INTERNATIONAL SOCIETY FOR THE STUDY OF HYPERTENSION IN PREGNANCY

ISSHP European Congress

24-26 September, 2015

PROGRAMME

www.euroisshp2015.com

CONTENTS

WELCOME

Dear Colleagues,

On behalf of the ISSHP and the Local Organising Committee, I am honoured and delighted to welcome you to the European Congress 2015 of the International Society for the Study of Hypertension in Pregnancy in Budapest, Hungary. We hope that the unique splendour of the Buda castle and the breathtaking panorama on the river Danube provides an ideal venue for an inspiring meeting that will surely be a remarkable experience for all participants.

We have made every effort to deliver a productive and informative congress that may expand the horizons of maternal care in preeclampsia. Our comprehensive programme aims to provide an innovative and complex overview of the latest developments and emerging challenges in the field of hypertensive disorders of pregnancy. We also attempt to provide a forum for the advancement of professional networking and collaboration.

We hope that the European Congress 2015 of ISSHP will be successful and a great experience for all of you, both scientifically and socially. We wish you a memorable stay in Budapest!

János Rigó Jr., MD, PhD, DSc
Chairman of the European Congress 2015 of ISSHP

COMMITTEES

CONGRESS CHAIRMAN

János Rigó Jr., Budapest, Hungary

INTERNATIONAL ADVISORY BOARD

Christopher Redman, Oxford, UK
Mark Brown (president of ISSHP), Sydney, Australia
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Annetine Staff, Oslo, Norway

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Gábor Szabó
András Szarka
Zoltán Veresh

GENERAL INFORMATION

CONGRESS DATE

24-26 September, 2015

CONGRESS VENUE

Hungarian House
H-1014 Budapest, Szentháromság tér 6.

CONGRESS WEBSITE

www.euroisshp2015.com

OFFICIAL CONGRESS LANGUAGE

The official language of the Congress is English. No interpretation will be provided.

CME CREDITS

European Congress of the International Society for the Study of Hypertension in Pregnancy (ISSHP) was granted maximum of 15 European CME credits (ECMEC) by the European Accreditation Council for Continuing Medical Education (EACCME).
The 'European Congress of the International Society for the Study of Hypertension in Pregnancy (ISSHP)' is accredited by the European Accreditation Council for Continuing Medical Education (EACCME) to provide the following CME activity for medical specialists. The EACCME is an institution of the European Union of Medical Specialists (UEMS), www.uems.net. The 'European Congress of the International Society for the Study of Hypertension in Pregnancy (ISSHP)' is designated for a maximum of 15 hours of European external CME credits. Each medical specialist should claim only those hours of credit that he/she actually spent in the educational activity.
Through an agreement between the European Union of Medical Specialists and the American Medical Association, physicians may convert EACCME credits to an equivalent number of AMA PRA Category 1 Credits™. Information on the process to convert EACCME credit to AMA credit can be found at www.ama-assn.org/go/internationalcme. Live educational activities, occurring outside of Canada, recognized by the UEMS-EACCME for ECMEC credits are deemed to be Accredited Group Learning Activities (Section 1) as defined by the Maintenance of Certification Program of The Royal College of Physicians and Surgeons of Canada.

SPEAKERS TECHNICAL INFORMATION

Please bring your presentations on USB memory sticks/cards. All PowerPoint presentations must be submitted to the congress staff in the posted room by the last coffee break prior to your scheduled presentation. Double slide, overhead projection and personal laptops cannot be used.

POSTERS INFORMATION

Poster size: 90 cm wide, 120 cm high
Poster set-up: 16.00 – 19.00 (Wednesday, 23 September) or 07.30 – 09.30 (Thursday, 24 September)
Poster removal: 13.00 – 14.00 (Saturday, 26 September)

All supplies needed to hang the posters will be available at the poster venue.

Poster session I: Thursday, 24 September	17.30 – 18.30
Poster session II: Friday, 25 September	17.00 – 18.00

PROGRAMME CHANGES

The organisers cannot assume liability for any changes in the programme due to external or unforeseen circumstances.

AWARDS

The Congress announces awards in two categories:

- The ISSHP Budapest 2015 meeting Award for Best Oral Presentation by New Investigator
- The ISSHP Budapest 2015 meeting Award for Best Poster Presentation by New Investigator.

INTERNET ACCESS

WIFI is available during the congress opening hours free of charge.

BADGES

The congress identification badges are provided along with other congress items upon registration. Please wear them at all times during the congress. Please note that your congress badge assures your entrance to conference premises, those without badges may be refused. The identification badges are also helpful when contacting the secretariat and other participants.

MEALS

Coffee breaks, lunches, welcome reception are included in the registration fee.

MOBILE PHONES

Please respect the speakers and presenters by ensuring your mobile phone is switched off at all the time during the scientific sessions.

OPENING HOURS OF THE REGISTRATION DESK AT HUNGARIAN HOUSE (1st floor)

Wednesday, 23 September	10.00 – 19.00
Thursday, 24 September	07.00 – 18.30
Friday, 25 September	07.30 – 18.00
Saturday, 26 September	07.30 – 14.00

REGISTRATION FEES

Type	Early bird fee until 30 June, 2015	Regular fee from 30 June, 2015	On site fee
ISSHP members	480 EUR	550 EUR	650 EUR
ISSHP non-members	600 EUR	670 EUR	770 EUR
ISSHP student	290 EUR	340 EUR	470 EUR
Non-member ISSHP student	350 EUR	430 EUR	550 EUR
ISSHP members from Eastern and South-Eastern European countries	190 EUR	240 EUR	290 EUR
ISSHP non-members Eastern and South-Eastern European countries	240 EUR	290 EUR	330 EUR
Accompanying fee	150 EUR	150 EUR	150 EUR
Daily ticket	150 EUR	150 EUR	150 EUR

The Registration fee includes
- Congress programme and abstracts
- Admission to all scientific sessions
- Exhibition & Lunch symposium
- Poster session
- Welcome Reception
- Lunches
- Coffee breaks

Daily ticket includes
- Congress programme and abstracts
- Admission to all scientific sessions and poster session on the chosen day
- Exhibition
- Coffee break and lunch on the chosen day

The fee for accompanying person includes
- Welcome Reception
- Lunches
- Sightseeing Tour

ACCOMMODATION

Hotel	
Hilton Budapest Hotel (on-site hotel)	H-1014 Budapest Hess András tér 1-3.
Mercure Budapest Buda	H-1013 Budapest, Krisztina körút 41-43.
Burg Hotel	H-1014 Budapest, Szentháromság tér 7-8.
Buda Castle Fashion Hotel	H-1014 Budapest, Úri utca 39.
Art'otel Budapest	H-1011 Budapest, Bem rakpart 16-19.
Carlton Hotel Budapest	H-1011 Budapest, Apor Péter utca 3.
Hotel Castle Garden	H-1012 Budapest, Lovas út 41.
Baltazár Hotel	H-1014 Budapest, Országház utca 31.
Erzsébet Guest House (on-site hotel)	H-1014 Budapest, Szentháromság tér 6.

SOCIAL PROGRAMMES

WELCOME RECEPTION

Thursday, 24 September, 2015, 18.30-20.00
Venue: Hungarian House (Congress venue)
Price: included in the registration fee

The ISSHP European Congress Welcome Reception is the first social opportunity to meet colleagues and friends in the vibrating city of Budapest. Do not miss this unique event and make sure to arrive to Budapest latest by Thursday evening.

EVENING GALA CRUISE

Friday, 25 September, 2015, 20.00 – 22.00
Price: 75 Euro / person
Departure: at 20.00 from Várkert Bazár, BKV port

Evening sightseeing-tour on the River Danube. Welcome-drink and a light dinner will be served on the boat. During the meal a Hungarian jazz trio plays evergreens. The boat is cruising from Margaret bridge to the National Theatre and the Palace of Arts, and you can enjoy the fascinating sight of the illuminated Budapest.

GUIDED VISITS TO SEMMELWEIS MUSEUM

Thursday, 24 September 2015, **16.30 – 18.00**
Friday, 25 September 2015, **10.00 – 11.30**
Saturday, 26 September 2015, **14.00 – 15.30**
Ticket price: 2 Euro/person (payable directly in the Museum)
Address: 1013 Budapest, Apród u. 1-3.
Meeting point for the guided tours: Congress registration desk, maximum capacity: 20 person/tour.

The lifework of Ignác Semmelweis can be followed up through a detailed representation. The Museum is found in the former house of – perhaps one of the most well-known Hungarian. The personal objects recall the atmosphere of the era and the turning points of his lifework. The permanent exhibition guides the visitors from ancient Egypt to the most modern times. The exhibition represents the development of biological knowledge, surgery and obstetrics techniques through scientific books, documents, paintings, statues, etc. The artistic expressions of disease, death and healing are demonstrated as well. Another important part of the exhibition is the demonstration of the Hungarian medical system. Serious changes in Hungary between the 10th and 20th centuries and the famous scientists between the 18th and 20th centuries made a lasting effect on the Hungarian medical science. Through these the Hungarian medical system rose to the top rank of the international medicine.

USEFUL INFORMATION

CLIMATE

The climate of Budapest is continental. In September usually nice warm weather can be expected with a max. temperature of 20-25 °C, while the lowest temperature during the night ranging between 12-15 °C. Nevertheless some rainy days can be expected.

INSURANCE

The registration fees do not include provision for the insurance of participants against personal accidents, illness, cancellation, theft, property loss or damage. Participants are advised to take adequate personal travel insurance.

CURRENCY

The Forint (HUF), the official national currency, is convertible. The exchange rates applied in Budapest banks, official exchange offices and hotels may vary. All the major credit cards are accepted in Hungary in places displaying the emblem at the entrance.
Exchange rate: 1 Euro = 314 HUF in September 2015.

CREDIT CARDS

In general, VISA, EC/MC and American Express credit cards are accepted in most restaurants, cafés, shops and petrol stations.

STORES AND SHOPPING

The opening hours of Budapest stores are generally 10.00-18.00 on weekdays and 10.00-13.00 on Saturday. The opening hours of Budapest stores are generally 10.00-18.00 on weekdays and 10.00-13.00 on Saturday. The big shopping centres are open from 10.00-20.00 from Monday to Saturday. On Sunday, big stores and shops are closed, while some smaller ones might be open from 10.00-18.00.

ELECTRICITY

The voltage in Hungary is 230V, 50 Hz AC.

RECOMMENDED TAXI COMPANY

To reach the Hotels or the Congress Venue and to avoid any inconvenience, please use the official **ISSHP2015 taxi company: City Taxi: +36 1 211 1111, www.citytaxi.hu, order@citytaxi.hu**
Credit card payment is available in every car of City Taxi.
Please note, that all licensed Budapest taxi companies have yellow cars and has same rates for all companies, placed clearly visible on the screens.

PARKING

If you drive a personal or rented car, always try to park at a guarded parking lot and do not leave any valuables in the car. Please note, that Budapest is divided into paying parking areas, with one parking meter in each street. The maximum parking time duration is 2 hours, tariffs may vary.
For detailed information on parking within the Castle District, please visit this site: www.budavarikapu.hu

TIME ZONE

Central European Summer Time (CEST): UTC+02:00

PROGRAMME OVERVIEW

THURSDAY, 24 SEPTEMBER

08.30 – 09.00	Opening Ceremony	
09.00 – 11.00	State of the Art Lecture, Plenary Lecture	Plenary Room
11.00 – 11.30	Coffee Break	
11.30 – 13.00	Oral communication – Genetics of preeclampsia	Plenary Room
	Oral communication – Pathophysiology of preeclampsia	Section Room
13.00 – 13.45	Lunch symposium (for detailed programme, see page 153)	
13.45 – 14.15	Break	
14.15 – 15.45	Oral communication – Markers of preeclampsia	Plenary Room
	Oral communication – Prediction of preeclampsia	Section Room
15.45 – 16.15	Coffee break	
16.15 – 17.30	Oral communication – Prevention of preeclampsia	Plenary Room
17.30 – 18.30	Poster	
18.30 –	Welcome reception	

FRIDAY, 25 SEPTEMBER

08.00 – 09.40	State of the Art Lecture, Plenary Lecture	Plenary Room
09.40 – 10.00	Coffee break	
10.00 – 11.00	Plenary Lecture	Plenary Room
11.00 – 12.30	Oral communication – Management of preeclampsia I.	Plenary Room
	Oral communication – Management of preeclampsia II.	Section Room
12.30 – 13.30	Break	
13.30 – 15.30	Oral communication – Immunology	Plenary Room
	Oral communication – Angiogenesis	Section Room
15.30 – 16.00	Coffee break	
16.00 – 17.00	Workshop	Plenary Room
17.00 – 18.00	Poster	
19.30 –	Gala dinner	

SATURDAY, 26 SEPTEMBER

08.00 – 10.00	State of the Art Lecture, Plenary Lecture	Plenary Room
10.00 – 10.30	Break	
10.30 – 12.15	Oral communication – Cardiovascular changes in preeclampsia	Plenary Room
	Oral communication – Long term complications of preeclampsia	Section Room
12.15 – 12.45	Coffee break	
12.45 – 14.15	Oral communication – Others I.	Plenary Room
	Oral communication – Others II.	Section Room
14.15 – 14.45	Closing Ceremony	

THURSDAY, 24 SEPTEMBER 2015

08.30 – 09.00 OPENING CEREMONY

Moderator: Katalin Cseh

Opening remarks:

János Mészáros
Deputy State Secretary for Health

Mark Brown
President of ISSHP

Gábor Tamás Nagy
Mayor of 1st district of Budapest

János Rigó Jr.
Chairman of the Congress

Ágoston Széll
Rector of Semmelweis University

09:00 – 11:00 STATE OF THE ART LECTURE, PLENARY LECTURE

Plenary Room

Chairs: Mark Brown – Annetine Staff – János Rigó Jr.

STA1

What's new in pre-eclampsia?

Mark Brown
St. George Hospital & University of NSW, Department of Renal Medicine, Sydney, Australia

STA2

Placentation and pre-eclampsia – Inflammatory and immunological issues

Christopher Redman
University of Oxford, Nuffield Department of Obstetrics and Gynaecology, Oxford, UK

STA3

Novel therapies for preeclampsia

Ananth Karumanchi
Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, USA

PL136

Renal disease before, during and after preeclampsia

Markus G. Mohaupt
University Hospital Bern, Department of Nephrology, Hypertension and Clinical Pharmacology, Bern, Switzerland

11:00 – 11:30 COFFEE BREAK

11:30 – 13:00 ORAL COMMUNICATION – GENETICS OF PREECLAMPSIA

Plenary Room

Chairs: Hannele Laivuori – Eric Moses

O4

Genome wide sequencing approaches to identify missing heritability of preeeclampsia

Eric Moses[1], Phillip Melton[1], Matthew Johnson[2], Dnyanada Gokhale-Agashe[1], Alex Rea[1], Richard Allcock[3], John Blangero[2], Shaun Brennecke[4]

[1]University of Western Australia, Centre for Genetic Origins of Health and Disease, Perth, Australia
[2]University of Texas Health Science Center at San Antonio, South Texas Diabetes and Obesity Institute, Brownsville, USA
[3]University of Western Australia, School Pathology and Laboratory Medicine, Perth, Australia
[4]Royal Women's Hospital / University of Melbourne, Pregnancy Research Centre, Department of Perinatal Medicine, Melbourne, Australia

O5

Next-generation sequencing studies in Finnish preeclampsia cohorts

Tea Kaartokallio[1], JIngwen Wang[2], Hong Jiao[2], Seppo Heinonen[3], Eero Kajantie[4], Juha Kere[2], Katja Kivinen[5], Anneli Pouta[6], Hannele Laivuori[1]

[1]University of Helsinki and Helsinki University Hospital, Medical and Clinical Genetics, Helsinki, Finland
[2]Karolinska Institute, Department of Biosciences and Nutrition, Center for Innovative Medicine and Science for Life Laboratory, Stockholm, Sweden
[3]University of Helsinki and Helsinki University Hospital, Obstetrics and Gynecology, Helsinki, Finland
[4]National Institute for Health and Welfare, Department of Chronic Disease Prevention, Diabetes Prevention Unit, Helsinki, Finland
[5]University of Cambridge, Division of Cardiovascular Medicine, Cambridge, UK
[6]National Institute for Health and Welfare, Department of Children, Young People and Families, Oulu, Finland

O6

Association between fetal congenital heart defects and maternal risk of hypertensive disorders of pregnancy in concurrent and subsequent pregnancies

Heather Boyd[1], Saima Basit[1], Ida Behrens[1], Elisabeth Leirgul[2], Henning Bundgaard[3], Jan Wohlfahrt[1], Mads Melbye[1], Nina Øyen[2]

[1]Statens Serum Institut, Department of Epidemiology Research, Copenhagen, Denmark
[2]University of Bergen, Department of Global Public Health and Primary Care, Bergen, Norway
[3]Copenhagen University Hospital (Rigshospitalet), Heart Centre, Copenhagen, Denmark

O7

Epigenome of the circadian clock pathway of placental and newborn tissues in pre-eclampsia

Caroline Van den Berg[1], Ines Chaves[2], Emilie Herzog[1], Sten Willemsen[3], Bert Van der Horst[2], Régine Steegers-Theunissen[1]

[1]Erasmus MC, Department of Obstetrics & Gynecology, Rotterdam, The Netherlands
[2]Erasmus MC, Department of Genetics, Rotterdam, The Netherlands
[3]Erasmus MC, Department of Biostatistics, Rotterdam, The Netherlands

O8

Cardiovascular risk factors, renin-angiotensin system gene polymorphisms, pregnancy course and outcomes in women with different forms of hypertension

Vasiliy Chulkov[1], Natalya Vereina[1], Sergei Sinitsin[1], Valentina Dolgushina[2]
[1]South Ural State Medical University, Russia, Faculty Therapy Department, Chelyabinsk, Russia
[2]South Ural State Medical University, Russia, Department of Obstetrics and Gynecology, Chelyabinsk, Russia

O9

The functional role of natriuretic peptides in preeclampsia

Gábor Szabó, Bálint Nagy, János Rigó Jr.
Semmelweis University, 1st Department of Obstetrics and Gynaecology, Budapest, Hungary

11:30 – 13:00 ORAL COMMUNICATION - PATHOPHYSIOLOGY OF PREECLAMPSIA

Section Room

Chairs: Attila Molvarec

O11

Evaluation of the endocannabinoid system in preeclampsia

Attila Molvarec[1], Gergely Fügedi[1], Miklós Molnár[2], Eszter Szabó[3], Júlia Schönléber[1], János Rigó Jr.[1]
[1]Semmelweis University, 1st Department of Obstetrics and Gynaecology, Budapest, Hungary
[2]Semmelweis University, Institute of Pathophysiology, Budapest, Hungary
[3]Semmelweis University, 1st Department of Pediatrics, Budapest, Hungary

O12

Analysis of the molecular and cellular mechanisms regulated by magnesium sulphate in an in vitro model of the human placenta

Rachel Williamson[1], Gerard O'Keeffe[2], Louise Kenny[1]
[1]University College Cork, 1st Department of Obstetrics and Gynaecology, Cork, Ireland
[2]University College Cork, Department of Anatomy and Neuroscience, Cork, Ireland

O13

Catechol-O-methyltransferase deficiency leads to hypersensitivity on the pressor response against angiotensin II

Norikazu Ueki[1], Satoru Takeda[1], Megumi Kanasaki[2], Daisuke Koya[2], Keizo Kanasaki[2]
[1]Juntendo University Faculty of Medicine, Department of Obstetrics and Gynecology, Tokyo, Japan
[2]Kanazawa Medical University, Department of Diabetology and Endocrinology, Ishikawa, Japan

O14

Is preeclampsia a variant of Liddles syndrome with enhanced activity of the epithelial sodium channel in the kidneys?

Lise Hald Nielsen[1], Per Ovesen[1], Boye Jensen[2]
[1]Aarhus University, Department of Gynecology and Obstetrics, Aarhus, Denmark
[2]Odense University Hospital, Department of Cardiovascular and Renal Research, Odense, Denmark

O15

Adipose tissue and adipocytokine in preeclampsia: New insights into danger signals and inflammation

Katsuhiko Naruse
Nara Medical University, Department of Obstetrics & Gynecology, Kashihara, Japan

O10

Increased maternal and fetal HDL cholesterol efflux capacity and placental CYP27A1 expression in pre-eclampsia

Hiten Mistry[1], Lesia Kurlak[2], Yosef Mansour[3], Line Zurkinden[1], Markus G. Mohaupt[4], Geneviève Escher[1]
[1]University of Bern, Department of Nephrology, Hypertension and Clinical Pharmacology, Berne, Switzerland
[2]University of Nottingham, Obstetrics and Gynecology, Nottingham, UK
[3]King's College London, Women's Health Academic Centre, London, UK
[4]University of Bern, Department of Nephrology, Hypertension and Clinical Pharmacology, Berne, UK

13:45 – 14:15 BREAK

14:15 – 15:45 ORAL COMMUNICATION – MARKERS OF PREECLAMPSIA

Plenary Room

Chairs: Annetine Staff – Christopher Redman

O16

Marinobufagenin as a promising preeclampsia risk assessment marker: Purification from toad venom and LC-MS identification in human plasma

Charline Lenaerts[1], Liz Bond[2], Robin Tuytten[2], Bertrand Blankert[1]
[1]University of Mons, Laboratory of Pharmaceutical Analysis, Faculty of Medicine and Pharmacy, Research Institute for Health Sciences and Technology, Mons, Belgium
[2]Metabolomic Diagnostics, Cork, Ireland

O18

Oxidative stress in preeclampsia

Hajnalka Héjja[1], Nóra Fekete[2], Bálint Alasztics[1], József Gábor Joó[1], Attila Molvarec[1], Katalin Szabó-Taylor[2], Edit Buzás[2], János Rigó Jr.[1], Éva Pállinger[2]
[1]Semmelweis University, 1st Department of Obstetrics and Gynaecology, Budapest, Hungary
[2]Semmelweis University, Department of Genetics, Cell- and Immunobiology, Budapest, Hungary

O19

Decreased plasma hemopexin activity in preeclampsia is associated with decreased plasma AT-1 receptor leves and increased placental and monocyte AT-1 receptor expression

Floor Spaan[1], Theo Borghuis[1], Paul De Vos[1], Harry Van Goor[1], Maria Van Pampus[2], Marijke Faas[1]
[1]University Medical Center Groningen, Department of Pathology and Medical Biology, Groningen, The Netherlands
[2]University Medical Center Groningen, Department of Obstetrics & Gynecology, Groningen, The Netherlands

O20

NT-pro-BNP levels as a marker of high clinical risk in pregnancy

Marcela Cleila Cabo Fustaret, Ana Escobar, Fedor Novo, Ricardo Illia, Carlos Rivas, Matias Uranga Imaz, Guillermo Lobenstein, Roberto Mayer, Patricia Olejnik, Tomas Garcia Balcarce, Guido Manrique

Hospital Alemán, Department of Cardiology / Obstetric and Gynecology, Buenos Aires, Argentina

O21

First trimester serum placental growth factor and hyperglycosylated human chorionic gonadotropin are associated with later pre-eclampsia

Elina Keikkala[1], Sini Koskinen[1], Piia Vuorela[1,2], Hannele Laivuori[1,3,4], Jarkko Romppanen[5], Seppo Heinonen[1], Ulf-Håkan Stenman[6]

[1]Obstetrics and Gynecology, University of Helsinki and Helsinki University Hospital, Helsinki, Finland
[2]Obstetrics and Gynecology, Porvoo Hospital, Porvoo, Finland
[3]Medical Genetics, University of Helsinki and Helsinki University Hospital, Helsinki, Finland
[4]Finnish Institute for Molecular Medicine, University of Helsinki, Helsinki, Finland
[5]Eastern Finland Laboratory Centre, Kuopio, Finland
[6]Clinical Chemistry, University of Helsinki and Helsinki University Hospital, Helsinki, Finland

14:15 – 15:45 ORAL COMMUNICATION – PREDICTION OF PREECLAMPSIA

Section Room

Chairs: Louise Kenny – Harald Zeisler

O22

Correlation of sFlt-1/PlGF ratio with time to delivery or preterm birth in PROGNOSIS (Prediction of short-term outcome in pregnant women with suspected preeclampsia study)

Harald Zeisler[1], Elisa Llurba[2], Frederic Chantraine[3], Manu Vatish[4], Anne Cathrine Staff[5], Maria Sennström[6], Matts Olovsson[7], Shaun P. Brennecke[8], Holger Stepan[9], Deirdre Allegranza[10], Carina Dinkel[11], Maria Schoedl[11], Martin Hund [10], Stefan Verlohren[12]

[1]Department of Obstetrics and Gynecology, Medical University Vienna, Vienna, Austria
[2]Department of Obstetrics, Maternal-Fetal Medicine Unit, Hospital Universitari Vall d´Hebron, Barcelona, AND Maternal and Child Health and Development Network (SAMID) RD12/0026, Instituto de Salud Carlos III, Spain
[3]Department of Obstetrics and Gynecology, University of Liege, CHR de la Citadelle, Liege, Belgium
[4]Nuffield Department of Obstetrics and Gynaecology, University of Oxford, Oxford, UK (previously University Hospitals NHS Trust, Coventry, UK)
[5]Department of Gynecology and Department of Obstetrics, Oslo University Hospital and University of Oslo, Oslo, Norway
[6]Department of Women's and Children's Health, Karolinska University Hospital, AND Karolinska Institute, Stockholm, Sweden
[7]Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden
[8]Pregnancy Research Centre, Department of Perinatal Medicine, Royal Women's Hospital and Department of Obstetrics and Gynaecology, University of Melbourne, Parkville, Victoria, Australia
[9]Department of Obstetrics, University of Leipzig, Leipzig
[10]Roche Diagnostics International Ltd, Rotkreuz, Switzerland
[11]Roche Diagnostics GmbH, Penzberg, Germany
[12]Department of Obstetrics, Campus Virchow-Klinikum Charité, Berlin, Germany

O23

STEPS (Study of Early Preeclampsia in Spain): sFlt-1/PlGF for the prediction of early-onset preeclampsia in singleton pregnancies

Alfredo Perales[1], Juan Luis Delgado[2], María de la Calle[3], José A García-Hernández[4], Ana Isabel Escudero[5], José Manuel Campillos[6], María Desamparados Sarabia[2], Begoña Laíz[1], Marta Duque[3], Mercedes Navarro[4], Pilar Calmarza[6], Martin Hund[7], Francisco V Álvarez[5]

[1]Hospital Universitario La Fe, Valencia, Spain
[2]Hospital Universitario Virgen de la Arrixaca, Murcia, Spain
[3]Hospital Universitario La Paz, Madrid, Spain
[4]Hospital Universitario Materno-Infantil, Gran Canaria, Spain
[5]Hospital Universitario Central de Asturias, Oviedo, Spain
[6]Hospital Universitario Miguel Servet, Zaragoza, Spain
[7]Roche Diagnostics International Ltd, Rotkreuz, Switzerland

O24

Prediction of pre-eclampsia in obese nulliparous women

Matias Vieira[1], Dharmintra Pasupathy[1], Robyn North[1], Lesley McCowen[2], Louise Kenny[3], Lucilla Poston[1]

[1]King's College London, Division of Women's Health, London, UK
[2]University of Auckland, Department of Obstetrics and Gynecology, Auckland, New Zealand
[3]University College Cork, Department of Obstetrics and Gynecology, Cork, Ireland

O25

Evaluation of the value of the first and third trimester maternal mean platelet volume (MPV) for prediction of pre-eclampsia

Maryam Kashanian

Iran University of Medical Sciences, 3rd Department of Obstetrics, Tehran, Iran

O27

Predicting preeclampsia in a second pregnancy

Doris Campbell, Sohinee Bhattacharya

University of Aberdeen, Department of Obstetrics & Gynecology, Aberdeen, UK

15:45 – 16:15 COFFEE BREAK

16:15 – 17:30 ORAL COMMUNICATION - PREVENTION OF PREECLAMPSIA

Plenary Room

Chairs: Mila Cervar-Zivkovic – Attila Molvarec

O28

Effect of folic acid supplementation in pregnancy on preeclampsia – Folic Acid Clinical Trial (FACT)

Shi Wu Wen, Ruth Rennicks-White, Josee Champagne, Natalie Rybak, Laura Gaudet, Mark Walker

The Ottawa Hospital, Department of Obstetrics, Gynecology and Newborn Care, Ottawa, Canada

O29

The impact of low dose aspirin after positive first trimester screening for pre-eclampsia

Ioana-Claudia Lakovschek[1], Bence Csapo[1], Vassiliki Kolovetsiou-Kreiner[1], Christina Stern[1], Karoline Mayer-Pickel[1], Uwe Lang[1], Barbara Obermayer-Pietsch[2], Mila Cervar-Zivkovic[1]

[1]Medical University of Graz, Department of Obstetrics & Gynecology, Graz, Austria
[2]Medical University of Graz, Department of Internal Medicine, Graz, Austria

O30

Diet and preeclampsia: A prospective multicentre unmatched case control study in Ethiopia

Mulualem Endeshaw
Rift Valley University, 3rd Department of Obstetrics, Ethiopia (Bahir Dar), Ethiopia

O31

Magnesium homeostasis and gestational hypertension

Ragnar Rylander
BioFAct Environmental Health Research Centre, Public Health, Lerum, Sweden

O32

Pre-eclampsia and thrombophilia: Prevention issues

Ekaterina Zhuravleva, Viktoriya Bitsadze, Alexander Makatsariya
First IM Sechenov Moscow State Medical University, Obstetrics and Gynecology, Moscow, Russia

17:30 – 18:30 POSTER

Chairs: Herbert Valensise – Markus G. Mohaupt

P34

Role of high-mobility group A1 protein in trophoblast invasion

Yuka Uchikura[1], Keiichi Matsubara[1], Yuko Matsubara[1], Miki Mori[2]
[1]Ehime University, Department of Obstetrics and Gynecology, Toon, Japan
[2]Ehime Prefectural Central Hospital, Department of Obstetrics and Gynecology, Matsuyama, Japan

P35

Novel interaction of placental caveolin-1 expression with markers of oxidative stress and the renin-angiotensin system (RAS) in pre-eclampsia

Hiten Mistry[1], Anna Czajka[2], Marta Hentschke[3], Carlos Poli-de-Figueiredo[3], Bartira Pinheiro da Costa[3], Fiona Broughton Pipkin[4], Lesia Kurlak[4]
[1]University of Bern, Department of Nephrology, Hypertension and Clinical Pharmacology, Berne, Switzerland
[2]King's College London, Diabetes Research Group, London, UK
[3]PUCRS, Laboratory of Nephrology, Porto Alegre, Brazil
[4]University of Nottingham, Department of Obstetrics & Gynecology, Nottingham, UK

P36

Identifying a novel link between preeclampsia and chronic hypertension in the MTHFR-gene using the population based Norwegian HUNT Study

Liv Cecilie Thomsen[1], Nina McCarthy[2], Phillip Melton[2], Gemma Cadby[2], Rigmor Austgulen[3], Eric Moses[2], Line Bjørge[4], Ann-Charlotte Iversen[3]
[1]Norwegian University of science and Technology (NTNU), Centre of Molecular Inflammation Research , Bergen, Norway
[2]University of Western Australia, Centre for Genetic Origins of Health and Disease, Perth, Australia
[3]Norwegian University of Science and Technology (NTNU), Centre of Molecular Inflammation Research , Trondheim, Norway
[4]Haukeland University Hospital, Department of Obstetrics & Gynecology, Bergen, Norway

P37

Alterations in maternal and fetal plasma soluble endothelial leukocyte adhesion molecule-1 (sE-selectin) concentrations in women with pre-eclampsia

Lesia Kurlak[1], Heidi Jamin[2], Markus G. Mohaupt[2], Hiten Mistry[2]
[1]University of Nottingham, Obstetrics and Gynecology, Nottingham, UK
[2]University of Bern, Department of Nephrology, Hypertension and Clinical Pharmacology, Berne, Switzerland

P38

Strong inhibitory effect of preeclampsia serum on angiogenesis using in vitro angiogenesis test

Jukka Uotila[1], Anita Virtanen[1], Tarja Toimela[2], Riina Sarkanen[2], Outi Huttala[2], Tuula Heinonen[2]
[1]Tampere University Hospital, Department of Obstetrics and Gynecology, Tampere, Finland
[2]FICAM, School of Medicine, Tampere, FICAM, Tampere, Finland

P39

Connection between placenta specific miRNA clusters and preeclampsia: A hypothetical miRNA-mRNA interaction network

Orsolya Biró, Bálint Nagy, János Rigó Jr.
Semmelweis University, 1st Department of Obstetrics and Gynecology, Budapest, Hungary

P40

MIR-21 A and MIR-221 overexpression in placental tissue of preeclamptic patients

Iveta Svecova[1], Martin Vazan[2], Pavol Zubor[1], Jan Danko[1], Zora Lasabova[2]
[1]Jessenius Medical Faculty, Comenius University, Department of Obstetrics & Gynecology, Martin, Slovakia
[2]Jessenius Medical Faculty, Comenius University, Institut of Molecular Biology, Martin, Slovakia

P41

The role of IL-10 polymorphism in pathology of hypertensive disorders in pregnancy

Pavol Zubor[1], Zora Lasabova[2], Eva Jezkova[1], Andrea Mendelova[1], Iveta Svecova[1], Jan Danko[1]
[1]Jessenius Medical Faculty, Comenius University, Department of Obstetrics & Gynecology, Martin, Slovakia
[2]Jessenius Medical Faculty, Comenius University, Institut of Molecular Biology, Martin, Slovakia

