the cases (20.21 ± 4.86 μg/dl) was significantly ($p = 0.046$) higher than controls (17.74 ± 3.53 μg/dl). Although the 11:00 PM mean serum cortisol value of cases (8.13 ± 3.52 μg/dl) was more than controls (6.97 ± 2.50 μg/dl) but difference was not statistically significant ($p = 0.187$).
Conclusion:Elevated cortisol level in CSCR patients strengthens the belief of its potential role in pathogenesis of disease. Also, regular posterior segment examination can reduce the ocular morbidity in patients with exo- or endogenous hypercortisolism. It is suggested that monitoring of cortisol levels could be beneficial in deciding the outcome of CSCR.

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Endocrinology

Cod: T149

HIGH-THROUGHPUT SCREENING OF STEROIDOGENESIS-RELATED GENES BASED ON A CUSTOM AMPLISEQ™ LIBRARY

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Objective. To test the reliability of a next-generation sequencing workflow (Ion Torrent PGM) for analysis of a panel of genes in patients with suspected adrenal deficiencies or inborn errors of steroidogenesis.
Methods. We designed a custom Ampliseq™ panel for massive-parallel sequencing of 7 human genes related to the steroid metabolism (CYP21A2, CYP17A1, CYP19A1, CYP11A1, CYP11B1, CYP11B2, HSD3B2) on an Ion PGM Sequencer. The pilot study group consisted in 8 genomic DNA samples (2 probands with their respective parents and 2 other single probands). Gene specific analysis was performed using Partek®Flow® software, version 5.0 (Partek Inc., St. Louis, MO, USA)
Results. The 117 amplicons (2 pools) covered a mean of 99.66% of the target sequence. Amplified Libraries were sequenced on an Ion Personal Genome Machine (PGM) sequencer (Life Technologies) using Ion 316 chip. The raw data (unmapped BAM files) were processed using Torrent Suite Software (v. 5.0.4) to generate read alignments which are filtered by the software into mapped BAM-files using the reference genomic sequence (hg19) of target genes. After trimming and filtering variants were detected using several bioinformatic instruments (e. g. Samtools 1.2, FreeBayes 1.0.1) and annotated by SnpEff. Bi-allelic variants with 20x coverage and a quality score of minimum 20 were called, so we identified for these 7 genes, in all subjects, 56 mutations (mostly single nucleotide variants): 1 pathogenic and 1 benign mutation in CYP21A2 gene, 1 pathogenic mutation and one novel mutation in CYP11B2 gene, one novel mutation in CYP11B1 gene (in one family, heterozygous in parents and homozygous in the proband), one benign mutation in CYP17A1 gene and one benign mutation in CYP19A1 gene (one family with all members heterozygous for that mutation).
Conclusions. Next-generation sequencing could be a powerful tool for screening of single nucleotide polymorphisms in steroidogenesis-related genes in patients with suspected adrenal deficiencies or inborn errors of steroidogenesis, for a better diagnosis and treatment of these patients.

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Endocrinology

Cod: T150

COMPARISON OF BPA AND ITS REPLACEMENTS ACTION ON STEROIDOGENIC BLTK1 LEYDIG CELL LINE

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Bisphenol A (BPA) is one of the most prevalent chemicals in daily-use materials and currently bisphenol S (BPS) and bisphenol F (BPF) are used as its substitutes in BPA free products. Unfortunately structural similarity of BPF and BPS to BPA and estradiol raises doubts about their safety.
The aim of the study was comparison of the effects of BPA and its replacements on BLTK1 Leydig cell steroidogenesis.
Cell viability was assessed after treatment for 24-72 hours with varying concentrations of BPA, BPF and BPS. Hormone release and changes in steroidogenesis-related gene expression using RT-qPCR after BPA, BPF and BPS exposure were also evaluated. Statistical analysis was performed by One-way ANOVA using GraphPad PRISM v.5.0.
Bisphenols had proliferation enhancing either cytotoxic effects depending on the range of dose. Extended exposure influenced steroid receptor and steroidogenesis-associated genes expression profile. Exposure to all studied compounds resulted in changes in steroidogenic genes expression. It has been demonstrated non statistically significant trend of BPA and BPS exposure to intensify CG-induced progesterone release.
BPS and BPF appear to have similar endocrine modulating capacity to BPA, therefore they may pose comparable potential hazards. Our results emphasize the need to prove the safety of replacement compounds prior to their introduction in manufacturing.

