THE 2014 PREGNANCY SUMMIT

ABSTRACT BOOK

6th - 8th October 2014
London, UK

EuroSciCon®
This summit will discuss our current understanding of pre-eclampsia research and treatments for the first two days.

The third day will focus on the technologies currently available to assess pregnancy and pregnancy-associated conditions.

This event has CPD accreditation
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Day 1: Pre-eclampsia research

Invited Speakers Abstracts

New prognostic marker(s) to determine the risk to develop early-onset preeclampsia?
Mr Joost Schuitemaker, Managing Director, IQ Products, The Netherlands

A maternal inflammatory response is characteristic for the maternal preeclampsia syndrome. During such a response, inflammatory factors play crucial roles in the onset of and also in sustaining the syndrome. Because of the complex interaction between processes, like conception, placentation and the immune system of the mother, the development of and the reason for preeclampsia are not completely clear yet. Making it difficult to develop an therapeutic to treat the disease, instead of the symptoms.

Several angiogenic and antiangiogenic markers, like placental growth factor, soluble endoglin (sEng) and soluble fms-like tyrosine kinase-1 (sFlt-1), have been found to have predictive value to determine the risk to develop preeclampsia. Depending on the moment they are evaluated during gestation, they have a better or worse sensitivity and specificity. Currently new biomarkers are evaluated that might contribute to this sensitivity and specificity and might bring the moment of use during gestation forward.

Implementing biomarkers into pre-eclampsia management.
Professor Andrew Shennan, Kings College London, UK

The role of angiogenic markers in the pathophysiology of pre-eclampsia has recently been more clearly elucidated. Their relationship to clinically important outcomes means they can be used to target prophylaxis to at risk pregnancies and tailor management at point of care in suspected cases. This talk will outline how this may be implemented.

Transport Kinetics of Alpha-aminoisobutyric acid and Leucine in Preeclampsia Model Human Placenta: In Vitro Study
Professor Nandakumaran Moorkath, Faculty of Medicine, University of Kuwait

Considering the difficulty of devising suitable animal model for study of preclamptic pregnancies, we have attempted to approximate an in vitro placental model for study of maternal-fetal transport of nutrients and pharmaco-active agents in humans. The plentalent pre-eclampsis model was designed to incorporate the major factor of compromised utero-placental blood flow of pre-eclamptic pregnancies as the major criterion of the model. We have studied maternal-fetal transport of two model amino acids, namely alpha-aminoisobutyric acid(AIB) and l-leucine using the above model and the results obtained in perfusions with placentae from pre-eclamptic women are used for evaluation of the findings in the case of AIB transport. Further studies are in progress.

Stress, immune system functioning and perinatal depression: the impact of heightened systemic inflammation and risk of CVD later in life. Is pre-eclampsia the right model?
Professor Meir Steiner, Professor Emeritus, McMaster University, Ontario, Canada

Depression and CVD are both inflammatory disorders. Their co-occurrence may be related to how the hypothalamic-pituitary-adrenal axis, serotonergic transmission and circulation, and the rennin-angiotensin-aldosterone system via angiotensin II are affected by the excess secretion of proinflammatory cytokines. Preliminary research attributes this systemic inflammation to a global deficiency in CD4+CD25+FOXP3 regulatory T cells, and the observed sex differences may be partially explained by the 17-β estradiol and progesterone mediated modulation of cytokine secretion. Hormones and reproductive events associated with hormonal fluctuations will be discussed in depth, along with an analysis of pre-eclampsia as a perinatal model of depression and CVD.

Placental Syncytiotrophoblast Vesicles In Normal Pregnancy And Pre-Eclampsia
Dr Dionne Tannetta, Senior Research Scientist, University of Oxford, UK

Extracellular vesicles (EV) are shed by numerous cell types as part of normal physiology and disease processes. In pregnancy, the placental surface epithelium (syncytiotrophoblast) is the primary source of fetal vesicles. Syncytiotrophoblast vesicles pass directly into the maternal circulation where they engage with the maternal immune and cardiovascular systems. Consequences of this are believed to be important for maintenance of normal pregnancy; constituting a major signalling mechanism between mother and fetus. Conversely, abnormal vesicle shedding has been implicated in pregnancy disorders, in particular pre-eclampsia. This talk will cover research at Oxford to better characterise syncytiotrophoblast vesicles in normal pregnancy and pre-eclampsia.
Central aortic pulse wave analysis parameters - a novel marker in prediction of hypertensive complications in pregnancy  
Dr Ludwina Szczepaniak-Chicheł, MD, PhD, adiunct, Dept. of Hypertensiology, Angiology and Internal Medicine, Poznan University of Medical Sciences, Poland  
In last decade in general population central blood pressure and arterial stiffness assessment based on pulse wave velocity (PWV) and pulse wave analysis (PWA) parameters such as augmentation index turned out to be more accurate for assessment of cardiovascular system and risk for future complications of arterial hypertension than traditional peripheral blood pressure assessment over brachial artery. Based on recent studies it seems to be true also for pregnant women. Assessment of arterial stiffness using PWA measured noninvasively with applanation tonometry method seems to be a promising new tool for prediction of preeclampsia before the onset of clinically detectable disease.

Regional versus General Anesthesia for C/S in Severe Preeclampsia  
Dr Kemal Tolga Saracoğlu, Assistant Professor of Anesthesiology and Reanimation, Marmara University School of Medicine Istanbul Turkey  
The optimal anesthetic method for Cesarean section for parturients with preeclampsia remains controversial. Recently there have been a dramatic shift away from general anaesthesia in obstetrics in favour of regional anaesthesia because of hazards related to difficult airway management and to the hemodynamic consequences of anesthesia induction, tracheal intubation and laryngoscopy. Historically spinal anesthesia was avoided in patients with severe preeclampsia due to the belief that it causes to decreased uteroplacental perfusion and severe hypotension. However, clinical trials conclude that parturients with severe preeclampsia experience less frequent, less severe perioperative hypotension than healthy parturients.

Preeclampsia and the immune system: a close relationship  
Dr Estibalitz Larestgoiti, Associate Professor, Attending Physician, American British Cowdray Medical Center, Mexico, School of Medicine, Monterrey Institute of Technology and Higher Education, Mexico  
Recent studies have revealed an active participation of the immune system in the origins and in the pathophysiology of preeclampsia. The presence of inflammatory cytokine microenvironments and the participation of various lymphocyte subsets in preeclampsia contribute to changes in immune system regulation and the persistence of inflammatory conditions in this syndrome. Neutrophils and auto-antibodies can also promote endothelial damage in preeclamptic patients. The immune system may be a key player in the pathophysiology of preeclampsia.

Podocyturia as a diagnostic and prognostic marker of preeclampsia  
Dr Vesna D. Garovic, Professor of Internal Medicine, Division of Nephology+Hypertension+Dept of Obstetrics+Gynaecology, Mayo Clinic, USA  
Preeclampsia is a hypertensive disease of pregnancy with multi-organ involvement, which is commonly, but not always, accompanied by either sudden onset or worsening of pre-existing proteinuria. Similar to other renal diseases, proteinuria in preeclampsia may represent a late marker of renal injury. Over the last 7 years, evidence has emerged indicating that either structural podocyte injury, as evidenced by down-regulation of podocyte-associated proteins, or urinary loss of viable glomerular epithelial cells –podocytes– (i.e., podocyturia) may play a central role in the renal involvement observed in preeclampsia. At the time of delivery, the number of podocytes positively correlates with the degree of proteinuria, suggesting a cause-effect relationship between ongoing podocyte loss and the onset and severity of proteinuria, i.e., that these are mechanistically related. Our recent data suggest that podocyturia may occur prior to the clinical features of preeclampsia, potentially representing an earlier marker of renal injury than proteinuria. In addition, two independent studies confirmed that podocyturia may persist postpartum, despite the resolution of proteinuria. Whether podocyte damage and shedding affect renal function years after preeclamptic pregnancies remains to be determined.

Porting Novel Preeclampsia Diagnostic Tools to the Clinical Market: Co-development of Two Complementary Technologies  
Robin Tuytten, Metabolomic Diagnostics, Ireland  
In order to equip healthcare professionals and pregnant women with novel and better tools to predict, prognose and diagnose preeclampsia, newly discovered biomarkers need to be developed into actual products. Two high potential preeclampsia technologies were identified and migrated into start-up companies: a blood-based metabolite profile to risk stratify pregnant women to their preeclampsia risk at 15 weeks of pregnancy and the detection of podocytes in urine collected at the end 2nd trimester to identify ongoing kidney damage that foregoes preeclampsia. An overview and discussion of the product development steps will be given.
Anesthetic Goals of Labor Analgesia in Preeclampsia

Dr Ayten, Assist. Prof. M.D., Department of Anesthesiology and Reanimation, Istanbul Bilim University Medical School, Turkey

The main goal of labor pain management for preeclamptic patients include both providing the adequate analgesia and hemodynamic stabilization. As long as there is no contraindication, neuraxial labor analgesia is suitable for patients with pregnancy induced hypertension. However sudden severe hypotension after regional procedures is the main concern in preeclamptic parturients. The treatment of labor pain decreases the sympathetic activity, leading to peripheral vasodilatation. Vasodilatation might lead to significant uteroplacental insufficiency because of reduced blood pressure. Intravenous opioid analgesia may be another method in order to obtain favorable outcome when neuraxial analgesia is contraindicated.