P42

TNF-ALPHA gene polymorphism in pathology of preeclampsia

Pavol Zubor[1], Andrea Mendelova[2], Imrich Zigo[1], Maria Skerenova[3], Eva Jezkova[2], Jan Danko[1]
[1]Jessenius Medical Faculty, Comenius University, Department of Obstetrics & Gynecology, Martin, Slovakia
[2]Jessenius Medical Faculty, Comenius University, Institut of Molecular Biology, Martin, Slovakia
[3]Jessenius Medical Faculty, Comenius University, Department of Medical Biochemistry, Martin, Slovakia

P43

Characterization of monocyte phenotype and polarization in preeclampsia and intrauterine fetal growth restriction

Thushari Alahakoon[1], Heather Medbury[2], Helen Williams[2], Nicole Fewings[2], Xin Wang[2], Vincent Lee[3]
[1]Westmead Hospital, Australia, Department of Obstetrics and Gynecology, Sydney, Australia
[2]University of Sydney, Sydney Medical School, Sydney, Australia
[3]Westmead Hospital, Australia, Department of Renal Medicine, Sydney, Australia

P44

Syncytiotrophoblast extracellular membrane vesicles from preeclamptic placentae show reduced abilities to guide monocyte maturation and activation as well as reduced activation of cytotoxicity of regulatory T-cells and NK-cells

Claudia Göhner[1], Jolien Fledderus[2], Justine Fitzgerald[3], Ekkehard Schleußner[3], Udo Markert[3], Torsten Plösch[1], Sicco Scherjon[1], Marijke Faas[2]

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[3]University Hospital Jena, Department of Obstetrics, Placenta-Lab, Jena, Germany

P45

Target cells of pregnancy-associated extracellular vesicles

Árpád Ferenc Kovács[1], Nóra Fekete[1], Bálint Alasztics[2], József Gábor Joó[2], Mária Prosszer[2], Edit Buzás[1], János Rigó Jr.[2], Éva Pállinger[1]

[1]Semmelweis University, Department of Genetics, Cell- and Immunobiology, Budapest, Hungary

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P46

Dysregulated levels of novel circulating autoantibodies in preeclampsia

Kjartan Moe[1], Harald Heidecke[2], Ralf Dechend[3], Anne Cathrine Staff[1]

[1]University of Oslo, Institute for Clinical Medicine, Oslo, Norway

[2]Celltrend GmbH, Luckenwalde, Germany

[3]The Charitè, Franz-Vollhard Clinic, HELIOS Clinic, Berlin, Germany

P47

First trimester urine and serum metabolomics to predict preeclampsia and gestational hypertension

Marie Austdal[1], Line Tangerås[2], Ragnhild Skråstad[3], Kjell Salvesen[4], Rigmor Austgulen[5], Tone Bathen[6], Ann-Charlotte Iversen[7]

[1]Norwegian University of Science and Technology and St. Olavs Hospital, Department of Circulation and Medical Imaging, Trondheim, Norway

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[3]Norwegian University of Science and Technology and St. Olavs Hospital, Department of Laboratory Medicine, Children's and Women's Health, Trondheim, Norway

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[5]Norwegian University of science and Technology (NTNU), Centre of Molecular Inflammation Research and Department of Cancer Research and Molecular Medicine, Trondheim, Norway

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[7]Norwegian University of Science and Technology, Centre of Molecular Inflammation Research and Department of Cancer Research and Molecular Medicine, Trondheim, Norway

P48

Possible laboratory markers and anthropometric women with preeclampsia – Preliminary results

Natine Fuzihara Rosa, Stephany Risnic Chvaicer, Ana Paula de Almeida Righi, Claudia Valéria Chagas Siqueira, Diego Gomes Ferreira, Maria Renata Lopes Natale Poltronieri, Rogerio Gomes dos Reis Guidoni, Sergio Floriano Toledo, Leda Ferraz, Patricia Lopes Andrade, Francisco Lazaro Pereira Sousa, Vivian Macedo Gomes Marçal

UNILUS - Lusiada Foundation, 1st Department of Obstetrics and Gynaecology, Santos, Brazil

P50

Microalbuminuria is a predictor of adverse pregnancy outcomes including preeclampsia

Mathini Jayaballa[1], Shreya Sood[2], Thushari Alahakoon[3], Suja Padmanabhan[4], Wah Cheung[4], Vincent Lee[1]

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P51

Screening for preeclampsia in the first trimester: A reduced fat mass increases the risk in normo BMI patients

Grazia Maria Tiralongo[1], Ilaria Pisani[1], Giulia Gagliardi[1], Damiano Lo Presti[1], Roberta Licia Scala[2], Barbara Vasapollo[3], Gianpaolo Novelli[4], Angela Andreoli[5], Herbert Valensise[1]

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P52

Prevalence of preeclampsia in patients of pre-gestational diabetic pregnancy in Bangladesh

Mobashera Jahan[1], Md Hasanuzzaman[1], Sharmin Mahbuba[1], K. Leena[2], Gias U. Ahsan[1], Thomas J. Kuehl[3], M. Uddin[3]

[1]North South University, Department of Public Health, Dhaka, Bangladesh
[2]Brac University, James P. Grant School of Public Health, Dhaka, Bangladesh
[3]Baylor College of Medicine, Houston, Texas, USA, Obstetrics and Gynecology, Houston, USA

P53

Body mass index before pregnancy and hypertensive disorders in following pregnancy

Ana Jakovljevic[1], Mirjana Bogavac[2], Aleksandra Nikolic[3], Mirjana Milosevic-Tosic[3], Zagorka Lozanov-Crvenkovic[4]

[1]University of Novi Sad Medical Faculty, Clinical Centre of Vojvodina, Centre for Laboratory Medicine, Novi Sad, Serbia
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[3]University of Novi Sad Medical Faculty, Clinical Centre of Vojvodina, Emergency Center, Urgent Laboratory at Department of Obstetrics and Gynecology, Novi Sad, Serbia
[4]University of Novi Sad Faculty, Faculty of Science Department of Mathematics and Informatics, Novi Sad, Serbia

08:00 – 09:40 STATE OF THE ART LECTURE, PLENARY LECTURE

Plenary Room

Chairs: Mark Brown – Louise Kenny

STA54

Preeclampsia – Myths are still stronger than scientific data

Berthold Huppertz
Medical University of Graz, Institute of Cell Biology, Histology & Embryology, Graz, Austria

STA55

Pathophysiology of preeclampsia from the view point of immunology

Shigeru Saito[1], Arihiro Shiozaki[1], Akitoshi Nakashima[1], Yasushi Nakabayashi[1], Attila Molvarec[2], János Rigó Jr.[2]
[1]University of Toyama, Obstetrics and Gynecology, Toyama, Japan
[2]Semmelweis University, 1st Department of Obstetrics and Gynecology, Budapest, Hungary

PL56

Long-term consequences of preeclampsia

Annetine Staff
University of Oslo,Oslo, Norway

PL138

Should we be using predictive tests for Pre-eclampsia in routine clinical practice?

Louise Kenny
University of Oslo, Norway

09:40 – 10:00 COFFEE BREAK

10:00 – 11:00 PLENARY LECTURE

Plenary Room

Chairs: Mark Brown – Louise Kenny

PL57

Angiogenic factors: From scientific data to clinical implementation

Holger Stepan
Leipzig University, Department of Obstetrics, Leipzig, Germany

PL58

Low molecular weight heparin for prevention of severe preeclampsia and other placental mediated complications

Michael Kupferminc
Tel Aviv Medical Center, Tel Aviv University, Obstetrics and Gynecology, Tel Aviv, Israel

PL59

The impact of classification of hypertensive disorders of pregnancy based on the ACOG 2013 and ISSHP 2014 criteria

János Rigó Jr., Bálint Alasztics, Anikó Árokszállási, Noémi Dobó, Mária Prosszer, József Gábor Joó, Attila Molvarec
Semmelweis University, 1st Department of Obstetrics and Gynecology, Budapest, Hungary

A new Database for all Preeclampsia Researchers. From the Global Pregnancy Collaboration

Christopher Redman
University of Oxford, Nuffield Department of Obstetrics and Gynecology, Oxford, UK

11:00 – 12:30 ORAL COMMUNICATION – MANAGEMENT OF PREECLAMPSIA I.

Plenary Room

Chairs: Helena Strevens – Herbert Valensise

O60

Treatment of hypertension in pregnancy

Csaba Farsang
St. Imre University Teaching Hospital, Budapest, Hungary

O61

The treatment of antenatal hypertension with labetalol: A prediction model for successful response

Daniel Stott, Mareike Bolten, Dana Paraschiv, Mona Salman, Katherine Clark, Nikos Kametas
King's College London, Department of Women's and Children's Health, London, UK

O62

Use of diuretics in the management of late-onset preeclampsia

Péter Tamás[1,2], Eszter Hantosi[1,2], Bálint Farkas[2], József Bódis[1,2]
[1]Department of Obstetrics and Gynecology, Faculty of Medicine, University of Pécs, Pécs, Hungary
[2]Doctorial School of Health Sciences, Faculty of Health Sciences, University of Pécs, Pécs, Hungary

O63

Removal of soluble Fms-like tyrosine kinase (sFlt-1) by plasma-specific apheresis: Pilot study in women with very preterm preeclampsia

Wiebke Schaarschmidt
Leipzig University, Obstetrics and Gynecology, Leipzig, Germany

O64

Timing of delivery in preeclampsia

Helena Strevens
Lund University, Department of Obstetrics and Gynecology, Lund, Sweden

O65

Is there evidence to inform antihypertensive prescribing in pregnancy complicated by chronic hypertension: A systematic review

Louise Webster, Frances Conti-Ramsden, Paul Seed, Catherine Nelson-Piercy, Lucy Chappell
King's College London, Women's Health Academic Centre, London, UK

Chairs: Michael Kupferminc – János Rigó Jr.

O66

Comparison of immediate delivery versus expectant management in women with severe early onset preeclampsia before 26 weeks of gestation

Miriam F. Van Oostwaard[1], Leonoor Van Eerden[2], Monique W. De Laat[3], Hans J. Duvekot[4], Jan Jaap H.M. Erwich[5], Kitty W.M. Bloemenkamp[6], Antoinette Bolte[7], Joost P.F. Bosma[8], Steven V. Koenen[9], René F. Kornelisse[10], Bente Rethans[3], Pieter Van Runnard Heimel[11], Hubertina C.J. Scheepers[12], Wessel Ganzevoort[3], Ben Willem J. Mol[13], Christianne J. De Groot[14], Ingrid P.M. Gaugler-Senden[15]

[1]Department of Obstetrics and Gynaecology, Beatrixziekenhuis, Gorinchem, The Netherlands
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[3]Department of Obstetrics and Gynaecology, Academisch Medisch Centrum, Amsterdam, The Netherlands
[4]Department of Obstetrics and Gynaecology, Erasmus Medisch Centrum, Rotterdam, The Netherlands
[5]Department of Obstetrics and Gynaecology, Universitair Medisch Centrum Groningen, The Netherlands
[6]Department of Obstetrics and Gynaecology, Leids Universitair Medisch Centrum, Leiden, The Netherlands
[7]Department of Obstetrics and Gynaecology, Radboud Universitair Medisch Centrum, The Netherlands
[8]Department of Obstetrics and Gynaecology, Isala Ziekenhuis, Zwolle
[9]Department of Obstetrics and Gynaecology, Universitair Medisch Centrum Utrecht, The Netherlands
[10]Department of Paediatrics, Erasmus Medisch Centrum, Rotterdam, the Netherlands
[11]Department of Obstetrics and Gynaecology, Maxima Medisch Centrum, Veldhoven, The Netherlands
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[15]Department of Obstetrics and Gynaecology, Jeroen Bosch Ziekenhuis, 's-Hertogenbosch, The Netherlands

O67

The cranial imaging in severe preeclampsia

XiaoDan Di[1], Hui Mai[2], JinYing Yang[1], HuiShu Liu[1]

[1]Guangzhou Women and Children's Medical Center, Department of Obstetrics, GuangZhou, China
[2]The third affiliated hospital of Guangzhou Medical University, Department of Radiology, GuangZhou, China

O68

Management of eclampsia and stroke during pregnancy

Yasumasa Ono

OHNO Ladies Clinic, Obstetrics and Gynecology, Iwakura, Japan

O69

Visual Evoked Potential as neurophysiological evaluation of patients with severe PE and visual disturbances

Ingrid Brussé[1], CB van den Berg[1], J.J. Duvekot[1], G.H. Visser[2,3]
[1]Department of Obstetrics and Gynecology, Division of Obstetrics and Prenatal Medicine,
Erasmus MC - University Medical Centre, Rotterdam, The Netherlands
[2]Department of Clinical Neurophysiology, Erasmus MC - University Medical Centre, Rotterdam, The Netherlands
[3]SEIN- Epilepsy Institute in the Netherlands, Heemstede, The Netherlands

O70

What is the optimal management for screening, diagnosis and management of preeclampsia today?

Mila Cervar-Zivkovic
Medical University of Graz, Department of Gynecology and Obstetrics, Graz, Austria

12:30 – 13:30 LUNCH BREAK

13:30 – 15:30 ORAL COMMUNICATION - IMMUNOLOGY

Plenary Room

Chairs: Shigeru Saito – Marijke Faas

O72

Monocyte-macrophage system in pregnancy complications from the prospective of extracellular vesicles

Éva Pállinger[1], Nóra Fekete[1], Anikó Árokszállási[2], József Gábor Joó[2], Edit Buzás[1], János Rigó Jr.[2]
[1]Semmelweis University, Department of Genetics, Cell- and Immunobiology, Budapest, Hungary
[2]Semmelweis University, 1st Department of Obstetrics and Gynaecology, Budapest, Hungary

O73

The role of Th17/Treg imbalance in normal pregnancy and pre-eclampsia

Dorota Darmochwal-Kolarz[1], Bogdan Kolarz[2], Magdalena Kludka-Sternik[3], Jan Oleszczuk[1]
[1]Medical University of Lublin, Department of Obstetrics and Perinatology, Lublin, Poland
[2]University of Rzeszow, Centre for Innovative Research in Medical and Natural Sciences, Rzeszow, Poland
[3]Medical University of Lublin, 3rd Department of Gynecology, Lublin, Poland

O74

Granulocyte and monocyte phagocytosis index affected by plasma factors in normal and preeclamptic pregnancy

Rudolf Lampé, Ágnes Kövér, Róbert Póka
University of Debrecen, Department of Obstetrics and Gynecology, Debrecen, Hungary

O75

B7 Costimulation and Intracellular Indoleamine-2,3-dioxygenase expression in peripheral blood of healthy pregnant and preeclamptic women

Gergely Toldi, Attila Molvarec, László Berta, Anna Bajnok, János Rigó Jr.
Semmelweis University, 1st Department of Obstetrics and Gynecology, Budapest, Hungary

O76

The role of costimulatory molecules in the pathogenesis of pre-eclampsia

Dorota Darmochwal-Kolarz[1], Bogdan Kolarz[2], Tomasz Chmielewski[3], Jan Oleszczuk[1]
[1]Medical University of Lublin, Department of Obstetrics and Perinatology, Lublin, Poland
[2]University of Rzeszow, Centre for Innovative Research in Medical and Natural Sciences, Rzeszow, Poland
[3]Medical University of Lublin, Depertment of Clinical Immunology, Lublin, Poland

O77

Functional screening of toll-like receptors in seven trophoblast cell lines

Lobke Gierman[1], Guro Stødle[1], Line Tangerås[1], Marie Austdal[2], Guro Olsen[1], Turid Follestad[3], Bente Skei[1], Kristin Rian[4], Astrid Gundersen[1], Rigmor Austgulen[1], Ann-Charlotte Iversen[1]
[1]Norwegian University of Science and Technology, Centre of Molecular Inflammation Research and Department of Cancer Research and Molecular Medicine, Trondheim, Norway
[2]Norwegian University of Science and Technology, Department of Circulation and Medical Imaging, Trondheim, Norway
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[4]Norwegian University of Science and Technology, Department of Laboratory Medicine, Children's and Women's Health, Trondheim, Norway

O78

The inflammatory role of HMGB1 in preeclampsia

Line Tangerås[1], Guro Stødle[1], Gabriela Silva[1], Liv Cecilie Thomsen[2], Lobke Gierman[1], Bente Skei[1], Karin Collett[3], Merete Myklebost[4], Anne Lise Beversmark[4], Ragnhild Skråstad[5], Rigmor Austgulen[1], Line Bjørge[2], Ann-Charlotte Iversen[1]
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O137

Developing, disseminating, and implementing a core outcome set for pre-eclampsia

James M. N. Duffy
On behalf of iHOPE: International Collaboration to Harmonise Outcomes for Pre-eclampsia, University of Oxford, Oxford, United Kingdom.

13:30 – 15:30 ORAL COMMUNICATION – ANGIOGENESIS

Section Room

Chairs: Ananth Karumanchi – Holger Stepan

O79

An intermediate sFlt-1/PlGF ratio without preeclampsia indicates preterm delivery

Victoria Ossada, Janine Hoffmann, Holger Stepan
University of Leipzig, Department of Obstetrics, Leipzig, Germany

O80

The SFLT-1/PlGF ratio associates with prolongation of pregnancy

Langeza Saleh[1,2], K. Verdonk[1], A.H.J. Danser[1], E.A.P. Steegers[2], H. Russcher[3], A.H. van den Meiracker[1],W. Visser[2]

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[3]Erasmus MC, Department of Clinical Chemistry, Erasmus MC, Rotterdam, The Netherlands

O81

The impact of uterine curettage post partum on maternal sFlt-1 concentration

Victoria Ossada, Alexander Jank, Holger Stepan

University of Leipzig, Department of Obstetrics, Leipzig, Germany

O82

Association between anti-angiogenic factor and signs of arterial aging in women with preeclampsia

Tansim Akhter[1], Anna-Karin Wikström[1], Marita Larsson[1], Anders Larsson[2], Tord Naessen[1]

[1]Uppsala University, Obstetrics and Gynecology, Uppsala, Sweden

[2]Uppsala University, Clinical Chemistry, Uppsala, Sweden

O83

Angiogenic factor imbalance contributes to the pathophysiology of preeclampsia among rural African women

Allen Meeme

Walter Sisulu University, Obstetrics and Gynecology, Mthatha, South Africa

O84

Hydrogen sulphide rescues the preeclampsia phenotype aggravated by high sFlt-1 in placenta growth factor deficient pregnant mouse

Shakil Ahmad, Keqing Wang, Asif Ahmed

Aston University, Birmingham, Medical School, Birmingham, UK

15:30 – 16:00 COFFEE BREAK

16:00 – 17:00 WORKSHOP

Plenary Room

WH85

Biomarker discovery in preeclampsia: Present and future challenges: Taking a biomarker into clinical practice

Lucy Chappell

King's College London, Women's Health Academic Centre, London, UK

WH86

Using proteomics for the discovery of biomarkers: Promise and pitfalls

Jenny Myers

University of Manchester, Maternal & Fetal Health Research Centre, Manchester, UK

17:00 – 18:00 POSTER

Chairs: Holger Stepan – Dorota Darmochwal-Kolarz

P33

Decreasing of placental progesterone induced blocking factor expression and spiral artery remodeling disturbance in mice preeclampsia model

Manggala Pasca Wardhana[1], Budi Wicaksono[1], Erry Gumilar Dachlan[1], Muhammad Ilham Aldika Akbar[1], Ernawati Ernawati[1], Agus Sulistyono[1], Aditiawarman Aditiawarman[1], Hermanto Tri Juwono[1], Widjiati Widjiati[2]

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P87

Alteration of Delta-like ligand 1 and Notch 1 receptor in various placental disorders with special reference to early-onset preeclampsia

Yota Shimanuki[1], Hiroyuki Mitomi[2], Yuki Fukumura[3], Shintaro Makino[1], Atsuo Itakura[1], Takashi Yao[3], Satoru Takeda[1]

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[3]Juntendo University Faculty of Medicine, Department of Human Pathology, Tokyo, Japan

P88

Pre-eclampsia risk stratification for low risk 1st pregnancies: First results of a new LC-MS based multiplex metabolite assay

Liz Bond[1], Grégoire Thomas[2], Caroline Nolan[1], Louise Kenny[3], Philip Baker[4], Robin Tuytten[1]

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[2]Squ4Re, Lokeren, Belgium

[3]Cork University Maternity Hospital, The Irish Centre for Fetal and Neonatal Translational Research, Cork, Ireland

[4]University of Auckland, Gravida: National Centre for Growth and Development, Auckland, New Zealand

P89

Biochemical parameters of the first trimester in preeclampsia

Mirjana Bogavac[1], Ana Jakovljevic[2], Aleksandra Nikolic[3], Mirjana Milosevic-Tosic[3], Zagorka Lozanov-Crvenkovic[4], Zoran Novakovic[5]

[1]University of Novi Sad Medical Faculty, Clinical Centre Vojvodina Department of Obstetrics and Gynecology , Novi Sad, Serbia

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[5]University of Novi Sad, Medical Faculty, Novi Sad, Serbia

P90

Effect of angiotensin II receptor subtype2 stimulant on the pathogenesis of preeclampsia

Keiichi Matsubara, Miki Mori, Yuka Uchikura, Yuko Matsubara

Ehime University, Obstetrics and Gynecology, Toon, Japan

P91

Possible therapeutics for preeclampsia: Drug repositioning by In Vitro screening via induction of placental growth factor

Kazuya Mimura
Osaka University Graduate School of Medicine, Department of Obstetrics and Gynecology, Suita, Japan

P92

When there is a lack of magnesium during pregnancy

Anna Vachulova[1], Monika Kaldararova[2], Andrea Vaskova[3], Peter Tittel[2]
[1]National Cardiovascular Insitute, Department of Arrhythmias and Permanent Pacing, Bratislava, Slovakia
[2]National Cardiovascular Insitute, Department of Functional Diagnostics, Bratislava, Slovakia
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P93

Early-onset eclampsia with intrauterine fetal death after placental abruption at 22 weeks gestation: A case report and literature review

Aiko Shigemitsu
Nara Medical University, Department of Obstetrics & Gynecology, Kashihara, Japan

P94

Preeclampsia in pregnancies with and without diabetes; the associations with placental weight. A population study of 655 842 pregnancies

Johanne Dypvik[1], Ellen Marie Strøm-Roum[1], Camilla Haavaldsen[1], Lars Johan Vatten[2], Anne Eskild[1]
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P95

Perinatal outcome of pregnant with severe preeclampsia and gestational diabetes mellitus in Rondőnia, Brazil: Case report

Gizeli Gimenez[1], Ticiana Albuquerque Gonçalves[1], Maiky Jose de Oliveira[2], Rita Ferreira Silva[1],
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P96

Neonatal outcome in women after kidney transplantation: Effect of immunosuppressive therapy on the risk of preeclampsia

Hester Zweers[1], Henk Van Hamersvelt[2], Renate Van der Molen[3], Olivier Van der Heijden[1]
[1]Radboud University Medical Centre Nijmegen, Department of Obstetrics and Perinatology, Nijmegen, The Netherlands
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P97

Chronic kidney disease and pregnancy – A case report

Sara Nascimento, Mariana Miranda, Teresa Matos, Fernanda Matos, Antónia Nazaré
Hospital Prof. Doutor Fernando Fonseca, EPE, Department of Obstetrics and Gynecology, Amadora, Portugal

P98

Maternal lipid- and steroid hormone concentrations during the course of pregnancy and in pregnancy pathologies

Ulrich Pecks[1], Nicola Kleine-Eggebrecht[2], Nicolai Maass[1], Geneviève Escher[3], Werner Rath[2], Markus G. Mohaupt[3]

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[3]University of Bern, Department of Nephrology, Hypertension and Clinical Pharmacology, Berne, Switzerland

P99

Use of high dose cortisosteroids in HELLP syndrome

Ioana-Claudia Lakovschek, Christiane Barthel, Bence Csapo, Vassiliki Kolovetsiou-Kreiner, Christina Stern, Karoline Mayer-Pickel, Uwe Lang, Mila Cervar-Zivkovic

Medical University of Graz, Department of Obstetrics & Gynecology, Graz, Austria

P100

Differences in depression scores between women with a history of term hypertensive pregnancy disorders and women with a history of uncomplicated pregnancies

Wietske Hermes[1], Floortje Van Kesteren[2], Marielle Van Pampus[3], Kitty Bloemenkamp[4], Arie Franx[5], Ben Mol[6], Christianne De Groot[7]

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P101

Cardiac function and ventriculo-arterial interaction11 years after preeclampsia complicated pregnancy

Maha Al-Nashi[1,5] ,Katarina Bremme[1,5], Thomas Kahan[3,5], Eva Östlund[4,5], Maria Eriksson[2,5]

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P102

Placental weight in the first pregnancy and risk for preeclampsia in second pregnancy: A population cohort study of 186 859 women

Sandra Larsen[1], Johanne Dypvik[1], Camilla Haavaldsen[1], Lars Vatten[2], Anne Eskild[1]

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P103

Relationship between severe preeclampsia onset with IUGR incidence at dr. Soetomo General Hospital in 2013

Budi Wicaksono[1], Ryan Intan[2], Budi Utomo[3]
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P104

Stromal derived factor-1A is a key to improving neonatal brain injuries

Miki Mori[1], Keiichi Matsubara[2], Yuko Matsubara[2], Yuka Uchikura[2], Hiroshi Ochi[1]
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SATURDAY, 26 SEPTEMBER 2015

08:00 – 10:00 STATE OF THE ART LECTURE, PLENARY LECTURE

Plenary Room

Chairs: Annetine Staff – Louise Kenny

STA105

PlGF: more than a pre-eclampsia biomarker. Results from the CoLAB Angiogenic Factor Study of 16 000 pregnancies

Anne Cathrine Staff AC[27],Burke Ó[1], Benton S[2], Szafranski P[1], von Dadelszen P[2], Buhimschi C[3], Cetin I[4], Chappell L[5], Figueras F[6], Galindo A[7], Herraiz I[7], Holzman C[8], Hubel C[9], Knudsen U[10], Kronborg C[10], Laivuori H[11], McElrath T[12], Moertl M[13], Myers J[14], Ness RB[15], Oliveira L[16], Olson G[17], Poston L[5], Ris-Stalpers C[18], Roberts J[9], Schistermann E[19], Steegers E[20], Stepan H[21], Lapaire O[22], Schlembach D[13], Timmermans S[20], Tsatsaris V[23], van der Post JA[18], Verlohren S[24], Villa PM[11], Williams D[25], Zeisler H[26], Zhang C[19], Redman C[1]

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[3]Yale University, New Haven, CT, USA
[4]University of Milan, Italy
[5]King's College London, London, UK
[6]University of Barcelona, Barcelona, Spain
[7]University of Madrid, Spain
[8]Michigan State University, East Lansing, MI, USA
[9]University of Pittsburgh, Pittsburgh, PA, USA
[10]Aarhus University, Aarhus, Denmark
[11]University of Helsinki, Helsinki, Finland
[12]Harvard Medical School, Boston, MA, USA
[13]University of Jena, Germany
[14]University of Manchester, Manchester, UK
[15]University of Texas, School of Public Health, Houston, TX, USA
[16]Federal University of Sao Paulo, Sao Paulo, Brazil
[17]University of Texas, Galveston, TX, USA
[18]University of Amsterdam, Amsterdam, The Netherlands
[19]National Institutes of Health, Bethesda, MD, USA
[20]Erasmus Medical Centre, Rotterdam, The Netherlands
[21]University of Leipzig, Germany
[22]University of Basel, Basel, Switzerland
[23]Université Paris Descartes, Paris, France
[24]Charité University Medicine, Berlin, Germany.
[25]University College London, London, UK
[26]University of Vienna, Austria
[27]University of Oslo, Oslo, Norway

STA106

Maternal cardiac function before and during preeclampsia: We must study the heart in pregnacy

Herbert Valensise

University of Tor Vergata, Biomedical Imaging, Rome, Italy

PL107

Monocytes in pregnancy and preeclampsia

Marijke Faas

University Medical Center Groningen, Department of Pathology and Medical Biology, Groningen, The Netherlands

PL108

Inflammatory mechanisms in preeclampsia

Attila Molvarec, János Rigó Jr.

Semmelweis University, 1st Department of Obstetrics and Gynecology, Budapest, Hungary

PL109

Corticosteroids in the management of severe preeclampsia: What evidence?

Alex Vidaeff

Baylor College of Medicine, Obstetrics and Gynecology, Houston, USA

10:00 – 10:30 COFFEE BREAK

10:30 – 12:15 ORAL COMMUNICATION – CARDIOVASCULAR CHANGES IN PREECLAMPSIA

Plenary Room

Chairs: Herbert Valensise – Asma Khalil

O110

Maternal left ventricular dysfunction and remodeling in pregnancy complicated with gestational hypertension

Orsolya Szenczi, János Rigó Jr.

Semmelweis University, 1st Department of Obstetrics and Gynecology, Budapest, Hungary

O111

The association between maternal haemodynamics and pre-eclampsia: Systematic review and meta-analysis

Silvia Selvi[1], Basky Thilaganathan[2], Francesco D'Antonio[2], Lamberto Manzoli[3], Asma Khalil[2]

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O112

Inotropy index and ratio of potential to kinetic energy: Two novel parameters derived from continuous-wave Doppler ultrasound

Sophie Bowe, Basky Thilaganathan, Elena Mantovani, Asma Khalil

St George's Hospital, University of London, Maternal-Fetal Department, London, UK

O113

Measurements of arterial stiffness and uterine artery Doppler for the prediction of preeclampsia in women presenting with gestational hypertension

Asma Khalil, Sophie Bowe, Basky Thilaganathan, Dimuthu Vinayagam, Elena Mantovani
St George's Hospital, University of London, Maternal-Fetal Department, London, UK

O114

Maternal cardiovascular changes in pregnancies complicated by small for gestational age neonate with or without maternal hypertension

Sophie Bowe, Basky Thilaganathan, Dimuthu Vinayagam, Asma Khalil
St George's Hospital, University of London, Maternal-Fetal Department, London, UK

O115

First trimester maternal vascular function is associated with fetal growth

Charlotte Iacobaeus[1], Thomas Kahan[1], Ellika Andolf[1], Malin Thorsell[1], Gun Jörneskog[1], Katarina Bremme[2]
[1]Karolinska Institute, Department of Clinical Science, Danderyd Hospital, Stockholm, Sweden
[2]Karolinska Institute, Department of Women's and Children's Health, Stockholm, Sweden

O116

Can maternal haemodynamics predict hypertensive disorders in pregnancy?

Asma Khalil
St George's Hospital, University of London, Maternal-Fetal Department, London, UK

10:30 – 12:15 ORAL COMMUNICATION – LONG TERM COMPLICATIONS OF PREECLAMPSIA

Section Room

Chairs: Manuel Bicho

O117

Role of some biomarkers in long term cardiovascular prognosis of pregnancy hypertensive disease

Manuel Bicho[1], Andreia Matos[1], Alda Pereira da Silva[1], Maria Clara Bicho[1], Maria José Areias[2], Irene Rebelo[3]
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O118

Subsequent preeclampsia is associated with worse subclinical left ventricular dysfunction

York Yann Chow[1], Deven Mahadavan[2], Gus Dekker[3], Noriko Warren[2], Melanie Wittwer[1], Vikki Clifton[4], Margaret Arstall[1]
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O119

Cardiovascular risk management after reproductive and pregnancy related disorders: A Dutch multidisciplinary evidence-based guideline

Karst Heida[1], Michiel Bots[2], Miram Cohen[3], Frederique Van Dunné[4], Christianne De Groot[5], Nurah Hammoud[1], Annemiek Hoek[6], Joop Laven[7], Angela Maas[8], Jeanine Roeters van Lennep[9], Birgitta Velthuis[10], Arie Franx[1]

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O120

Increased myeloperoxidase is a cardiovascular risk biomarker in women with previous preeclampsia

Andreia Matos[1], Alice Rivera[2], Alda Pereira da Silva[1], Ana Portelinha[3], Maria José Areias[4], Irene Rebelo[5], Manuel Bicho[1], José R. Romero[6]

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[6]Brigham and Women's Hospital and Dept. of Medicine, Harvard Medical School, Div. of Endocrinology, Diabetes and Hypertension, Boston, USA

O121

Maternal metabolic outcomes in women with a history of hypertensive pregnancy disorders

Laura Benschop[1], Jeanine E. Roeters-van Lennep[2], Sarah Schalekamp-Timmermans[1], Vincent W.V. Jaddoe[3], Nienke E. Bergen[1], Eric A.P. Steegers[1]

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O122

The role of framing in modifying behavior to reduce cardiovascular risk after preeclampsia, a vignette study

Anouk Bokslag[1], Wietske Hermes[2], Christianne De Groot[1], Pim Teunissen[3]

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O123

Hypertensive disorders of pregnancy and subsequent risk of cancer – A population-based cohort study

Ida Behrens[1], Saima Basit[2], Allan Jensen[3], Jacob Lykke[4], Lars Peter Nielsen[5], Jan Wohlfahrt[2], Susanne Krüger Kjaer[3], Mads Melbye[2], Heather Boyd[2]

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[5]Statens Serum Institut, Department of Autoimmunology and Biomarkers, Copenhagen, Denmark

12:15 – 12:45 COFFEE BREAK

12:45 – 14:15 ORAL COMMUNICATION – OTHERS I.

Plenary Room

Chairs: Lucy Chappell – Katsuhiko Naruse

O124

Preeclampsia: Two different clinical phenotypes – Two different pregnancy outcomes

Zulfiya Khodzhaeva

Moscow Federal Research Center for Ob-Gyn & Perinatology, Maternal-Fetal Department, Moscow, Russia

O125

Ethnicity: An independent risk factor for adverse perinatal outcome in women with chronic hypertension

Louise Webster[1], Kate Bramham[1], Paul Seed[1], Michelle Homsy[1], Catherine Nelson-Piercy[1], Basky Thilaganathan[2], Lucy Chappell[1]

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O126

Postnatal neurological development follow-up of newborns from pregnancies with hypertension associated intrauterine growth restriction (IUGR)

József Gábor Joó, Boróka Ujvárosi, Anna Beke, János Rigó Jr.