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Endocrinology

Cod: T151

ASSOCIATION ANALYSIS BETWEEN KCNJ11 GENE AND ZINC LEVELS IN GESTATIONAL DIABETES MELLITUS: A RETROSPECTIVE STUDY

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BACKGROUND:Gestational Diabetes mellitus (GDM), is a common medical disorder characterized by impaired glucose tolerance during pregnancy and confers 4-to 7-fold greater risk of incident type 2 diabetes mellitus (T2DM). The KCNJ11 gene, has a key role in insulin secretion and is a substantial candidate gene for T2DM. E23K mutation in KCNJ11 gene increases the risk of T2DM and also considered to be associated with GDM. Additionally, it is known that zinc is involved with the formation, storage and secretion of insulin and required for normal glucose metabolism. It enhances the insulin-induced transportation of glucose into cells by effecting insulin signaling pathway. Therefore, we aimed to investigate the association between T2DM gene KCNJ11 and zinc levels in GDM patients.
METHODS: 91 pregnant (24-28 gestational weeks) individuals who are admitted to Selcuk University Faculty of Medicine, Endocrinology Polyclinic were included in our study. Zinc levels of 54 GDM patients and 37 healthy pregnants, whose KCJN11 genes were genotyped for E23K mutation previously, were evaluated. Paired t test for independent samples and ANOVA analysis were used. A p value < 0.05 was considered statistically significant.
RESULTS: According to descriptive statistics, there was no significant difference for zinc levels of patient [11.56 (10.91-12.25) #mol/l] and healthy [11.13 (10.50-11.79) #mol/l] pregnant groups (p=0.363). We did not determine a significant association between E23K mutation and GDM (p=0.214).
CONCLUSIONS:Comparing of patient and healthy groups individually, we did not determine any relation between G/G, G/A and A/A genotypes E23K mutation and zinc levels (p=0.488 and p=0.205). Seen from this aspect, further studies with more sample numbers are needed to clarify the relations.

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Endocrinology

Cod: T152

DIABETES MELLITUS AND THYROID DYSFUNCTION

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Background: Diabetes mellitus type 2(T2DM) has an intersecting underlying pathology with thyreiod dysfunction.Hyper and hypothyreoidism have been associated with insulin resistance which has been reported to be the major cause of impaired glucosa metabolism in T2DM.Polyendocrinal multidysfunction leads to stimulation cascade of reaction which are actuelly antihomeostatic.We aimed to evaluate the relationship between serum TSH,FT4, and HbA1C in our T2DM population.
Methods: Subjects (64 females and 56 males) were grouped into two age groups:
I group 20-40 years old (n=60) and II group 40-60 years old (n=60). Serum levels of TSH and FT4 measured by immunochemiluminesce using Cobas e 411 Roche . HbA1Cc was measured using Beckman Coulter AU-680.
The diagnostic assessment of the thyroid gland done by thyreodologist was consisted of physical exam thorough anamnesis of the patients. Thyroid ultrasound exam was done on every each of the patients.
Results:Prevalence of subclinical hypothyreoidism is 8% in the I group,14% in II group.
Prevalence of subclinical hyperthyreoidism is 4%in the Igroup,6% in IIgroup
I group: HbA1C 68 ±11 mmol/mol
II group: HbA1C 77±9 mmol/mol
Conclusions:On the one hand,results of this investigation reflect age is the risk factor of thyroid disease in T2DM.On the other hand,the results also provide information about hypo and hyperthyroidism in T2DM.