Oral Presentation Abstracts

PRE-ECLAMPSIA: FOUR DECADES OF CLINICAL CARE AND YET THE AETIOLOGY REMAINS ILLUSIVE
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The author’s involvement in the clinical care and research in preeclampsia and eclampsia is traced from 1980s. Edampsia was at its height in 1983-88 (66/100000) in one east coast state in Malaysia he worked. The maternal mortality in 2011 was 29/100000 with 14 % of deaths related to hypertensive disorders. The results of local research are utilised to develop an argument that despite enormous research done in understanding the pathophysiology of preeclampsia, specific health strategies in antenatal and prenatal care were pivotal in reducing morbidity and mortality related to preeclampsia. Traditional approaches based on clinical manifestations continue to guide clinicians in management of preeclampsia. Anticonvulsant therapy with MgSO4 and antihypertensive remain the mainstay of management. Ophthalmic changes have been described in preeclampsia. When 78 such mothers were reviewed in 2011 hypertensive retinopathy was evident in 59% (grade 1 in 41 and grade 2 in 5 patients. A significant relationship with severity of hypertension was noted (p=0.001). This evaluation is the effect of disease rather than the cause. Predictive factors have remained elusive in diagnosis of preeclampsia. In understanding placental pathology related to preeclampsia reference is made to research done in this institute on immunological and ultrastructure changes namely reduced trophoblastic keratin 18 and 19 expression and its link to placental ultrastructure. In another study Type 1 (AT1) and Type 2 (AT2) angiotensin II receptor subtypes in the mechanism of PIH were studied. A disruption of AT1:AT2 receptor balance was seen in preeclampsia which could contribute to placental ischemia seen in this disorder. The author opines that research on placental pathology and ultra-structural placental abnormalities seen in preeclampsia at best helps understand more about disease development. Such findings point to outcome of the disease and would have little clinical impact.

The role of serum markers are revisited through prospective studies on normal and hypertensive mothers (n=20). An inverse relationship between sFlt-1 and PI GF was seen with disease prevalence evident prolonged exposure to sFlt-1 through pregnancy. Such abnormal balance between biochemical markers could contribute to abnormal angiogenesis seen in preeclampsia. This observation may have some meaningful role in disease prediction in the local context. In another prospective study hypoxia inducible alpha-1 transcription factor is studied. Hypoxia-inducible alpha-1 transcription factor was measured in preeclampsia and controls (n=20) and significant increases were seen in the former. Though the sample size was small there appears to be yet another biochemical marker that may be used as a predictive marker for this disease. The author concludes that despite advances in research on preeclampsia, after four decades of managing preeclampsia the aetiology remains poorly understood; predictive factors lack specificity and preventive measures like antioxidants have not stood the test of time. Clinical manifestations and timely intervention with indicated termination of pregnancy continue to dictate management of preeclampsia.

DETERMINATION OF THE PLACENTAL GROWTH FACTOR (PLGF) LEVELS IN GESTATIONAL AGE 9-18 WEEKS: EARLY PREECLAMPSIA (PET) SCREENING IN CZECH REPUBLIC

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Introduction

Early preeclampsia is the cause of fetal and maternal mortality in 12-20%. Pathogenesis of this disease is multifactorial, with genetic disposition. Abnormal PI GF levels correlate with the risk of development of preeclampsia. Based on the current literature it can be assumed, that the lower level of PI GF is found, the higher risk of early preeclampsia can be expected. Aim of the study was to establish physiological levels of PI GF for pregnancies within the range of gestational week 9 to 18. With the knowledge of these results,
screening of PET by PlGF, placenta associated plasma protein A (PAPP-A) and doppler ultrasound examination, is now possible to be introduced to clinical practice.

Material and methods
Retrospectively, 800 blood samples from women with physiological pregnancy were assessed to obtain normal PlGF levels in the first and second trimester. Procedure was performed by the Delfia Xpress (Perkin Elmer) device. PAPP-A levels were measured by Kryptor (Brahms). Potential risk of early PET in the first trimester was calculated by Preeclampsia Predictor software.

Results
Percentile norms of the PlGF levels in the first trimester were determined for the population of pregnant women in Czech Republic. The results correspond with the European standards for gestational age 9-13 weeks. Risk of the PET can be also assessed in the second trimester by using our standards for the weeks 14-18, something that current software doesn’t allow. Linear increase of PIGF levels is in accordance with published studies. Results can be seen in attached tables.

Discussion
Establishing of percentile charts for PIGF levels in both first and second trimester allowed us to develop guidelines for screening of preeclampsia with the possibility of early detection of pregnancies in risk, followed by early treatment by acetylsalicylic acid.

Supported by: CZ.2.16/3.1.00/24022 and project, Moderni terapie “(University hospital Motol, Praha).

GENETIC PREDISPOSITION TO DYSLIPIDEMIA AND RISK OF PREECLAMPSIA
KK Ryckman, CN Spracklen, AF Saftlas, EW Triche, PJ Breheny, AT Dewan, JG Robinson, J Hoh, B Keating, A Bjonnes, R Saxena.

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Background Large epidemiologic studies support the role of dyslipidemia in preeclampsia; however, the etiology of preeclampsia or whether dyslipidemia plays a causal role is still unestablished. We aim to examine the association between the genetic predisposition to dyslipidemia and risk of preeclampsia using validated genetic markers of dyslipidemia.

Methods Preeclampsia cases (N=177) and normotensive controls (N=116) were selected from live birth certificates to nulliparous Iowa women during the period August 2002-May 2005. Disease status was verified by medical chart review. Genome-wide genotyping of buccal cell derived DNA was performed at the Rockefeller University Genomics Resource Center using the Affymetrix Genome-wide Human SNP Array 6.0 (Affymetrix, Santa Clara, CA). Genetic predisposition to dyslipidemia was estimated by four genotype risk scores (GRS) (total cholesterol, LDL-cholesterol, HDL-cholesterol, and triglycerides) on the basis of established loci for blood lipids. Logistic regression analyses were used to evaluate the relationships between each of the four genotype scores and preeclampsia. Replication analyses were performed in an independent US population of preeclampsia cases (N=516) and normotensive controls (N=1,097) of European ancestry.

Results The GRS related to higher levels of total cholesterol, LDL-cholesterol, and triglycerides demonstrated no association with the risk of preeclampsia in either the Iowa or replication populations. A trend toward an association between the GRS related to lower levels of HDL-C and increased risk for preeclampsia (OR=1.04, 95% CI=0.99-1.10, p=0.10) was observed in the Iowa population. In the independent replication population the association between the HDL-C GRS was marginally significant (OR=1.03, 95% CI=1.00-1.07, p=0.04).

Conclusions The most common patterns of dyslipidemia experienced during preeclampsia are elevated triglycerides and reduced HDL-C levels. Our data suggest that lower HDL-C may be a component or an effect modifier along the causal pathway to preeclampsia. This finding is intriguing as HDL-C has anti-thrombotic properties, the ability to inhibit inflammation and oxidation, and is reported to enhance endothelial repair. The classic hallmark of preeclampsia is endothelial dysfunction; therefore, having lower levels of HDL-C is plausible as a candidate mechanism in the pathogenesis of preeclampsia.
ORTHOSTATIC SHIFTS OF CARDIOVASCULAR MEASUREMENTS DIFFER BETWEEN SUBTYPES OF HYPERTENSIVE DISEASES IN PREGNANCY.
A. Staelens, S. Vonck, K. Tomsin, T. Mesens and W. Gyselaers
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Introduction
Impedance cardiography (ICG) is a promising technical device to determine the cardiovascular function in pregnant women. ICG enables orthostatic testing in which the patient is moved from supine to standing position which might elucidate differences of maternal hemodynamic function and cardiovascular (mal) adaptation in different types of maternal hypertensive disorders. The aim of this study was to evaluate the shift of ICG cardiovascular measurements from supine to standing position, in uncomplicated and hypertensive pregnancies.

Patients and methods
Cardiovascular function was evaluated in pregnant women using ICG (NICCOMO, Medis Medizinische Messtechnik GmbH, Ilmenau, Germany) according to a standardized protocol in supine and standing position. Exclusion criteria were twin-pregnancies, preexisting maternal comorbidity, atypical preeclampsia, HELLP-syndrome and non-hypertensive gestational complications. Measurements of blood pressure, aortic flow velocities (VI: velocity index; ACI: acceleration index), left ventricular output (HR: heart rate; CO: cardiac output; SV: stroke volume), pre-ejection period (PEP) and thoracic fluid (TFC) were assessed. Orthostatic index (OI) was calculated as value_supine/value_standing for all parameters (OI >1: decrease from supine to standing, OI <1: increase from supine to standing).