Semmelweis University, 1st Department of Obstetrics and Gynecology, Budapest, Hungary

O127

Low levels of plasma protein S, protein C and coagulation factor XII during early pregnancy and adverse pregnancy outcome

Yasuhiko Ebina[1], Masahiro Ieko[2], Sumiyoshi Naito[3], Gen Kobashi[4], Masashi Deguchi[1], Hisanori Minakami[5], Tatsuya Atsumi[6], Hideto Yamada[1]

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O128

Placental vascularization indices and uterine artery peak systolic velocity in pregnancy hypertension

Ábel Tamás Altorjay[1], Andrea Surányi[1], Tibor Nyári[2], Gábor Németh[1]
[1]University of Szeged, Department of Obstetrics and Gynecology, Szeged, Hungary
[2]University of Szeged, Department of Medical Physics and Informatics, Szeged, Hungary

12:45 – 14:15 ORAL COMMUNICATION – OTHERS II.

Section Room

Chairs: Marijke Faas – Péter Tamás

O130

Urinary congophilia in women with preeclampsia and chronic kidney disease

Fergus McCarthy[1], Adedamola Adetoba[2], Carolyn Gill[2], Kate Bramham[2], Maria Bertolaccini[2], Guillermina Girardi[2], Lucilla Poston[2], Lucy Chappell[2]
[1]King's College London, Women's Health Academic Centre, London, UK
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O131

Pravastatin protects against glucose-induced anti-proliferative, anti-invasive and anti-angiogenic milieu in cytotrophoblasts

M. Nasir Uddin
Texas A&M Health Care Centre, Department of Obstetrics & Gynecology, Temple, USA

O132

Comparison of groups with and without diabetes mellitus and preeclampsia in pregnancy: a retrospective case-control comparison

M. Nasir Uddin
Texas A&M Health Care Centre, Department of Obstetrics & Gynecology, Temple, USA

O133

Fetal renal vascularisation in pregnancy induced hypertension complicated by gestational diabetes or intrauterine growth restriction

Andrea Surányi, Ábel Altorjay, Gábor Németh
University of Szeged, Department of Obstetrics & Gynecology, Szeged, Hungary

O134

Polycystic ovary syndrome as a risk factor of pregnancy induced hypertension – Review of the literature

Szabolcs Várbíró[1], Eszter Horváth[2], Nándor Ács[1]
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[2]Institute of Human Physiology and Clinical Experimental Research, Semmelweis University, Budapest, Hungary

O135

HELLP??? – A case

Eva-Christine Weiss, Gordana Tomasch, Uwe Lang, Wolfgang Schöll
Medical University of Graz, Department of Obstetrics & Gynecology, Graz, Austria

STA1

What's new in pre-eclampsia?

Mark Brown
St. George Hospital & University of NSW, Department of Renal Medicine, Sydney, Australia

Introduction: Pre-eclampsia and other hypertensive disorders of pregnancy have major world-wide consequences, with high maternal and perinatal mortality.
Objective: To describe attempts to improve outcomes for women with pre-eclampsia.
Methods: Review of some recent literature and statements from ISSHP.
Results: Improved outcomes depend upon a) translation of factors behind 'success' in pre-eclampsia management in developed countries to LMIC in a culturally sensitive and practical way; b) improved understanding of the cause(s) of this disorder, and c) improved management of all hypertensive disorders during pregnancy, d) recognition of the long-term cardiovascular consequences of pre-eclampsia and chronic hypertension, the latter often detected for the first time during pregnancy.
Recent advances in the pathogenesis of pre-eclampsia include greater understanding of the links between inflammatory and antibody-initiated stimulation of anti-angiogenic factors and the downstream effects of these changes on endothelial function, endothelin release and the renin-angiotensin system. A concern in recent management is an increasing tendency to utilise 'predictive' tests with apparent certainty even though such certainty does not exist.
For the first time we now have randomised trial evidence that 'tight' BP control is associated with greater maternal protection than 'less tight' control and further suggestive evidence that a conservative approach is appropriate in the management of women with mild pre-eclampsia pre-term. Some disturbing evidence shows that physicians lag behind obstetricians in recognising pre-eclampsia as a cardiovascular risk factor, even though this is now highlighted by major cardiac societies.
Conclusions: ISSHP has developed a 7-point plan designed to make a difference to the short (during pregnancy) and long-term outcomes of women who have hypertension during their pregnancy. This is an ongoing plan that involves groups working with LMIC, improved dissemination of research, greater public awareness of the impacts of pre-eclampsia, and support for young investigators.

STA2

Placentation and pre-eclampsia – Inflammatory and immunological issues

Christopher Redman
University of Oxford, Nuffield Department of Obstetrics and Gynaecology, Oxford, UK

Early and late onset disease are subsets of pre-eclampsia (PE). The late onset variety (LOPE) seems to be caused by placental hypoxia that occurs at term when the placenta outgrows the capacity of the uteroplacental circulation. Typically it is not associated with feta
University of Oxford, Nuffield Department I growth restriction. Early onset pre-eclampsia (EOPE) arises from inadequate placentation particularly affecting spiral artery remodelling. Poor placentation has many potential causes of which none is well defined. It is a pathology that underlies fetal growth restriction whether or not the mother has PE.
A potential cause of poor placentation is immune disparity between mother and fetus. Placentation depends on invasion of the placental bed by extravillous cytotrophoblast which is the only subset

of trophoblast to express a major polymorphic transplantation antigen (HLA-C).This can interact with decidual natural killer cells and T cells. Specific maternal-fetal combinations are known to increase the risk of PE and the presumed mechanisms point to dysfunctional trophoblast invasion of the placental bed (placentation). This interaction could explain the first pregnancy preponderance of PE as well as the increased risk with a short interval between first coitus and conception, by a particular partner (primipaternity). There is evidence that preconceptual exposure to a partner's semen promotes favourable immunoregulation which stimulates local (uterine) tolerance to paternal antigens expressed by extravillous trophoblast.
But other inflammatory mechanisms may be relevant.
One of the distinguishing features of EOPE is its increased likelihood of recurrence in later pregnancies compared to LOPE. Recurrence is also a feature of women with underlying medical disorders such as pregestational hypertension, which is a major risk factor for PE, as much for EO as for LO disease. Chronic hypertension, as well as conditions associated with insulin resistance (for example obesity), is associated with, possibly even caused by, vascular inflammation. This would be expected to involve the uteroplacental circulation and could unfavourably modify interactions between trophoblast, particularly endovascular trophoblalst, and maternal endothelium, down regulating trophoblast invasion of spiral arteries. This would constitute an inflammatory cause of deficient placentation distinct from the immune cause described above.
The evidence for these concepts will be presented.

STA3

Novel therapies for preeclampsia

Ananth Karumanchi
Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, USA

Imbalance of angiogenic growth factors in the maternal circulation contributes to the pathogenesis of preeclampsia. Soluble fms-like tyrosine kinase 1 (sFlt1), an endogenous anti-angiogenic protein that antagonizes vascular endothelial growth factor (VEGF) and placental growth factor (PlGF) appears to be a central player in this paradigm. In this presentation, I will focus on novel strategies for targeting sFlt1 in preeclampsia including therapeutic apheresis, antagonists of sFLT1 and small molecules that inhibit placental production of sFlt1.

PL136

Renal disease before, during and after preeclampsia

Markus G. Mohaupt
University Hospital Bern, Department of Nephrology, Hypertension and Clinical Pharmacology, Bern, Switzerland

In patients with chronic kidney disease the decision to get pregnant is complicated by reduced fertility rates and the risk of adverse fetal and maternal outcomes. This suggests informed and shared decision making of the patient and the attending physician. The counseling should cover the best preparation for a pregnancy, the risk for hypertensive disorders and preeclampsia, the risk for a renal functional deterioration and required therapeutical modalities, the risk for a nephrotic syndrome, and the risk for any fetal consequences such as IUGR. Long-term consequences such as an increased cardiovascular and renal risk for mother and child given certain pregnancy-related diseases should also be approached.
As with chronic hypertension, the rate for maternal pregnancy complications including gestational

hypertension, preeclampsia, eclampsia or death is several fold elevated in all major analysis. Also fetal complications such as premature birth, low birth weight with both IUGR and SGA, neonatal mortality, and even stillbirth are quite variable in between studies, in general they are increased. Given different renal diseases, with increasing renal functional impairment the likelihood of a permanent renal devastation is rising. This requires in those patients to even consider the impact of the renal disease on a later successful renal transplantation. Any type of de novo renal disease is conceivable in pregnancy, yet infrequent. However, unknown preexisting renal pathologies might be revealed upon pregnancy.

The most frequent de novo renal disease and an imminent threat to those patients with low renal function constitutes preeclampsia. This multisystem endothelial disease appears to be related to a reduced functional nephron number, a finding supported by the heightened rate of preeclampsia after living kidney donation prior to being pregnant. Novel recognized risks such as gestational diabetes and abnormal ADAMTS-13 availability further contribute. Preeclampsia monitoring is hindered in prior proteinuric and hypertensive disease states, yet can be successfully performed by following sFlt-1/PlGF ratios.

In certain cases, in might be preferable to await renal transplantation which allows for an improved rate of successful pregnancies as compared to progressed renal functional decline or even end-stage renal disease on dialysis. Renal transplantation is effectively supporting pregnancy if stable though hampered by a reduced fetal birth weight.

If preeclampsia has been encountered during pregnancy, the mothers are subjected to an increased risk for hypertension and renal disease. The number of affected pregnancies seems to heighten this risk and may even lead to end-stage renal failure. A very intriguing assumption is to consider the impact of the compromised angiogenetic signaling on podocyte survival leading to focal and segmental glomerulosclerosis and progressive renal deterioration due to hyperfiltration of the remaining glomeruli. Likewise, the children of these mothers often affected by reduced birth weight are demonstrate a reduced functional renal mass leading to symptoms such as salt-sensitive blood pressure increases and ultimately to end-stage renal disease.

Given all these considerations pregestational counseling, very subtle peripregnancy follow-up and postpartal assessment are highly recommended to avoid individual affliction and to relieve the societies healthcare expenses.

O4

Genome wide sequencing approaches to identify missing heritability of preeeclampsia

Eric Moses[1], Phillip Melton[1], Matthew Johnson[2], Dnyanada Gokhale-Agashe[1], Alex Rea[1], Richard Allcock[3], John Blangero[2], Shaun Brennecke[4]

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[2]University of Texas Health Science Center at San Antonio, South Texas Diabetes and Obesity Institute, Brownsville, USA

[3]University of Western Australia, School Pathology and Laboratory Medicine, Perth, Australia

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Introduction: Genome-wide mapping approaches have been successfully used to identify several candidate susceptibility genes for preeclampsia (PE). Of note is the identification of the ACVR2A gene on chromosome 2 that was originally identified by our group by linkage and fine mapping studies in a cohort of 34 multiplex preeclampsia families from Australia and New Zealand. Genetic association of preeclampsia risk to variants in or near this gene has now been validated in three independent population studies from Norway, Turkey and Brazil. Most recently, a Dutch study has demonstrated a plausible functional role in trophoblast invasion/spiral artery remodelling for the ACVR2A SNP variant showing strongest association. Despite these successes there remains

a substantial portion of the heritable risk of PE unaccounted for. We propose that family-based sequencing is an optimal study design for the identification of potentially rare novel risk variants of moderate to large effect.
Objective: To identify the missing heritability of PE risk in the cohort of 34 Australian/New Zealand families previously used in linkage mapping studies by our group.
Methods: Whole exome and whole genome DNA sequencing using Illumina and Life Technologies massively parallel DNA sequencing platforms. We have completed whole exome sequencing in the entire 34 family cohort and are currently doing whole genome sequencing in a subset, representing the largest five families.
Results: Our preliminary bioinformatic interrogation has identified 428,229 variants from targeted exonic sequencing and 68,933 of these are non-synonymous (i.e., a nucletide substitution that changes the amino acid sequence of a protein), with 15,024 of these variants being determined to be deleterious using specific bioinformaric software tools including SIFT (≤ 0.05) and Polyphen2 (≥0.453). A total of 3,664 of these non-synonymous deleterious variants are detectable in more than four individuals indicating a high potential for identifying rare functional variants impacting PE.
Conclusion: We are currently applying linkage, association and pathway lineage specific filtering on this data in an effort to identify rare risk variants segregating/shared among affected and non-affected family members. We are initially focusing on deleterious non-synonymous coding sequence variants and variants in the most likely regulatory regions of genes.

O5

Next-generation sequencing studies in Finnish preeclampsia cohorts

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Preeclampsia is a heterogeneous disease and deciphering its genetic background has proven difficult. The clinical disease presumably results from the additive effects of multiple sequence variants from the mother and the fetus together with environmental factors. Recent studies have demonstrated substantial advantages for studying the role of rare variation in complex phenotypes in founder populations like the Finns. Some rare alleles are enriched in Finland due to bottleneck effect, genetic drift and population expansion.
Next-generation sequencing (NGS) holds the promise to broaden our understanding of the genetic background of preeclampsia, because rare sequence variants can be identified using this technology. It is plausible that variants predisposing to preeclampsia are under negative evolutionary selection and do not reach high frequencies in a population. We have applied several NGS strategies to explore genetic predisposition to preeclampsia. In RNA sequencing study on preeclamptic placentae we identified several genes involved in the biological processes relevant for the development of preeclampsia such as immunological and vascular functions. In two ongoing studies in the Finnish Genetics of Preeclampsia Consortium (FINNPEC) and the Finnish Preeclampsia Family cohorts we have used exome sequencing. The results from these studies will be presented in the meeting.

O6

Association between fetal congenital heart defects and maternal risk of hypertensive disorders of pregnancy in concurrent and subsequent pregnancies

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Introduction: Pregnant women carrying fetuses with heart defects and women with hypertensive disorders of pregnancy (HDP) both often exhibit angiogenic imbalances, suggesting that the same underlying processes may play a role in the etiology of heart defects and the pathology associated with HDP.

Obejctives: To determine whether fetal heart defects are associated with an increased risk of maternal HDP, and whether the mechanisms driving the association are primarily maternal or fetal.

Methods: Using Danish national registers, we constructed a cohort comprising all singleton pregnancies without chromosomal abnormalities continuing to at least 20 completed weeks gestation in Denmark, 1977-2011. We then identified both pregnancies complicated by offspring congenital heart defects and those complicated by HDP (severe preeclampsia [PE]/eclampsia, moderate PE, gestational hypertension [GH]). Using polytomous logistic regression, we estimated odds ratios (ORs) for the association between carrying a fetus with a congenital heart defect and maternal risk of an HDP in the second half of pregnancy, overall and for specific heart defects. We also estimated ORs for the association between 1) an HDP in a previous pregnancy and the risk of carrying a child with a heart defect in subsequent pregnancies, and 2) fetal congenital heart defects in a previous pregnancy and the risk of HDP in subsequent pregnancies.

Results: Carrying a child with a heart defect was associated with a 3-fold increase in the risk of severe PE later in pregnancy (OR 3.02, 95% confidence interval [CI] 2.71-3.37) and a modest increase in the risk of moderate PE (OR 1.29, 95% CI 1.18-1.41), but not with the risk of GH (OR 1.08, 95% CI 0.93-1.25). These associations did not appear to depend on the type of offspring heart defect. Having a child with a heart defect in a previous pregnancy was also associated with PE (severe PE: OR 1.57, 95% CI 1.24-1.97; moderate PE: OR 1.32, 95% CI 1.16-1.51) but not with GH (OR 1.00, 95% CI 0.82-1.22) in subsequent pregnancies. Similarly, a history of PE in a previous pregnancy, but not of GH alone, was associated with an increased risk of offspring heart defects in later pregnancies (severe PE: OR 1.46, 95% CI 1.21-1.77; moderate PE: OR 1.13, 95% CI 1.01-1.27; GH: OR 1.12, 95% CI 0.91-1.37).

Conclusion: Our findings suggest that the same pathophysiological mechanisms may be involved in both congenital heart defects and severe PE (but are less important in less severe forms of HDP), and that these processes are most likely maternal, rather than fetal.

O7

Epigenome of the circadian clock pathway of placental and newborn tissues in pre-eclampsia

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Introduction: The placenta is important in providing a healthy environment for the fetus and plays a central role in the pathophysiology of pre-eclampsia (PE). The circadian rhythm is implicated in fetal and placental growth and development. We hypothesize that derangements in prenatal epigenetic programming of circadian clock-related genes in placental and newborn tissues are associated with disease severity of PE.

Objectives: To investigate DNA methylation programming of circadian clock-related genes in patients with early-onset or late-onset PE and controls.

Methods: From the Rotterdam periconception cohort, patients with early-onset (n=13) and late-onset (n=16) PE were selected and compared with fetal growth restriction (FGR, n=26) or preterm birth (PTB, n=20) as controls, complications often occurring in PE, as well as with controls without PE, FGR or PTB (n=36). Genome-wide methylation analysis (Illumina 450KA methylation array) was performed at 936 CpGs of 38 circadian clock-related genes in umbilical cord white blood cells (UCWBC), endothelial cells (HUVEC) and placental tissue. For statistical analysis a pathway approach was used and ANCOVA was applied with adjustment for gestational age at sampling. Bonferroni adjustment was used for multiple comparisons.

Results: DNA methylation differed between early-onset PE and PTB at 5 circadian clock-related CpGs in placental tissue ($10\text{-}4 < P \leq .01$) and at 22 CpGs in UCWBC ($10\text{-}6 < P \leq .05$)). The same comparison with controls revealed differences at 2 CpGs ($P < .01$) in placental tissue and 10 CpGs in UCWBC ($10\text{-}4 < P \leq .05$). Moreover, in early-onset PE compared with FGR differences at 4 CpGs in UCWBC ($10\text{-}4 < P \leq .03$) were observed. Late-onset PE showed no differences between groups and tissues.

Conclusion: Here we show variations in epigenetic programming of the circadian clock pathway in early-onset PE only. Differences in placental and UCWB programming of circadian clock genes of interest and severity of PE are suggested. Future research should address whether these tissue specific epigenetic profiles can be used as early predictors of short and long term health.

O8

Cardiovascular risk factors, renin-angiotensin system gene polymorphisms, pregnancy course and outcomes in women with different forms of hypertension

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Introduction: The hypertensive disorders of pregnancy remain the leading causes of maternal and perinatal morbidity and mortality. Each form of hypertension during pregnancy has its outcome. The investigations of characteristics of genetic and cardiovascular risk factors in different forms of hypertension are necessary to carry out.

Objectives: The aim of our research was to study the frequency of cardiovascular risk factors, renin-angiotensin system gene polymorphisms, pregnancy course and outcomes in women with different forms of hypertension.
Methods: Prospective cohort study. The study included 300 patients (200 – with hypertension, 100 – without hypertension). Women with hypertension were divided into 4 groups: 106 patients with chronic hypertension (CH), 63 patients with gestational hypertension, 10 patients with preeclampsia (PE), 21 with PE superimposed on CH. Control group included 100 women without hypertension. Molecular genetic testing was used for detection of three polymorphic variants in angiotensin-converting enzyme (ACE I/D), angiotensinogen (AGT 174 T/M) and angiotensin II type 1 receptor (ATR1 1166 A/C) genes by polymerase chain reaction («Lytech», Russia). Statistical analysis was performed using the statistical software package version 11.5.0 MedCalc®. Gene-gene interactions were studied using entropy-based multifactor dimensionality reduction (MDR) method (software version 3.0.2).
Results: Pregnant women with CH and with PE superimposed on CH were more frequently of age over 35 years, overweight, obese and smoking and a high incidence of hypertension in the family history compared with pregnant women without hypertension. In pregnant women with CH a higher frequency of D allele and DD-genotype of ACE (I/D) and C allele of ATR1 (A1166C) were observed and compared with a control group. In pregnant women with PE a higher frequency of M allele and MM-genotype AGT (T174M) was noted. To assess independent associations of clinical and genetic factors with combined adverse outcome (fetal growth restriction or/and premature delivery or/and small gestational age) we have used MDR. The best interaction model included: age > 35 years, hypertension in the family history, failure to achieve target blood pressure to 27-28 weeks and C allele of ATR1 (A1166C). The established model precisely predicted combined adverse outcome in 79,5% cases.
Conclusion: Analysis of cardiovascular risk factors, renin-angiotensin system gene polymorphisms may be helpful for evaluation adverse outcomes in pregnant women with different forms of hypertension.

O9

The functional role of natriuretic peptides in preeclampsia

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Background: Natriuretic peptide family is believed to have evolved for the common homeostatic purpose of volume, osmosis and pressure regulation of the circulatory system. The activities of natriuretic peptides and endothelins are associated with each other. In the last three decades many members of the natriuretic peptide family was identified. BNP is the member of this family and with the sympathetic nervous system and other hormones they play key roles, like an endogeneous system in the regulation of the body fluid homeostasis and blood pressure. In the last years the potential use of the elevated BNP levels for diagnosis of pre-eclampsia was examined. There is a variable tandem repeat polymorphism in the 5'-flanking region of the natriuretic peptide precursor B gene (NPPB). A previous study showed association of the (TTTC) small tandem repeat (STR) variants of this gene and essential hypertension in females.
Methods: In our studies blood samples were collected from healthy pregnant normotensive women (n=235) and patients having severe pre-eclampsia (n=220). DNA was isolated and fluorescent PCR and DNA fragment analysis was performed for the detection of (TTTC) repeats. The concentration of the BNP was measured by fluorescence immunoassay -Triage BNP test- method.

Results: The overall distribution of alleles and genotypes was significantly different between the control and pre-eclamptic groups. We detected 12 different (TTTC) repeats on the NPPB gene in the studied population. The pre-eclamptics were a homogeneous population, with only 10 types of alleles and 20 types of genotypes, contrary to control group with 12 types of alleles and 32 types of genotypes. The 11 homozygote patients have a higher frequency among the severe-pre-eclamptics. I found higher levels of BNP in those who had the genotype 11 homozygotes in both groups, significantly higher in pre-eclamptics. The concentration of the BNP is higher pre-eclamptic pregnancies, it shows association with the (TTTC) genotypes. The concentration of BNP was higher in early onset pre-eclamptic patients than in late onset pre-eclamptics. Intrauterine growth restriction shows no connection with BNP levels in severe pre-eclampsia.
There was a significant inverse correlation between plasma BNP levels of preeclamptic patients and sodium and total protein concentrations and a significant positive correlation was observed between plasma levels of BNP and 24 hour proteinuria.
The cut-off value < 24.5 pg/ml seems to be a powerful discriminative indicator excluding preeclampsia.
Conclusions: We introduced a F-PCR and DNA fragment analysis method for the fast and reliable detection of the STR in the 5'-flanking region of the natriuretic peptide precursor B gene. Further investigations may help to understand the details of molecular biology, biochemistry and clinical relevance of natriuretic peptides.

O10

Increased maternal and fetal HDL cholesterol efflux capacity and placental CYP27A1 expression in pre-eclampsia

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Introduction: Pre-eclampsia is a pregnancy-specific condition affecting 2-7% of women, causing perinatal and maternal morbidity/mortality and predisposes both mother and fetus to increased risks of adult cardiovascular disease. A disturbance in the flow of cholesterol is linked to atherosclerosis and cardiovascular disease.
Objective: We measured cholesterol efflux capacity, apoA1, apoE and oxysterols, in maternal and fetal plasma and placental sterol 27-hydroxylase (CYP27A1) and apo-A1-binding-protein (AIBP) expression in normotensive control and pre-eclamptic pregnancies.
Methods: Cholesterol efflux assays were performed in RAW264.7 cells with maternal and matched fetal plasma of normotensive control or pre-eclamptic pregnancies (n=17 in both). ApoA1, apoE were measured by ELISAs. Oxysterols were also measured by gas-chromatography-mass-spectrometry. Placental mRNA and protein expression/localisation of CYP27A1 and AIBP were measured in the same women by qPCR and immunohistochemistry.
Results: In pre-eclampsia, maternal and fetal cholesterol efflux capacity and fetal apoE were all increased ($P<0.05$ for all), yet fetal cholesterol efflux capacity and apoE were lower in the small-for-gestational-age (SGA) subgroup (n=6; $P<0.05$ for both). Fetal 27-hydroxycholesterol (27-OHC) concentrations were lower in babies born to pre-eclamptic mothers ($P<0.05$) with no other

observed differences in oxysterols. Fetal apparent CYP27A1 activities (calculated by ratios of 27-OHC / (27-OHC + total serum cholesterol) were also lower in the pre-eclampsia group ($P<0.05$). Protein expression was localised around fetal vessels; CYP27A1 and AIBP proteins increased in pre-eclampsia ($P=0.04$), but no differences were found in gene expression.
Conclusions: Increased maternal and fetal cholesterol efflux capacity in pre-eclampsia, which is a key step in reverse cholesterol transport, coupled with increased placental CYP27A1, could be a rescue mechanism to remove cholesterol from cells thus trying to reduce lipid peroxidation. However, increased placental AIBP suggests disturbed lipid homeostasis, which could disrupt placental angiogenesis, contributing to the endothelial dysfunction so characteristic of pre-eclampsia.

O11

Evaluation of the endocannabinoid system in preeclampsia

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Introduction: The endocannabinoid system plays a key role in female reproduction, including implantation, decidualization and placentation. A growing number of studies indicate that placental and peripheral blood anandamide levels correlate closely with both spontaneous miscarriage and ectopic pregnancy. Anandamide has also been implicated in blood pressure regulation.
Objectives: In this study, we aimed to analyze placental expression and localization of cannabinoid receptor 1 (CB1), CB2 and fatty acid amid hydrolase (FAAH), as well as circulating anandamide levels in normal pregnancy and preeclampsia.
Methods: We determined CB1, CB2 and FAAH expressions by Western blotting and immunohistochemistry in placental samples collected directly after Cesarean section in 18 preeclamptic patients and 18 normotensive, healthy pregnant women. Serum anandamide concentrations were measured by high performance liquid chromatography-mass spectrometry (HPLC-MS) technique in 43 preeclamptic patients and 71 healthy pregnant women. Serum total soluble fms-like tyrosine kinase-1 (sFlt-1) and biologically active placental growth factor (PlGF) levels were assessed by electrochemiluminescence immunoassay.
Results: CB1 expression semi-quantified by Western blotting was significantly higher in preeclamptic placenta, and these findings were confirmed by immunohistochemistry. CB1 immunoreactivity was markedly stronger in syncytiotrophoblasts, the mesenchymal core, decidua, villous capillary endothelial and smooth muscle cells, as well as in the amnion in preeclamptic samples compared to normal pregnancies. However, we did not find significant differences between preeclamptic and normal placenta in terms of CB2 and FAAH expressions and immunoreactivity. Serum levels of anandamide were significantly lower in preeclamptic patients than in healthy pregnant women. Preeclamptic patients had significantly higher sFlt-1 levels and significantly lower PlGF concentrations as compared to healthy pregnant women. Serum anandamide concentrations did not correlate with serum levels of sFlt-1 and PlGF in our healthy pregnant and preeclamptic groups.
Conclusion: We observed markedly higher expression of CB1 protein in preeclamptic placental tissue. Increased CB1 expression might cause abnormal decidualization and impair trophoblast invasion, thus being involved in the pathogenesis of preeclampsia. Nevertheless, we did not find significant differences between preeclamptic and normal placental tissue regarding CB2 and FAAH expressions. Furthermore, serum anandamide concentrations were decreased in women with preeclampsia. While the detailed pathogenesis of preeclampsia is still unclear, the endocannabinoid system could play a role in the development of the disease.

O12

Analysis of the molecular and cellular mechanisms regulated by magnesium sulphate in an in vitro model of the human placenta

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Introduction: Pre-eclampsia is a multi-systemic pregnancy disorder and characterised as a hypertensive condition which consists of symptoms such as high blood pressure and proteinuria in women in their second trimester (around 20weeks gestation). It globally affects 2-8% of all pregnancies and remains the leading pregnancy disorder. Magnesium sulphate (MgSO4) is commonly administered for the prevention and treatment of life-threatening seizures in women with preeclampsia and fetal neuroprotection before anticipated preterm birth. Despite this the mechanisms of action of MgSO4 are poorly understood, partly due to a lack of good cellular models. We have developed an in vitro placental model to investigate the effects of MgSO4 on (1) cytotrophoblast differentiation (syncytialisation) and (2) on preventing placental inflammation.
Objectives: To investigate the effects of MgSO4 on (1) cytotrophoblast differentiation (syncytialisation) and (2) on preventing placental inflammation.
Methods: Cytotrophoblast viability was examined at 24hrs and 48hrs post treatment with Lipopolysaccharide (LPS) (10-1000ng/ml) and MgSO4 (100nM-1mM) by MTT assay. Pyknotic nuclei morphology was identified by immunofluorescence. Syncytial formation was assessed by β-HCG production via ELISA methodology and assessed by desmoplakin architectural staining of cells treated with MgSO4 (1mM), LPS (200ng) and Forksolin (25μM) for 72hours. Quantitative real-time PCR was used to evaluated ACVR2A mRNA and TNF-α mRNA expression.
Results: MgSO4 has a dose dependent effect on cytotrophoblast viability. BeWo cells treated with 200ng/ml LPS had a statistically significant effect on cell viability (30% viable cells) after 48hrs. 1mM MgSO4 pre-treatment of cells resulted in an increase in viability to 57% compared to controls. Similarly, 1mM MgSO4 pre-treatment reduced development of pyknotic nuclei compared to controls. MgSO4 reduced the mRNA expression of ACVR2A and TNF-α. Finally MgSO4 may have the potential to alter cytotrophoblast differentiation.
Conclusion: MgSO4 provides protection against LPS-induced inflammation by modulating syncytialisation and reducing pro-inflammatory cytokine expression in vitro.

O13

Catechol-O-methyltransferase deficiency leads to hypersensitivity on the pressor response against angiotensin II

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Introduction: Women with preeclampsia (PE) exhibit hypersensitivity on the pressor response against angiotensin II (AngII). Catechol-O-methyltransferase (COMT) metabolizes 2-hydroxyestradiol (2-OHE2) into 2-methoxyestradiol (2-ME) and COMT deficiency has shown to be associated with PE. Objectives: We have hypothesized that COMT deficiency is reasonable to explain the molecular mechanisms of the hypersensitivity on the pressor response against AngII.

Methods: We utilized C57BL/6 male mice for all experiments. Mice were subjected to COMT inhibitor (COMTi: 25 mg/kg/day) or olive oil (Control) for 4 weeks, with or without low-dose AngII infusion (ANGII: 70ng/kg/min) for last 3 weeks. The AngII-infused mice were treated with 2-ME (10 ng/day), 2-OHE2 (10 ng/day), or vehicle for last 1 week. At the end of the protocol, we obtained following 6 experimental groups; Control, ANGII, COMTi, COMTi+ANGII, COMTi+ANGII+2-ME, and COMTi+ANGII+2-OHE2. Also we performed similar experiments utilizing in vivo administration of siRNA of COMT (20 nmol/week) instead of COMTi.
Results: NeitherANGII nor COMTi exhibited significant alteration in blood pressure through the experimental protocol compared with Control. When compared to ANGII or COMTi, COMTi+ANGIIdisplayed significantly higher blood pressure; COMTi+ANGII+2-ME decreased in blood pressure significantly when compared to COMTi+ANGII. 2-OHE2 treatments did not suppress the blood pressure of COMTi+ANGII. When COMT protein was analyzed in several organs of siRNA-administered mice (COMTsi); COMT protein level was significantly suppressed in liver when compared to control siRNA treated mice (Csi): either heart, kidney, or aorta was not affected. There was no difference in blood pressure between COMTsi and Csi; AngII infusion increased blood pressure in COMTsi but not in Csi: 2-ME administration significantly suppressed blood pressure of COMTsi+ANGII. The levels of soluble fms-related tyrosine kinase 1and placental growth factorwere not significantly associated with blood pressure of any groups of mice; plasminogen activator inhibitor(PAI)-1 level was significantly higher in both AngII-infused COMT deficient mice (COMTi+ANGII and COMTsi+ANGII) compared to control mice of each experiment. Such PAI-1 induction was suppressed by 2-ME.
Conclusion: Deficiency in COMT and 2-ME are associated with the hypersensitivity on the pressorresponse against AngII infusion. Similar mechanisms could be relevant to pregnant status and PE.

O14

Is preeclampsia a variant of Liddles syndrome with enhanced activity of the epithelial sodium channel in the kidneys?

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Introduction: Preeclampsia is characterized by hypertension accompanied by proteinuria. The plasma protease plasmin is aberrantly filtered to pre-urine in preeclampsia and may activate the epithelial sodium channel ENaC in the renal collecting ducts. This mechanism could contribute to impaired sodium excretion, suppression of renin-angiotensin-aldosterone and hypertension which are features of preeclampsia.
Objectives: It was hypothesized that established hypertension of pregnancy/preeclampsia share features with Liddles syndrome and display hyper-active ENaC and therefore blood pressure is more sensitive to NaCl intake compared to normal pregnancy whereas the renin-angiotensin-aldosterone system is suppressed and less sensitive. Experiments were designed to test the effect of controlled high and low dietary salt intake in patients with preeclampsia, healthy pregnant controls and non-pregnant controls. 24h urine Na excretion, blood pressure, cardiac output - and extracellular volume (ECV) and plasma renin and aldosterone were measured.
Secondary outcomes were pulsatile index (PI) in the umbilical artery and in the uterine artery.
Methods: The study (clintrialsgov NCT01828138) which is ongoing, is a randomized, cross-over, double-blinded, dietary intervention study (Ethic committee approval: 1-10-72-600-12). 7

patients with PE, 15 healthy pregnant women and 11 non pregnant women were included. The intervention was a fixed low-sodium diet (50-60mmol/24h) with addition of either placebo or salt tablets (200mmol) for 4+4 days.24h urine was collected for dietary compliance. After baseline measurements, outcome was measured after each of the two interventions.