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Endocrinology

Cod: T154

ASSESSMENT OF HbA1c AS AN ALTERNATIVE TOOL FOR DETECTION OF GESTATIONAL DIABETES MELLITUS AT UNIVERSITY MALAYA MEDICAL CENTRE, MALAYSIA

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Background:
The Malaysian 2010 National Obstetrics Registry (NOR) reported incidence of Gestational Diabetes Mellitus was 9.9% among Malaysian women. Current screening criteria to diagnose gestational diabetes mellitus (GDM) in Malaysia are adopted from the Malaysian 2015 Clinical Practice Guidelines (FPG ≥5.1mmol/L and/or 2HPP 7.8mmol/L). The clinical utility of glycohemoglobin A1c (HbA1c) as a screening tool for GDM remains controversial and has yet to been validated.
Objective:
We undertook this study to assess if HbA1c may be used as a surrogate screening tool for GDM in our antenatal women.
Materials and Method:
447 pregnant women were evaluated for GDM using OGTT based on the Malaysian 2015 CPG criteria. HbA1c testing was also performed at the same time utilizing the Abbott Architect C4000 enzymatic assay. ROC curve was used to evaluate the diagnostic performance of HbA1c. Sensitivity and specificity for different HbA1c cut-off points were calculated.
Results:
Of the 447 pregnant women, 131 were excluded due to anemia. The mean gestational age for the participants was 28.1 weeks with values of HbA1c ranging from 4% to 8%. ROC curve was drawn to determine the sensitivity and specificity of HbA1c in detecting GDM. The area under the curve of HbA1c to detect GDM was 0.717. The mean + SD HbA1c value in women with GDM was 5.3 + 0.59% while it was 4.98 + 0.34% in women without GDM. The difference in the two HbA1c values was found to be statically significant. HbA1c at 5% cut-off of had the high sensitivity (72.92%) in screening for GDM but had a low specificity (60.82%). Highest specificity (99.25%) for diagnosing GDM was found at HbA1c value of more than 5.7% but exhibited lowered sensitivity (10.42%).
Conclusion:
This study suggests that HbA1c may be a reasonably sensitive screening measure of GDM. Further prospective studies are warranted to verify this conclusion, and to evaluate the specificity of HbA1c as a screening test for GDM before it can be adapted into clinical practice.

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Endocrinology

Cod: T155

EVALUATION OF HbA1c FOR DETECTION OF TYPE 2 DIABETES MELLITUS AT UNIVERSITY MALAYA MEDICAL CENTRE, MALAYSIA

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Background:
HbA1c has recently been recognized as an alternative tool for the diagnosis of Type 2 Diabetes Mellitus. Most Malaysian public hospitals still depend on the Oral Glucose Tolerance Test (OGTT) and are reluctantly moving to the utilization of HbA1c for the diagnosis of Type 2 DM. The Malaysian 2015 Clinical Practice Guideline (CPG) advocate a HbA1c cut off value of 6.3% versus 6.5% as recommended by the World Health Organization (WHO).
Objective:
This study was conducted to evaluate the clinical utility of HbA1c to diagnose Type 2 DM in UMMC against the reference Oral Glucose Tolerance Test (OGTT
Materials and Method:
208 patients scheduled for Oral Glucose Tolerance test in the Division of Laboratory Medicine, UMMC were recruited. Simultaneous HbA1c testing was performed by the Abbott Architect C4000 enzymatic assay. These patients were evaluated for Type 2 DM using HbA1c value based on the WHO criteria in addition to the Malaysian 2015 CPG guidelines against OGTT.
Results:
Of the 208 patients on whom OGTT was performed, 105 (50.5%), 64 (30.8%) and 88 (42.3%) participants were diagnosed as Diabetes Mellitus by using OGTT, HbA1c ≥6.5% and HbA1c cut-off ≥6.3% criteria respectively. The HbA1c at ≥6.3% had a sensitivity and specificity of (71.43%) and (69.90%) respectively while the HbA1c ≥6.5% had the highest specificity (93.2%) but lower sensitivity (54.29%).
Conclusion:
HbA1c with a cut-off value of 6.3% as per our Malaysian 2015 CPG guidelines demonstrated superior sensitivity and may be adapted as a screening tool for newly diagnosed Type 2 DM. However, the challenge remains to wean off the OGTT testing practice in favor of HbA1c in our Malaysian public hospitals.