Patients were divided into 5 groups: uncomplicated pregnancies (UP), essential hypertension (EH), gestational hypertension (GH), early-onset preeclampsia (EPE, <34weeks) and late-onset preeclampsia (LPE, ≥34weeks). Measurements were compared using Mann-Whitney U test (significance at the level of α<0.05) in SPSS 22.0.

Results
A total of 211 patients were assessed: 41 UP, 9 EH, 59 GH, 35 EPE and 67 LPE. In UP, aortic flow velocities, blood pressure and PEP increase from supine to standing position (OI<1). This trend is also true for the GH group, but ACI increases significantly less than in UP (p=.017). In EH, blood pressure hardly changes (OI around 1). In EPE and LPE, aortic flow velocities decrease from supine to standing position (OI>1). In the LPE group, blood pressure increases similarly to UP, but it hardly changes in the EPE group (p<0.050). In EPE, PEP increases significantly more compared to UP (p=.001) and LPE (p=.012). OI of left ventricular output parameters and TFC were not different between groups.

Conclusion
Hypertensive gestational diseases have different cardiovascular orthostatic responses which are unique for each group. Orthostatic impedance cardiography testing shows all characteristics needed for an instantaneous differential diagnostic test between GH and preeclampsia.

A POTENTIAL ROLE OF CXCR2 IN EARLY-ONSET PREECLAMPSIA: PLACENTA CXCR2 EXPRESSION IS RELATED TO INCREASED BLOOD PRESSURE AND SERUM LDH LEVEL
Rong Zhou, Hong Li, Xijing Liu,

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Background: Preeclampsia, an idiopathic obstetric disease that occurs after 20 weeks of pregnancy, is a main cause of maternal and perinatal morbidity and mortality. Although the exact cause of preeclampsia is not completely understood, it is widely accepted that the genesis of preeclampsia, especially the early-onset one, is associated with inadequate trophoblast invasion and failure of spiral artery transformation leading to generalized endothelial dysfunction and an exaggerated inflammatory response. CXCR2 has been shown to bind the ELR+CXC chemokines with high affinity, which has been reported to exert important role in trophoblast invasion and be involved in the pathogenesis of preeclampsia. This study was designed to determine the changes in and significance of placenta expression of CXCR2 in preeclampsia.
Methods: Women with early-onset preeclampsia, late-onset preeclampsia and healthy pregnancy were included in the study, from March 2012 to October 2012. After immunolocalized in human placenta, the levels of CXCR2 protein and mRNA were detected by Western blot, ELISA and Real-time quantitative PCR. Correlations between parameters were examined using Pearson or Spearman’s correlation coefficients.

Results: The expression of CXCR2 was found in the syncytiotrophoblasts and vascular endothelial in all groups with no difference between maternal and fetal side. The placental CXCR2 protein as well as CXCR2-mRNA expression of early-onset preeclampsia were significantly lower than those of healthy pregnancy and late-onset preeclampsia. The placental CXCR2 protein expression of early-onset preeclampsia correlated negatively with systolic blood pressure and LDH.

Conclusions: Significant abnormality of placental CXCR2 expression in early-onset preeclampsia, and correlations between placenta CXCR2 protein expression of early-onset preeclampsia and some clinical parameters of early-onset severe preeclampsia were discovered, suggesting CXCR2 may play role in pathogenesis of early-onset preeclampsia.

ELEVATION OF URINARY ADIPSIN IN PREECLAMPSIA: CORRELATION WITH URINE PROTEIN CONCENTRATION AND THE POTENTIAL USE FOR RAPID DIAGNOSTIC TEST
Tao Wang*, Rong Zhou*, Linbo Gao, Yanyun Wang, Changping Song, Yunhui Gong, Jin Jia, Wei Xiong, Li Dai, Lin Zhang, Huaizhong Hu

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Early diagnosis and treatment of preeclampsia is essential for prevention of seizure development and fetus maturation. Although various methods have been developed for predicting or monitoring the onset of preeclampsia, a simple assay that can be used as a home or point of care test remains unavailable. We attempted to find a urinary protein that could be used as a biomarker for developing such a test. Urinary samples were collected from 124 preeclampsia and 135 healthy pregnant women for screening using a protein array technology and quantification by enzyme-linked immunosorbent assay. A urinary protein, adipsin, was found significantly increased, and the adipsin creatinine ratio was closely correlated with the urinary 24-hour protein in preeclampsia patients. When combined with the increased diastolic blood pressure (≥90 mmHg), the sensitivity was 90.3% and the specificity reached 100.0% for preeclampsia diagnosis. We then developed a laminar flow immunoassay for rapid diagnosis, and the sensitivity and specificity was 89.04% and 100%, respectively, when combined with increased diastolic blood pressure. Because of the easiness of sample collection, assay conduction and result interpretation, this urine test can be potentially used as a home test for monitoring preeclampsia onset for high risk pregnant women and as a rapid test for a preliminary diagnosis for emergency patients at hospitals.

SYNCYTIOTROPHOBLAST EXTRACELLULAR VESICLES FROM PRE-ECLAMPTIC PATIENTS AFFECT PLATELET FUNCTION

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Introduction: Pre-eclampsia complicates around 3% of all pregnancies and is one of the most common causes of maternal mortality worldwide. It is caused by the placenta and is manifest as raised blood pressure, proteinuria and vascular inflammation in the mother. The placenta sheds increased numbers of syncytiotrophoblast extracellular vesicles (STB EV) into the maternal circulation. Platelet reactivity, size and counts may be altered in pre-eclamptic women who develop pre-eclampsia for reasons that are not yet understood. Here we investigated if this increase in platelet reactivity could be caused by STB EV that are released from the placental surface into the mother’s blood.

Methods: STB EV were isolated using a modified dual placental perfusion system. Platelet rich plasma and washed platelets were prepared from whole blood by differential centrifugation. Platelet preparations from 3 healthy female donors were each exposed to 3 separate samples of STB EV from both healthy and pre-
eclampsia placentas. Aggregation was measured in response to agonists following incubation with STB EV, and in response to STB EV alone. To investigate whether platelets bind STB EV, platelets were incubated with STB EV and fixed at various time points, then analysed by either flow cytometry or electron microscopy. Immunoblotting of STB EV treated platelets was performed to investigate activation of signalling pathways. Finally thrombus formation in response to STB EV was tested using DIOC

Results: STB EV associate rapidly with platelets and were found to cause increased tyrosine phosphorylation indicating platelet activation, which was increased with STB EV isolated from pre-eclamptic pregnancy placentas compared to those from healthy pregnancy. We also found that STB EV from pre-eclampsia complicated pregnancy, but not healthy pregnancy, induced reversible aggregation at high platelet concentration and that the treatment of platelets with aspirin, the current therapy given to women at high risk of pre-eclampsia, removes this affect. Finally, STB EV stimulated thrombus formation and the effect was more pronounced with STB EV from preeclampsia placentas.

Conclusion: We provide direct evidence that STB EV could contribute to the platelet dysfunction that characterises pre-eclampsia.

MATERNAL PLASMA AND PLACENTA MIRNAS EXPRESSION PROFILING OF PREECLAMPTIC PREGNANCIES BY MICROARRAY.
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Abstract:
The role of posttranscription regulation in preeclampsia is largely unknown. MicroRNAs (miRNAs) regulate the expression of nearly 30% of all the human genes and participate in all fundamental cell processes. Genome-wide analysis shows that human placenta expresses more than 600 miRNA species, including placenta-specific ones with high level of expression during different stage of pregnancies. miRNAs have emerged as key regulators of gene expression stability implicated in cell proliferation, apoptosis, and development. Comparative analysis also has revealed many differentially expressed miRNAs with either high or low levels of expression in human placentas from preeclamptic and normal pregnancies. Recently, circulating miRNAs of maternal plasma are considered as potential useful noninvasive biomarkers in pregnancies. This study purpose investigated differentially expressed of miRNAs in placenta and maternal plasma from patients with preeclampsia (PE) and normal term (NT) pregnancies.

Using microarray profiling of human miRNAs (1368 probe) were measured in samples collected from 18 PE cases and 18 NT. The analysis indicated that 406 of these miRNAs in all placentas and 42 of these miRNAs in all maternal plasma were expressed. The relative expression of 12 miRNAs (P < 0.05 and >2-fold) in maternal plasma (hsa-miR-191*, hsa-let-7b*, hsa-let-7f-1*, hsa-miR-1539, hsa-miR-23c, hsa-miR-33b*, hsa-miR-425*, hsa-miR-4313, hsa-miR-550a, hsa-miR-933, hsa-miR-877* and hsa-miR-1183) was differentially expressed in PE and NT.