Results: A significantly elevated systolic blood pressure (4 mmHg) was found in the healthy pregnant group (P= 0,008) on a high salt diet.

Plasma renin decreased significantly on a high salt diet in the healthy pregnant groups (P=0,02) and in non-pregnant group (P<0,0000) but not in the pre-eclamptic group (P=0,4). Comparing the delta values between groups, there was no difference.

Plasma aldosterone decreased significantly on a high salt diet in all groups. Delta aldosterone was not different betweengroups.

There was no statistically significant difference in cardiac output found in any of the groups.

ECV increased significantly on a high salt diet in all groups.

Umbilical artery PI was unaltered due to the intervention in both pregnant groups. PI in the uterine artery was significantly decreased in the group of preeclamptic women on a low salt diet (P=0,02) contrary to the healthy pregnant group (P=0,9).

Conclusion: There was a reduced reactivity of plasma renin concentration to altered salt intake in the pre-eclamptic group. Low salt intake was well-tolerated. PE/hypertension in pregnancy with proteinuria display features compatible with impaired sodium excretion that could involve ENaC activity.

O15

Adipose tissue and adipocytokine in preeclampsia: New insights into danger signals and inflammation

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Recently, the pathophysiological mechanism of preeclampsia has been gradually revealed. The latest key thesis being the so-called 2-step theory, which suggests that the cause of preeclampsia may occur in the early stage of pregnancy and that the pathological change is manifested later after the increase in physiological load of pregnancy. Our study aimed to investigate the inflammation and insulin resistance in the course of pregnancy mainly by adipose tissue metabolism and the so-called danger-signal molecules (Damage-associated molecular pattern molecules: DAMPs), which may be a key of the second steps of the theory.

Cytokines derived from adipose tissue (adipocytokines) were peripherally altered in the patients with a normal pregnancy course and in those with preclampsia. In the normal pregnancy group, the decreased adiponectin levels (increases insulin resistance and decreases anti-TNF action) and increased free fatty acid levels (induces inflammation within adipose tissue via Toll-like receptor) suggest an increase of inflammatory action ("homeostatic inflammation"). However, the chemokine MCP-1 level was decreased in the normal pregnancy group but increased in preeclampsia, indicating that it may contribute to the pathological inflammation in the disease. The high-molecular weight adiponectin level was increased in lean patients with severe preeclampsia, mainly in early-onset, which was experimentally demonstrated as the result of brain natriuretic peptide stimulation by cell line culture of adipocytes.

Inflammatory change and increased oxidative stress was demonstrated to genetically occur in adipose tissues, with increasing apoptosis using our novel culture method with or without serum samples from the patients of severe preeclampsia. However, increases of some genes in the regulation of Th2 predominance and anti-oxidative stress were also shown, suggesting the protective action of the adipose tissue in the patients of preeclampsia.
The peripheral level of HMGB1, a receptor for advanced glycation end-product (RAGE)-ligand that is regarded as a DAMP and a major surface marker of trophoblastic microparticles, was increased in patients with early-onset preeclampsia. This increase in HMGB1 level may support the 2-step theory, as it is the first finding that may connect the first and second steps of the underlying mechanism of preeclampsia. Therefore, our established thesis of the pathological mechanism of preeclampsia may explain the cause and onset of the disease in relation to placentation and immune response of adipose tissue, which may be associated not only to preeclampsia but to other fetomaternal complications and later hypertensive disorder or metabolic syndromes that may occur throughout a woman's lifetime.

O16

Marinobufagenin as a promising preeclampsia risk assessment marker: Purification from toad venom and LC-MS identification in human plasma

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Introduction: Marinobufagenin (MBG) is an endogenous bufadienolide cardiac inotrope which is demonstrating growing interest in the early diagnosis of volume expansion-mediated hypertensive states such as preeclampsia (PE) and end-stage renal disease hypertension.
Mammalian MBG is an inhibitor of the α1 isoform of Na+,K+-ATPase with vasoconstrictive and cardiotonic properties,resulting in hypertension and natriuresis. Elevated endogenous MBG levels have been described in pregnant mammals and especially in preeclamptic patients[1-3]. The rise of endogenous MBG appears prior the development of the main symptoms of PE, leading us to consider MBG as one of the potential target in the biomarker panel for PE.
A sensitive and accurate analytical method is needed to assess MBG in as lower level as possible in plasma. Currently, only marinobufagenin-like material has been found in humans using two published quantification methods based each on immunoassays[4,5]. These techniques suffer from a lack of specificity due to cross-reactivity and tend to exhibit high variability at low concentrations[6].
Objective: Our aim is to develop a MBG assay using a more specific and easy to access technique, such as LC-MS/MS. An algorithm dealing with the MBG plasma levels might be established by clinicians in the future, in order to predict, in combination with other clinical and biological markers, the risk for preeclampsia in pregnant women.
Methods: As the major source for MBG is located in the parotid glands of the Bufo Marinus toad, we developed a purification method from toad venom in order to get pure MBG standard.
A pre-extraction procedure was elaborated to concentrate and clean the plasma sample prior to its analysis.
A LC-MS based assay designed to determine MBG in human plasma is being optimized, giving us the opportunity to investigate MBG in non-pregnant healthy volunteers plasma as well as in early pregnant women plasma.

Results and discussion: Pure MBG has been successfully extracted from the Bufo Marinus toad venom and the identity of the compound has been confirmed.
An extraction procedure for MBG from plasma has been set up by use of solid phase extraction cartridges.
Preliminary results allowed us to authenticate the presence of MBG by LC-MS/MS in non-pregnant women as well as in early pregnancy.
Futher optimization and validation of the LC-MS assay are needed to quantify MBG plasma levels. However, these pioneering observations, are giving the clinicians a promising perspective for early preeclampsia risk assessment in pregnant women.

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O18

Oxidative stress in preeclampsia

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Introduction: Preeclampsia (PE) is characterized by hypertension and proteinuria that affects 5-10% of pregnancies. Risk factors of PE cause the release of reactive oxygen species, which lead to increased vascular cell proliferation and hypertrophy, apoptosis, inflammation and extracellular matrix remodeling.
Objectives: Our purpose was the complex monitoring of in vivo oxidative stress in preeclamptic patients in order to find possible biomarkers that might be used in the prognosis or in the early diagnosis of PE.
Methods: We examined the effects of oxidative stress on the level of proteins by measuring thiol content on the surface of peripheral blood mononuclear cells (PBMC) and circulating extracellular vesicles by DyLightMaleimide staining and also in the plasma by DTNB assay. The oxidative damage of DNA was measured by flow cytometric detection of oxoguanin-8. Multicolor FACS was used for the investigation of the regulatory molecules of the redox homeostasis including the expression levels of sirtuin 3, 4, 5, and both the cell surface and intracellular expression of thioredoxin1 (TRX1) and peroxiredoxin1 (PRDX1) in PBMC. Plasma soluble PRDX1 level was also detected by ELISA.
Results: The total exofacial thiol content of PBMC was significantly higher in preeclamptic women, implying increased activation of these immune cells, and the total thiol content of plasma proteins was also elevated. In contrast, we could not detect any differences in the oxoguanine 8 expression of PBMCs, a marker of oxidative DNA damage. Significantly higher expression levels of extracellular PRDX1 and lower content of intracellular PRDX1 were detected in preeclamptic patients. The

intracellular PRDX1 content of lymphocytes and monocytes showed positive correlations with the plasma soluble PRDX1 level in PE. Both the cell surface expression and the intracellular content of TRX1 were significantly higher both in lymphocytes and monocytes in the preeclamptic group. The levels of intracellular Trx1 and Prdx1 are known to increase under inflammatory conditions. They act as direct ROS scavengers, as molecular chaperones and as regulators of different signaling pathways. Both extracellular Trx1 and Prdx1 are known to have pro-inflammatory effects.
Conclusion: Our results suggest that preeclampsia might be characterized by different markers of oxidative stress. Changes of the cell surface or intracellular expressions of regulatory molecules, including PRDX1 and TRX1 may be also associated with cell activation and inflammatory conditions.

O19

Decreased plasma hemopexin activity in preeclampsia is associated with decreased plasma AT-1 receptor leves and increased placental and monocyte AT-1 receptor expression

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Introduction: Hemopexin (Hx), apart from being a free heme scavenger, also has protease activity. While during healthy pregnancy, Hx activity was increased as compared with non-pregnant individuals, in preeclampsia, Hx activity was decreased as compared with healthy pregnant women. Since we have previously shown that active Hx was able to shed the angiotensin II type 1 receptor (AT-1R) from various cell types in vitro, we now hypothesized that the increased Hx activity in pregnancy leads to increased shedding of the AT-1R from the vascular wall and subsequently decreased angiotensin II sensitivity. In preeclampsia the decreased Hx activity may lead to decreased shedding of the AT-1R and therefore increased angiotensin II activity.
Objective: We aimed to evaluate whether decreased Hx activity in preeclampsia was associated with increased AT-1R expression (on placental tissue and monocytes) and reduced presence of the AT-1R in the circulation.
Methods: We obtained peripheral blood samples from non pregnant (n=21), healthy pregnant (n=25) and (early onset) preeclamptic (n=26) women. We measured plasma Hx activity (colorimetric assay) and plasma AT-1R levels (Western blotting) and monocyte AT-1R expression (flow cytometry). From another group of healthy pregnant (n=15) and (early onset) preeclamptic women (n=24), we collected placental biopsies, in which we measured placental AT-1R expression using immunohistochemistry and qPCR.
Results: The increase in plasma Hx activity in healthy pregnant women vs non-pregnant women ($p<0.05$) was associated with decreased monocyte AT-1R expression ($p<0.01$) and increased plasma AT-1R levels ($p<0.01$) in healthy pregnant women vs non pregnant women. In women with preeclampsia as compared with healthy pregnant women, the decreased plasma Hx activity ($p<0.05$) was associated with increased monocyte AT-1R expression ($p<0.01$) and increased plasma AT-1R levels ($p<0.05$). In addition, placental AT-1R protein expression (immunohistochemistry) and placental AT-1R mRNA were also increased ($p<0.01$) in preeclamptic women vs healthy pregnant women.
Conclusions: Our data suggest that also in vivo active Hx sheds the AT-1R from tissues, such as monocytes and placenta. Therefore active Hx may play a role in the development of the decreased responsiveness to angiotensin II in healthy pregnancy, while the decreased Hx activity in preeclampsia may contribute to increased angiotensin II sensitivity in this disease.

O20

NT-pro-BNP levels as a marker of high clinical risk in pregnancy

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Introduction: NT-pro-BNP proved to be a useful prognostic marker of unfavorable outcome in cardiac failure. There were few data about its clinical significance in pregnant women (PW) and maternal health prognosis, correlated to adverse events during pregnancy.

Objectives: Evaluate the correlation between NT-pro-BNP levels and primary end-points: death, HELLP, preeclampsia and cardiac failure in PW.

Methods: We analyzed prospectively 218 asymptomatic PW who consulted Private Hospital between 2009 -2015. Patients with diabetes, renal chronic failure and cardiac disease were excluded. We performed: clinical and cardiological evaluation, blood and urine determinations included NT-pro-BNP. PW were followed-up during pregnancy and post-delivery. Association between: death, HELLP, preeclampsia and cardiac failure, as combined end-points were evaluated during follow-up and confronted by statistical analysis with NT-pro-BNP levels during follow-up. The best cutoff point value for NT-pro-BNP was 125pg/ml. Statistical analyses was performed: chi-square test for parametrical nominal data, Fisher's exact test with Yates correction.

Results: PW average age was 33.7 years, 106 PW had Hypertensive Gestational Syndromes (HGS), in this group: gestational age at delivery 35.2 weeks, birth average weight 2469.6 gr, first pregnancy 50%, fetal growth restriction 18.5%, oligoamnios 21.2%, stillbirth 5.3%, maternal cardiac failure 6%, peripartum cardiopathy 1%. NT-pro-BNP average in HGS: 646.7pg/ml, non HGS: 60.3pg/ml. In this population: in 140 PW (69.4%) NT-pro-BNP was below 125pg/ml, and 78 PW (30.6%) above this value. In the group with NT-pro-BNP above 125pg/ml 71 PW (75.2%) showed combined end-point vs. 35 PW (24.7%) in the NT-pro-BNP normal value group, with a significant statistical association (p 0.001) by chi-square correlation 59.21 df, Cramer's V 0.6887, OR 0.82 (CI 0.56-0.92) showing a negative predictive value in the prospective follow-up. There was no correlation between NT-pro-BNP and fetal health.

Conclusion: NT-pro-BNP levels were strongly associated with adverse clinical events during pregnancy. Its early determination could be a successful tool in high risk pregnancy diagnosis, even for post-delivery events.

O21

First trimester serum placental growth factor and hyperglycosylated human chorionic gonadotropin are associated with later pre-eclampsia

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Introduction: First trimester serum placental growth factor (PlGF) predicts early-onset pre-eclampsia (diagnosis < 34+0 weeks of gestation) when combined with pregnancy-associated plasma protein-A (PAPP-A), uterine artery pulsatility index and maternal clinical risk factors. We recently showed that a lower percentage of serum hyperglycosylated human chorionic gonadotropin (hCG-h) of total hCG (%hCG-h) in the first trimester predicts early-onset pre-eclampsia.

Objectives: To study the accuracy of using combined maternal serum %hCG-h, PlGF, PAPP-A and maternal risk factors in prediction of pre-eclampsia.

Methods: We determined gestational-age-adjusted concentrations of PlGF, PAPP-A, hCG (Perkin Elmer Wallac Oy, Turku, Finland) and hCG-h (in-house immunofluorometric assay)in maternal serum at 8-13 weeks of gestation. The study consisted of 98 women who later developed pre-eclampsia and 177 pregnant controls. Of the cases, 24 developed preterm pre-eclampsia (diagnosis < 37+0 weeks of gestation) and 37 severe pre-eclampsia (blood pressure > 160/110 mmHg, proteinuria > 5g/24 hours and/or hemolysis, elevated liver enzymes and low platelet count –syndrome).

Results: Serum PlGF, %hCG-h and PAPP-A were lower in women with later preterm or severe pre-eclampsia than in controls. In receiver-operating characteristics (ROC) curve analysis the area under the curve (AUC) was 0.680 for PlGF, 0.699 for %hCG-h and 0.714 for PAPP-A to predict preterm pre-eclampsia. AUC values for prediction of severe pre-eclampsia were 0.677, 0.702 and 0.677, respectively. When PlGF, %hCG-h and PAPP-A were combined by logistic regression analysis the AUC value was 0.830 for preterm pre-eclampsia and 0.824 for severe pre-eclampsia. Combination of PlGF, %hCG-h, PAPP-A and maternal risk factors including nulliparity and first-trimester mean arterial pressure (MAP) gave an AUC value of 0.805 for preterm pre-eclampsia and 0.882 for severe pre-eclampsia. When PlGF was removed from the analysis the AUC value was 0.803 for preterm pre-eclampsia and 0.878 for severe pre-eclampsia. When %hCG-h was removed the AUC values were 0.756 and 0.840, respectively.

Conclusions: Combining %hCG-h with PlGF, PAPP-A and maternal risk factors in first trimester improves prediction of later preterm or severe pre-eclampsia. %hCG-h tended to give better AUC values than PlGF when combined with PAPP-A and maternal risk factors. Thus, in first trimester %hCG-h might be superior to PlGF for prediction of preterm or severe pre-eclampsia and it should be further investigated in risk models of pre-eclampsia.

Table 1. Area under the curve (AUC) values and 95% confidence intervals (CIs) for serum markers and their combinations with maternal clinical risk factors.

	Preterm pre-eclampsia (n=24)		Severe pre-eclampsia (n=37)	
	AUC	95% CI	AUC	95% CI
PlGF	0.680a	0.572 - 0.788	0.677a	0.591 - 0.794
%hCG-h	0.699a	0.577 - 0.821	0.702b	0.610 - 0.794
PAPP-A	0.714a	0.612 - 0.849	0.677a	0.581 - 0.774
PlGF, %hCG-h, PAPP-A	0.830b	0.747 - 0.913	0.824b	0.759 - 0.889
PAPP-A, PlGF, MAP, nulliparity	0.756b	0.651 - 0.861	0.840b	0.771 - 0.910
%hCG-h, PAPP-A, MAP, nulliparity	0.803b	0.696 - 0.910	0.878b	0.816 - 0.940
%hCG-h, PAPP-A, PlGF, MAP, nulliparity	0.805b	0.699 - 0.912	0.882b	0.821 - 0.942

aP<0.05 or bP<0.001 by ROC curve analysis as compared to controls.

O22

Correlation of sFlt-1/PlGF ratio with time to delivery or preterm birth in PROGNOSIS (Prediction of short-term outcome in pregnant women with suspected preeclampsia study)

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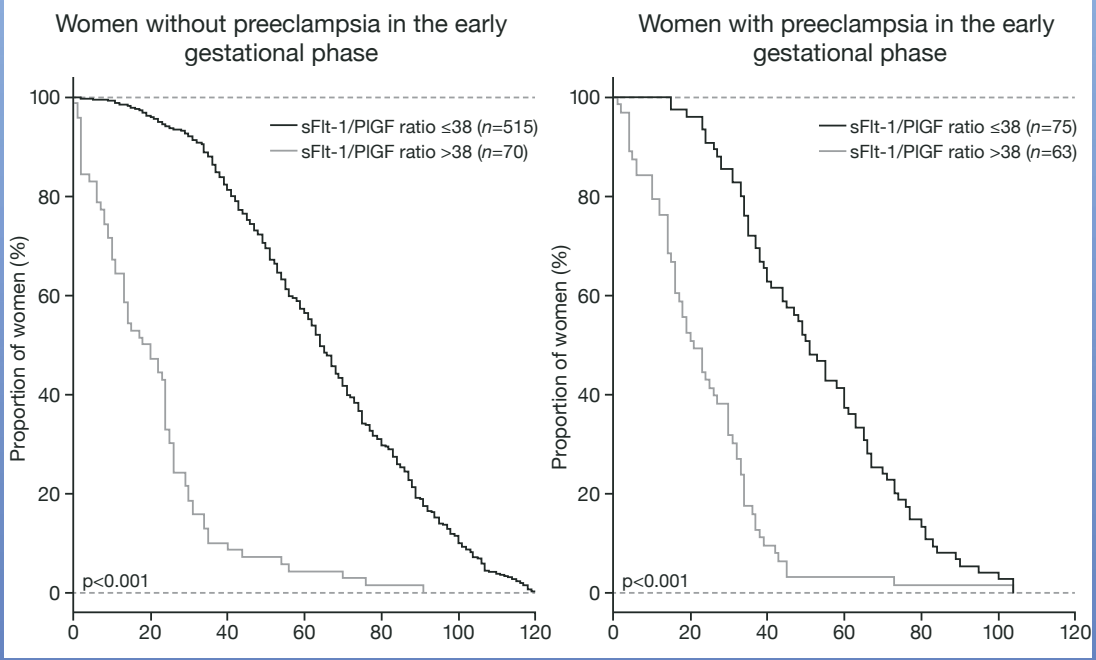
Introduction: PROGNOSIS reported a negative predictive value of 99.3% (95% CI 97.9–99.9) for ruling out preeclampsia/eclampsia/HELLP syndrome within 1 week using a soluble fms-like tyrosine kinase 1 (sFlt-1)/placental growth factor (PlGF) ratio cut-off of 38 in women with suspicion of the syndrome. The sFlt-1/PlGF ratio may also help identify women likely to deliver preterm.
Objectives: Correlation of the sFlt-1/PlGF ratio with (a) time to delivery and (b) preterm delivery (<37wks) were secondary objectives.

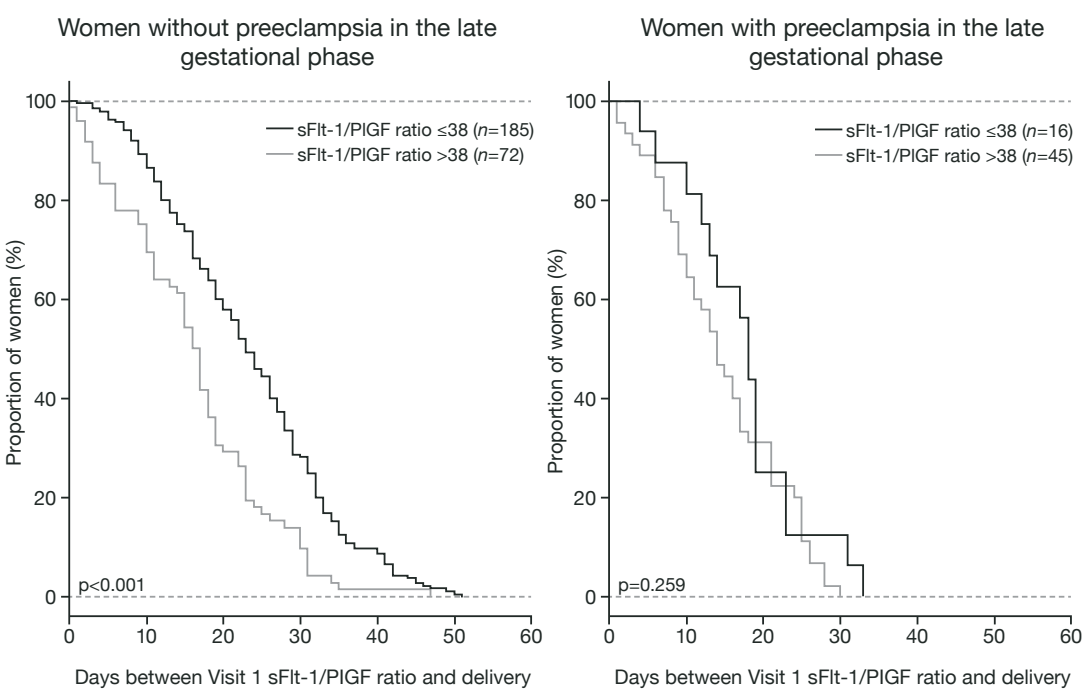
Methods: PROGNOSIS (prospective/non-interventional) enrolled pregnant women (≥18 years; gestational age 24wk+0d–36wk+6d at visit 1) with suspected preeclampsia (having clinical features of the syndrome). Maternal serum sFlt-1 and PlGF were measured (fully automated Elecsys® sFlt-1 and PlGF assays; cobas e electrochemiluminescence platform; Roche Diagnostics, Mannheim, Germany) and analyzed at the study end. Assessment points: Visit 1; Visit 2 (7+2d); Visits 3, 4, and 5 (each 7±2d after previous visit); delivery; postpartum. Early and late gestational phases were defined as 24wk+0d–33wk+6d and 34wks to delivery, respectively. Cox-regression analysis was adjusted for gestational age and preeclampsia status.

Results: sFlt-1/PlGF ratio >38 at Visit 1 was associated with shorter time to delivery, particularly in the early gestational phase (Figure). With a median 15 (SD 11) day difference the immediate risk for delivery was higher for women with sFlt-1/PlGF ratio >38 versus ≤38 (HR 2.9 [95% CI 2.5–3.5]), independent of preeclampsia status/gestational age. Women with sFlt-1/PlGF ratio ≤38 had longer pregnancy duration (no preeclampsia [n=720]: median 270 days, interquartile range [IQR] 262–279; preeclampsia [n=91]: median 262 days, IQR 248–269) than in women with a ratio >38 (no preeclampsia [n=159]: median 255 days, IQR 224–266; preeclampsia [n=108]: median 251 days, IQR 232–262). These trends were consistent when the sFlt-1/PlGF ratio at any pre-delivery visit was examined (not shown). Women without preeclampsia, who had iatrogenic preterm delivery had a higher Visit 1 median sFlt-1/PlGF ratio (35.3 [IQR 6.8–104], n=171), than women with non-iatrogenic preterm delivery (8.4 [IQR 3.4–30.6], n=25) or term delivery (4.3 [IQR 2.4–10.9], n=584). For women who developed preeclampsia and delivered preterm, the median sFlt-1/PlGF ratio at Visit 1 was 121 (IQR 66.2–231, n=53).

Conclusions: The maternal sFlt-1/PlGF ratio gives further information on preterm delivery risk. Women with high sFlt-1/PlGF ratios (>38) should be closely monitored, regardless of preeclampsia.

Figure: Time to delivery by sFlt-1/PlGF ratio at Visit 1





O23

STEPS (Study of Early Preeclampsia in Spain): sFlt-1/PlGF for the prediction of early-onset preeclampsia in singleton pregnancies

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Introduction: The soluble fms-like tyrosine kinase 1 (sFlt-1)/placental growth factor (PlGF) ratio is CE-mark approved for short-term prediction of preeclampsia in women with clinical suspicion of the syndrome (gestational age 24weeks+0d–36weeks+6d).

Objectives: We evaluated sFlt-1/PlGF as a predictive marker for early-onset preeclampsia in women at high risk of preeclampsia.

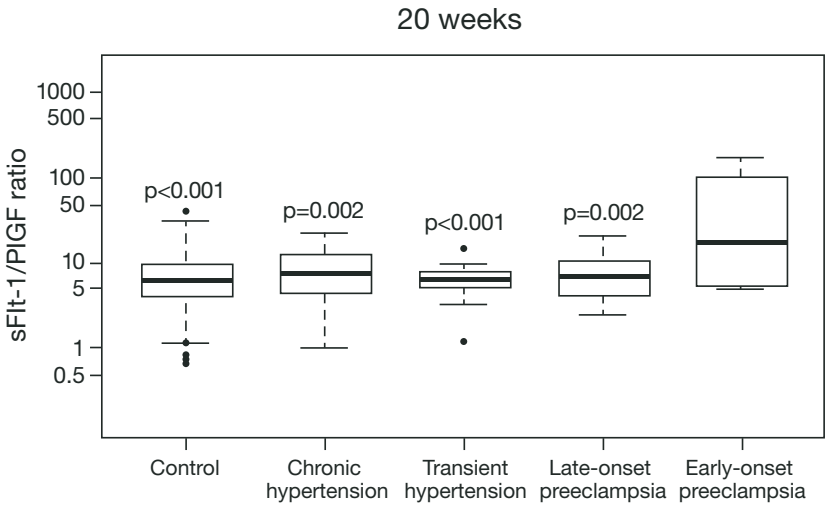
Methods: STEPS (prospective/multicenter) included pregnant women with preeclampsia risk factors (including history of IUGR/preeclampsia/eclampsia/HELLP syndrome, pre-gestational diabetes, antiphospholipid antibodies, and abnormal uterine artery Doppler). Primary objective: to show that sFlt-1/PlGF was predictive of early-onset preeclampsia (<34 weeks+0d) at 20/24/28 weeks' gestation. Secondary objectives included evaluation of sFlt-1/PlGF to: predict late-onset

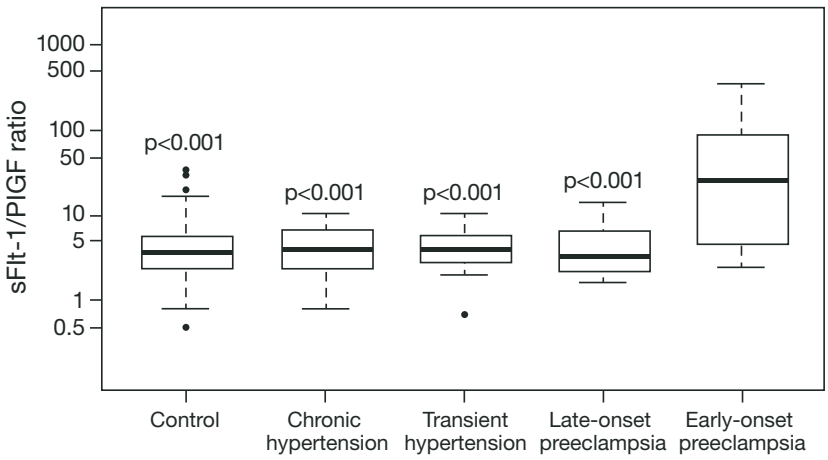
preeclampsia; and differentiate preeclampsia from hypertension. At gestational age 20, 24, and 28 weeks subjects had: serum sFlt-1/PlGF measurement (fully automated Elecsys® sFlt-1 and PlGF assays, cobas electrochemiluminescence platform, Roche Diagnostics, Germany); bilateral uterine artery Doppler; blood pressure/proteinuria/preeclampsia status assessment. Results were compared by ANOVA/Dunnet and Wilcoxon signed-rank test. For prediction of early-onset preeclampsia, the area under the curve (AUC) of receiver operating characteristic curves (ROC) was calculated. Singleton pregnancies are reported.

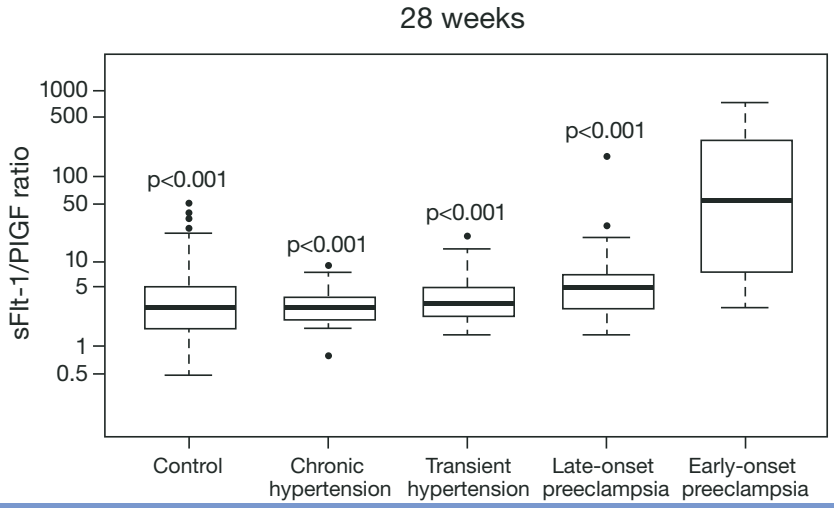
Results: 819 subjects were enrolled. Of 442 women with singleton pregnancies 42 (9.5%) developed preeclampsia (14 early-onset/28 late-onset). The mean (SD) sFlt-1/PlGF ratio at 20, 24, and 28 weeks was: 7.86 (8.61), 5.9 (12.38) and 4.59 (5.65) for subjects who did not develop preeclampsia (control); 53.15 (61.79), 69.25 (105.53) and 180.37 (241.83) for early-onset preeclampsia; and 7.81 (4.45), 5.09 (3.34) and 13.39 (34.52) for late-onset preeclampsia. Compared with early-onset preeclampsia the sFlt-1/PlGF ratio was significantly lower for control, chronic hypertension, transient hypertension, and late-onset preeclampsia (Figure). Prediction of early-onset preeclampsia (ROC AUC [95% CI]) was best for sFlt-1/PlGF plus clinical data (0.94 [0.90–0.98], 0.94 [0.89–1.0], 0.94 [0.86–1.0], at 20, 24 and 28 weeks) vs sFlt-1/PlGF alone (0.78 [0.62–0.95], 0.82 [0.65–0.98], 0.86 [0.72–1.0]) or Doppler alone (0.71 [0.56–0.86], 0.73 [0.54–0.91], 0.87 [0.74–1.0]).

Conclusion: The sFlt-1/PlGF ratio can improve prediction of early-onset preeclampsia for women at high risk of preeclampsia.

Figure: sFlt-1/PlGF ratio for control subjects, and those who developed chronic hypertension, transient hypertension, late-onset preeclampsia or early-onset preeclampsia (p values indicate the comparison with early-onset preeclampsia)




24 weeks
sFlt-1/PIGF ratio
1000
500
100
50
10
5
1
0.5
p<0.001
p<0.001
p<0.001
p<0.001
Control
Chronic hypertension
Transient hypertension
Late-onset preeclampsia
Early-onset preeclampsia


28 weeks
sFlt-1/PIGF ratio
1000
500
100
50
10
5
1
0.5
p<0.001
p<0.001
p<0.001
p<0.001
Control
Chronic hypertension
Transient hypertension
Late-onset preeclampsia
Early-onset preeclampsia

O24

Prediction of pre-eclampsia in obese nulliparous women

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Introduction: Obese women have an increased risk of pre-eclampsia and may have a distinct mechanism of disease due to factors associated with adiposity and insulin resistance.
Objective: To develop a prediction model for pre-eclampsia in obese women.
Methods: SCOPE was a prospective cohort study of 5690 primiparous women. We investigated whether in obese SCOPE participants (BMI>30kg/m2) clinical factors and biomarkers measured at 15 weeks gestation, and ultrasound parameters at 20 weeks gestation could predict pre-eclampsia (blood pressure ≥140/90 mmHg after 20 weeks' gestation with either proteinuria ≥ 300mg/24 hour urine or protein: creatinine ratio ≥30mg/mmol or urine dipstick protein ≥++ or any multisystem complication of pre-eclampsia). The variables of interest were selected based on a-priory hypothesis.Univariate logistic regression selected factors ($p<0.05$) for a multivariate model. In the multivariate model, stepwise selection was based on Bayesian information criterion (BIC) criteria. The performance of the test was assessed by receiver operating characteristic (ROC) curves and detection rate at a 10% or 25% false positive rate.
Results: 834 (14.7%) of the SCOPE participants comprised the study population for this analysis. Median BMI was 33.1kg/m2 (IQR 31.3-36.1kg/m2). Median gestation at delivery was 40 weeks (IQR 38-41 weeks) and median birth weight was 3520g (IQR 3150-3850g). 9.2% (77 cases) developed pre-eclampsia. Factors associated with pre-eclampsia in univariate analysis were family history of venous thromboembolism (VTE) or cerebrovascular accident (CVA) ($p<0.001$); family history of pre-eclampsia or gestational hypertension ($p=0.029$); hip circumference at 15 weeks ($p=0.020$); HDL cholesterol ($p=0.003$); adiponectin ($p=0.037$); natriuretic peptide A (ANP) propeptide ($p=0.046$); natriuretic peptide B (BNP) ($p=0.031$); placental growth factor (PLGF) ($p<0.001$) and abnormal uterine artery Doppler (UtA-RI) ($p=0.002$). In multivariate analysis family history of VTE or CVA (OR 2.7; 95%CI 1.5-4.7); HDL cholesterol <50mg/dl (OR 2.7; 95%CI 1.5-5.1) and PLGF (per log unit) (OR 0.6; 95%CI 0.4-0.7) were selected by stepwise procedure. The final model had an area under (AU) ROC of 0.68 (95%CI 0.62-0.75). Detection rates were 25.9% and 53.2% for a false positive rate of 10% and 25%, respectively.
Conclusion: The factors associated with later onset of pre-eclampsia in obese women are mainly cardiovascular but have only a moderate predictive performance.