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Endocrinology

Cod: T156

STANDARDIZATION AND HARMONIZATION* OF ORTHO-CLINICAL DIAGNOSTICS THYROID FUNCTION TESTS -VITROS® IMMUNODIAGNOSTIC PRODUCTS TSH AND FREE T4 ASSAYS

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Background: The International Federation of Clinical Chemists (IFCC) has an ongoing program of standardization and harmonization for Thyroid function tests (C-STFT). The project aims to develop reference measurement systems (reference materials/reference methods) to establish traceability of free thyroid hormone and TSH assays. The IFCC intends that; FT4 assays will become traceable to the conventional reference measurement procedure based on equilibrium dialysis isotope dilution-liquid chromatography/tandem mass spectrometry (ED ID-LC/MS/MS), TSH assays to the statistically inferred all-procedure trimmed mean (APTM).
Methods: Ortho generated data as part of the IFCC Phase IV Harmonization and Standardization study by testing two panels of samples (90 FT4 & 102 TSH samples), results returned to the C-STFT. The committee provided Ortho with panel member results as determined by ED ID-LC/MS/MS for FT4 and the statistically derived APTM values for the TSH panels. Ortho then adjusted the values of their master reference calibrators to achieve closer agreement to these values. To achieve the best possible agreement of the VITROS® TSH assay to the APTM values at doses <0.3mIU/mL Ortho introduced two additional reference standards to their master reference calibrator set.
Results: Prior to the recalibration exercise slopes of 0.69 and 1.05 were obtained for the VITROS® Free T4 and TSH assays respectively. After adjustment of Ortho's internal reference standards, slopes of 1.02 and 1.00 were obtained for the VITROS® Free T4 and TSH assays.
Conclusion: Agreement of the VITROS® TSH assay (at doses below 0.3mIU/mL) against the IFCC APTM panel was improved by introduction of two additional master reference calibrator levels, and manipulation of the assigned doses. Manipulation of the master reference calibrator values for the VITROS® Free T4 assay can improve the correlation to ED ID-LC/MS/MS. However the VITROS® Free T4 assay is a true free hormone assay which is currently well aligned with other immunoassays.

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Endocrinology

Cod: T157

ASSOCIATION BETWEEN SERUM LIPOPROTEIN RATIOS AND INSULIN RESISTANCE IN TURKISH ADULTS

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Background: Researchers have attempted to evaluate insulin resistance (IR) using various serum lipid concentration ratios. Most of the studies have suggested the triglyceride to high-density lipoprotein cholesterol ratio (TG/HDL-C) as a surrogate marker of insulin resistance. However, there are conflicting findings about this association in different populations. The purpose of this study was to determine the most strongly IR-predictive lipid profile ratio by studying associations between lipid concentration ratios and IR in Turkish adults

Methods: The data were collected from 2591 individuals referred to the Marmara University Pendik E&R Hospital Outpatient Clinic. Among them, 1789 individuals who were older than 20 years of age with a fasting plasma glucose < 126 mg/dL and without a history of diabetes were enrolled in the study. Lipid ratios included TG/HDL-C, the low density lipoprotein cholesterol (LDL-C)/HDL-C, non-HDL-C (LDL-C + TG/5)/HDL-C and the total cholesterol (TC)/HDL-C. We divided subjects into 4 groups according to lipid profile ratio quartiles for a comparison of homeostasis model assessment (HOMA)-IR values. Insulin resistance was defined as the HOMA-IR values greater than the 80th percentile. The areas under the curves (AUC) of the receiver operating characteristic (ROC) curves were used to compare the power of these serum lipoprotein ratios as markers.

Results: Statistically significant differences were observed among all 4 sets of quartile groups (mean TG/HDL-C, LDL-C/HDL-C, non-HDL-C/ HDL-C, TC/HDL-C ratios; p-values <0.001). HOMA-IR values tended to increase as the lipid ratios increased. All of the lipid profile ratios were significantly correlated with HOMA-IR ($P<0.001$). The highest correlation was observed with the TG/HDL ratio ($r=0.354$; $P<0.001$). The area under the ROC curve of the TG/HDL-C for predicting insulin resistance in women was 0.69 (95% CI, 0.656 to 0.724).