Results showed that there were differentially expressed placenta and maternal plasma miRNAs in patients with PE and control cases. These plasma miRNAs might be used as notable biomarkers for diagnosis of preeclampsia.

Poster Presentation Abstracts

EVALUATION OF BIOMARKERS FOR THE PREDICTION OF PRE-ECLAMPSIA IN WOMEN WITH TYPE 1 DIABETES MELLITUS: A SYSTEMATIC REVIEW
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Background
Pre-eclampsia is a leading cause of maternal and foetal morbidity and mortality. Women with type 1 diabetes mellitus are at an increased risk of developing pre-eclampsia, compared to the background population.
Research has increasingly focused on biomarkers to predict pre-eclampsia development. To date, this has not been systematically reviewed in women with type 1 diabetes.

Objective
To systematically review the literature about the effectiveness of serum biomarkers for the prediction of pre-eclampsia in women with type 1 diabetes.

Methods
We developed a systematic search strategy and conducted the search in March 2014. We searched 7 electronic databases, which included Medline, Embase, Maternity and Infant Care, CINAHL, Scopus and Web of Science. Reference lists were also reviewed for further studies. A data extraction form was used to extract data from included studies. The QUADAS tool was used to assess quality of included studies.

Results
17 studies out of 1962 studies identified met the inclusion criteria. A wide range of biomarkers were measured including HbA1c, anti-angiogenic and angiogenic factors (PIGF,sEng and sFlt-1), adhesion molecules, urinary protein and fat-soluble vitamins. Biomarkers that were found to be significantly different include PIGF, sEng, sFlt-1, HbA1c and urinary albumin. PIGF:sEng and sFlt-1:PIGF ratios were amongst the most effective predictors of pre-eclampsia.

Discussion
No single biomarker was identified as being useful in prediction of pre-eclampsia. Evidence would suggest that a combination of biomarkers and maternal characteristics would be more beneficial in the prediction of pre-eclampsia, rather than a single biomarker. More research should be conducted in this high-risk group to identify possible predictive markers to aid targeting of resources to those most at risk. This may also allow for further understanding of the pathophysiology of pre-eclampsia.

COMPARATIVE TRANSCRIPTOME ANALYSIS IMPLICATES THE PLACENTAL ACTION OF HTRA SERINE PEPTIDASE 1 (HTRA1) IN PREECLAMPSIA: A VIEW FROM EVOLUTIONARY MEDICINE
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Preeclampsia (PE) is a human specific disorder associated with placental dysfunction. Because the placenta is the site of both cooperative and competitive interactions between mother and the embryo and fetus, we asked whether genes implicated in PE are highly evolutionarily constrained. We obtained transcriptome data for: first, second, and term placenta from normal pregnancies (Mehkeev et al., 2008); placenta-specific expressed genes (Dezo et al., 2008; Saben et al., 2014); and, genes differentially expressed in PE compared with normal placenta (Kleinrouweler et al., 2013; Tejera et al., 2013). Human transcript IDs were mapped to the human genome and orthologous gene IDs for non-human primates (Pongo pygmaeus, Callithrix jacchus, Otolemur garnettii) downloaded from Ensembl database v.74 using Biomart. All cDNA sequences were translated into protein sequences via perl scripts and aligned using MUSCLE v.3.8. We first identified 12,276 orthologous genes across the 4 species of primates and then calculated the dN/dS ratio, a measure of natural selection, for each gene using CodeML from PAMLv4.7. Evidence for lineage-specific selection was determined by maximum likelihood. Among genes differentially expressed over the course of pregnancy, 3 are under strong purifying selection in humans, an indication of their critical and evolutionarily constrained functions. In placental-specific genes, only HtrA serine peptidase 1 (HTRA1) is under selection in humans and, remarkably this gene is differentially regulated in preeclampsia. HTRA1 is implicated in the structural integrity of blood vessels through its actions on pro-collagen peptides. This evolutionary perspective offers a new approach to narrow the focus on particular candidate genes for preeclampsia.

METYLENTETRAHYDROFOLATE REDUCTASE (MTHFR) C677T POLYMORPHISM AND RISK OF PREECLAMPSIA IN TURKISH PREGNANT WOMEN

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Although the aetiology of preeclampsia (PE) is still not clear, placental, immune and genetic factors are thought to play an important role in its pathophysiology. The aim of the present study was to investigate whether there is an association between Methylentetrahydrofolate Reductase (MTHFR) C677T polymorphism and PE. In this study, 82 preeclamptic and 38 normotensive pregnant women was genotyped for MTHFR C677T polymorphism by RFLP analysis and the distribution of genotype and allele frequencies belonging to these polymorphism in preeclampsia and controls were also evaluated. Among controls, the MTHFR C677T genotypes of CC, CT and TT were observed in 68%, 13%, and 18% respectively, whereas the CC, CT and TT genotypes were observed in 61%, 24%, and 15% of case patients, respectively. CT genotype was found higher in preeclampsia than controls (PE:24%; control:13%), but there was no statistically significant difference in frequencies of three genotypes of MTHFR C677T polymorphism between PE and controls (p=0.361). The C allele frequency was 73% in PE patients while it was 75% in controls (p=0.764). The T allele frequency was 27% in PE patients while it was 25% in controls (p=0.764).

In conclusion, it was not found any difference in allele and genotype frequencies between preeclampsia and controls for MTHFR C677T polymorphism. It is not known whether C677T polymorphism has a functional effect on the MTHFR gene. So it was not possible to determine whether this polymorphism promotes the progression of PE because of no statistically significant difference between PE and controls.

**Key Words:** Preeclampsia; MTHFR C677T, Polymorphism, Pregnant women

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**PLASMA BIOMARKERS FOR EARLY IDENTIFICATION OF WOMEN AT RISK FOR PREECLAMPSIA**

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**Introduction:** Preeclampsia (PE) is a multi-systemic pregnancy complication with complex pathophysiological changes characterized by new onset hypertension and proteinuria, that develop after 20 weeks of gestation in previously normotensive women. PE complicates 2–10% of pregnancies and leads to increased maternal and fetal morbidity and mortality. No reliable screening markers exist to detect at-risk pregnancies, thereby offering no opportunity for intervening therapies prior to the onset of the symptoms.

**Samples & Methods:** Blood samples for this case-control proteome study were collected prospectively from pregnant women at approximately 11 weeks of gestation. After delivery, 10 samples from cases that subsequently developed early severe PE and 10 from cases with normal healthy outcomes were analysed by two-dimensional gel electrophoresis (2-DE) and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS) in order to identify biomarkers for PE.

**Results:** Gel comparison revealed 12 proteins differentially expressed in maternal plasma in women that subsequently developed PE. Six proteins, Alpha-1-antitrypsin (A1AT), CD5 antigen-like molecule (CD5L) Keratin, type I cytoskeletal 9 (K1C9), Myeloid cell nuclear differentiation antigen (MNDA), Serotransferrin (TRFE) and Vitamin D-binding protein (VTDB) were up-regulated and six, Alpha-2-HS-glycoprotein (FETUA), Beta-2-glycoprotein 1 (APOH), Complement factor B (CFAB), Haptoglobin (HPT), Vitronectin (VTNC) and Zinc-alpha-2-glycoprotein (ZA2G) were down-regulated. The differential expression of ZA2G VTNC and FETUA was further verified by Western blot Western blot and densitometric analysis.

**Conclusions:** This pilot study indicates that proteomics could be a useful tool for the detection of new PE screening markers. All differentially expressed proteins are candidate biomarkers for the early identification of women at risk for PE. As these are preliminary findings, follow-up experiments are needed for their evaluation.

**Acknowledgment:** The study was funded by «Aristeia», through the operation program «Education and lifelong learning» co-financed by EU and the Greek state.

**EARLY IDENTIFICATION OF WOMEN WITH HELLP SYNDROME WHO NEED PLASMA EXCHANGE AFTER DELIVERY**

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Abstract

Objectives: To compare the laboratory course of HELLP syndrome between patients who recover and those who progress to postpartum thrombotic microangiopathic syndrome (PTMS) and require postpartum plasma exchange (PPEX) and to describe maternal characteristics and morbidity in women with PTMS.

Methods: In this retrospective analysis, 81 patients recovered and 5 progressed. Values for aspartate aminotransferase (AST), lactate dehydrogenase (LDH), bilirubin, platelets (Plt), urea, and creatinine at 0, 8, 16, 24, 48, and 72 hours postpartum in both groups were analyzed and compared. We also described maternal characteristics and morbidity of patients who progressed to PTMS.

Results: Patient groups differed significantly at 72 hours postpartum for Plt and LDH values and at 24 and 48 hours for bilirubin. Trends for AST and Plt differed significantly between the recovery and progression groups in the first 48 hours. All patients who progressed had severe morbidity: acute kidney injury (5), respiratory failure (5), neurological complications (3) and severe bleeding (3) including one case of maternal death.