O25

Evaluation of the value of the first and third trimester maternal mean platelet volume (MPV) for prediction of pre-eclampsia

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Introduction: Pre-eclampsia is one of the most serious complications of pregnancy and one of the major causes of maternal mortality. Thus its prediction is a matter for serious concern.
Objective: The purpose of the present study is to determine the value of mean platelet volume (MPV) measurement in the first and third trimester of pregnancy for the prediction of pre-eclampsia.
Method: A prospective nested case-control study was performed on pregnant women who were at 9-12 weeks of pregnancy. Inclusion criteria were: gestational age between 9-12 weeks (with a

reliable LMP and ultrasound confirmation), singleton, and maternal age between 15-45 years old. Exclusion criteria were, any known maternal systemic disorder (including chronic hypertension, diabetes mellitus, collagen vascular disorders, and ischemic heart disease and kidney disorders), using immunosuppressive drugs and anticoagulants, history of previous poor pregnancy outcomes like recurrent abortions, intrauterine fetal death (IUFD), pre-eclampsia, intrauterine growth restriction (IUGR) and smoking.In the first trimester and again in 26-28 weeks, MPV was calculated. All eligible women were then monitored to delivery and MPV of women who were pre-eclamptic was compared with the MPV of normotensive women.

Results: 35 pre-eclamptic women were compared with 269 normotensive women. MPV at the first trimester of pre-eclamptic women was significantly higher than normotensive women (10.2±1.06 fl VS 9.68±1.09 fl, P=0.008). Also, MPV at the third trimester of pregnancy of pre-eclamptic women was more than normotensives. (10.16±1.23 fl VS 9.62±1.12 fl, P= 0.009).

Area under the curve in Receiver Operating Characteristics (ROC) curve was calculated 0.64 for the predictive value of MPV at the first and third trimester of pregnancy, which showed a low value of this test for predicting of pre-eclampsia.

Conclusion: MPV at the first and third trimester of pregnancy are higher in women who eventually would be pre-eclamptic, but has low predictive value and is not a good predictor of pre-eclampsia.

O26 CANCELLED

Prediction of IUGR and preeclampsia – The role of Doppler in a selected high-risk population

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O27

Predicting preeclampsia in a second pregnancy

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Introduction: Preeclampsia is known to recur in a second pregnancy with earlier work from Aberdeen (1985) showing a rate in second pregnancies similar to that of first pregnancies in those who had preeclampsia in a first . Since then other factors relating to the first pregnancy such as pregnancy outcomes as well as maternal characteristics have been studied to determine what influence these might have on incidence in the second pregnancy.
Objectives: This study aimed to determine in a total population whether preeclampsia in a second pregnancy could be predicted from what was known about the first pregnancy and thus more intensive monitoring in a second could be considered.
Methods: Data was obtained from Information and Services Division of NHS Scotland (SMR02) for all first singleton pregnancies occurring in Scotland between 1981 and 2008 with a subsequent singleton live or stillbirth till 2010. (N=380684) Logistic reression was used to develop models for prediction of preeclampsia in a second pregnancy adjusting for confounding factors.
Results: Univariate analysis revealed that the type of first pregnancy, namely live birth, ectopic pregnancy, miscarriage, termination, stillbirth, other influenced the rate of preeclampsia in a second pregnancy, ranging from 2.2% in those with a previous live birth to 4.7% for those with a previous ectopic pregnancy.
The first model included age at first pregnancy, cigarette smoking both before and during first pregnancy, deprivation category, type of first pregnancy and interpregnancy interval. This showed that compared to those with a live birth the major influence was type of first pregnancy with ectopic pregnancy having an odds ratio for preeclampsia in the second of 4.29 (95%CI 1.55-11.87). All the remining types of pregnancy has ORs of between 2-2.7.
The second model examined those women who had live births in both pregnancies. The variables used were those listed above plus previous preeclampsia and gestation at delivery of the first birth. This showed that the main predictor of preeclampsia in the second delivery was preeclampsia in the first delivery, OR 7.59 (95%CI 6.81-8.45). preterm dilevery in the first also had an ibfluence OR 1.82 (95%CI 1.59-2.09).
Conclusion: The most important predictor of preeclampsia in the second pregnancy was previous preeclampsia.. Previous pregnancy loss and preterm delivery were also associated with an increased risk of preeclampsia in the second pregnancy.

O28

Effect of folic acid supplementation in pregnancy on preeclampsia – Folic Acid Clinical Trial (FACT)

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Introduction: FACT is an international, multi-centre, double-blind, placebo-controlled, Phase III trial of 3,656 women, sponsored by the Ottawa Hospital Research Institute (OHRI) and funded by the Canadian Institutes of Health Research (CIHR).
Observational studies suggest that folic acid supplementation during pregnancy reduces the risk of preeclampsia (PE). FACT is the first and only trial to date to examine the effect of folic acid supplementation for at-risk women in late pregnancy on the primary outcome of PE.
Objectives: FACT (trial registration: NCT 01355159) aims to determine efficacy of a PE prevention strategy using high dose (4mg per day) folic acid supplementation from early pregnancy until delivery in women at high risk of developing PE.
Methods: Subjects
Pregnant women between 80/7 - 166/7 weeks gestation, aged > 18 years, taking < 1.1mg of folic acid supplementation with at least 1 of the following risk factors for PE:

- Pre-existing hypertension
- Pre-pregnancy diabetes
- Twin pregnancy
- History of PE
- BMI > 35kg/m2

Primary Outcome
PE, defined as > d90 mmHg on 2 occasions > 4hrs apart and proteinuria developed in pregnancy > 200/7 weeks gestation.
Or
HELLP (Haemolysis, Elevated Liver Enzymes, Low Platelets)

- Haemolysis
- Serum LDH > 600U/L
- Serum AST > 70U/L
- Platelets <100x109/L

Or
Superimposed PE, defined as history of pre-existing hypertension with new proteinuria.
Proteinuria is defined as:

- Urinary protein >300mg/24hrs, or
- >2+ protein dipstick, or
- Random protein-creatinine ratio >30mg protein/mmol

Results: As of May 19th, 1,833 participants (1,058 Canadian, 220 Australian, 111 Argentinean, 49 Jamaican and 395 UK participants) have been randomized into the trial.
To date, 63 sites across 5 countries are recruiting in FACT, with a total monthly recruitment averaging 80 participants. In June 2015, 16 sites in the Netherlands and 12 additional sites in the UK will begin recruiting thereby increasing anticipated recruitment to an average of 100 participants per month for a projected completion in November 2016.

The Data and Safety Monitoring Board (DSMB) has recommended that FACT continue without modifications and interim analysis is anticipated in December 2015. To date, there are no reported Serious Adverse Events related to the use of study treatment and only 0.52% of the 786 participants who have completed the trial have incomplete outcome data.

Conclusions: Results will establish if high dose folic acid supplementation is an effective preventative strategy in women at high risk of developing PE.

O29

The impact of low dose aspirin after positive first trimester screening for pre-eclampsia

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Introduction: Pre-eclampsia is a major cause of maternal and perinatal morbidity and mortality. The prophylactic use of low dose aspirin (50-150 mg/day) is associated with a reduction in the incidence or severity of pre-eclampsia between 50-90% if the treatment begins before the 16th week of gestation. Promising multifactorial screening models in first trimester of pregnancy are in use to predict pre-eclampsia, especially early onset disease before the 34th week of gestation.

Objectives: Combining this issues we conducted an observational study and evaluated the outcome of women on low dose aspirin after a positive first trimester screening test for pre-eclampsia based on two different risk calculations models.

Methods: We have completed outcome data of 401 women with performed multifactorial screening test for pre-eclampsia at 12-14 weeks of gestation in a clinical setting, from June 2012 until September 2014 using two different risk-calculation software. In the first time period until October 2013 we used the Pre-eclampsia Predictor™ Software by PerkinElmer (group PE). Thereafter the prediction algorithm in Viewpoint® (group VP) was used to calculate the risk for pre-eclampsia. Women who were screened positive for the development of early and late onset of pre-eclampsia (early: < 34th week of gestation e.g. late >34th week of gestation) in the group PE and for early onset pre-eclampsia (< 34th week of gestation) in the group VP were prescribed low dose aspirin (75-100mg/day) starting before 16 gestational weeks and until 34 completed weeks of gestation. Descriptive and explorative statistical analyses were performed. A two-sided p-value of less than 0.05 was considered as significant.

Results: There were 214 women in the PE group and 187 in the VP group. In the PE group 17 (7.9%) women were screened positive for early onset pre-eclampsia and 46 (21.5%) for late onset pre-eclampsia. In the VP group 44 (23.5 %) were screened positive for early onset pre-eclampsia. Regarding screening positive for early onset pre-eclampsia groups differ significant ($p = 0.000$). Comparing prescription of low dose aspirin and outcome of pre-eclampsia (4 (1.8%) cases in the PE and 5 (2,7%) cases in the VP group) there were no significant differences between the two groups. There was no cases of early onset or severe form of pre-eclampsia in both groups.

Conclusion: The both used predication algorithms are not similar but were similarly applied so that the outcome of women were not different. Using a multifactorial first trimester screening test with subsequent administration of low dose aspirin in a screening-positive group of pregnant women is a promising strategy to reduce early onset and severe forms of pre-eclampsia, but cut offs of algorithms should be improved.

O30

Diet and preeclampsia: A prospective multicentre unmatched case control study in Ethiopia

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Background: Preeclampsia is one of the most commonly encountered hypertensive disorders of pregnancythat accounts for 20–80% of maternal mortality in developing countries, including Ethiopia. For many years diet have been suggested to play a role in preeclampsia. However, the hypotheses have been diverse and often revealed inconsistent results across studies, and this has not been studied in Ethiopia

Objectives: The objective of this study was to determine the effect of dietary habits on the incidence of preeclampsia Bahir Dar, Ethiopia

Methods: A prospective multicentre unmatched case- control study was conducted among 453 (151 cases and 302 controls) pregnant women attending antepartum or intrapartum care in public health facilities of Bahir Dar City Administration. Interviewer administered face to face interview, measurement of mid-arm circumference (MUAC) and document review were conducted using a standardized and pretested questionnaire. Data entry and cleaning was done by Epi.info version 3.5.3.The data were transported to SPSS version 20 for analysis. Both bivariate and multivariate logistic regression analyses were applied. Backward stepwise unconditional logistic regression analysis was employed to determine the putative association of predictive variables with the outcome variable and to control for the effect of confounding variables. A P-value < 0.05 was considered to declare statistically significant throughout the study.

Result: For every 1-cm increase of MUAC, there was an increase in the incidence rate of preeclampsia by a factor of 1.35 (AOR=1.35, 95%CI:1.21, 1.51).). A higher incidence of preeclampsia was found in women who reported to have consumed coffee daily during pregnancy (AOR = 1.78, 95%CI: 1.20, 3.05). Similarly for women who had anemia during the first trimester the incidence of preeclampsia 2.5 times higher than their counterparts(AOR=2.47, 95%CI: 1.12,7.61). This study also revealed consumption of fruit or vegetables at least three times a week during pregnancy to be protective against preeclampsia (AOR= 0.51, 95%CI: 0.29, 0.91; AOR=0.46, 95%CI: 0.24, 0.90, respectively). In addition compliance with IFA during pregnancy has shown a significant independent effect on the prevention of preeclampsia in this study (AOR=0.16, 95%CI: 0.08, 0.29)

Conclusion and recommendation: Adequate vegetable and fruit consumption and compliance to folate intake during pregnancy are independent protective factors of preeclampsia. On the other hand, higher mid upper arm circumference, anemia and daily coffee intake during pregnancy are risk factors for the development of preeclampsia. Audience specific education and promotion for the use of the protective factors identified in this study should be strengthened. The risk factors identified can be used for prediction and early diagnoses of preeclampsia allowing timely interventions to be performed to minimize deaths associated with severe preeclampsia/eclampsia.

O31

Magnesium homeostasis and gestational hypertension

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Introduction: Magnesium (Mg) is important for the normal functioning of muscles and blood vessels. A deficiency has been related to an increase in blood pressure and acute death in heart infarction and stroke..
Objectives: To review the literature regarding a relation between magnesium homeostasis and gestational hypertension (GH) during pregnancy.
Methods: A survey of published studies on the subject.
Results: Mg homeostasis is determined by intake through food and drinking water. A diet rich in proteins and poor in vegetables will increase the excretion of acids in the urine, resulting in a decrease of the normal reabsorption of Mg in the kidneys. Several population studies show that pregnant women often have a Mg intake below the recommended nutritional values.Pregnant women have also been found to have a higher expression of a gene regulating the uptake of Mg from the intestine, suggesting an increased demand for Mg during pregnancy. The incidence of pre-eclampsia (PE) is higher in developing countries, where the risk of nutritional insufficiencies including Mg is high.
On the cellular level, results from studies of erythrocyte membranes, brain cells and cerebrospinal fluid suggest that women with PE have lower Mg values than women with normal pregnancies. Several studies show that Mg deficiency during pregnancy is been linked to high blood pressure and PE..
Regarding intervention, Mg sulphate intravenously has long been used in the treatment of PE. Data from investigations in four different countries show that supplementation with Mg during pregnancy decreased the risk of GH. The expression of Mg responsive genes has been related to diastolic blood pressure and duration of delivery. Available data thus indicate that GH and PE are related to a lack of Mg.
Conclusion: From a public health point of view, further studies on Mg homeostasis in pregnancy and intervention in terms of supplementation have a high priority, with the ultimate aim to develop prevention programs.

O32

Pre-eclampsia and thrombophilia: Prevention issues

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The purpose: Evaluation of effectiveness of prophylaxis treatment to prevent reccurent PE in patients with thrombophilia.
Materials and methods: 158 patients with thrombophilia (genetic, acquired or combined) and severe PE in their medical history: 88 patients with PE in anamnesis who were under the supervision from a fertile cycle (I subgroup), and 70 patients with PE in anamnesis who addressed us when already pregnant (week 6 till week 13 of gestation) – II subgroup.
Control group – 105 women with noncomplicated pregnancy (noncomplicated obstetrics, thrombotic and family anamnesis).
Lab methods: DIC-syndrome markers: D-dimer, TAT, prothrombin time, prothrombin fragments F1+2, level of fibrinogen, AT III. Detection of aggregation of platelets. Detection of homocystein level. Detection global function of protein C. Detection of antiphospholipid antibodies circulation. Gene tests: FV Leiden, prothrombin G20210A, PAI-1 G4/G5 polymorphism, t-PA «I/D» polymorphism, gene MTHFR C677T, platelets glycoproteins polymorphism: GP IIb/IIIa, GP Ia/IIa, GPIba, GP ADP.

Results: The outcome of pregnancy in this group of the patients were the following: fetal growth retardation syndrome was noted in 18 patients out of the group, in 6 patients from the subgroup I and in 12 patients from subgroup II. The premature delivery was not observed in any patients in subgroup I, in subgroup II it was observed in 5 and no patients in control group had premature delivery. We were able to prevent severe PE, but moderate PE was in 5 patients from II subgroup.
Preventive therapy of the patients include: LMWH (Enoxaparin 20-60 mg), micronized progesterone, antioxidants (Vitrum® Cardio Omega 3), vitamin B (Multi-
tabs B-complex), folic acid (folacin) since fertile cycle, aspirin (except the I trimester of pregnancy and lactation).
All the patients delivered via cesarean section. In the control group only 24 (22,8%) patients delivered via cesarean section, mostly elective one: due to high degree of myopia, scar on the uterus after the cesarean section surgery, pelvic presentation of fetus. 158 live children were born, with mean weight 3,250±250 g, height 51±2 cm, Apgar score 71%- 8-9 points and 29%- 7-8 points. Early neonatal period was unremarkable.
Conclusions: The most effective prophylaxis of recurrent severe PE- preventive therapy since fertile cycle, which must include LMWH, micronized progesterone, folic acid, group B vitamins and antioxidants.

STA54

Preeclampsia – Myths are still stronger than scientific data

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Introduction: During pregnancy close interactions between the maternal and fetal system exist with the placenta as the organ situated between the two individuals. In cases where this crosstalk is disturbed, preeclampsia may develop. During the last decades a number of hypotheses have been developed to describe the etiology of this syndrome. However, so far all of them have failed.
Objectives: One of the current hypotheses – although wrong as well - is still strongly supported by the scientific community although it has become clear in recent years that a variety of arguments that are needed to support this hypothesis are not valid at all.
Methods: This list comprises the following arguments, known to be wrong today:
1. Failure in trophoblast invasion is a prerequisite for preeclampsia.
2. Placental hypoxia is present in cases suffering from preeclampsia.
3. During preeclampsia, the placenta is the main source for angiogenic factors in maternal blood.

Additionally, another important issue needs attention:
(4) The quality of a biomarker only depends on its concentration in maternal blood.
Results: These four arguments and issues will be discussed. It will become clear that
(1) changes in trophoblast invasion are not related to preeclampsia;
(2) placental hypoxia is not existing at all in cases with preeclampsia;
(3) the maternal vascular system is the main source for angiogenic factors; and
(4) pre-analytics are increasingly important to maintain the quality of samples to test for biomarkers.
Conclusion: Due to the availability of new data it is more than needed to update the hypotheses on the etiology of preeclampsia. It is quite detrimental to keep with old but no longer valid hypotheses and hindering the rise of newer and better hypotheses. Therefore, the above mentioned arguments including trophoblast invasion, placental hypoxia and the source of angiogenic factors need to be taken into account when further discussing the etiology of preeclampsia.

STA55

Pathophysiology of preeclampsia from the view point of immunology

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Introduction: The pathogenesis of preeclampsia remains largely unknown. However, many researches support the immune maladaptation hypothesis. Epidemiological findings show that first pregnancy, the use of barrier contraceptive method or short cohabitation, oocyte donation cases and obesity are the risks for preeclampsia. These factors seem to be independent.

Objective: We tried to explain the relationship between the epidemiological risks for preeclampsia and immune maladaptation.

Method: We have studied the immune system in preeclamptic cases and oocyte donation cases using flow cytometry and immunohistochemical examination.

Results: Human pregnancy represents a semiallograft to the maternal host, therefore tolerance system is required. In oocyte donation cases, all the MHC of the fetus are allograft to maternal host, therefore more strict tolerance system is needed. Nevertheless, our study showed the number of regulatory T (Treg) cells which induce tolerance were scare at fetomaternal interface. Moreover, macrophage, T cell and NK cells that play important roles for vascular remodeling were also scare in placental bed biopsy samples.Importantly, vascular remodeling was inadequate in oocyte donation cases regardless of the presence or absence of preeclampsia. These findings suggest that macrophage, T cell and NK cells play an important role for vascular remodeling of spiral artery and poor placentation is present in oocyte donation pregnancy.We also showed that effector Treg cells decreased and exhausted Treg cells increased in peripheral blood of preeclampsia. Expression of Bcl-2 in Treg cells was decreased and expression of Bax in Treg cells was increased suggesting that Treg cells in preeclampsia are more likely to die by apoptosis.

In our mice model, seminal plasma plays an important role for induction of paternal antigen specific Treg in the uterus. This finding explains barrier contraceptive method or short cohabitation are the risk of preeclampsia.

We also showed the positive relationship between BMI and the frequencies of cytotoxic T cells and cytotoxic NK cells.

Conclusion: These findings support that immune maladaptation is one of the mechanisms of preeclampsia.

PL56

Long-term consequences of preeclampsia

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Introduction: There is a clearly documented increased risk of long-term maternal cardiovascular disease after pregnancy complications such as preeclampsia, premature birth and fetal growth restriction. The risk is highest in pregnancies with both maternal and fetal manifestations of abnormal placentation. We lack today however the mechanistic understanding of the association. We also lack the evidence-based recommendations on how and how frequent to follow up these women at risk, both pre- and postmenopausally.

Objective and Methods: The talk will briefly review the epidemiological associations, with emphasis on cardiovascular disease (CVD) after preeclampsia. In addition, the talk will review common risk factors for preeclampsia and CVD, as women developing preeclampsiamay have

risk factors in common with older persons developing CVD. Additionally, the talk will suggest how preeclampsia and other placentally-mediated disorders may themselves contribute to an augmented cardiovascular burden that may directly or indirectly affect long-term vascular health.
Results: Further understanding of the process underlying maternal and placental mediators of preeclampsia may help cast light on development of cardiovascular disease later in life. Further research is needed to ascertain whether specifically targeted group of women with such pregnancy complications benefit from prevention strategies, such as with oral statins or aspirin, similarly to other population groups at risk, and therebyimprove long-term maternal health.
Conclusion: This talk will suggest how longitudinal pregnancy cohorts and biobanks across the world may improve the understanding of CVD in parous women. Options for such studies from pregnancy biobanks within the Global CoLaboratory research network are presented.

PL138

Should we be using predictive tests for pre-eclampsia in routine clinical practice?

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Pre-eclampsia is responsible for considerable maternal and neonatal morbidity and mortality, particularly in low to middle income countries. Despite an evolving understanding of the pathophysiology of the disorder, there are currently few preventative strategies and no cure other than delivery of the placenta. Nevertheless, there is considerable interest in the development of a clinically useful screening test as this would aid in risk stratification, personalised antenatal care, targeting of limited resources to those at greatest risk, and facilitating research by the identification and subsequent focus on those most likely to develop the disorder. Over 200 hundred screening tests have been proposed including blood borne biomarkers, ultrasound based tests and combinations of both. Several tests are now commercially available and they report greatest clinical utility for the detection of early onset pre-eclampsia.
However, none have yet been shown to be of benefit in rigorous randomised controlled trials. As the only cure for pre-eclampsia is delivery, a perception of increased risk on the basis of a screening test alone is associated with the real risk of increased iatrogenic prematurity. Moreover, globally, the vast majority of maternal and neonatal deaths from pre-eclampsia are associated with disease that develops at or close to term. The narrow focus on screening for early onset disease will have little impact on global morbidity and mortality. Therefore, the clinical deployment of any screening test for pre-eclampsia should be suspended until there is evidence of benefit without harm. The research community should redouble collaborative efforts to validate proposed and new screening tests in sufficiently powered cohorts, which include women in low to middle income settings, with a focus on term as well as pre-term disease.

PL57

Angiogenic factors: From scientific data to clinical implementation

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The pathogenesis of preeclampsia is still not completely known; however, in the recent decade, there have been tremendous research efforts leading to impressive results highlighting the role of a disturbed angiogenic balance as one of the key features of the disease. Soluble fms-like tyrosine kinase 1 (sFlt-1), induces a preeclampsia-like phenotype in experimental models and circulates at elevated levels in human preeclampsia. The elevation of sFlt-1 in maternal circulation is detectable weeks prior to the onset of clinical symptoms. In parallel, serum levels of placental growth factor (PlGF) are decreased. The increased ratio of both biomarkers (sFlt-1/PlGF) in women with preeclampsia reflect the altered (anti)angiogenic state. Although preeclampsia seems to be a clearly defined disease, clinical presentation, and particularly the dynamics of the clinical course can vary enormously. The only available tools to diagnose preeclampsia are blood pressure measurement and urine protein sampling. However, these tools have a low sensitivity and specificity regarding the prediction of the course of the disease or maternal and perinatal outcome. The sFlt-1/PlGF ratio can now by determined by a rapid, automated immunoassay and can differentiate between preeclampsia and other hypertensive pregnancy disorders. Particularly, the reliable ruling out of preeclampsia is clinically useful and can lead to a step down management in women with signs and symptoms of preeclampsia. The ratio can indicate the severity and progression of the disease and gives hereby a short term prognosis that is useful for clinical management. Thus, the sFlt-1/PlGF ratio has developed from an aid in diagnosis to a robust biomarker for prediction and risk stratification. Moreover, strategies aiming at restoring the angiogenic balance are a promissing approach for possible future therapies of preeclampsia.

PL58

Low molecular weight heparin for prevention of severe preeclampsia and other placental mediated complications

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Placental mediated complications, including preeclampsia, placental abruption, fetal growth restriction (FGR) and late pregnancy loss, affect over 5% of pregnancies and can result in significant maternal and perinatal morbidity and mortality.
The risk of recurrence of early or severe preeclampsia is 40-60% and the risk of recurrence of other placental mediated complications such as FGR < 5 percentile, late pregnancy loss and severe placental abruption is 50-60%.
With the use of low does aspirin (LDA) there is has a modest effect in preventing preeclampsia, preterm birth, fetal or neonatal death and FGR.
Recently, several studies has been shown that low molecular weight heparin (LMWH) in women with previous placental mediated complications reduces significantly the occurrence of preeclamsia, severe preeclampsia, FGR placental abruption, late fetal loss and IUFD compared to no treatment or compared to LDA.
In women with severe preeclampsia or placental abruption the use of LMWH was associated with a reduction of 65% of preeclampsia and of 60% of composite adverse outcome.
In thrombophilic women with prior fetal death, treated with LMWH, there was less fetal death recurrences (10.3% vs. 23.2%, p=0.0007), higher live birth (70.3% Vs. 50.2%; p<0.0001), less

severe PE (2.25 vs. 8.3%, p=0.024), less early onset PE (0.7% vs. 6.1%, p=0.03, and less preterm births (12.5% vs. 25%, p=0.0106).
In women with adverse pregnancy outcome and significant placental lesions without thrombophilia treatment with LMWH was associated with only 9% complications in the following pregnancy compared to 60% in non treated women.
These findings of reduction in preeclampsia and other placental mediated complications are evident regardless of the thrombophilic state. When only randomized controled trials are considered, LMWH use was associated with reduction of 60-80% of severe preeclampsia or any preeclampsia, reduction of 50% of FGR < 5 percentile, reduction of 60 % of fetal loss > 20 weeks, and reduction of 60% in preterm delivery < 34 weeks.
Thus, the use of LHWH to prevent severe preeclampsia and other placental mediated complications seems as promising therapy providing that their effectiveness in women with placenta-mediated pregnancy will be confirmed in future studies.

PL59

The impact of classification of hypertensive disorders of pregnancy based on the ACOG 2013 and ISSHP 2014 criteria

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Introduction: A standardized classification of hypertensive disorders of pregnancy would be highly needed to achieve the comparability of the studies and the adequate management of the patients. In the last two years, the American College of Obstetricians and Gynecologists (ACOG), as well as the International Society for the Study of Hypertension in Pregnancy (ISSHP) revised the classification of hypertensive disorders in pregnancy.
Objectives: In Hungary,the ACOG 2002 criteria were used in the last decade to classify hypertensive disorders during pregnancy. This study aimed to determine the impact of the ACOG 2013 and ISSHP 2014 criteria on the occurrence of different forms of hypertensive disorders, as well as on perinatal outcome compared to the ACOG 2002 criteria.
Methods: All pregnant women with hypertensive disorders and singleton pregnancies who delivered in the 1st Dept. of Ob-Gyn. at the Semmelweis University between 1 Jan 2012 and 31 Dec 2014 (n=755) were enrolled in this study. We determined the prevalence of different forms of hypertensive disorders according to the ACOG 2002, ACOG 2013 and ISSHP 2014 criteria. We also examined the reasons for re-classification of chronic hypertensive (CHT) and gestational hypertensive (GHT) patients to the preeclampsia (PE) group, as well as its impact on the perinatal outcome.

Results:

	ACOG 2002	ACOG 2013 n=755	ISSHP 2014
Gestational hypertension (cases)	248 (32.9%)	204 (27.0%)	160 (21.2%)
Preeclampsia (cases)	286 (37.9%)	330 (43.7%)	374 (49.5%)
Chronic hypertension (cases)	140 (18.5%)	122 (16.2%)	98 (13.0%)
Superimposed preeclampsia (cases)	81 (10.7%)	99 (13.1%)	123 (16.3%)
Preeclampsia +superimposed preeclampsia (cases)	367 (48.6%)	429 (56.8%)	497 (65.8%)

The extended definition of PE according to ACOG 2013 and ISSHP 2014 classifications raised the incidence of PE by 8,2% and 17,2% compared to the ACOG 2002 classification.
The most frequent cause of re-classification of GHT and CHT patients to the PE group were abnormal laboratory findings in 35% of cases according to ISSHP 2014 classification and subjective symptoms in 36% of cases according to ACOG 2013 classification.
The median values of fetal birth weight were significantly lower in women with GHT (3330g (IQR: 2985-3750g) vs. 2735g (IQR: 2125-3375g), p<0,001) and CHT (3330g (IQR: 2980-3650g) vs. 2605g (IQR: 1720-3350g), p<0,001) who were re-classified to the PE group compared to those who remained in the original group.
There was no statistically significant difference between the median values of gestational age at delivery and birth weight in PE patients based on ACOG 2002 and ISSHP 2014 classifications: 36 weeks (IQR: 32-38 weeks) vs. 36 weeks (IQR: 33-38 weeks), 2450g (IQR: 1540-3180g) vs. 2530g (IQR: 1650-3260g).
Conclusions: The extended definition of PE in both ACOG 2013 and ISSHP 2014 classifications raised the incidence of PE but did not influence perinatal outcomes significantly.

O60

Treatment of hypertension in pregnancy

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Introduction: Several international (2013 ESH/ESC guidelines, AHA/ISH guidelines, JNC-8) and national (NICE, French, Canadian, Hungarian, Chinese) guidelines have been published recently with recommendations for management of hypertension in pregnancy.
Objectives: Data-based opinions onantihypertensive treatment initiation and target blood pressure (BP), and drugs of choice are not similarly described in these guidelines. Main objectives of the presentation are to summarise data of the relevant literature.
Methods: Review of the recently published guidelines.
Results: Treatment initiation: in addition to life-style changes, there is consensus that drug treatment of severe hypertension(≥160 /110 mmHg) in pregnancy is indicated and beneficial. The suggestion, in the 2007 European Society of Hypertension (ESH) and European Society of Cardiology (ESC) Guidelines,for considering treatment in all pregnant women with persistent elevation of

BP ≥150/95 mmHg is supported by recent US data, showing an increasing trend in the rate of pregnancy-related hospitalizations with stroke — especially during the postpartum period — and by an analysis of stroke victims with severe pre-eclampsia and eclampsia.However, the benefits of antihypertensive therapy are uncertain in pregnant women with mildly to moderately elevated blood pressure (≤160/110 mmHg), either pre-existing orpregnancy-induced, except for a lower risk of developing severe hypertension.Despite lack of evidence, the Task Force of2013 ESH/ESC Guidelines reconfirms that physicians should consider early initiation of antihypertensive treatment atvalues of BP ≥140/90 mmHg in women with (i) gestational hypertension(with or without proteinuria), (ii) pre-existing hypertension with thesuperimposition of gestational hypertension or (iii) hypertension withasymptomatic organ damage (OD) or symptoms at any time during pregnancy.
Target blood pressure: Guidelines mostly agree on that BP should be normalised (to<140/90 mm Hg) in pregnant women with hypertension.
Drug treatment: Drug treatment can be considered in pregnant women with persistent elevation of BP ≥150/95 mmHg, and in those with BP ≥140/90 mmHg in the presence of gestational hypertension, subclinical OD or symptoms due to increased BP. The recommendations to use methyldopa, labetalol and nifedipine as the only calcium antagonist really tested in pregnancy was confirmed in recent European and US guidelines. Beta-blockers (possibly causing foetal growth retardation if given in early pregnancy) anddiuretics (in pre-existing reduction of plasma volume) should be used with caution, only if other indications exist (e.g. ischemic heart disease, severe tachycardia, excess fluid retention). All agents interfering with the renin-angiotensin system (ACE inhibitors, angiotensin AT-1 receptor blockers, renin inhibitors) should absolutely be avoided. In emergency (pre-eclampsia), intravenous labetalol is the drug of choice with sodium nitroprusside (only for short term) or nitroglycerin in intravenous infusion being other options.
Conclusions: According to recent guidelines,in the absence of randomised clinical trials recommendations how hypertension should be treated in pregnant women, can only be guided by experts' opinion based on case reports and their meta-analyses.

O61

The treatment of antenatal hypertension with labetalol: A prediction model for successful response

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Objectives: The aim of this study was to create and validate a prediction model for the response to labetalol in women who have hypertension in pregnancy. This prediction model is based on maternal demographics and haemodynamics.
Methods: This was a prospective observational study that ran over three phases. In the first phase, 50 women attending King's College Hospital's antenatal hypertension clinic, needing antihypertensive treatment, were commenced on labetalol and followed to delivery. We recorded maternal demographics and haemodynamic characteristics at presentation and created a prediction model for the successful treatment with labetalol. In the second phase, this model was internally validated, with a further 50 patients who were treated with either labetalol or alternatively, a vasodilator, based on their haemodynamics at presentation and with reference to our prediction model. In the third phase, we monitored 50 patients' haemodynamics serially, and we adjusted antihypertensive treatment at each visit according to our prediction model.