Conclusions: In conclusion, a higher lipid profile ratios especially TG/HDL-C ratio, which are widely accessible on routine laboratory tests, could be a convenient surrogate markers for insulin resistance. However, additional large-scale studies will be required to evaluate the optimum cut-off values for the lipid profile ratios used to determine IR in each sex.

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Endocrinology

Cod: T158

IMPORTANCE OF THE EVALUATION OF FOLIC ACID STATUS IN PSYCHIATRIC PATIENTS

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Background
The incidence of folic acid deficiency is high in patients with various psychiatric disorders including depression, dementia and schizophrenia. The aim of this study is to associate folic acid status and the presence of macrocytic anaemia with psychiatric patients.
Methods
Cross-sectional study. Folic acid deficiency was established in 3.65 ng/mL according to reference interval used in our laboratory. Anaemia was established in 12 g/dL (women) and 13 g/dL (men) in haemoglobin value and mean corpuscular volume above 100 fL. Two groups were selected, one from psychiatry and the other from non-psychiatry. Trend analysis was performed with STATA13.
Results
A total of 1020 patients were studied from January 2012 to December 2012, divided in two groups, one of them consisted of 520 non-psychiatric patients and the other of 500 psychiatric patients in psychiatric. Folic acid medium levels were 8.04 ng/mL (95% IC: 7.63 to 8.44 ng/mL) and 6.69 ng/mL (95% IC: 6.32 to 7.07 ng/mL) respectively. Prevalence of folic acid deficiency was 15.77 % in non-psychiatric patients group and 26.60% in the other (OR: 1.94 (95% CI: 1.42 to 2.63)). Prevalence of folic acid deficiency was increased in psychiatric patients. Folic acid deficiency in absence of anaemia was 9.87% in non-psychiatric patients and 20.40% in psychiatric patients (OR: 2.34 (95% CI: 1.59 to 3.44).
Conclusion
Psychiatric patients have more prevalence associated with folic acid deficiency without macrocytic anaemia than those with non-psychiatric disease.

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Endocrinology

Cod: T159

APPLICATION OF THE NEW RANDOM ACCESS, FULLY AUTOMATED BIOCHIP ANALYSER EVIDENCE EVOLUTION TO SIMULTANEOUSLY MEASURE ANALYTES RELATED TO ENDOCRINE FUNCTION

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Background. Cortisol and dehydroepiandrosterone-sulphate (DHEAS) are produced in the adrenal glands, the cortisol/DHEAS ratio regulates multiple body functions and has been found to be a better predictor of health outcomes than the level of either hormone alone. The availability of effective analytical tools enabling the simultaneous detection of these two analytes is therefore beneficial in the process of measuring fundamental circulating hormones, valuable in regulating endocrine function. This study reports the application of the simultaneous quantitative measurement of cortisol and DHEAS from a single sample on the first high throughput, random access, fully automated biochip analyser, Evidence Evolution. This application, based on biochip array technology, represents a new valuable multi-analytical tool to facilitate the understanding of endocrine function.
Methods. Simultaneous chemiluminescent competitive immunoassays were applied to the automated Evidence Evolution analyser. Analytical sensitivity and intra-assay precision were evaluated using serum based precision material. Serum patient samples (n = 45 for cortisol and n = 42 for DHEAS) were assessed and the results were compared with a commercially available method.
Results. Analytical sensitivity values of 0.13 µg/dL for cortisol and 0.16 µg/dL for DHEAS were obtained. Intra-assay precision, expressed as CV(%), showed values of 7.1%, 4.7% and 2.9% (cortisol) and 5.5%, 3.3% and 6.5% (DHEAS) using low, medium and high levels of cortisol and DHEAS in serum based precision material. The method comparison, based on the assessment of serum samples, showed following regression analysis r values of 0.96 and 0.99 for cortisol and DHEAS respectively.
Conclusion. The data indicate optimal analytical performance when cortisol and DHEAS are measured simultaneously from a single serum sample. This first high throughput, random access with STAT capabilities, fully automated biochip analyser is applicable as a reliable multi-analytical tool to facilitate the understanding of endocrine function.