Conclusions: Women with HELLP syndrome without clear Plt and AST improvement in the first 48 hours and with acute kidney injury, neurological impairment, or respiratory distress syndrome are at risk of progressing to PTMS. They should be administered PPEX between 24–72 hours postpartum.

Acknowledgments
The study was financially supported by grants IGA NT/14104-3/2013, No. 2 RVO-FNO/2013 and No. 22 RVO-FNO/2014.

Day 2: Pre-eclampsia treatment and management

Invited Speakers Abstracts

Vitamin D3 deficiency during pregnancy and preeclampsia
Dr Stella Nowicki, Professor Microbiology and Immunology, Meharry Medical College, Nashville, TN, USA
Vitamin D3 levels in both maternal and umbilical cord compartments are low in preeclampsia. Vitamin D3 regulates angiogenesis and has direct influence on molecular pathways important in the pathogenesis of preeclampsia. Therefore maternal vitamin D3 deficiency may be an independent risk factor for preeclampsia. The objective of this study was to characterize the effect of vitamin D3 on the function of monocytes and macrophages during pregnancy. We hypothesized that vitamin D3 would modify the expression of monocytes and macrophage CD55 (complement inhibitor) to prevent chronic inflammation during pregnancy. We developed an experimental ex vivo model system to quantify the immune-responsiveness of primary monocytes isolated from pregnant patients.

Human monocytes and macrophages, were treated with inflammatory signaling and with or without 1,25 dihydroxy vitamin D3 for multi time points. The real time PCR was used to quantify CD55 mRNA. CD55 protein expression was assayed using immune-confocal microscopy and immunohistochemistry. Vitamin D3 significantly regulate CD55 expression in monocytes and macrophages exposed to inflammatory signaling. CD55 expression regulates macrophages' detachment, that preventing the excessive accumulation of activated macrophages in chronic inflammation which is implicated in preeclampsia. Our results support our hypothesis that there are inherent differences in the proinflammatory responsiveness between individuals and that vitamin D3 signaling may play a role in maintaining elevated anti-inflammatory CD55 levels. These findings help us to understand on molecular level how vitamin D3 deficiency may increase risk for preeclampsia and gives us some explanation why vitamin D3 deficiency has been linked to an increased risk for the development of preeclampsia. All together suggests that vitamin D3 supplementation in early pregnancy should be explored for preventing preeclampsia and promoting neonatal well-being.

Pre eclampsia - a charity perspective
Ms Ann Marie Barnard, Chief Executive Officer, Action on Pre-eclampsia

Action on Pre-eclampsia is the only UK charity dedicated to supporting those affected by the disease. Founded in 1992 by Professor Chris Redman and Isable Walker APEC runs a helpline for those affected, study days for midwives and convenes an annual conference for experts in the field.

APEC has gained a wide knowldege of the personal impact of pre eclampsia, the devastation it casue and the ways in which patients percieve their care could have been improved. The aim of this session is to share feedback from both patients and professionals of their pre eclampsia experiences.

The hemostatic changes in preeclampsia, is there a place for anticoagulation treatment for the prevention of this syndrome?
Professor Offer Erez, Director of Risk Management and Patients Safty Unit, Acting Director Maternal Fetal Medicine Unit, Soroka University Medical Center, Ben Gurion University of the Negev, Israel
Heparin is one of the most frequent drugs used during pregnancy. The most common indication is for the prevention and treatment of thromboembolic disease. In the recent years heparins and mainly low molecular weight heparin are also being used for the prevention of pregnancy complications. There is evidence suggesting that women with preeclampsia have increased thrombin generation, resulting from activation of the coagulation cascade as well as systemic maternal inflammation. A recent randomized trial suggested a beneficial effect of low molecular heparin in the prevention of the early form of the disease in women with thrombophilia. Raising the question whether heparin can be used for primary or secondary prevention of preeclampsia.

**Pre-eclampsia casts a long shadow**

*Professor Fiona Broughton Pipkin*, Professor Emeritus of Perinatal Physiology, University of Nottingham Medical School, UK

Pre-eclampsia is associated with higher incidence of hypertension, ischaemic heart disease, stroke, renal and metabolic disease in later life, all these occurring at a younger age than in women whose pregnancies remained normotensive. Is hypertensive pregnancy the unmasking of an existing pre-disposition to these conditions, or does it sow the seeds of future disease? Can we improve the routine 6-week post-natal check to allow us to identify women at increased later risk? Prevention is better than cure - we should be trying.

**Gestational hypertension, preeclampsia and the risk of cardiomyopathy in and after the peripartum period**

*Ms Ida Behrens*, Department of Epidemiology Research, Statens Serum Institut, Denmark

Preeclampsia is associated with an increased risk of peripartum cardiomyopathy, but whether it is also associated with cardiomyopathy later in life is unknown. Using Danish health register information on >1 million women giving birth from 1978 to 2012, we compared rates of 1) peripartum cardiomyopathy and 2) later cardiomyopathy, in women with and without a history of preeclampsia/gestational hypertension. Apart from markedly increased risks of peripartum cardiomyopathy (5- to 23-fold, depending on severity of the gestational hypertensive disorder), women with a history of preeclampsia or gestational hypertension also had a lasting two-fold increase in cardiomyopathy risk later in life.

**Angiogenic Factors in Preeclampsia: Potential for Diagnosis and Treatment**

*Dr Sarosh Rana*, MD, Assistant Professor, Harvard Medical School/ Beth Israel Deaconess Medical Center, Boston, MA, USA

The talk will summarize new observations of key roles for circulating angiogenic factors in diagnosing, managing and, treating preeclampsia. We will review the literature that alterations in circulating angiogenic factors in preeclampsia correlate with the diagnosis and adverse outcomes particularly when the disease presents prematurely. Measurement of these angiogenic biomarkers has also shown to differentiate preeclampsia and its complications from other disorders that present with similar clinical profiles. We will also review the evidence that modulating these factors can have therapeutic effects suggesting a future role for angiogenic factors in treatment and prevention of preeclampsia.

**Oral Presentation Abstracts**

**PLACENTAL PROTEIN 13: PRECONDITIONING OF UTERINE ARTERIES, A POSSIBLE AGENT TO PREVENT THE DEVELOPMENT OF PREECLAMPSIA**

S. Gizurarson, H. Helgadottir, T. Drobnjak, B. Huppertz, M. Mandala, M. Sammar, G. Osol and H. Meiri

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**Objectives**

Placental protein 13 (PP13), a placenta specific protein, is a galectin specifically made by the placenta with high affinity to carbohydrate residues. A meta analysis of 18 clinical studies by Huppertz et al (2013) have shown that its level is is reduced in the first trimester of pregnant women who subsequently develop preeclampsia. A naturally occurring PP13 deletion of thymidine at position 221 (DelT221) is a rare mutation identified among black Africans and is associated with an increased frequency of severe preeclampsia. The DelT221 variant is unable to bind carbohydrates. In this study we compared the effect of PP13 with its DelT221 variant in pregnant rats.

**Methods**

Full length PP13 (“wildtype”) or its DelT221 (“truncated”) variant were tested in gravid rats, by continuous administration over a period of 5 days starting from day 8 of pregnancy, using a mini osmotic pump (0.625 ng/h) implanted subcutaneously during placentation.
Results
Animal exposed to prolonged PP13 application or its truncated variant have a lower (about 20 mm Hg) blood pressure that is reversible after the pump released its entire content. When sacrificed at day 15 or after delivery the animals treated with PP13 but not with its truncated varried has expanded uterine veins and also a larger placentae and heavier pups.

Conclusion
This study emphasizes the importance of PP13 in blood pressure control and utero-placental remodeling in pregnancy. Understanding the structure/function relationship underlying the role of PP13 molecule in pregnancy in general and placental development and preeclampsia in particular may shed light on PP13 regulatory functions in normal pregnancy development and placental impairment. The results are consistent with the assumption that PP13 precondition the uterine vasculature, facilitating proper placentation or even prevent preeclampsia, turning replenishing with PP13 into a novel pharmacological agent against preeclampsia.

ASSOCIATION BETWEEN SUICIDAL IDEATION AND INTIMATE PARTNER VIOLENCE AMONG LOW-INCOME POSTPARTUM WOMEN IN SÃO PAULO, BRAZIL.

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Background: The purpose of this investigation is to examine the relationship between exposure to intimate partner violence (IPV) and risk of suicidal ideation (SI) among postpartum women.

Methods: Participants were recruited between May 2005 and March 2007 from primary health care units in São Paulo, Brazil. A total of 701 postpartum women were included in the analysis. Postpartum SI was assessed using the Clinical Interview Schedule-Revised (CIS-R). Crude and adjusted risk ratios with 95% confidence intervals (95% CI) were estimated using Poisson regression with robust variance to examine the association between IPV and the risk for postpartum SI.