Outcome measures: The prevalence of severe pre-eclampsia (PE) over the three phases of the study.
Statistics: Multivariate logistic regression with bootstrapping and the $\chi 2$-test and $\chi 2$-for-trend.
Results: In the first study, 50 patients were treated with labetalol. Of these 37 (74%) responded and 13 (26%) did not, despite dose maximisation. From the non-responders 10 (77%) were admitted with severe pre-eclampsia whilst from the responders only 1 was admitted (3%) ($\chi 2$-$p<0.001$). A prediction model for the response to labetalol was created. The area under the receiver operating characteristic curve was 0.9626 and this was confirmed in the validation study. Using the prediction model to guide treatment, the PE rate fell from 20% to 10% and 6%, respectively over the three phases of the study ($\chi 2$ for trend $p<0.001$).
Conclusion: Maternal demographics and haemodynamics can provide a sensitive prediction tool to anticipate the response to labetalol in hypertensive pregnancies, with a subsequent reduction in severe pre-eclampsia rates

O62

Use of diuretics in the management of late-onset preeclampsia

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Introduction: Hemodynamic examinations revealed high cardiac output (CO) in a portion of preeclamptic patients. These cases in our study population met the criteria for late-onset subtype of the disease as hypertension and proteinuria appeared beyond the 33rd gestational week.
Objectives: To decrease enormously high blood volume, as the possible reason for hypertension and edema, diuretics were applied in preeclamptic women with high CO, and edema.
Methods: After a short rest on the left lateral recumbent position, blood pressure (BP), and, by the use of impedance cardiography, CO and systemic vascular resistance (SVR) were determined. In the absence of relative hemoconcentration (hematocrit < 37 l/l) 40 mg of furosemide was administrated orally in 10 cases. Examinations were repeated after 60 minutes of rest. Looking for the effects of the diuretics identical data (before and after furosemide medication) were compared by paired t-test. Significant difference was determined as $p < 0.05$.
Results: In most of cases furosemide administration resulted in a lowering of CO and also BP. Heart rate and SVR remained stable, therefore change of CO was due to blood volume decrease.

	Systolic BP (mm Hg)	Diastolic BP (mm Hg)	Heart rate (beat/min)	CO (l/min)	SVR (dyn.sec.cm-5)
Before furosemide administration	151 ± 44.2**	94 ± 27.5	81.2 ± 24.3	8.34 ± 2.6	1192.8 ± 359.3
After furosemide administration	136 ± 13.5	84 ± 13.2	82.6 ± 10.9	7.44 ± 0.31	1146.2 ± 167.3
p	< 0.01	0.02	NS	0.01	NS

**Data are presented as mean ± SD

Conclusion: Our preliminary data draw attention to the possible use of diuretics in the management of late-onset preeclampsia and support the presumption that increased water retention may play a role in the development of hypertension in late-onset gestational hypertension or preeclampsia. Our data also suggest that the pathogenesis of late-onset preeclampsia is basically different from "classical" preeclampsia characterized by low CO.
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O63

Removal of soluble Fms-like tyrosine kinase (sFlt-1) by plasma-specific apheresis: Pilot study in women with very preterm preeclampsia

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Background: Preeclampsia is a devastating complication of pregnancy affecting both mother and fetus. Soluble Fms-like tyrosine kinase-1 (sFlt-1) is a potential therapeutic target in preeclampsia. We evaluated the safety and efficacy of treating women with very preterm preeclampsia using a plasma-specific dextran sulfate (PSDS) column to remove circulating sFlt-1.
Methods: This was an open study of up to three extra-corporeal PSDS-apheresis treatments in 10 women with very preterm preeclampsia to determine the extent of sFlt-1 and proteinuria reduction, and its safety for mother and fetus.
Results: Six patients with very preterm preeclampsia (mean gestational age 29 + 2 weeks) underwent one PSDS-apheresis treatment; three were treated twice, and one for three times. The apheresis volumes ranged from 400-1500 ml. Mean starting sFlt-1 concentration was 18,342 pg/mL (range 8,243-35,301 pg/mL) with a 17% mean reduction per treatment (range 6-28%). Mean starting protein:creatinine(P/C) ratio was 6.4 g/g (range 0.4-16.9 g/g); mean reduction per treatment was 39% (range 88% reduction to 30% increase). Among women treated multiple times, pregnancy continued on average for 11 days (range 7-19 days). The most common side effect during treatment was transient blood pressure reduction (~10-20 mmHg), managed by withholding antihypertensive therapies before treatment, saline prehydration, and reducing blood flow through the apheresis column. There were no adverse effects to fetuses or neonates.
Conclusions: Therapeutic apheresis reduces circulating sFlt-1 and proteinuria in women with very preterm preeclampsia, enabling pregnancy to continue. A controlled trial is needed to determine whether apheresis to remove sFlt-1 safely prolongs pregnancy.

O64

Timing of delivery in preeclampsia

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Since the only cure of preeclampsia is delivery, and timing of delivery is so essential for maternal and perinatal outcome, one would expect that our profession would have been able to develop clear guidelines as to when to deliver a preeclamptic pregnancy. Yet the decision concerning the timing of delivery remains a complex one. Administrating the cure of delivery too prematurely can have devasting consequences for the baby, as can a prolonged delay in a rapidly progressing disorder, causing a threat both to the mother and the fetus.
Existing guidelines offer assistance mainly in decisions regarding the premature pregnancies before 34 weeks (expectant management), and even then with exceptions for the severly ill mother or the compromised fetus, whereas the more confident advice of delivery in preeclampsia after 36 weeks doesn't entirely help us very much with our difficult decisions. Recommendations for pregnancies week 34 to 36 are all but clear cut. And still we are continuously getting timing of delivery wrong and harming mothers and babies alike.
The HYPITAT and PIERS studies have provided us with more evidence concerning the benefits and risks of delaying or delivering the pregnancy in preeclampsia at different gestational weeks, and the

parameters by which we can monitor maternal disease, in order to identify risk patients to monitor more closely or deliver, aswell as non-risk patients, where delivery might be harmful and should rather be avoided. But perinatal outcomes are perhaps yet not sufficiently considered in these studies. And treatment paradox poses a problem.
A standardized timing of delivery according to gestational age alone does not seem to be the best solution, if optimal perinatal outcome is to be achieved, neither does it seem wise to delay delivery until substantial signs of maternal mobidity are apparent. Rather than standardizing timing of delivery, it might be prudent to standardize the model of monitoring in preeclampsia according to certain pre-specified risk groups. The final decision of when to deliver should be individualized in every preeclamptic women but based on an optimal monitoring.
A model for standardized monitoring practised in Lund is presented. Ideally such a model should include early markers of a hypertensive disorder in progression, markers reflecting even a small degree of endotheliosis, and able to closely reflect every increase in endothelial swelling as a prognostic marker for the rate of deteriation in maternal disease. Pollak and Nettles showed serum urate to be such a marker in ground-breaking renal biopsy studies and this variable is widely used as a prognostic marker in Scandinavia.
Similarly other GFR markers have been shown to be strongly associated with the degree of renal endotheliosis due to the endothelial swelling decreasing the glomerular filtration of water.
Some such markers seem to reflect, due to their size and charge, the filtration of certain particles rather than of water which increases their potential as prognostic markers in preeclampsia

O65

Is there evidence to inform antihypertensive prescribing in pregnancy complicated by chronic hypertension: A systematic review

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Introduction: Chronic hypertension (CHT) complicates 1-5% of all pregnancies. The importance of optimising blood pressure control has been highlighted by the results of the Control of Hypertension In Pregnancy Study. The frequency of severe hypertension in pregnancy directly affects maternal morbidity and mortality. Effective anti-hypertensive treatments (AHTs) for CHT in pregnancy that reduce this risk need to be identified.
Objectives: To perform a systematic review of randomised controlled trials (RCTs) in women with CHT in pregnancy to determine the incidence of severe hypertension with AHT use (vs. none) and by drug class, together with incidence of adverse maternal and fetal/neonatal outcomes.
Method: Medline (via OVID), Embase (via OVID) and the Cochrane Trials Register were searched from their earliest entries until 30.4.15. All RCTs evaluating AHTs for CHT in pregnancy were included. Additional data were found from references of papers identified from the original searches. Two review authors (LW and FCR) extracted and tabulated relevant data. Data were analysed in Stata 13.1 (StataCorp, College Station, Texas), using the metan suite of commands (Higgins et al. 2003). Where there was significant evidence of heterogeneity, the DerSimonian & Laird (1986) method was used.
Results: 10 RCTs of AHT vs other AHT or placebo/no AHT were identified for a pre-defined CHT cohort and an additional 5 RCTs reported outcomes for a CHT subgroup; all data were from studies completed prior to 2000. A clinically important reduction in the incidence of severe hypertension was seen with AHT use vs no AHT (4 studies, 244 women; risk ratio (RR) 0.37; 95% confidence interval (CI) 0.22 to 0.64; I2 0.0%). Additionally two small studies reported incidence of severe hypertension when comparing β-blockers with methyldopa, but results are ambiguous (86 women; RR 0.85, CI 0.5 to 1.37; I2 66.1%).

There was no clear difference in the incidence of superimposed pre-eclampsia for women on AHTs vs no AHTs (6 studies, 525 women; RR 0.77, CI 0.50 to 1.18; I2 37.3%). No significant difference in birthweight (g) was demonstrated with AHT treatment of CHT in pregnancy (7 studies, 731 women; weighted mean difference -78.23; CI -164.59 to 8.13; I2 59.9%).
Conclusion: A considerable paucity of data exists from RCTs to guide AHT prescribing for CHT in pregnancy. Given the increasing incidence of CHT in pregnancy and that AHTs reduce the incidence of severe hypertension, head-to-head RCTs of the commonly used AHTs are urgently required to inform prescribing.

O66

Comparison of immediate delivery versus expectant management in women with severe early onset preeclampsia before 26 weeks of gestation

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Introduction: Severe early onset preeclampsia (PE) is a rare pregnancy disorder with a high maternal and neonatal mortality and morbidity. At an extremely premature gestational age, severe preeclampsia is rare. It causes a distinctive dilemma, as foetal and maternal interests conflict. Prolongation of pregnancy (expectant management) may improve foetal prognosis on one hand, but increases maternal risks of severe morbidity and mortality on the other hand.
Objectives: To compare maternal and neonatal outcomes of immediate delivery or expectant management in women with severe, early onset preeclampsia before 26 weeks' gestation.
Methods: We conducted a nationwide retrospective cohort study. We included women diagnosed with severe preeclampsia, who delivered between 22 and 26 weeks' gestation in all tertiary perinatal care centres in the Netherlands between 2008 and 2014. Patients were identified through computerized hospital databases. We collected data using the medical records. Maternal complications, neonatal mortality and neonatal complications were the primary outcomes.
Results: We studied 133 women, of whom 99 (74%) were managed expectantly, while 34 women (26%) were treated with immediate delivery. Time interval between admittance and delivery was 4 days longer in the expectant group (6 versus 2 days, 95%CI 2.45 – 5.55). Expectant management

was less often associated with perinatal death than immediate delivery (50% versus 88%; OR: 0.079, 95%CI: 0.02 - 0.37), but no differences were found for maternal (69% versus 68%; OR: 3.1, 95%CI: 0.22 – 44) or neonatal complications (81% versus 80%; OR: 3.3, 95%CI: 0.068 – 159). In 46 reported ongoing subsequent pregnancies, 17 (37%) women had recurrent preeclampsia. While no evident trend over time can be found in management or neonatal survival over the study period, a peak appears in caesarean section rate in 2011 and the occurrence of maternal complications seem to decrease.
Conclusion: In women with severe, early onset preeclampsia, expectant care was often applied in the Netherlands. The maternal complication rate is high. Therefore, women need to be counselled carefully, weighing expectant care versus high perinatal mortality in case of immediate delivery.

O67

The cranial imaging in severe preeclampsia

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Introduction: Preeclampsia occurs in 5-6% of all pregnancies, some of the most serious complications of preeclampsia involve neurologic symptoms and include uncontrolled vomiting, severe and persistent headache, visual disturbances, unexplained seizure (eclampsia), coma and death. The mechanism of eclampsia is still controversial.
Objectives: The purpose of this study was to analyse the cranial imaging in severe preeclampsia, and to find the value of cranial imaging in severe preeclampsia.
Methods: Thirty six patients with a clinical diagnosis of severe preeclampsia were retrospectively selected, magnetic resonance imaging or computed tomography were evaluated at hospital. Compared the patients with abnormal imaging findings and without abnormal imaging findings.
Results: Abnormal cranial imaging was in 20(55.55%) patients. Brain edema was found in 13 patients, focal chronic ischemia was found in six patients and cerebral hemorrhage was found in one patients. 24 patients with headache, 9 patients with dizzy, 9 patients with visual disturbance, 5 patients with vomiting, 4 patients with stomachache. In patients with abnormal imaging findings, systolic pressure, uric acid were significantly higher than those without abnormal imaging findings ($p=0.043$, $p=0.026$, respectively). Although patients with abnormal imaging findings showed higher diastolic pressure as compared to those without imaging findings, there was no statistically significant difference ($p=0.092$).
Conclusion: The abnormal cranial imaging can be found in severe preeclampsia without convulsion. If the patients had some neural symptoms, the cranial imaging should be taken. The higher blood pressure and uric acid may related with the cerebral lesions.

O68

Management of eclampsia and stroke during pregnancy

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Introduction: Eclampsia and stroke during pregnancy are major couses of maternal death in the world. Despite the ubiquity of these conditions and their public health impact, neither their etiologies nor therapeutic strategies for their treatment have been established.
Objectives: To establish the etiologies and therapeutic strategies for eclampsia and stroke during pregnancy.

Methods: We performed a questionnaire based long-term survey in Aichi prefecture, Japan in 2007, 2010, and 2013. Aichi prefecture accounts for 7% of the Japanese population as well as 7% of annual births in Japan. The questions were desighed to obtain detailed information about the cases of eclampsia and stroke during pregnancy experienced by the participating institutions between 2005 and 2012 including the number of cases of each condition; their locations, outcomes, and prognoses; and the treatments employed. Questionnaire recovery rate was 100%.
Results: This survey revealed the following findings; 66% of deliveries were managed in primary medical facilities, 38% of eclampsia and 39% of stroke occurred at primary medical facilities, and 26% of stroke occurred at home. 37% of eclampsia and 18% of stroke occurred during labor. More than half of them were associated with hypertension firstly detected after the onset of labor (labor onset hypertension). We revealed that 24% of pregnant women who remained normotensive throughout pregnancy developed labor onset hypertension. We also investigated a lot of cases with eclamspia and/or stroke and revealed important issues regarding their management. In case with eclampsia, we should give priority to emergent care and fetal heart rate monitoring. Accurate antihypertensive and anticonvulsive treatment are necessary. While discrimination between eclampsia and stroke is difficult, brain CT and MRI can detected most of hemorrhagic stroke. When stroke is detected, collaborative treatment with neurosurgeon should be started. Detailed blood pressure measurement during labor is also important especially on having thought about the existence of labor onset hypertension.
Conclusion: These findings might aid the development of therapeutic strategies for pregnant women with eclampsia or stroke.

O69

Visual Evoked Potential as neurophysiological evaluation of patients with severe PE and visual disturbances

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Introduction: Visual symptoms are present in about 25% of women with pre-eclampsia (PE). The origin of these visual disturbances is localized in either the neurological or ophthalmic pathway. The exact causative factors of these disturbances have not been elucidated yet. Cerebral edema may affect the visual cortex, which can even lead to cortical blindness. The occipital cortex seems to be more susceptible for preeclampsia related breakthrough of the cerebral autoregulation. Because the vertebrobasilar system is less innervated with sympathetic nerves, this part of the brain is less capable to regulate cerebral blood flow with rising blood pressure.
Objectives: The objective of the study was to describe the neurophysiological changes by means of visual evoked potentials (VEPs) in patients with PE. A VEP measures the functional integrity of the visual pathway from retina to the occipital cortex of the brain. Our hypothesis is that women with PE have a longer VEP latency and lower amplitude compared to normotensive pregnant women.
Methods: From October 2005 till July 2008 a prospective study was performed. Normotensive pregnant women were recruited at the outpatient clinic from a gestational age of 12 weeks. They underwent clinical and neurophysiological measurements at 5 different time points: at a gestational age of 12-14 weeks, 26-28 weeks, 32-34 weeks, 36-40 weeks and 6-8 weeks postpartum. Women

PE were recruited at the moment of diagnosis and investigated during pregnancy and 6-8 weeks postpartum. The visual evoked potentials were measured using a checkerboard pattern (Viking 4 device).
Results: VEP measurements of 29 normotensive controls, 15 mild PE and 34 severe PE were performed. The absolute values of the mean latency and amplitude was not significantly different between the groups. When compared to normative values of a group of women in the age of 20-59 year in the normotensive controls a higher proportion of women in the severe PE group had a latency time >107 (left eye: controls 31.0%, mild PE 41.7%, severe PE 52.9%, p=0.215; right eye: controls 10.3% , mild PE 26.7%, severe PE 38.2%, p=0.041).
Conclusion: This study showed that a higher percentage of women with PE had a longer latency. We are now studying the association between the VEP results and the cerebral blood flow measured with transcranial Doppler in these women.

O70

What is the optimal management for screening, diagnosis and management of preeclampsia today?

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Preeclampsia is a pregnancy associated syndrome with multifactorial etiology, pathophysiology and clinical expression. The endothelial damage and dysfunction at the heart of the disease canoccur in maternal, fetal and placental compartment or combined. It causes various combinations of clinical issues like maternal hypertension and proteinuria, liver-, renal-, cerebral and/or placental dysfunctions, which are associated with endothelial damage, vasospasm and thrombosis in microcirculation.
Furthermore, the clinical symptoms, the onset of the disease and maternal and/or fetal outcome are not unique. It will be proposed that the early onset form (<34 weeks), usually associated with the fetal growth restriction (FGR), is due to trophoblast dysfunction in the utero-placental vasculature, whereas the late forms are caused by massive endothelial damage in maternal vasculature. However, the severe forms of HELLP Syndrome late in pregnancy, during and immediately after delivery, suggest a unique variantpossibly associated with shallow re-remodeling of spiral arteries and impaired intravascular trophoblast apoptosis.
In the last two years, different approaches for prediction and management of the different forms of preeclampsia were established and introduced in clinical practice, including the assessment of various biomarkers at different times of pregnancy. In the first trimester, the multifactorial algorithms include placental growth factor (PLGF) and placenta associated protein A (PAPP-A) for prediction and prevention initiated by aspirin for early onset form. However, for the prediction of the onset of disease in the second and third trimester of pregnancy, predominately endothelial biomarkers, as solublefms-like tyrosine kinase-1(sflt-1) and PLGF, will be used. Moreover, the management of diseasewill be even more dependent on the dynamics of biomarkers and the use well-defined cut-offs.
Thenew ongoing and coming approaches will notonly help the differentiation of this multifactorial disease, but also lead to better prediction, prevention and management, mostly by reducingthe frequency of emergency management with itshigh potential for fatal maternal and fetal consequences.

O72

Monocyte-macrophage system in pregnancy complications from the prospective of extracellular vesicles

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Introduction: Successful pregnancy is based on the immunological balance between the maternal immunity and the feto–placental immune system. The activity of the monocyte-macrophage (MO-Mph) system is a critical step in placental homeostasis. The bilateral effects between Mo-Mph-derived extracellular vesicles (EVs) and neighboring cells or the microenvironmental EVs and MO-Mph are well-known. On the one hand, EVs released from Mph-s have both autocrine and paracrine effects including the regulation of the differentiation of local MOs into Mph-s, the induction of inflammation-induced apoptosis, or the regulation of antigen presentation. It is also well-defined that infections modify the content of Mph-derived EVs which than stimulate pro-inflammatory responses and may have a role in pregnancy complications.
Objective: The aim of our study was the characterization of the interactions between circulating EVs and the MO-Mph system in pregnancy complications.
Methods: Characterization of in vivo apoptosis and circulating MO subsets and also the effects of circulating MVs on MO function were followed up. Multicolor flow cytometry was used for the characterization of circulating microvesicles (MVs) and apoptotic bodies (ABs), and an in vitro co-culture system was designed for the identification of the effects of pregnancy associated circulating MVs.
Results: Significantly higher amounts of circulating ABs could be detected in pre-eclamptic plasma compared to the healthy pregnants. The binding ability of circulating MVs to human leukocytes did not differ. The distribution of MO subsets was typical for preeclampsia: higher amounts of CD14+/HLA-DR+ Mo-s and significantly lowers levels of CD14dim+ MOs could be detected. On the other hand, neither the expression level of HLA-DR on circulating MOs differed, nor the circulating MVs modified the HLA-DR expression in an in vitro culture system.
Conclusion: Our studies on the interactions between trophoblast derived MVs (tMVs) and infections in the development of preeclampsia suggested that tMVs induced IL-6 production in human leukocytes and the combined effect of LPS and tMVs resulted in an upregulation of the synthesis of the pro-inflammatory cytokines, IL-6 and TNFa.
Our results confirm a reciprocal effect between circulating MVs and maternal MO-Mph system which may have both local and systemic consequences in the development of preeclampsia.

O73

The role of Th17/Treg imbalance in normal pregnancy and pre-eclampsia

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Introduction: The etiology and pathogenesis of pre-eclampsia are not yet fully understood. Many of the findings support a hypothesis that an inappropriate activation of immune system is associated with the development of this syndrome.

Objectives: The aim of the study was to estimate the prevalence of CD3+CD4+ T lymphocytes producing IL-17, IL-2, IFN-γand IL-4, as well as CD4+CD25+FoxP3+ Tregulatory cells (Tregs) in peripheral blood of patients with preeclampsia and healthy women in the third trimester of normal pregnancy. Furthermore, the purpose of our study was to assess the immunosuppressive activity of Treg cells of patients with preeclampsia in comparison with the controls.
Methods: Thirty four patients with preeclampsia and 27 healthy women in third trimester of pregnancy were included to the study. The percentage of CD4+CD25+FoxP3+ Treg cells and CD3+CD4+ T lymphocytes with intracellular expressions of cytokines were estimated using monoclonal antibodies and flow cytometry. The in vitro functional assays were performed with the use of Treg Cells Isolation Kit and 3H-thimidine.
Results: The percentages of T CD3+CD4+ lymphocytes producing IL-17A were significantly higher in preeclampsia when compared to healthy normotensive pregnant women in the third trimester of normal pregnancy ($p<0.001$). The population of CD4+CD25+FoxP3+ Treg cells was significantly lower in the study when compared to the control group ($p<0.05$). There were no changes in the stimulation index of CD3+CD4+CD25- T lymphocytes of patients with preeclampsiaduring in vitro assay without Treg cells and after the addition of autologous Tregs. In normal pregnancy the stimulation index of CD3+CD4+CD25- T lymphocytes was significantly higher without Treg cells when compared to this response after addition of autologous Tregs ($p<0.05$).
Conclusions: The results obtained suggest the up-regulation of Th17 immune response in preeclampsia. It seems that the decreased number and function of Treg cells may be responsible for the activation of inflammatory response in this disorder. In preeclampsia the predominance of Th17 immunity can act through the modulation of Th1/Th2 immune response.

O74

Granulocyte and monocyte phagocytosis index affected by plasma factors in normal and preeclamptic pregnancy

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Introduction: Phagocytic function of neutrophil granulocytes and monocytes is poorly examined in healthy and preeclamptic pregnancies. Phagocytosis in an important function of innate immune system which protects the mother and the fetus with elimination of microbes and probably microparticles.
Objectives: We examined the phagocytic index of non-pregnant, healthy pregnant and preeclamptic women. We also described the effect of different plasma samples on phagocytic function of neutrophil granulocytes and monocytes of the three groups.
Methods: Five healthy pregnant, preeclamptic pregnant and non-pregnant women were enrolled into our study. Cells and plasma samples were isolated from peripherial blood samples. Cells of the three groups were incubated in autologous and different plasma samples and evaluated by their phagocytic index with an immunofluorescent microscope after internalization of zymosan molecules.
Results: Phagocytic index of monocytes and granulocytes was decreased in healthy pregnancy and further decreased in preeclampsia. Phagocytic index of cells from non pregnant women was inhibited by plasma from healthy pregnant women and further decreased by plasma from preeclamptic women. Phagocytosis of cells from healthy pregnant women was increased by plasma from non-pregnant women and decreased by plasma from preeclamptic women. Phagocytic index of cells from preeclamptic women was increased by plasma from healthy pregnant women and further increased by plasma from non-pregnant women

Conclusion: Phagocytic function of granulocytes and monocytes decreased significantly in healthy pregnancy and further decreased in preeclampsia compared with non-pregnant controls. The reduced phagocytic index of neutrophils and monocytes in healthy pregnancy may be caused by immunosuppressive factors present in maternal plasma. This mechanism can be part of the maternal immunosuppression for the protection of the fetus. Failure of this mechanism and further inhibition of phagocytosis in preeclampsia may take part in the pathogenesis of preeclampsia.

O75

B7 Costimulation and intracellular Indoleamine-2,3-dioxygenase expression in peripheral blood of healthy pregnant and preeclamptic women

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Introduction: B7 costimulatory molecules are expressed on antigen presenting cells (APCs) and are important regulators of T cell activation. We investigated their role in the development of the systemic maternal immune tolerance during healthy pregnancy (HP) and preeclampsia (PE).
Objectives: We also aimed to investigate the intracellular expression of indoleamine-2,3-dioxygenase (IDO) and plasma levels of tryptophane (TRP), kynurenine (KYN) and kynurenic acid (KYNA), important molecules with immunoregulatory properties, in order to describe their potential contribution to the pregnancy-specific maternal immune tolerance.
Methods: We determined the frequency of activated (CD11b+) monocytes expressing B7-1, B7-2, B7-H1, and B7-H2, and that of T cells and CD4+ T helper cells expressing CD28, CTLA-4, PD-1, and ICOS in peripheral blood samples of 20 PE, 20 HP and 14 non-pregnant (NP) women using flow cytometry. We also examined the intracellular expression of IDO applying flow cytometry and plasma levels of TRP, KYN and KYNA using high-performance liquid chromatography.
Results: A significant increase in the prevalence of CD28+ T cells was observed in HP compared to NP women. At the same time a decrease was shown in the expression of CTLA-4 on these cells. The frequency of B7-1 and B7-2 expressing monocytes and that of IDO expressing T lymphocytes was lower in PE than in HP. The prevalence of IDO-expressing T cells and monocytes was higher in HP compared to NP women. Plasma KYN, KYNA and TRP levels were lower, while at the same time, the KYN/TRP ratio was higher in HP than in NP women. We found a positive correlation between the expression of B7-2 and IDO within activated monocytes.
Conclusion: Costimulation via CD28 may not contribute to the immunosuppressive environment, at least in the third trimester of pregnancy. The development of the pregnancy-specific immune tolerance in the mechanism of B7 costimulation may be more related to the altered expression of B7 proteins on APCs rather than that of their receptors on T cells. The elevated intracellular IDO expression in monocytes and T cells, as well as higher plasma enzymatic IDO activity are likely to contribute to the systemic immunosuppressive environment in the third trimester characteristic for healthy gestation. Lower expression of B7-1 and B7-2 proteins on peripheral monocytes in PE might indicate a secondary regulatory mechanism in response to the ongoing systemic maternal inflammation. Immunosuppression by IDO may play an important role in the pregnancy-specific immune tolerance, and might be a contributing factor in the pathogenesis of PE.

O76

The role of costimulatory molecules in the pathogenesis of pre-eclampsia

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Introduction: B7-H1 and B7-H4 molecules belong to the newly discovered immunomodulatory protein family which down-regulates T cell responses.
Objectives: The aim of the study was to estimate the expressions of B7-H1 and B7-H4 molecules on myeloid and plasmocytoid dendritic cells (DCs) in peripheral blood of patients with pre-eclampsia, normal pregnant women and healthy non-pregnant women.
Methods: Thirty three patients with pre-eclampsia, 26 normal pregnant women and 12 healthy non-pregnant women were included in the study. Dendritic cells were isolated from peripheral blood, stained with monoclonal antibodies against blood dendritic cell antigens and B7-H1 and B7-H4 molecules and estimated using flow cytometry.
Results: The expressions of B7-H1 and B7-H4 molecules were significantly higher on CD1c+ myeloid and BDCA-2+ plasmocytoid DCs in the first trimester of pregnancy when compared to the luteal phase of the ovarian cycle. Moreover, the expressions of B7-H1 molecule on CD1c+ DCs in the second trimester of normal pregnancy were significantly higher when compared to the first trimester. In the third trimester they decreased when compared to the second trimester. The expressions of B7-H1 molecule on CD1c+ myeloid and BDCA-2+ plasmocytoid DCs were significantly lower in pre-eclampsia when compared to healthy third trimester pregnant women.
Conclusions: It seems that the higher expressions of B7-H1 and B7-H4 molecules on CD1c+ myeloid and BDCA-2+ plasmocytoid DCs in the first trimester of pregnancy suggest their role in the immunomodulation during early pregnancy. Lower expressions of B7-H1 molecule on myeloid CD1c+ DCs in the third trimester of normal pregnancy may suggest their decreased tolerogenic activities before the labour. It seems possible that the lower expressions of B7-H1 tolerance molecule on CD1c+ myeloid and BDCA-2+ plasmocytoid DCs in pre-eclampsia may be associated with the increased inflammatory response which is observed in this syndrome.

O77

Functional screening of toll-like receptors in seven trophoblast cell lines

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Introduction: Pregnancy is considered a natural inflammatory condition, but pregnancy complications such as preeclampsia and miscarriage are linked to excessive inflammation in the placenta. Toll-like receptors (TLRs) serve as sensors for danger signals and are crucial for initiating inflammation. A successful pregnancy depends on proper function of fetal trophoblasts, the main cell type in the placenta. We have shown broad functional TLR expression in primary first trimester trophoblasts (Tangerås et al, J Reprod Immunol 2014), and trophoblast TLR activation may contribute substantially to placental inflammation. Trophoblast cell lines are commonly used as surrogates for primary trophoblasts for in vitro research. With respect to TLR mediated inflammation, the translatability of trophoblast cell lines warrants examination.

Objectives: This study aimed to assess TLR1-10 gene expression and activation in seven trophoblast cell lines of different origins and compare to primary first trimester trophoblasts.
Methods: The choriocarcinoma trophoblast cell lines BeWo, JAR, JEG-3, AC1M-32 and ACH-3P and the SV40 transformed extravillous trophoblast cell lines HTR-8/SVneo and SGHPL-5 were included and compared to primary first trimester trophoblasts (n=6).Gene expression of TLR1-10 was analyzed using RT-qPCR. Following specific TLR ligand activation for 24 hours,trophoblast release of interleukin (IL)-1β, IL-6, IL-8, IL-9, IL-10, IL-12 (p70), interferon (IFN)-γ-inducible protein (IP)-10, tumor necrosis factor (TNF)-α, IFN-γ, and vascular endothelial growth factor (VEGF)-A was measured by multiplex immunoassay.
Results: All choriocarcinoma cell lines demonstrated broad TLR gene expression, but lacked functional cytokine response to TLR ligand activation. On the contrary, the SV40 transformed cell lines showed restricted TLR gene expression, and responded to activation of TLR2, TLR3 and/or TLR4 by significantly upregulated production of inflammatory cytokines such as IL-6, IL-8 and/or IFN-γ. The primary first trimester trophoblasts demonstrated both a broad TLR gene expression profile and prominent cytokine response to TLR ligand activation. Only SGHPL-5 showed a TLR activated cytokine response comparable to primary first trimester trophoblasts.
Conclusion: Most of the trophoblast cell lines tested showed markedly lower inflammatory TLR properties compared to primary first trimester trophoblasts, and SGHPL-5 and HTR8/SVneo were most TLR responsive. This warrants caution when translating trophoblast immune function from cell line studies.

O78

The inflammatory role of HMGB1 in preeclampsia

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Introduction: Preeclampsia is characterized by an aberrant inflammatory response to pregnancy, leading to hypertension and proteinuria after mid-gestation. Although the pathogenesis remains unclear, there is a strong association between abnormal placentation and excessive inflammation in preeclampsia. Toll-like receptors (TLRs) serve as sensors for danger signals and are crucial for initiating inflammation. The danger signal high-mobility group box 1 (HMGB1) induces inflammation through TLR2 and TLR4 and has been linked to inflammatory diseases, such as atherosclerosis. Studies have suggested involvement of HMGB1 both in the placenta and maternal circulation in preeclampsia, albeit with conflicting results.
Objective: The aim of this study was to investigate HMGB1 expression and activation in the placenta and maternal serum of normal and preeclamptic pregnancies.

Methods: Third trimester placental samples from 36 pregnancies were obtained after cesarean delivery (23 preeclamptic and 13 uncomplicated pregnancies). Placental expression of TLR2, TLR4 and HMGB1 was analyzed by immunohistochemistry. Maternal blood samples were taken before delivery from 34 preeclamptic and 43 healthy pregnant women, and 28 healthy non-pregnant women. HMGB1 serum levels were measured by ELISA and ten selected cytokines were analyzed by multiplex immunoassay. Explant cultures of isolated placental chorionic villi from five normal pregnancies and the trophoblast cell line SGHPL-5 were incubated for 24h with or without addition of HMGB1, and cytokine release in the culture supernatant was measured by multiplex immunoassay.
Results: Maternal serum HMGB1 was significantly higher in normal and preeclamptic pregnancies compared to non-pregnant women. HMGB1 and its receptor TLR4 were expressed by the syncytiotrophoblast in all placentas. TLR4 expression in the syncytiotrophoblast was significantly increased in preeclamptic pregnancies, while cytoplasmic HMGB1 expression was significantly increased in preeclamptic pregnancies when combined with fetal growth restriction. HMGB1 stimulation of chorionic villi explants and SGHPL-5 trophoblasts induced release of the inflammatory cytokine IL-8. In addition, the level of IL-8 in maternal serum was significantly higher in preeclampsia compared to normal pregnancies.
Conclusion: Our findings demonstrate a role for HMGB1 in promoting inflammation both in normal and complicated pregnancies. HMGB1 activation of TLR4 may represent an important mechanism linking harmful placental and systemic inflammation in preeclampsia.

O137

Developing, disseminating, and implementing a core outcome set for pre-eclampsia.