Findings: The prevalence of postpartum suicidal ideation was 4%. Among those with postpartum SI, 70% reported IPV during pregnancy. We found a statistically significant association between IPV SI during the postpartum period. Compared to non-IPV counterparts, women who reported IPV had an increased risk for suicidal ideation (Relative Risk (RR) 7.25, 95% CI: 3.23-16.27). In the fully adjusted model, the risk for SI remained significantly higher for women who experienced IPV compared to those who did not (RR 3.00, 95% CI: 1.24-7.25).

Interpretation: In our sample of low-income women living in Brazil, intimate partner violence in pregnancy is associated with postpartum suicidal ideation. These findings present clinical implications for screening for violence and suicidal thoughts during pregnancy and the postpartum.

Poster Presentation Abstracts

HAZARDOUS EFFECTS OF DILLAPIOLE ON MATURATION OF MOUSE OOCYTES, FERTILIZATION, AND FETAL DEVELOPMENT

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Abstract
Previously, we reported that dillapiole, a phenylpropanoid with antileishmanial, anti-inflammatory, antifungal and acaridical activities, is a risk factor for normal embryonic development that triggers apoptotic processes in the inner cell mass of mouse blastocysts, causing decreased embryonic development and cell viability. In the current study, we investigated the deleterious effects of dillapiole on mouse oocyte maturation, in vitro fertilization (IVF), and subsequent pre- and postimplantation development both in vitro and in vivo. Notably, dillapiole significantly impaired mouse oocyte maturation, decreased IVF rates, and inhibited subsequent embryonic development in vitro. Preincubation of oocytes with dillapiole during in vitro maturation induced an increase in postimplantation embryo resorption and a decrease in mouse fetal weight. In an in vivo animal
model, 2.5-10 μM dillapiole, provided in drinking water, caused a decrease in oocyte maturation and IVF, and led to deleterious effects on early embryonic development. To our knowledge, this is the first study investigating the impact of dillapiole on maturation of mouse oocytes, fertilization, and sequential embryonic development.

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A CASE OF POSTPARTUM CARDIOMYOPATHY AFTER BROMOCRIPTINE USE TO TREAT DEPRESSION

Authors: Yumiko Goto¹, Atsuko Togo², Akane Kondo³, Toshinari Muramatsu¹, Hitoshi Ishimoto²

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Abstract:

Backgrounds
Postpartum cardiomyopathy is a rare disease which women without heart disease happen to have a heart failure like dilated cardiomyopathy during pregnancy or postpartum. Though the cause of a disease has not been elucidated, there are some hypothesis that it is caused by virus infection, pregnancy itself, immunopathy, endocrine abnormality. Recently, atypical prolactin is reported as a cause of postpartum cardiomyopathy. In those cases, Bromocriptine was effective as a treatment.

Case
A 28 year old, 0 gravida 0 para, woman visited our hospital at 25 gestational weeks for PIH, FGR and depression. She admitted because of threatened premature delivery at 26 weeks and she delivered at 33weeks. She took bromocriptine because depression had not been stable. She had a good course after delivery. However post partum day 9, she came emergency room with asthma-like condition. She was diagnosed for heart failure (EF20%, hypokinetic LV, significant MR). She needed a control under IABP urgently.

Discussions and conclusions
In this case, she was able to stop lactation by bromocriptine but she appeared acute heart failure which seemed severe postpartum cardiomyopathy. Postpartum cardiomyopathy may have various factor not only prolactin.

THE PRERATIO STUDY IS THE SFLT-1/PLGF RATIO A SUITABLE MARKER TO DIAGNOSE PREECLAMPSIA AND TO PREDICT ITS ADVERSE MATERNAL/NEONATAL OUTCOMES?

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Background:
Hypertensive disorders of pregnancy such as preeclampsia (PE) remain a leading cause of maternal and fetal morbidity and mortality. Accumulating evidence suggests that an imbalance between proangiogenic factors such as placental growth factor (PIGF) and antiangiogenic factors such as soluble fms-like tyrosine kinase 1 (sFlt1) derived from the placenta play a fundamental role in the pathogenesis of preeclampsia. We evaluate the potential value of sFlt1 and PIGF and its ratio in diagnosing preeclampsia, predicting the development of adverse outcomes and to get to know if there is any valuable information of these markers in the differential diagnosis of different phenotypes of PE.

Methods: The aim of this prospective multicenter cohort study is to include 600 women suspected of PE. For the preliminary results a total of 44 women are analysed: 17 with normal pregnancy outcome, 3 patients with HELLP, 3 with gestational hypertension (GH) and 21 with PE including 2 samples of superimposed PE.

Results: The sFlt1/PIGF ratio is significantly increased in patients with both early as late onset PE/HELLP in comparison to controls and GH. PIGF seems to be more related to fetal outcomes compared to sFlt-1. A ratio of
A high sFlt-1/PlGF ratio is associated with PE/HELLP and has a significantly increased risk for delivery.

**Keywords:** placental growth factor, PlGF, soluble fms-like tyrosine kinase, sFlt-1, preeclampsia, gestational hypertension

**A SUPEROXIDE DISMUTASE MIMETIC EFFECTS ON THE BLOOD FLOW IN MERINO EWE’S FETUS**

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**Background:** The vascular endothelium is a critical regulator of vascular function. Diverse stimuli such as Nitric Oxide (NO) and oxidative stress modulate endothelial function and thereby impact on the development of vascular disease states. Therefore, identification of the regulatory factors that mediate the effects of these stimuli on endothelial function is of considerable interest. Tempol (4-hydroxy-2,2,6,6-tetramethyl piperidinoxy) is a superoxide dismutase mimetic which scavenges free radicals. In this study, we analysed the mechanism how Tempol act on endothelium in hypertensive conditions.

**Materials and Method:** Pregnant Merino ewes (n=5) were surgically prepared between 0.85 and 0.90 full gestation. A catheter was inserted into the femoral artery to measure blood pressure continuously. Another catheter was inserted into a tarsal vein. The angiotensin II (0.05ug/min) was infused continuously for 9-12 days until the blood flow was blocked. Thereafter, Tempol (300umol/kg) was administered to improve blood flow. The volume flow rate, diameter and pressure were digitised. The Doppler quadrature signals were relayed to a spectrum analyser and the digital data output to computer in real time. NO concentration, blood flow velocity and aortic diameter were analysed by ANOVA.

**Result:** The pre-administration NO was 1.9±0.4 nM, AI was 0.35±0.14. 10 min after administration of AngiotensinII both measurements were NO=0nM, AI= 0.35±0.14. After tempol administered, NO=6.1±1.5 nM and AI= 0.35±0.14. Infusion of tempol promotes endothelium produces NO which improved the reverse flow.

**Conclusion:** Dysfunction of endothelium cause arteriosclerotic changes which end up disruption and reverse flow. In this study, we showed that Tempol lower the oxidative stress and promote NO which improve blood flow. We believe this may offer a new antihypertensive treatment strategy in the future.

**TWO CASES OF POSTERIOR REVERSIBLE LEUKOENCEPHALOPATHY SYNDROME (PRES) ASSOCIATED WITH PREECLAMPSIA**

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**Introduction:** Clinical features of posterior reversible leukoencephalopathy syndrome (PRES), also known as reversible posterior cerebral edema syndrome, include headache, nausea, vomiting, seizures, visual disturbances, altered consciousness, and mental abnormalities. PRES is characterized as reversible changes of MRI signals in the white matter of the occipital and parietal lobes, pathogenesis of which is a form of vasogenic edema. We here present two cases of PRES secondary to preeclampsia.

**Case 1)** A 39-year-old woman, gravida 2, para 2, was referred to our high risk care unit at 30 weeks of gestation because of manifestation of preeclampsia and HELLP syndrome. Her blood pressure was 190/110mmHg. Sonography showed retroplacental hematoma indicative of placental abruption. An urgent cesarean section was performed and a female neonate with a body weight of 1146 g was delivered. Apgar scores were 8 and 9 at 1 and 5 minutes, respectively. Postoperatively, she was treated with intravenous magnesium sulfate and nicardipin. Laboratory data had normalized. Three days after the delivery, the patient complained of visual disturbance. Cranial magnetic resonance imaging (MRI) demonstrated high signal intensity in the left occipital lobe on T2-weighted image (T2WI) and fluid-attenuated inversion-recovery (FLAIR) image. On the 6th day after the delivery, a follow-up MRI demonstrated disappearance of the abnormal lesion. Blood pressure had normalized and visual disturbance was improved. She was discharged on the 10th postoperative day.

**Case 2)** A 40-year-old primigravida underwent in vitro fertilization. At 40 weeks 3 day gestation, labor began spontaneously with a complaint of a headache. Blood pressure was 143/94mmHg. Two hours later, a generalized seizure occurred, and her blood pressure was 190/103mmHg. She was immediately transferred to our institution, and an emergency cesarean section was carried out. A healthy 2710g female baby was delivered with Apgar scores of 8 and 9 at 1 and 5 minutes, respectively. MRI after 2 hours revealed a high signal intensity in the left occipital lobe on T2WI and fluid-attenuated inversion-recovery (FLAIR) image.
signal density area in the bilateral occipital lobes on T2W1 and FLAIR images. Intravenous magnesium sulfate was administered for 5 days. Her blood pressure was normalized, and puerperal eclampsia did not occur. On the 8th day after the delivery, a follow-up MRI showed disappearance of the high signal area. She was discharged. She was discharged on the 11th day.