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Introduction: Pre-eclampsia is a serious complication of pregnancy. Clinical studies evaluating therapeutic interventions for pre-eclampsia have reported many different outcomes and outcome measures. Such variation contributes to an inability to compare, contrast, and combine individual trials, limiting the usefulness of research to inform clinical practice.
Objectives: Develop, disseminate, and implement a core outcome set for pre-eclampsia
Methods: An international steering group has been formed to guide the development of this core outcome set. Potential outcomes will be identified through a comprehensive literature review and semi-structured interviews with patients. Potential core outcomes will be entered into an international, multi-perspective Delphi survey. The Delphi method encourages whole and stakeholder group convergence towards consensus 'core' outcomes. High quality outcome measures will be associated with core outcomes.
Results: A comprehensive literature review has been completed. The search retrieved 1938 articles. Seventy six studies (84 references) were potentially eligible and were retrieved in full text. Seventy four studies (78 references) met our inclusion criteria. Eighteen studies (21 references) were excluded. Thousands of reported outcomes have been organised into 165 outcome domains, including 80 maternal domains and 67 offspring domains. Semi-structured interviews with patients have commenced.
Conclusions: Embedding the core outcome set within future clinical trials, systematic reviews, and clinical practice guidelines will advance the usefulness of research to inform clinical practice, enhance patient care, and improve maternal and offspring outcomes.

O79

An intermediate sFlt-1/PlGF ratio without preeclampsia indicates preterm delivery

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Introduction: Current concepts understand preeclampsia (PE) as an altered angiogenic state that is indicated by an increased sFlt-1/PlGF ratio. This ratio is a valid biomarker for the diagnosis of PE and correlates closely with the severity of the disease. A case control study developed new, gestational age-dependent cut-offs framing an intermediate zone.
Objectives: In this retrospective study we analysed patients in the intermediate zone with an sFlt-1/PlGF ratio between 33 and 85 (<34 weeks) respectively 33 and 110 (≥ 34 weeks) according to pregnancy outcome, PE rate, re-testing and preterm delivery.
Methods: All women with tested sFlt-1/PlGF ratio in clinical routine in 2012 and 2013 were included in this retrospective cohort study. SFlt-1 and PlGF concentrations were measured using the automated Elecsys® platform (Roche Diagnostics GmbH).
Results: Of all 553 tested woman, 86 (16%) showed an sFlt-1/PlGF ratio in the intermediate zone between 33 and 85/110. 16 of them were tested < 34 weeks with a preterm birth rate of 94% (15/16). 31% of them developed PE (5/16) with a mean sFlt-1/PlGF ratio of 70 , 69% (11/16) showed no preeclampsia-related conditions: multiple pregnancy (n=5), gestational diabetes, lupus erythematodes, pre-existing maternal cardiac or kidney disease, IUGR or pathological perfusion with a mean sFlt-1/PlGF ratio of 57. Re-testing was performed in 18% of all cases.
Conclusion: As expected, patients with ratio in the intermediate zone show an increased risk for developing PE. Notably, in patients < 34 weeks without later PE an intermediate sFlt-1/PlGF ratio is associated with preterm delivery. Thus, an intermediate sFlt-1/PlGF ratio indicates adverse outcome and identifies pregnancies at risk for preterm birth, independent from PE.

O80

The SFLT-1/PlGF ratio associates with prolongation of pregnancy

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Introduction: The sFlt-1/PlGF ratio has emerged as a biomarker for the timely diagnosis of preeclampsia (PE) and prediction of pregnancy outcome. Because of this property we hypothesized that this ratio.
Objective: To evaluate whether a single determination of the serum sFlt-1/PlGF ratio associates with pregnancy prolongation in women with suspected or confirmed preeclampsia (PE).
Methods: In this ongoing observational Dutch multicenter study (600 pts to be enrolled) blood was drawn at admission. Values of sFlt-1 and PlGF were measured postpartum using the automated Elecsys system to prevent influence of this information on decision-making of the treating physicians and the defining time point of delivery. Clinical characteristics and pregnancy outcomes were retrieved from medical records. Cutoffs of <33 to rule out and ≥85 to rule in the occurrence of delivery for selected time points were used.

Results: So far complete data of 147 patients (age 18 to 48 yrs. singleton pregnancies, median pregnancy duration 32 weeks (range 20-36 weeks) are available. At time of inclusion 67 pregnancies were complicated with PE, of which 12 with superimposed PE, 8 with HELLP, 20 with gestational hypertension (GH) and 60 without pregnancy induced hypertension (PIH). The median (range) ratio in patients who delivered within 7 days was 146 (9-1803) compared to 14 (1-469) in those who delivered after >7 days ($p<0.001$). Delivery within 7 days occurred in 59% patients with a ratio >85 compared to 7% with a ratio <33 ($p=0.002$) and 39% with a ratio 33-85 ($p=0.048$).
Conclusion: In this high risk group a low ratio is inversely correlated with prolongation of pregnancy.

Diagnosis at time of inclusion	Ratio <33, n= 77 Prolongation of pregnancy		Ratio 33-85, n=32 Prolongation of pregnancy		Ratio >85, n=38 Prolongation of pregnancy	
	≤7 days	> 7 days	≤7 days	> 7 days	≤7 days	> 7 days
Non PIH (n=60)	2 (4%)	46 (96%)	1 (13%)	7 (88%)	3 (75%)	1 (25%)
PE/HELLP (n= 67)	4 (21%)	15 (79%)	11 (55%)	9 (45%)	18 (64%)	10 (36%)
GH (n= 20)	-	10 (100%)	-	4 (100%)	3 (50%)	3 (50%)

O81

The impact of uterine curettage post partum on maternal sFlt-1 concentration

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Introduction: The anti-angiogenic biomarker sFlt-1 is closely related to the pathobiology and the clinical presentation of preeclampsia. A uterine curettage post partum is a known therapeutic option for eclamptic seizures or HELLP syndrome after delivery.
Objectives: Our purpose was to investigate the influence of a uterine curettage on the immediate maternal sFlt-1 concentration post partum.
Methods: Forty six patients booked for delivery via primary caesarean section were included in a prospective open, case control study. Eighteen of them achieved an intraoperative curettage and formed the treatment group, 28 patients without curettage were enrolled in the control group. Maternal sFlt-1 serum values were measured immediately before and 24 hours after delivery.
Results: Patients who underwent a uterine curettage showed a relative decrease of 70 % (from median 3670 ± 1110 pg/ml to 1143 ± 270 pg/ml) in comparison to the control group with 65 % (from median 3132 ± 636 pg/ml to 1098 ± 611 pg/ml; p=0,558). Additionally, three patients with preeclampsia and curettage were included, who showed a relative decrease of 76 %.
Conclusion: A uterine curettage may slightly accelerate the fall of the postpartal sFlt-1 concentration. The previously described benefit of curettage in preeclamptic patients regarding faster recovery or treatment of post partum seizures may be partly explained as mediated by anti-angiogenic factors.

O82

Association between anti-angiogenic factor and signs of arterial aging in women with preeclampsia

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Introduction: Preeclampsia (PE) is a state of exaggerated inflammation and is associated with increased risk of cardiovascular disease later in life. Soluble fms-like tyrosine kinase-1 (s-Flt1) is an antiangiogenic factor and is increased, whereas placental growth factor (PlGF) is an angiogenic factor and is decreased in PE.

Objectives: Aim of this study was to assess s-Flt1, PlGF and s-Flt1/PlGF and its correlation with common carotid artery (CCA) intima, media and intima/media ratio (I/M) in women with and without PE.
Methods: We measured serum s-Flt1 and PlGF using commercially available enzyme-linked immunosorbent assay kits and individual CCA intima and media thicknesses were estimated by high-frequency (22 MHz) ultrasound in 55 women at PE diagnosis and in 64 women with normal pregnancies at a similar gestational age and about one year postpartum. A thick intima, thin media and high I/M are signs of a less healthy artery wall.
Results: During pregnancy, we found higher values of s-Flt1, lower values of PlGF and thicker intima, thinner media and higher I/M in women with PE than in women with normal pregnancy (all $p < 0.0001$). Further, s-Flt1 and s-Flt1/PlGF showed a positive correlation with intima thickness and I/M but a negative correlation with media thickness (all $p < 0.0001$). About one year postpartum, s-Flt1 and s-Flt1/PlGF values had decreased in both groups but there was still a significant group difference (all $p < 0.0001$). No significant correlation with CCA wall layers (except for s-Flt1 and intima thickness, $p = 0.007$) was found at postpartum.
Conclusion: We found substantially higher values of s-Flt1 and s-Flt1/PlGF in women with PE and these higher values were associated with signs of arterial aging. Our findings support the findings of increased risk of cardiovascular disease in women with PE.

O83

Angiogenic factor imbalance contributes to the pathophysiology of preeclampsia among rural African women

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Introduction: Preeclampsia remains one of the leading causes of maternal morbidity and mortality. An imbalance in the angiogenic factors has been hypothesised to contribute to the pathophysiology of this condition. The condiition favors an increase in the antiangiogenic factors like vascular endothelial growth factor receptor 1(sFlt-1) and a decrease in the proangiogenic factors like placental growth factor (PlGF). Although this has been found in the Caucasian populations, it is not known whether that imbalance exists among the rural African population.
Objectives: The aim of this study was to determine whether there is an imbalance in angogenic factors among preeclamptic and normotensive pregnant rural African women
Methods: The levels of antiangiogenic factor sFlt-1 and proangiogenic factor PlGF were quantified using their specific enzyme linked immunosorbent assays (ELISAs) among both preeclamptic and normotensive pregnant women in Nelson Mandela Academic Hospital in Mthatha. Ethical approval was obtained from the Walter Sisulu University Faculty of Health Sciences research and ethics committee and participants were given informed consent. Preeclampsia participants (105) were selected on the basis of a persistent blood pressure of >140/90mmHg on two separate occasions 4-6hrs apart or a single reading of >160/100mmHg and a proteinuria of >1+ in two random specimens collected atleast 4hours apart (or a 24hr urine protein of >300mg/l) from 20 weeks of gestation as defined by the international society for study of hypertension in pregnancy (ISSHP). Controls (110) were age- and gestation age-matched normotensive pregnant women attending antenatal clinic or admitted for other obstetric conditions other than hypertension or diabetes.

Bloods were drawn, centrifuged and stored at -70 degrees C until analysis. Values were summarised as means+- standard error of the mean and were compared using the Students' t-test. Statistical significance was set at $p<0.05$.

Results: Compared to the controls, circulating levels of sFlt-1 were higher in preeclampsia (2087.3+-200.2pg/ml vs 1546.5+- 91.9pg/ml; $p<0.01$). In contrast, PlGF levels were significantly lower in cases compared to controls (90.26+-8.99pg/ml vs 172.80+-20.24pg/ml; $p<0.01$). The sFlt-1/PlGF ratio was also significantly greater in the cases compared to the controls (66.77+-18.66 vs 22.26+-2.95; $p<0.01$).

Conclusion: Thus, similar to the results from the Caucasian populations, there exists an imbalance in agiogenic factors among rural African women. This suggests that this imbalance could be a contributing factor in the pathophysiology of preeclampsia in this population.

O84

Hydrogen sulphide rescues the preeclampsia phenotype aggravated by high sFlt-1 in placenta growth factor deficient pregnant mouse

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Low circulating levels of placenta growth factor (PlGF) is strongly associated with the onset of preeclampsia, a maternal hypertensive disorder characterized by high blood pressure and proteinuria after 20 weeks of gestation. Although, PlGF-deficient mice are born healthy and fertile at a Mendelian ratio, the physiological importance of PlGF in the pathogenesis of preeclampsia is unknown. We hypothesised that decreased levels of PlGF in pregnancy exacerbates the fetal growth restriction associated with preeclampsia in the presence of high sFlt-1.Pregnant PlGF-/- mice were injected with adenovirus encoding sFlt-1 (Ad-sFlt-1) at high (i) 1x108 pfu/ml and low (ii) 1x109 pfu/ml doses. Mean arterial blood pressure (MBP), biochemical and histological assessments of maternal kidney, placenta and embryos were performed. Ad-sFlt-1 significantly increased MBP and induced severe glomerular endotheliosis in PlGF-/- mice at E10.5 gestation compared to wild-type animals. High sFlt-1 also significantly elevated albumin-creatinine ratio and increased levels of urinary kidney injury molecule-1, a marker for proximal tubule injury.At a high dose of sFlt-1, there was complete fetal resorption in the pregnant PlGF-/- mice, and even the lower dose of sFlt-1 induced severe fetal resorption and abnormal placental vascularization. Hydrogen sulphide-releasing agent, GYY4137, significantly reduced resorption, hypertension and proteinuriain Ad-sFlt-1 treated pregnant PlGF-/- mice. To determine if placental PlGF is critical for preventing fetal growth restriction associated with preeclampsia, we generated haploinsufficientPlGF+/- placentas and embryos were generated in wild-time dams and exposed to high sFlt-1 environment. This resulted in reduced fetal resorption, gestational hypertension and proteinuria when compared to pregnant PlGF-/- micePlacental PlGF is a critical protective factor against the damaging effects of high sFlt-1 associated with preeclampsia and activation of the hydrogen sulphide pathway may rescue preeclampsia phenotype even under low PlGF environment.

WH85

Biomarker discovery in preeclampsia: Present and future challenges: Taking a biomarker into clinical practice

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The search for new predictive and diagnostic biomarkers for pre-eclampsia has continued for decades, but the pathway for taking a biomarker from discovery to clinical practice is fraught with hurdles. The World Health Organization criteria for a suitable biomarker include: well-defined disorder with known prevalence; effective, accepted treatment; cost effective screening; easily introduced test using available infrastructure; acceptable follow-up of the high-risk group; simple, safe test; known distribution of test values in affected and unaffected populations with small overlap, defined cut-off point; accessible. There is a potential need for diagnostic markers in women who present with suspected pre-eclampsia, in order to confirm (or refute) the diagnosis, allowing appropriate stratification of care and to optimise decision-making around time of delivery, and for predictive markers in low and high risk populations to improve the targeting of prophylactic treatments. Heterogeneity of the pre-eclampsia syndrome makes both tasks challenging.
Decreased serum concentrations of placental growth factor, a pro-angiogenic factor synthesised by the trophoblast (and other maternal and fetal tissues), in women with pre-eclampsia were first described in the late 1990s and many reports, initially from case-control studies and subsequently from cohort studies, have followed. Numerous other blood-based biomarkers have also been investigated including placental (e.g. pregnancy associated plasma protein-A, placental protein 13), maternal (e.g. markers of inflammation or endothelial activation), fetal (e.g. cell-free fetal DNA) together with biophysical markers such as uterine artery Doppler imaging, but none are routinely recommended for widespread clinical practice, due to lack of external validation, and limitations of test performance. Considerable research is now ongoing in order to refine the choice of biomarker combinations for prediction and diagnosis, including evidence synthesis of the studies already published, individual patient data meta-analysis for first trimester prediction, well-designed cohort studies of first trimester predictive panels (using candidate and proteomic panels) and randomised controlled trials of placental growth factor at presentation with suspected disease, with embedded health economic evaluations. These projects will need to evaluate the test effectiveness and the downstream impact of the test on maternal and perinatal outcomes.

WH86

Using proteomics for the discovery of biomarkers: Promise and pitfalls

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Preeclampsia is largely unpredictable, particularly in healthy nulliparous pregnant women. Accurate preeclampsia prediction in this population would transform antenatal care. As mass spectrometry techniques have advanced, proteomics has promised much in terms of novel biomarker discovery. However, this has not yet translated into clinically useful biomarkers for most diseases. In order to progress the identification of novel biomarkers for pre-eclampsia, we have undertaken several parallel mass spectrometry studies using samples collected through the SCOPE consortium. Two different strategies have been employed to identify candidate proteins in plasma specimens collected

at 14-16 and 19-21 weeks' gestation from women who later developed preeclampsia and women without preeclampsia. Candidate proteins were then verified in cohorts recruited from Australia and New Zealand and Europe, respectively. Algorithms were developed and tested which met predefined criteria: sensitivity ≥50% at 20% positive predictive value (PPV). Eight models detected 50-56% of preeclampsia cases in the training and validation sets; the detection rate for preterm preeclampsia cases was 80%.
In another series of experiments, the high specificity, sensitivity and multiplexed nature of selected reaction monitoring (SRM) as a tool for the verification and validation of putative candidate biomarkers was tested. Realisation of the potential of this technique involves establishing a high throughput, cost effective, reproducible sample preparation workflow. We developed a semi-automated HPLC-based sample preparation workflow prior to a label-free SRM approach. This workflow has been applied to the verification of novel predictive biomarkers for PE.We obtained reproducible protein quantitation across the 100 samples and demonstrated significant changes in protein levels, even with as little as 20% change in protein concentration. The SRM data correlated with a commercial ELISA, suggesting that this is a robust workflow suitable for rapid, affordable, label-free verification of which candidate biomarkers should be taken forward for thorough investigation. The complexities of biomarker discovery in the context of the prediction of pre-eclampsia will be discussed.

STA105

PlGF: more than a pre-eclampsia biomarker. Results from the CoLAB Angiogenic Factor Study of 16 000 pregnancies

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Low maternal circulating concentration of placental growth factor (PlGF) has been investigated as a diagnostic and prediction marker of pre-eclampsia, but may represent a marker for syncytiotrohoblast stress and placentally associated pregnancy complications. These complications are common and represent a major threat to maternal and/or offspring health globally. Large study populations are required to define subsets of these placenta associated complications, that may have different pathophysiological background.

In a collaboration study organized by The Global Pregnancy CoLlaboration (CoLAB; pre-empt. cfri.ca/colaboratory/global-pregnancy-colaboratory), multiple and heterogeneous cohorts were aggregated (22 cohorts and 16,462 pregnancies), including PlGF analyses from four disparate analytical platforms. Inter-platform standardization and merging algorithms were preformed. Two merging algorithms, using Z-Score and Multiple of Median transformations, were applied. Best reference curves (BRC), based on merged, transformed PlGF measurements in uncomplicated pregnancy across six gestational age groups, were estimated.
The CoLab study has demonstrated the feasibility of merging PlGF concentrations from different analytical platforms and the talk will present how "low PlGF" identifies more than pre-eclampsia in this large merged pregnancy study.

STA106

Maternal cardiac function before and during preeclampsia: We must study the heart in pregnacy

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Objective: Most studies during pregnancy have assessed maternal left ventricular (LV) function by load-dependent indices, assessing only chamber function. The aim of this study was to assess afterload-adjusted LV myocardial and chamber systolic function at 24 weeks' gestation and 6 months postpartum in high-risk normotensive pregnant women.
Methods: A group of 118 high-risk women with bilateral notching of the uterine arteries underwent an echocardiographic examination to evaluate midwall mechanics (midwall shortening (mFS%) and stress-corrected midwall shortening (SCmFS%)) of the LV at 24 weeks' gestation and 6 months postpartum. Patients were followed until delivery and pregnancies were classified retrospectively as uneventful (uncomplicated outcome) or complicated.A control group of 54 low-risk women with uneventful pregnancies without bilateral notching was also enrolled.
Results: The pregnancy was uneventful in 74 (62.7%) women, whereas 44 (37.3%) developed complications. At 24 weeks' gestation, mFS% and SCmFS% were greater in the uncomplicated-outcome compared withthe complicated-outcome group (25.9 +/-4.8 vs 18.8 +/-5.0%, $P < 0.001$ and 107.9 +/18.4 vs 77.9 +/-20.7%, $P < 0.001$, respectively). At 6 months postpartum, SCmFS% remained greater in the uncomplicated-outcome compared with the complicated-outcome group (100.4 +/-21.6 vs 87.8 +/-19.1, $P < 0.05$). In the uncomplicated outcome group, SCmFS% was higher during pregnancy than it was postpartum, whereas in the complicated outcome group, it was lower during pregnancy than it was postpartum ($P < 0.05$).
Conclusions: Maternal cardiac midwall mechanics appear to be enhanced (SCmFS% increased compared with controls) during pregnancy compared with postpartum inhigh-risk patients with uncomplicated pregnancy, whereas midwall mechanics are depressed both during pregnancy and postpartum in patients with pregnancy complications

PL107

Monocytes in pregnancy and preeclampsia

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Monocytes are short lived circulating leukocytes. Their main function is phagocytosis, antigen presentation and cytokine production. After a few days of circulating, they migrate into tissues to become macrophages. Monocytes can be subdivided into classical and non-classical monocytes. In humans, an intermediate subpopulation between classical and non-classical monocytes exists, intermediate monocytes. They are often grouped together with non-classical monocytes. Increased numbers of non-classical and/or intermediate monocytes are usually associated with pro-inflammatory conditions.

Monocytes are changed during pregnancy and preeclampsia. During healthy pregnancy, monocytes are phenotypically activated, and function (i.e. cytokine production) is changed. During preeclampsia they are even further activated, with further changes in funciton. The pro-inflammatory condition of pregnancy and preeclampsia is further endorsed by the fact that during pregnancy non-classical monocytes are increased as compared with non-pregnant individuals. During preeclampsia, the numbers of non-classical monocytes are even further increased as compared with healthy pregnancy. The question arises whether the non-classical monocyte subset plays a role in the pathophysiology of preeclampsia. We tried to answer this question by using rat models for preeclampsia. Similar to human pregnancy, during rat pregnancy, monocytes are activated and increased numbers of non-classical monocytes are found. We studied 3 rat models of preeclampsia, i.e. the low dose LPS infused pregnant rat, the ATP infused pregnant rat and the pregnant rat injected with sFlt-1 adenovirus. In all 3 models of experimental preeclampsia, numbers of non-classical monocytes were increased as compared with healthy pregnant rats. Moreover, only these non-classical monocytes, but not the classical monocytes, appeared to be phenotypically activated.

Activation of monocytes, especially non-classical monocytes, may play a role in the pathophysiology of preeclampsia. These data support the view that pro-inflammatory factors produced by the stressed placenta during preeclampsia, may activate monocytes (and other immune cells) which in turn induce the full blown syndrome of preeclampsia.

PL108

Inflammatory mechanisms in preeclampsia

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Introduction: Preeclampsia is a severe complication of pregnancy characterized by an excessive maternal systemic inflammatory response.

Objectives: Our aim was to determine cellular and humoral components of the innate and adaptive immune system in normal pregnancy and preeclampsia.

Methods: In our case-control studies, we used flow cytometry, multiplex suspension array, ELISA, immunoturbidimetry and radial immunodiffusion for our measurements.

Results: High-throughput multiplex cytokine measurements demonstrate an overall pro-inflammatory systemic environment in preeclampsia with elevated amounts of pro-inflammatory cytokines, chemokines and adhesion molecules in the maternal circulation. In addition, circulating levels of positive acute phase proteins increase, whereas those of negative acute phase proteins

decrease in preeclampsia, indicating an acute phase response. The complement system is activated systematically with increased terminal complex formation, as shown by the elevated amounts of activation markers in the systemic circulation. All three complement pathways (the classical, lectin and alternative) are involved in the excessive complement activation in preeclampsia. Regulatory T cells (Tregs) play an important role in the development of pregnancy-specific immune tolerance. The frequency of conventional CD4+ CD25high FoxP3+ and non-conventional CD4+ CD25- FoxP3+ Tregs is lower in preeclampsia, suggesting inadequate induction of tolerance to paternal antigens. The prevalence of the functionally most active effector Tregs is decreased, while that of exhausted Tregs is increased in preeclampsia.The combination of lower effector Treg and higher exhausted Treg prevalence may account for the decrease in the functionality of Tregs in preeclampsia. There is a shift not only in the Th1/Th2, but also in the Th17/Treg balance favouring skewness towards a pro-inflammatory status in preeclampsia. The prevalence of IL-17-producing CD8 (Tc17) and NK cells is also elevated in this pregnancy-specific disorder.

Conclusion: Our results indicate that both the innate and adaptive arms of the immune system are involved in the development of the exaggerated maternal systemic inflammation observed in preeclampsia.

PL109

Corticosteroids in the management of severe preeclampsia: What evidence?

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Introduction: The fundamental premise that has governed the proposal relative to the use of corticosteroids for the purpose of disease modification in severe preeclampsia was that preeclampsia is a condition characterized by an inappropriate maternal systemic inflammatory response and possibly immune-mediated impairment in maternal-fetal communication, while corticosteroids have the capacity to exercise anti-inflammatory and immunosuppressive effects.

Objective: The presentation will review the evidence behind this proposal. The risks associated with such an approach, especially in fetuses manifesting growth restriction and umbilical artery absent end-diastolic flow, will also be discussed.

Methods: The literature published between 1990 and 2015 was searched for papers dealing with corticosteroids treatment for disease modification in preeclampsia and HELLP syndrome, using a combination of keywords including "HELLP syndrome", "preeclampsia", "corticosteroids" and "maternal and fetal outcomes". The MEDLINE bibliographic database yielded studies heterogeneous as methodology including retrospective analyses, randomized trials, and meta-analyses.
Published studies were assessed for quality according to Jadad's quality assessment scale.

Results: On the basis of a critical interpretation of the available literature, we argue that corticosteroids administration, either antepartum or postpartum, does not improve the outcome of pregnancies affected by severe preeclampsia.

Conclusion: Until more convincing data become available, corticosteroids for disease modification in women with preeclampsia should not be used outside the setting of an approved investigational protocol.
In antepartum HELLP syndrome, if a brief period (not to exceed 48 hours) of expectant management is elected to allow optimal exposure to corticosteroids strictly for fetal benefit, intensive surveillance of both mother and fetus is indicated.

O110

Maternal left ventricular dysfunction and remodeling in pregnancy complicated with gestational hypertension

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Introduction: During normal pregnancy, stroke volume and heart rate increase and peripherial vascular resistance (PVR) decreases. In pregnancy complicated with gestational hypertension (GH), however PVR increases and produces pressure overload on the left ventricle.
Objectives: The purpose of our study was to asses the impact of GH on left ventricular performance and structure in previously normotensive heart.
Methods: 30 pregnant females suffering from pregnancy induced hypertension in the third trimester and 30 normotensive pregnant females were enrolled. Left ventricular function was assesed using 2D echocardiography, Doppler and tissue Doppler technique. Left ventricular mass normalized on body surface (LVMI), relative wall thickness (RWT), and isovolumetric relaxation time (IVRT) was calculated. Parameters of mitral inflow (E/A, DT, E'), TDI (E/E') and pulmonary vein flow (S/D, AR, ARdur-Adur) was also assessed.
Results: In GH, IVRT was increased (92+17 ms vs 79+13 ms), E/A was lower (1,1+0,2 vs 1,6+0,3), E/E' was higher (8,2+3,1 vs 5,3+1,5) and AR was also increased (0,26+0,4, m/s vs 0,22+0,2 m/s). Women who developed GH had increased RWT (0,39+0,06 mm vs 0,32+0,05 mm) and LVMI (82+16 g/m2 vs 66+9 g/m2 $p<0,05$). There were 7 women with concentric remodeling (23%) and 2 pregnant with exncentric hypertrophy (2%). There were no significant differences in ejection fraction.
Conclusion: GH is associated with preserved left ventricular systolic function and subclinical diastolic dysfunction. Women who developed GH had increased left ventricular mass and wall thickness and had higher prevalence of left ventricular concentric remodelling compared with normotensive pregnancies.

O111

The association between maternal haemodynamics and pre-eclampsia: Systematic review and meta-analysis

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Objective: Pre-eclampsia (PE) is associated with marked maternal cardiovascular changes before its clinical onset, at the time of clinical diagnosis, and in the postpartum period.These changes vary according to the timing of onset (early vs late) or the severity (mild vs severe) of PE.The aim of this study was to perform a systematic review and meta-analysis to quantify these cardiovascular changes associated with PE.
Methods: MEDLINE, EMBASE, CINAHLand The Cochrane Library were searched, using combinations of the terms pre-eclampsia, cardiac, vascular resistance, stroke volume (SV) and pregnancy hypertension. Reference lists within relevant articles and reviews were hand-searched for additional reports. Randomised controlled trials, cohort and case-control studies were included. Studies reporting data on cardiac output (CO), cardiac index (CI), SV, systemic vascular resistance (SVR) and its index (SVRI) were included. Between-study heterogeneity was assessed using the I2 test.

Results: The search yielded 1943 citations, of which 56 studies were included in the review. A significant increase in SVR (weighted mean difference [WMD] 446.42, $p<0.001$) and SVRI (WMD 923.34, $p<0.001$) and a decrease in the CI (WMD -0.54, $p<0.001$) were observed in women with PE compared with women with normotensive pregnancies. SVR was significantly higher (WMD 866, $p<0.001$) while the SV was significantly lower (WMD -2.6, $p<0.001$) in early-onset compared to late-onset PE. Screening studies have reported significantly higher SV in the first trimester in pregnancies that later developed PE compared to those which remained normotensive (WMD 1195, $p<0.001$). Both the heart rate (WMD 5.87, $p=0.002$) and SVR (WMD 317.33, $p=0.004$) were significantly lower, while the SV (WMD -9.00, $p=0.002$) was significantly higher after the incident pregnancy (postpartum), when complicated by PE.
Conclusion: Women who develop PE have significantly elevated SVR, both at the time of the clinical diagnosis and postpartum. SV may also be useful in first trimester screening for PE. However, changes in CO were not significantly different in PE before its clinical onset, at the time of diagnosis, or postpartum.

O112

Inotropy index and ratio of potential to kinetic energy: Two novel parameters derived from continuous-wave Doppler ultrasound

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Objective: In pregnancies complicated by hypertension, antihypertensive therapy should be tailored to the type of hypertension, whether cardiogenic or vasogenic. However, current clinical assessment does not allow this differentiation. Inotropy is a measure of the myocardial contractility, while the ratio of potential to kinetic energy (PKR) is a measure of arterial impedance. In a recent report, both Smith-Madigan inotropy index (SMII) and PKR could be derived from a continuous-wave Doppler ultrasound technique. The aim of this study was to investigate these two novel cardiovascular parameters in pregnancies complicated by hypertensive disorders compared to uncomplicated pregnancies.
Methods: This was a prospective case-control study including a group of women presenting with hypertension in the second half of the pregnancy and a group of uncomplicated pregnancies recruited after 20 weeks' gestation. Cardiovascular parameters were assessed using a continuous-wave Doppler ultrasound technique (USCOM®). Pregnancies were followed up and the outcome ascertained. Mann-Whitney test and regression analysis were used for statistical analysis.
Results: We recruited 94 women with hypertensive disorders in pregnancy and 106 controls. Compared to normotensive controls, the cases had significantly higher SMII (median 1.96W/m2, IQR 1.64-2.40 vs 1.75W/m2, IQR 1.47-2.03, $p<0.001$), higher PKR (median 26.27, IQR 19.0-37.07 vs 20.94, IQR 15.69-27.73, $p<0.001$), higher systemic vascular resistance index (median 2622dynes-sec/cm5/m2, IQR 2170-3023 vs 1877dynes-sec/cm5/m2, IQR 1561-2233, $p<0.001$), but significantly lower cardiac index (median 3.34L/min/m2, IQR 2.97-4.0 vs 3.72 L/min/m2, IQR 3.17-4.40, $p=0.003$).
Conclusion: Women presenting with hypertensive disorders in pregnancy demonstrate significant changes in cardiac contractility and dynamic arterial impedance. It remains to be established whether these indices may be used prospectively for the individualized triage and management of these pregnancies.

O113

Measurements of arterial stiffness and uterine artery Doppler for the prediction of preeclampsia in women presenting with gestational hypertension

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Objective: While gestational hypertension (GH) and chronic hypertension are usually benign, pre-eclampsia (PE) is more commonly associated with adverse maternal and fetal outcomes. About 15-25% of women initially diagnosed with GH will develop PE, but only 10% of women who develop GH after 36 weeks of gestation will develop PE. Pulse wave velocity (PWV) and augmentation index (AIx) are markers of arterial stiffness and endothelial dysfunction, while uterine artery Doppler pulsatility index (UtA PI) reflects the resistance in the uteroplacental circulation. These parameters have been shown to be associated with the risk of PE. The main aim of this study was to investigate whether maternal cardiovascular changes can discriminate pregnancies which will subsequently develop PE among those presenting with GH.
Methods: This was a prospective cohort study in women with singleton pregnancies presenting with GH at St George's Hospital (n=112). Another group of uncomplicated singleton pregnancies were recruited as controls. PWV, AIx and aortic systolic blood pressure (SBPAo) were recorded using the Arteriograph® (TensionMed Ltd., Budapest, Hungary). The uterine artery Doppler was recorded on both sides and the mean PI was calculated. Mann-Whitney and Chi-Square tests were used to compare the groups, while regression analysis was used to identify and adjust for potential confounders. The predictive accuracy for the development of PE was assessed using the ROC curve analysis.
Results: The analysis included 105 pregnancies with GH and 356 controls. Compared to the group that remained as GH (n=82), the group that developed PE (n=23) had significantly higher AIx (25.9%, IQR 12.8-34.3 vs 15.8%, IQR 6.1-25.6; p=0.019) and SBPAo (141 mmHg, IQR 130-158 vs 130 mmHg, IQR123-142; p=0.005) at the initial assessment. They also had significantly higher UtA mean PI at 20-24 weeks (1.10, IQR 0.78-1.47 vs 0.83, IQR 0.68-1.04;p=0.008). AIx was significantly associated with the risk of development of PE (odds ratio 1.05; 95% CI 1.01-1.09, p=0.016). For a cut-off of 31.18%, AIx had sensitivity of 41.2% (95% CI 18.4-67.1%) and specificity of 93.2% (95% CI 83.5-98.1%) and LR 6.07 (AUC 0.69; 95% CI 0.53-0.84, p=0.019).
Conclusion: Arterial stiffness and SBPAo measured at the initial assessment of GH can potentially discriminate the pregnancies that will develop PE. Identification of women who will develop PE among those who initially present with PIH is likely to facilitate targeted antenatal surveillance and possibly intervention.