Conclusion) An acute onset of hypertension is likely to be an episode that heralds PRES, of which obstetricians should be aware. Prompt and appropriate control of both blood pressure and seizure are required for a better prognosis.

Day 3: Technologies to assess pregnancy and pregnancy-associated conditions

Invited Speakers Abstracts

Pregnancy complicated by cervical cancer
Dr Wojciech Kolawa, Senior lecturer, University Hospital, Department of Gynecology and Oncology, Jagiellonian University, Krakow, Poland

Incidence of invasive cervical cancer in pregnancy is low: 1-5/100 000. Incidence of preinvasive lesions on the cervix is at least 10 times higher. Cervical cancer complicating pregnancy is an ambiguous phenomenon as it affects the organ where foetus develops. Diagnosis of cervical cancer creates a need for a satisfactory, possibly non-invasive diagnostic process, and a challenge to choose optimal treatment. The aim of the presentation is to discuss the following topics based on current literature and individual experience. What is the influence of pregnancy on cancer progression? Is there a way to avoid conisations in pregnant patients with HSIL cytology and with a colposcopical suspicion of microinvasion while in vast majority no invasion occurs? Is delay of cancer treatment an optimal proceeding? What is the impact of chemotherapy on foetus? How to choose the optimal procedure considering foetal maturation and cancer stage?

Fetal haemodynamic assessment by magnetic resonance imaging
Dr Mike Seed, Pediatric Cardiologist and Radiologist, SickKids, Toronto, Canada

Ultrasound provides high spatial and temporal resolution imaging of the fetal heart and Doppler yields a wealth of information about fetal cardiovascular physiology. However, due to inherent limitations of the technique, ultrasound is not routinely used to measure an important parameter of haemodynamics; blood flow. Furthermore, ultrasound provides no information about a second key parameter of cardiovascular function, the oxygen content of blood. We sought to develop a MRI technique to measure fundamental elements of fetal circulatory physiology including oxygen delivery, oxygen consumption, cardiac output and the distribution of blood flow and oxygen across the fetal circulation.

Information about prenatal examinations - A challenge in antenatal care
Associate Professor Susanne Georgsson Öhman, Senior Lecturer, Karolinska Institutet Department of women’s and children’s health, Stockholm, Sweden

In Sweden pregnant women are offered ultrasound in the second trimester. Combined Ultrasound and Biochemical screening (CUB) may be offered for risk estimation for chromosomal aberrations but new non invasive test methods with this purpose are in an explosive development. Invasive test; amniocentesis or chorion villus sampling, is offered when the risk for chromosomal aberrations is high due to screening test results, due to the maternal age or due to increased worry. It is essential for the parents to be to have access to correct, non-directive information to be able to make decisions, informed choices, about prenatal examinations, and this is a great challenge for the antenatal health care.

The role of nutrition and genetics during pregnancy
Dr Anne Parle-McDermott, Lecturer in Genetics, Dublin City University, Ireland

The B vitamin, folate, is an important nutrient during pregnancy in the prevention of birth defects. While it is widely accepted that a folic acid supplement can prevent neural tube defects (NTD) if taken preconceptionally, the exact mechanism of how prevention is occurring is not clear. What also needs to be considered is whether folate supplementation has any additional effects outside of NTD prevention. This talk will describe the latest discoveries in relation to how human genetic variation can impact on pregnancy and how folic acid supplement could potentially be modifying our genome.

Catheter Ablation of Arrhythmia in Pregnant Women
Dr John Ferguson, Associate Professor, University of Virginia Medical Center, USA

Oral Presentation Abstracts

WHOLE-OF-POPULATION STUDY OF TERM AND POST-TERM GESTATIONAL AGE AT BIRTH AND CHILDREN’S DEVELOPMENT
LG Smithers, A Searle, C Chittleborough, W Scheil, S Brinkman, JW Lynch
Background: In Australia, over 90% of births are ≥37 weeks, and therefore term (37-41) and post-term (≥42 weeks) comprise the majority of births and the majority of children with developmental problems. The debate over which gestational age at birth is associated with the lowest risk has been predominantly focussed on short-term birth outcomes. The objective of this study is to examine the longer-term risks to children's development according to the week of gestation at birth, among children born at ≥37 weeks gestation.

Methods: This population-based study in South Australia involved linking routinely-collected perinatal data from all birth ≥37 weeks gestation from 1999-2005 to children's development at school entry (n=12601). The best estimate of gestational age at birth was recorded in weeks according to a dating ultrasound at 8-13 wk, which was supported by the first day of the last menstrual period or by review of other ultrasound. Children's development was documented by teachers during a national census of children attending their first year of school in 2009, using the Australian Early Development index (AEDI). Children scoring in the lowest 10% of the national distribution of AEDI scores were considered developmentally vulnerable.

Results: There percentage of children vulnerable on one or more AEDI domains for the following gestational ages at birth 37, 38, 39, 40, 41, 42-45 weeks was 24.9%, 22.4%, 20.7%, 20.1%, 20.4% and 24.5%, respectively. Across all domains of the AEDI, the adjusted relative risk of developmental vulnerability was 9-34% higher for children born at 37 weeks and 10-102% higher for children born ≥42 weeks, compared with children born at 40 weeks, although the confidence intervals were wide.

Conclusion: Children born at 40 to 41 weeks gestation have the lowest risk of developmental vulnerability at entry to school. The longer-term effects of gestational age at birth on child development should be taken into consideration in perinatal care.

USE OF SBAR TOOL FOR HANDOVER IN DELIVERY SUITE AND MATERNITY WARD

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SBAR, defined as Situation, Background, Assessment and Recommendation, has been introduced into the medical world from the aviation industry to improve patient safety and culture of teamwork. SBAR, as in any other department, has been recommended as the main tool of communication in the guidelines between staff members at the Obstetrics Department in Peterborough City Hospital. Hence, I performed an audit, first of its kind in the department, to assess the compliance with use of tool when handing over the patients between Maternity Triage, Delivery Suite and Maternity Ward.

I did a retrospective study of 50 case notes of the year 2013 based on the Maternity Guidelines at Peterborough City Hospital. There were no age or co-morbidities restrictions. The proforma assessed the presence of SBAR sticker or Assessment when transferring patient from Maternity Triage to Delivery Suite as 'Antenatal Handover of Care' and filling in of SBAR tool in Maternity Notes when handing over patient from Delivery Suite to Maternity Unit as 'Postnatal Handover of Care'. The restrictions employed were on any patients directly reaching Delivery Suite as planned deliveries without going through Maternity Triage, any patient transferred to Maternity Ward antenatally for observation/induction or any patient leaving Delivery Suite to any other ward except Maternity Ward.

The results clearly showed that there is a significant margin of improvement especially in completely filling in the SBAR tool page. It was concluded that there is still quite a lack of understanding in the importance of providing complete information when handing over the patient between different teams looking after the patient. It was recommended to include the use of word 'SBAR' several more times in the guidelines to emphasize its importance and to precisely use the word 'Assessment Sticker (a form of SBAR Sticker used at PCH)' when referring to its full completion in the guidelines. Also recommendations were put in to repeat the Audit in about 6-9 months' time to assess the compliance in the year 2014.

The only limitation that I came across was unfortunately secondary to my proforma that did not allow me to completely scrutinise the SBAR tool page to see how often that we missed part of Situation, Background, Assessment and Recommendation along with Date, Time and Name of Transferring and Receiving Midwives.
OBSTETRIC ADMISSIONS TO THE INTENSIVE CARE UNIT IN A TERTIARY CENTRE
Yeo S, Tagore S, CF Yim, KH Tan, Kwek K

Introduction: Obstetric complications relating to pregnancy, delivery and the puerperium can result in severe maternal morbidity and mortality. Understanding risk factors for obstetric WICU admissions will therefore identify high-risk pregnancies and early intervention may improve maternal outcomes.

Aims and objectives: The primary aim of this study was to assess facility-based incidence, case fatality rate and possible risk factors for obstetric Women’s Intensive Care Unit (WICU) admission.

Methods: Retrospective review of all WICU admissions for one year between January 2009 and December 2009 at KK Women's and Children's Hospital (KKH). Maternal characteristics, and all variables concerning pregnancy and delivery were recorded, together with specific data associated with the ICU stay, including indication for admission and major interventions.

Results: There were 67 obstetric WICU admissions, with a hospital-based incidence of 5.6 per 1,000 deliveries. The vast majority of these admissions were postnatal. There was no maternal mortality during the period under review. The most frequent indications for postnatal WICU admission were hypertension during pregnancy (42.6%) followed by major obstetric haemorrhage (39.4%). The other factors associated with a higher risk for WICU admission, and hence severe maternal morbidity, were maternal age above 30, parity above two, and gestational age below 37 weeks.

Conclusion: Hospital-based incidence of WICU admission was 5.6 per 1,000 deliveries. Hypertension during pregnancy, major obstetric haemorrhage, maternal age above 30 and parity above two appear to be significant risk factors for severe maternal morbidity.

ANAEMIA OF PREGNANCY, PERINATAL OUTCOMES AND CHILDREN'S DEVELOPMENTAL VULNERABILITY: A WHOLE-OF-POPULATION STUDY
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Background: There is limited longitudinal data from high-income countries on the sequelae of anaemia during pregnancy. The aim of this study is to examine whether anaemia of pregnancy is associated with adverse perinatal outcomes and with children's developmental vulnerability.

Methods: We conducted a population-based study to link routinely-collected government administrative data that involved all live births in the state of South Australia 1999-2005 (n=124061), and a subset for whom developmental data were collected during a national census of children attending their first year of school in 2009 (n=13654). Perinatal outcomes were recorded by midwives using a validated, standardised form. Development was recorded by school teachers using the Australian Early Development index (AEDI). Children in the lowest 10% of AEDI scores are indicative of developmental vulnerability.

Results: There were 8764/124061 (7.1%) cases of anaemia. After adjustment for a range of potentially confounding factors, anaemia of pregnancy was associated with a higher risk of fetal distress (relative risk (RR) 1.20 (95% CI 1.13, 1.27)) and preterm birth <37 weeks gestation (RR 1.23 (1.15, 1.31)), slightly higher birthweight (14 g (2, 26)) and newborns were less likely to require resuscitation (IRR 0.94 (0.91, 0.097)). Anaemia of pregnancy was not associated with children's developmental vulnerability after adjustment for maternal, obstetric and sociodemographic covariables, either in complete case analyses (n=11949) or after imputation for missing data (n=13654).

Conclusions: Anaemia of pregnancy is associated with perinatal complications but not with children's development at school entry.
CHROMOSOMAL ABNORMALITIES IDENTIFIED AT PRENATAL DIAGNOSIS OF 7050 PREGNANCIES IN TURKEY

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Purpose: Prenatal diagnosis of fetal chromosomal abnormalities is the most common indication for invasive prenatal testing. Amniocentesis is a very crucial diagnostic procedure for preventing the birth of genetically defective fetuses in order to decrease the prevalence of genetic diseases in populations.

Method: A retrospective review of our amniocentesis database for the period from January 2000 to June 2014 was carried out. The karyotyping of 7050 fetuses was carried out in Department of Medical Biology from the samples of amniotic fluids which were sent from department of Gynecology and Obstetrics of Balcali Hospital. A standart nomenclature has been developed to describe each of types of abnormality found in human chromosomes. The current version was developed by the International Standing Committee on Human Cytogenetic Nomenclature and adopted in 1995 (ISCN, 1995).

Results: A total of 7050 amniocentesis specimens were processed during the study period. 436 fetuses (6.18%) had various chromosomal abnormalities. The group of advanced maternal age had the highest rate of chromosomal abnormalities and followed by positive triplescreening. Chromosomal abnormalities associated with maternal age. 60.1% of abnormal karyotypes (262 cases) were numerical and 37.38% (163 cases) were structural. Both numerical and structural chromosomal aberrations were observed in 11 cases (2.52%). The numerical abnormalities were as: trisomy 21 (43.9%), trisomy 18 (18.7%), monosomy X (11.45%), trisomy 13 (6.1%), triploidy (5.25%), Klinefelter Syndrome (4.2%), trisomy X (1.52%), XYY Syndrome (1.14%), mosaics and the others. The frequent structural abnormalities were as: 46,XX/XY, inv(9) (35.6%), 46,XX/XY, 1qh(+) (6.74%), 46,XX/XY 16qh(+) (5%), 46,XY, Yqh(-) (4.3%) and 46,XY, Yqh(+) (3%). Balanced and unbalanced translocations, deletions and duplications were also found.

CONCLUSIONS: According to the literature and our results, advanced maternal age is the main cause of fetal chromosomal abnormalities. So fetal chromosomal abnormalities could be associated with advanced maternal age. Fetal chromosomal abnormality ratio that we found was 6.18%. This ratio emphasize the importance of prenatal diagnosis.

Key Words: Chromosomal abnormality, Cytogenetic, Prenatal diagnosis, Indication, Advanced maternal age

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THE OUTCOME OF PERINATAL MANAGEMENT OF FETAL GROWTH RESTRICTION IN TERTIARY-CARE UNIT IN POLAND

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MATERIALS AND METHODS The aim of the study was to evaluate the outcome of FGR management according to perinatal morbidity and mortality. It was retrospective analysis of 53 women admitted to the Department of Obstetrics and Gynaecology of the Institute of Mother and Child in Warsaw between 2009 and June 2014 with the diagnosis of FGR. Patients included to the study group were women with a singleton fetus at 25 to 36 weeks' gestation with abdominal circumference (AC) < 10th percentile and umbilical artery Doppler pulsatility index > 95th percentile. Patients were divided into 2 groups: 1st group - with adverse perinatal/neonatal outcome (n=14) and 2nd group – without adverse perinatal/neonatal outcome (n=39).

RESULTS Perinatal mortality rate was 13,19%. Adverse perinatal/neonatal outcome occurred in 14 (26,4%) cases. There was no significant difference between the groups according to patients age, parity, coexistence of hypertensive disorders, the presence of oligohydramnion and the mode of delivery as well. In both groups the majority of patients delivered by cesarean section (92,9% vs 97,4% p=0,44 ). The most common indications for delivery were fetal causes. Gestational age at FGR diagnosis was smaller in the group with adverse
pregnancy/neonatal outcome (28.5 weeks vs 32.15 weeks, p=0.003). The same relation was revealed according to gestational age at delivery (29.2 weeks vs 32.8 weeks, p=0.0004). Birth weight was significantly lower in the group with adverse pregnancy/neonatal outcome than in the second group (774g vs 1416g, p=0.0001). Female fetuses predominated in the group without adverse outcome (64.1%), whereas male fetuses in the group where adverse outcome occurred (64.3%). This difference was statistically significant (p=0.03). 1st minute Apgar score was substantially lower in the group with adverse pregnancy/neonatal outcome than in the second group (4.4 vs 7.8, p=0.0003). There was no difference between the groups in 5th minute Apgar score evaluation (p=0.83).

CONCLUSIONS
1. In pregnancies with fetal growth restriction gestational age at diagnosis, gestational age at delivery and birth weight are the most important determinants of adverse neonatal outcome. 2. The most common mode of delivery for fetuses with growth restriction is cesarean section. 3. There is a need to perform more detailed analysis according to the coexistence of hypertensive disorders and FGR and its relation with neonatal death and severe morbidity. 4. Perinatal mortality and morbidity rates in fetal growth restriction are still high and the management of such pregnancies is a big challenge, so it should take place in the reference obstetric units, where detailed diagnostics, monitoring and treatment of fetal and neonatal complications can be performed.

IMPROVING PATIENT EDUCATION POST CAESAREAN SECTION, THE NEED FOR A SIMPLE PATIENT LETTER
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With the growing incidence of caesarean sections performed in western medicine, patient understanding post lower section caesarean section (LSCS) delivery is of great importance. A through de-brief of a patient post LSCS helps to decrease patient uncertainty about Vaginal birth after caesarean section (VBAC) as a future delivery mode. We assessed how patients in a district general hospital are reviewed post LSCS and what proportion had the appropriate documentation about their future delivery modes on their discharge summary.

A prospective audit assessing which information about future deliveries was given to women post emergency and elective caesarean section over a 4 week period. There were 69 records of recorded births as documented in EuroKing. Of these, 7 were instrumental deliveries and were excluded. A total of 62 LSCS were collated, 34 Emergency LSCS and 28 Elective LSCS. Patient discharge summaries were reviewed and the ward diary for which patient was seen.

Of the 62 LSCS recorded in a 4 week period, all of these patients had a review by a doctor one day after their LSCS. Four patients did not have a discharge summary. There were 9 patients who underwent an elective LSCS for whom VBAC in the next pregnancy would not be suitable; none of these 9 patients had this documented in their discharge summary. Of the 34 patients who had Emergency LSCS, 15 had documentation on their discharge summary about future delivery mode recommendations, 19 did not. There were 14 patients who underwent elective LSCS who would be suitable for future VBAC, 5 had this documented on their discharge summaries, 9 did not.

There were a total of 48 patients who underwent LSCS in a four week period who VBAC was suitable mode of delivery in their next pregnancy, only 42% had this documented on their discharge summary. This highlights the need for further enhancement of the written documentation and education given to patients post discharge, with the hope to improve future VBAC initiatives with a simple patient letter to be given to every patient post LSCS.