O114

Maternal cardiovascular changes in pregnancies complicated by small for gestational age neonate with or without maternal hypertension

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Objective: The literature describing the maternal cardiovascular changes in pregnancies complicated by fetal growth restriction and maternal hypertension is limited, conflicting and does not discriminate the two pathologies. The aim of this study was to investigate maternal cardiovascular changes in pregnancies complicated by small for gestational age (SGA) neonates with or without maternal hypertension.

Methods: This was a prospective case-control study including pregnancies resulted in SGA neonate (n=159) and a group of uncomplicated pregnancies (n=473), recruited after 20 weeks' gestation. The SGA group was further divided according to fetal Doppler to define fetal growth restriction (FGR; n=51) and maternal hypertension (n=51). FGR was defined as estimated fetal weight below the 10th centile with abnormal umbilical artery Doppler (pulsatility index [PI] above the 90th centile or absent or reversed end-diastolic flow). Maternal cardiac output (CO), cardiac index (CI), systemic vascular resistance (SVR), systemic vascular resistance index (SVRI) were recorded using the USCOM®, while the augmentation index (AIx) was assessed using the Arteriograph®.Uterine artery (UtA) mean PI was assessed at the same visit. Mann-Whitney test and regression analysis were used for statistical analysis.
Results: Compared to controls, the SGA pregnancies had significantly lower CO (median 6.08L/min, IQR 5.31-6.86 vs 6.65L/min, IQR 5.68-7.79, p=0.006), but significantly higher SVR (median 1091 dynes-sec/cm5, IQR 998-1359 vs 1040 dynes-sec/cm5, IQR 878-1263, p=0.008). Both AIx and UtA mean PI were significantly higher in the SGA pregnancies compared to controls (p=0.002 and p<0.001, respectively). In normotensive SGA, the results were similar (p<0.05). However, after correcting for body surface area, neither cardiac index nor SVR index were significantly different between the two study groups (p=0.209 and p=0.139, respectively). In normotensive FGR pregnancies, SVR, AIx and UtA mean PI were significantly higher (p<0.01 for all), while CO was not significantly different (p=0.429).
Conclusion: FGR is associated with maternal cardiovascular changes. The conflicting results reported by previous studies could be explained by failure to correct for maternal body surface area, incorrectly labelling SGA pregnancies as FGR, or lack of distinction between FGR with or without maternal hypertension.

O115

First trimester maternal vascular function is associated with fetal growth

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Introduction: It has been suggested that preeclampsia (PE) and intrauterine growth restriction arise from a maternal predisposition to endothelial dysfunction existing already before the pregnancy, and this contributes to an impaired placental implantation. The first trimester thus represents an interesting time window for research on the early mechanisms that influence fetal growth and the development of PE.
Objective: To investigate the relationship between first trimester endothelial function , assessed both in the brachial artery and in the forearm skin microcirculation, and fetal growth.
Methods: Vascular function was assessed in 58 pregnant women during gestational week 11-14. Vascular reactivity in the in the brachial artery was evaluated by post-ischemic hyperaemia induced flow mediated vasodilatation (FMD) and by administration of sublingual glyceryl trinatrate (GTN). Forearm skin microcirculation was investigated by laser Doppler perfusion imaging during iontophoresis of acetylcholine (Ach) and sodium nitroprusside (SNP) to assess endothelium-

dependent and endothelium-independent microvascular vasodilatation, respectively. Fetal growth during pregnancy was measured in each trimester and birth weight centile was calculated.
Results: FMD and GTN was associated with birth weight centile. By multivariate analysis (adjusted for brachial artery diameter at rest, blood pressure, age and heart rate), β was 1.7 (95% CI 0.06–3.34), r2 = 0.26, p = 0.043 for FMD. For GTN, β was 2.6 (95% CI 0.44–4.68) r2 = 0.15, p = 0.020. Endothelium-dependent and independent microvascular reactivity was also associated with birth weight centile: β for Ach = 7.8 (95% CI 1.8-13.8) r2 = 0.12 p = 0.029 and β for SNP = 6.2 (95%CI 1.2 – 11.3) r2 0.11 p = 0.016 respectively. These significant associations for FMD and ACh to birth weight centile were no longer retained when adjusted for responses to GTN and SNP, respectively.
Conclusion: Fetal growth is associated with first trimester maternal vascular dilative capacity, rather than to endothelial function specifically. These findings were consistent in, both in the brachial artery and the forearm skin microcirculation.

O116

Can maternal haemodynamics predict hypertensive disorders in pregnancy?

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Pre-eclampsia (PE), a major cause of maternal and fetal complications, is associated with maternal cardiovascular changes. Increased arterial stiffness is demonstrated firstly in women with clinically established PE; secondly, several months after delivery in women who had PE in pregnancy; thirdly, in healthy non-pregnant individuals who subsequently develop cardiovascular disease; and fourthly, in hypertensive patients at increased risk of death from cardiovascular disease. Our studies have shown that these changes are detected as early as 11 weeks' gestation. Itis therefore likely that the abnormal cardiovascular findings in early pregnancy in women who subsequently develop PE may predate conception. This is known for patients with chronic hypertension but, as demonstrated in our studies, may also be true for women who are normotensive at the start of pregnancy. Current obstetric practice relies on the measurement of peripheral blood pressure. However, central haemodynamics could be more valuable in understanding cardiovascular pathophysiology and have been shown to relate more strongly to vascular hypertrophy, extent of atherosclerosis, and cardiovascular events than does brachial blood pressure.
The effectiveness of screening for PE by maternal haemodynamics is unrelated to the gestational age at delivery. In contrast, abnormal uterine artery Doppler and reduced serum pregnancy associated plasma protein (PAPP-A), reflecting impaired placentation, are more marked in those developing early rather than late-PE. This is compatible with the concept that PE may be the common phenotypic expression of two distinct processes: one based on a predisposition for cardiovascular disease that under the physiological stress of pregnancy manifests as either early- or late-PE, and another that results in early-PE due to impaired trophoblastic invasion of the maternal spiral arteries.
Recent evidence suggests that the prophylactic use of low-dose aspirin from early pregnancy can potentially halve the rate of PE. In the UK, The National Institute for Health and Clinical Excellence (NICE) recommends that all women should be routinely screened in the first trimester for their risk of PE based on maternal characteristics and previous history, and those at high-risk should be treated with aspirin.The detection rate of PE is improved by combining maternal factors with the vascular parameters at 11-13 weeks' gestation. The extent to which such combined testing, undertaken before conception (allowing for earlier administration of aspirin), could result in further reduction in the prevalence of PE is the subject of future studies.

O117

Role of some biomarkers in long term cardiovascular prognosis of pregnancy hypertensive disease.

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Introduction: There is a growing evidence that preeclampsia (PE) is a risk factor for development of cardiovascular disease even before the menopause. Stratification of risk can be based not only in haemodynamic and anthropometric parameters, but also in intermediate phenotypes and functional genetic polimorphisms of pathogenic pathways in hypertension.
Objectives: to study the modulation, of some distant and intermediate phenotypes associated with hypertension in women with history of previous PE, by some genetic functional polimorphisms of pathways involved in the pathogenesis of those diseases.
Methods: A prospective study was done in a sample of 138 women (35.2±5.48 years old), 90 of those presented PE 2 to 16 years ago. We evaluated demographic, anthropometric, haemodynamic and biochemical parameters: hsCRP, liver function tests, lipid profile, nitrites, nitrates and myeloperoxidase. Functional polymorphisms of some genes belonging to those pathways were determined by molecular biology techniques (PCR, PCR-RFLP). Statistical analyses were performed by parametric or non-parametric tests when apropriate. Results: Hypertension develops significanty ($p<0,001$) in 47,7% of women with history of PE compared with only 10.3% hypertensive women that didn`t have previous PE. Only some of the genotype carriers of those studied genes presents already alterations in those parameters in normotensive women with history of previous PE compared with those without PE.
Conclusions: Some potential biomarkers including the genetic ones at different biological levels, of risk for the development of future cardiovascular diseases can be identified in women with previous PE.

O118

Subsequent preeclampsia is associated with worse subclinical left ventricular dysfunction

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Introduction: Preeclampsia is associated with cardiac dysfunction and long-term cardiovascular disease. A novel echocardiography technique measuring cardiac strain using speckle tracking myocardial deformation is closely related to the functional state of the myocardium and is more sensitive in the early detection of subtle left ventricular changes.
Objective: Evaluate cardiac structure and function using novel echo assessment in preeclampsia
Methods: We evaluated 14 preeclampsia women, 5 of whom had previous preeclampsia, aged 29±5, BMI 37±12 at 36.1±2.2 weeks of gestation within 1 week diagnosis of new onset hypertension (>140/90mmHg) and proteinuria (spot urine protein/creatine ratio >30mg/mmol). 20 women with uncomplicated pregnancy were matched for age, BMI and gestation. Echocardiography of

left ventricular mass index, ejection fraction and global longitudinal strain were assessed. Statistical analysis included Student's t-test and one-way ANOVA.
Results: There was a significantly higher left ventricular mass index in women with preeclampsia (97.52±14.51g/m2 vs. 82.61±13.21g/m2) (p=0.02). Conventional echo assessment of ejection fraction using Simpson biplane was not different between control and preeclampsia. However global longitudinal strain was significantly reduced in preeclampsia group (-17±2.69 vs. -20.2± 1.49)(p=0.0004). Preeclampsia women with history of preeclampsia was associated with further impairment of global longitudinal strain (one-way ANOVA, $p<0.05$).
Conclusion: Our data confirm previous studies that preeclampsia is associated with subclinical left ventricular dysfunction measured by speckle tracking. In addition, we have demonstrated that this deterioration is incrementally worse with subsequent preeclampsia events. These preliminary findings will be explored further both in pregnancy and the postpartum period.

O119

Cardiovascular risk management after reproductive and pregnancy related disorders: A Dutch multidisciplinary evidence-based guideline

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Introduction: In the past decades evidence has accumulated that women with reproductive and pregnancy related disorders are at increased risk of developing cardiovascular disease (CVD) in the future. Up to now there is no standardized follow-up of these women since guidelines on cardiovascular risk management for this group are lacking. However, early identification of high-risk populations followed by prevention and treatment of CVD risk factors, has the potential to reduce CVD incidence.
Objective: The Dutch Society of Obstetrics and Gynaecology initiated a multidisciplinary working group (gynecologists, cardiologist, vascular internist, radiologist, general practitioner, epidemiologist and representatives of patient associations) to develop a guideline for cardiovascular risk management after reproductive and pregnancy related disorders.
Methods: The guideline was developed using the "Appraisal of Guidelines for Research and Evaluation" instrument. The guideline addresses the cardiovascular risk consequences of gestational hypertension, preeclampsia, preterm delivery, small-for-gestational-age infant, recurrent miscarriage, polycystic ovary syndrome and premature ovarian insufficiency. The best available evidence on these topics was gathered by systematic review and the relation between the reproductive or pregnancy related disorders and CVD risk and risk factors was assessed by meta-analysis. Recommendations for clinical practice were formulated based on the number and quality of the studies and presence or absence of a relative risk >2 of developing CVD events and/or risk factors from the meta-analysis. The Dutch societies of gynaecologists, cardiologists, vascular internists, radiologists, and general practitioners endorsed the guideline to ensure support for implementation in clinical practice.
Results: For all reproductive and pregnancy related disorders only a moderate increased relative risk (<2) was found for overall CVD, except for preeclampsia (relative risk 2.15, 95% CI 1.76-

2.61). Based on the current available evidence, follow-up is only recommended for women with a history of preeclampsia. A cardiovascular risk profile should be offered at the age of 50 years. Assessment of CVD risk and treatment of cardiovascular risk factors should be performed according to the Dutch guideline for cardiovascular risk management. For all reproductive and pregnancy related disorders optimization of modifiable cardiovascular risk factors is recommended to reduce the risk of future CVD.
Conclusion: In this guideline we present the recommendations for cardiovascular risk management after reproductive and pregnancy related disorders. To the best of our knowledge we are the first to make such recommendations in a national guideline.

O120

Increased myeloperoxidase is a cardiovascular risk biomarker in women with previous preeclampsia

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Introduction: There is growing evidence showing that women who have had preeclampsia have an increased risk of developing cardiovascular disease (CVD). Various groups have proposed increased levels of the vasoconstrictor, Endothelin-1 (ET-1), in the pathophysiology of preeclampsia via increased angiotensin II and reactive oxygen species (ROS) through mechanisms that remain unresolved. Myeloperoxidase (MPO) is an enzyme that catalyzes ROS formation and is a critical factor of the innate immune responses that may contribute to tissue damage during inflammation. Indeed, increased MPO levels predict the risk of CVD and are proposed as a target for therapeutic intervention. MPO is secreted from azurophilic granules in activated leukocytes and participates in respiratory burst responses. However the relationship between MPO, leukocytes and ET-1 levels in women that had preeclampsia in the past is unclear.
Objectives: To evaluate the effect of activation of ex vivo human leukocytes with ET-1 on MPO production and its genotype-phenotype relationship in women that had preeclampsia.
Methods: We studied 150 women, aged 35.1±5.5 years [60 (40%)] that had normal blood pressure during pregnancy (NBPP) and compared them to women [90 (60 %)] that had preeclampsia (PE) 2 to 16 years ago and measured HS-C-reactive protein (CRP) and MPO levels.
Results: Our results show dose-dependent increases of MPO from ex vivo human leukocytes treated with either endothelin-1 or angiotensin II via activation of endothelin-1 or angiotensin II receptors, respectively. Consistent with these data, we observed higher circulating MPO levels in PE when compared with NBPP women ($n=55$; $P < 0.04$) that were associated with increased HS-CRP levels in a cohort of our subjects. We then determined the genetic variants of the MPO gene by PCR-RFLP in a larger sample size and observed that PE was associated with increased MPO risk genotype (GG) ($n= 71$; $P < 0.02$).
Conclusion: Our results suggest that in PE, activated leukocytes and genetic variants of MPO contribute to increased MPO levels. Thus MPO measures may serve to improve CVD risk stratification among women that had PE.

O121

Maternal metabolic outcomes in women with a history of hypertensive pregnancy disorders

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Introduction: Women with preeclampsia or pregnancy induced hypertension (PIH) show metabolic aberrations during pregnancy similar to the metabolic syndrome. These women also are at increased risk of cardiovascular disease later in life.

Objective: To assess whether women with preeclampsia or PIH have more unfavorable metabolic outcomes six years after pregnancy compared to normotensive women.

Methods: This study was embedded in the Generation R study, a population-based prospective cohort study. Information on pregnancy and metabolic outcomes six years after pregnancy was available in 4933 women. We measured total body and abdominal fat distribution, weight and plasma lipid concentrations (total cholesterol, LDL-c, HDL-c, triglycerides, Apolipoprotein-B (Apo-B), lipoprotein (a) (lp-a)).

Results: Compared with normotensive women, women with PIH had higher Apo-B (0.05g/l; 95%CI 0.02, 0.08), LDL-c (0.13mmol/l; 95%CI 0.04, 0.22), triglyceride (0.11mmol/l; 95%CI 0.01, 0.21) and total cholesterol concentrations (0.15mmol/l; 95%CI 0.02, 0.29) and lower HDL-c concentrations (-0.06mmol/l; 95%CI -0.11, -0.01). No differences were observed in lipid concentrations between normotensive and preeclamptic women.

Women with PIH or preeclampsia both had higher body fat percentages (0.03%; 95%CI 0.02, 0.04 and 0.02%; 0.00, 0.04), higher BMI (3.6kg/m2; 95%CI 2.9, 4.2 and 2.4kg/m2; 1.4, 3.4, respectively) and increased risk of clustering of metabolic risk factors (OR 2.2; 95%CI 1.4, 3.3 and OR 2.3; 95%CI 1.3, 4.3, respectively) compared with normotensive women. These associations attenuated after adjustment for maternal weight gain after pregnancy. Early pregnancy weight seems to be a predictor for these unfavorable outcomes (figure 1).

Conclusion: Hypertensive pregnancy disorders, especially PIH, were associated with adverse metabolic outcomes and an increased risk of clustering of metabolic risk factors six years after pregnancy compared to normotensive women. We therefore advise to perform regular metabolic check-up on these women after delivery.

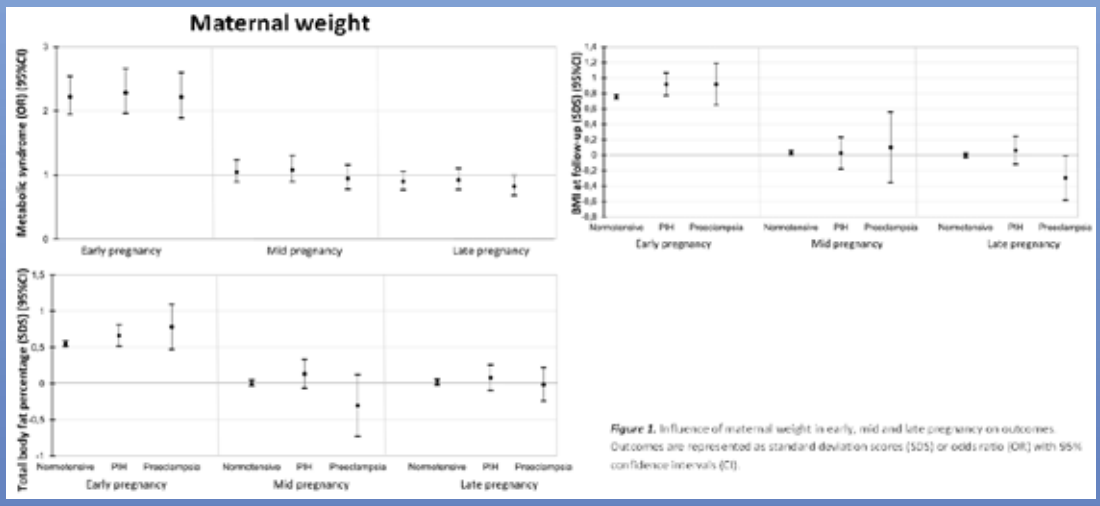

Figure 1. Influence of maternal weight in early, mid and late pregnancy on outcomes. Outcomes are represented as standard deviation scores (SDS) or odds ratio (OR) with 95% confidence intervals (CI).

O122

The role of framing in modifying behavior to reduce cardiovascular risk after preeclampsia, a vignette study

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Introduction: Observational studies have consistently described that women with a history of hypertension in pregnancy have a markedly increased risk of cardiovascular disease (CVD)later in life. Pregnancy is suggested as a "stress test" that identifies women who are at risk for developing clinical cardiovascular disease in later life. This opens up the opportunity for preventive measures at a relatively young age. Helping women to address their cardiovascular risk by modifying lifestyle has proven difficult. Motivation to change behaviour is crucial for effective interventions. Research on promoting healthy lifestyle has demonstrated that even subtle differences in message framing can affect (intentions to improve) health-related behavior. So, framing risk information could be effective in motivating these women too. Perceived probability of developing a disease appears to be another important factor influencing people's motivation to modify behavior.
Objectives: Investigating the impact of framing information as a health score versus a risk score and the impact of high versus low probability of developing CVD on the willingness to modify behavior after preeclampsia.
Methods: Obstetric nurses (n=165) were invited to participate in a questionnaire containing two hypothetical scenarios, a case with mild preeclampsia and a case with severe preeclampsia.Scores of their willingness to modify behaviour were analysed on a Likert scale by ANOVA.
Results: We found no significant effect of framing F(3,287)= 1.932, p 0.166. A significant main effect was found of the severity of the case (F (3,287)= 11.12, p 0.001) and a non-significant interaction between severity and framing on the willingness to modify behavior (F(3,287)= 0.592, p 0.442).
Conclusions: Framing information in health or risk score and its interaction with probability is not of influence in motivating women to modify their lifestyle to decrease cardiovascular risk after preeclampsia. Framing in health or risk score does not seem to be contributing in clinical practice. Those who are presented with a higher risk are more motivated to change their lifestyle.

O123

Hypertensive disorders of pregnancy and subsequent risk of cancer – A population-based cohort study

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Introduction: Women with preeclampsia often have higher levels of anti-angiogenic factors than women with normotensive pregnancies. Since angiogenesis is necessary for solid cancer growth and spread, women with a history of preeclampsia may have a reduced risk of solid cancers.

Objectives: To investigate the association between hypertensive disorders of pregnancy (HDP: preeclampsia and gestational hypertension) and later risks of solid and non-solid cancers.
Methods: We applied Cox regression to Danish health register data and estimated hazard ratios (HRs) for solid and non-solid cancers, comparing women with and without a history of HDP.
Results: In a cohort of 1.08 million women with ≥1 birth in 1978-2011, 68,236 women had ≥1 pregnancy complicated by HDP; during follow-up, 42,236 and 1,899 women developed solid and non-solid cancers, respectively. A history of HDP was not associated with the rate of solid cancer (HR 0.96, 95% confidence interval [CI] 0.92-1.00), regardless of HDP severity, nor was it associated with delayed solid cancer onset. Interestingly, prior HDP were modestly associated with the rate of non-solid cancer (HR 1.21, 95% CI 1.02-1.45). In analyses of specific cancer subtypes, prior HDP were associated with reduced rates of breast (HR 0.89, 95% CI 0.83-0.95) and lung cancer (HR 0.66, 95% CI 0.54-0.79) and increased rates of leukemia (HR 1.43, 95% CI 1.12-1.83), endometrial (HR 1.62, 95% CI 1.33-1.97) and urinary tract cancer (HR 1.42, 95% CI 1.09-1.97).
Conclusion: Prior HDP were not associated with overall solid cancer risk, suggesting that observed associations with specific cancer subtypes are probably not explained by an angiogenic imbalance.

O124

Preeclampsia: Two different clinical phenotypes – Two different pregnancy outcomes

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Introduction: Preeclampsia (PE) affects 3-5% of all pregnancies. Recently PE may be better segregated into two distinct phenotypes, with differing etiologies and manifestions and different impact on pregnancy outcome.
Objectives: To use modern multidisciplinary approach for proving evidence of early and late onset PE.
Methods: 200 pregnant women were divided into 3 groups: I – 50 women with early onset PE, II – 50 with late PE and 100 women - as control. Samples of placental bed were obtained during CS after prior patient's informed consent. Urine samples, placental tissue were also analysed. Clinical, morphological, immunohistochemical, molecular methods were used for systemic analysis of PE's pathogenesis. Mitochondrial morphology in thin vital slices of placenta and in trophoblast cells and systemic biology approach for detecting peptidomic candidate predictors for early and late onset PE were used.
Results: Women in group I delivered at 33,1±2,3 wks, in group II at 38,1±1,0 wks ($p<0.01$). Women with early PE were younger and had lower BMI values compared to those with late PE (27.2 ± 2.2 yrs vs 33.4 ± 2.5 yrs, $P<0.01$; BMI 26.7 ± 1.3 vs 34.1 ± 1.1 kg/m2, $p<0.01$) and control. Re-PE had 22% and 10%, IUGR occurred in 68% and 22%, respectively ($p<0.01$). 28% of young primigravidas with early PE conceived within 6 months after marriage. Birth weight was significantly lower for early PE ($p<0,01$). Placental bed disorders (CKW+ cell's in placental bed tissue, Vimentin+ elements in endometrium, CD34+ in vessels, percentage of nonremodeled spiral arteries, expression of SMA, HIF-1, VEGF, VEGFR, miR-34A) were pronounced and mitochondrial fragmentation in trophoblast cells expressed in group I ($p<0.05$).
Conclusion: Our results confirm that PE should no longer be considered as a single disease. Pathophysiologic mechanisms are likely to contribute differently to the development of early vs late PE. We have identified more profound disturbances in the area of placentation and in trophoblast cells in early PE. These changes that have led to deficient physiologic vessel transformation are likely to be immunohistochemical markers of spiral arteries remodeling and endothelial dysfunction. Besidesthe level of mtDNA may serve as a marker of compensatory mechanism in PE. miR-34A is dysregulated in early-onset PE and could possibly play a role in trophoblast invasion. The further researches on the onset of PE will promote development of the pathogenetic basis for prediction, early diagnosis, and adequate treatment .

O125

Ethnicity: An independent risk factor for adverse perinatal outcome in women with chronic hypertension

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Introduction: Ethnic variation in incidence of adverse perinatal outcomes has been previously described, but similar data from pregnancies exclusively in women with chronic hypertension are limited.

Objectives: To perform a retrospective cohort study of pregnant women with chronic hypertension to assess the impact of ethnicity as an independent risk factor on adverse perinatal outcome.

Method: Demographic and delivery data of women with chronic hypertension and singleton pregnancies from two tertiary obstetric units between 2000 and 2015 were extracted from maternity databases. Women were allocated to one of four groups of ethnicity (aligned to those used by the UK Office for National Statistics) for analysis: White, Black, Asian and other. Risk ratios and risk differences were calculated by generalised linear models, with a log or linear link respectively, together with risk ratios adjusted for baseline characteristics (maternal age, parity, body mass index, smoking); the statistical package Stata version 1.3 (StataCorp, College Station, Texas) was used.

Results: 4713 singleton pregnancies in women with chronic hypertension were included. All adverse perinatal outcomes occurred more frequently in Black women compared to White women (Table, showing percentages and adjusted risk ratios with 95% confidence intervals using White women as the referent category). Asian women also were at increased risk, though to a lesser extent.

	White n=2146	Black n=1631	Asian n=341
Stillbirth	0.5%	3.7% 7.11 (2.30 to 13.8)	1.7% 3.48 (1.28 to 9.47)
SGA-10th centile	18.4%	31.0% 1.72 (1.53 to 1.95)	20.8% 1.18 (0.94 to 1.49)
SGA-3rd centile	7.3%	16.3% 2.22 (1.83 to 2.70)	11.8% 1.68 (1.21 to 2.34)
LGA-90th centile	7.4%	6.5% 0.82 (0.64 to 1.05)	10.4% 1.35 (0.95 to 1.93)
Preterm birth <37 weeks	9.6%	20.3% 2.11 (1.78 to 2.49)	16.7% 1.87 (1.42 to 2.44)
Preterm birth <34 weeks	3.3%	10.4% 3.28 (2.47 to 4.35)	6.6% 2.26 (1.42 to 3.58)
Pre-eclampsia	14.2%	17.5% 1.28 (1.09 to 1.49)	17.3% 1.31 (1.01 to 1.69)

Conclusion: Black women with chronic hypertension are at markedly increased risk of many adverse perinatal outcomes compared to White women, with features of placental disease. Further research is needed to explore the pathophysiology underpinning these disparities in outcome. Ethnic differences in incidence of chronic hypertension and response to antihypertensive agents in non-pregnant individuals exist. Antihypertensive treatments prescribed in pregnancy may need to account for ethnic variation in response to therapy and an awareness of these potential differences should inform stratification of antenatal care pathways.

O126

Postnatal neurological development follow-up of newborns from pregnancies with hypertension associated intrauterine growth restriction (IUGR)

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Introduction: Postnatal neurological deficiencies are among the most important late complications of intrauterine growth restriction (IUGR).
Objective: The aim of our study is the neuropsychological follow-up of newborns with intrauterine growth restriction from pregnancies that were associated with hypertension, which enables the analysis of the results in light of clinical data.
Methods: In the study we involved newborns with intrauterine growth restriction who were born from pregnancies with hypertension between 2006 and 2009 (n=37). Another study group was formed of pregnancies, where in addition to hypertension eutrophic fetal development was confirmed (n=28). Physiological pregnancies, with normal blood pressure of the expectant where eutrophic fetal development was observed, belonged to the control group (n=35). During the neuropsychological follow-up KQ (sensomotoric coordination quotient), BQ (speech development quotient) and SQ (sociability quotient) quotients have been identified from which an aggregate FQ (developmental quotient) was calculated.
Results: The Apgar values and the FQ1 and FQ2 values measured later in relation to newborns with IUGR, showed no significant correlation with each other, however a highly significant relationship was proven between the Apgar scores and the Binet-IQ score; both the 1 and the 5 minute higher values were associated with the Binet-IQ higher values (p=0,007). Statistically significant correlation was found between the length of the treatment at the neonatal intensive care of retarded newborns and the FQ1 and FQ2 values (p=0,032). Statistically significant relationship was not verifiable between the FQ1, FQ2 and Binet-IQ values of the children involved in the study and the flowmetrial test results during pregnancy. Significant relationship between the onset condition of high blood pressure during pregnancy and postnatal FQ1, FQ2 and Binet-IQ values were not justified neither in the test nor in the control group.
Conclusions: The neurological development follow-up confirmed that the severity of the disease is not a relevant factor in terms of the development of most of the early postnatal neurological functions however, the development of speech and coordination related to posture is significantly affected by intrauterine atrophy. The „catch-up growth" that occurs in the first year of life of a newborn with intrauterine growth restriction contributes to as little operational decline of neurological functions as possible. This is supported by the fact that the length of the after birth neonatal intensive treatment in the first three years of the postnatal period shows a significant relation to the FQ1 and FQ2 values, however similar statistical relationship cannot be established with the Binet-score at 36 to 54 months of age. The significant correlation between the postpartum 5 and 10 minute Apgar score and the Binet IQ suggests that the nervous system development in newborns with IUGR is closely related to the conditions during labor.

O127

Low levels of plasma protein S, protein C and coagulation factor XII during early pregnancy and adverse pregnancy outcome

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Objectives: A meta-analysis has revealed that women with pre-eclampsia/ eclampsia are more likely to have protein S (PS) deficiency and protein C (PC) deficiency, whereas another study has found no association between pre-eclampsia/ eclampsia and PS or PC deficiency. Coagulation factor XII (FXII) is involved in the initiation of the intrinsic coagulation pathway, fibrinolysis, bradykinin production, and the complement system. FXII deficiency causes a defect in fibrinolysis activation resulting in abnormal hemostasis. Many cases of VTE in FXII deficiency have been reported, but it remains unclear whether FXII deficiency is associated with an increased risk of thrombosis, and little is known about an association between FXII deficiency and adverse pregnancy outcomes.The aim of this cohort study was to evaluate whether low levels of plasma protein S (PS) activity, free PS, protein C (PC) activity and coagulation factor XII (FXII) during early pregnancy were related to adverse pregnancy outcomes.

Methods: The institutional ethics board approved this study. Peripheral blood samples were obtained at 8–14 gestational weeks (GW) from a consecutive series of 1,220 women with informed consent. The levels of plasma PS activity, free PS, PC activity, and FXII were measured. Cut-off values were defined as <1st, <5th, and <10th percentiles of values obtained from 933 women whose pregnancies ended in normal deliveries without complications. The low levels of plasma PS, free PS, PC and FXII during early pregnancy were evaluated for risks of adverse pregnancy outcomes occurring subsequently.

Results: PS activity of <10th percentile yielded risks of pregnancy-induced hypertension (PIH) and severe PIH, while free PS level of <5th percentile yielded a risk of pre-eclampsia. FXII level of <1st percentile yielded a risk of premature delivery (PD) at <34 GW. None was associated with PD at <37 GW, fetal growth restriction or fetal loss. A multivariate analysis demonstrated that PS activity of <10th percentile (odds ratio 5.9, 95% CI 1.7-18.1) and body mass index (BMI) ≥ 25 kg/m2 (4.3, 1.1-13.3) were independent risk factors for severe PIH. Similarly, free PS level of <5th percentile (4.4, 1.0-14.3) and BMI ≥ 25 kg/m2 (4.0, 1.3-10.9) were independent risk factors for pre-eclampsia.

Conclusion: Women with low levels of plasma PS activity and free PS during early pregnancy might have increased risks of PIH, severe PIH or pre-eclampsia. Women with low FXII level might have an increased risk of PD at <34 GW.

O128

Placental vascularization indices and uterine artery peak systolic velocity in pregnancy hypertension

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Introduction: Hypertension during pregnancy affects about 6-9% of pregnant women, it is a leading cause of maternal and fetal morbidity and mortality, and remarkable portion of pregnancy hypertension cases are accompanied by gestational diabetes (GDM). There is a great effort worldwide on reaching greater effectiveness in prediction and prevention in these pathologycal pregnancies.

Objectives: The aim of the study was to analyze placental vascularization, uterine artery peak systolic velocity (PSV), placental volume and pre-gestational BMI for the better prediction rate of adverse pregnancy outcomes in pregnant women with essential hypertension (EH), EH associated with gestational diabetes (EH+GDM), pregnancy induced hypertension (PIH), and PIH associated with gestational diabetes (PIH+GDM) compared to a normal blood pressure (NBP) group.

Methods: We measured placental 3-dimensional power Doppler indices, such as vascularization index (VI), flow index (FI) and vascularization flow index (VFI), and uterine artery PSV in pregnancies complicated with EH (N=51), EH+GDM (N=13) PIH (N=57) and PIH+GDM (N=23), and compared these to pregnancies with NBP (N=146) with the help of 3-dimensional analysing VOCAL program. We analyzed the correlation between the above mentioned indices, volume of the placenta, pre-gestational BMI, and gestational age.

Results: VI and VFI were significantly higher in pregnancies with EH (VI:13.27%±9.77; VFI:5.94±4.99(mean±SD)) and significantly lower in pregnancies with PIH (VI:7.75%±6.50; VFI:3.00±2.3(mean±SD)) than in pregnancies with NBP (VI:10.18%±6.16; VFI:5±3.49(mean±SD)) ($p<0.01$). FI was significantly lower in EH (FI:41.50±7.74) and PIH (FI:38.90±9.59) as well compared to NBP (FI:45.89±8.39) ($p<0.01$). Although FI was higher in EH than in PIH but the difference we found was not significant ($p>0.01$).

FI (31.35±12.48) and VFI (1.87±1.20) were significantly ($p<0.01$) lower in the PIH+GDM group compared to the PIH group, although we did not find a signifiant difference in VI (9.52±6.30) ($p>0.01$). VI (4.13±2.77) and VFI (1.70±1.31) were significantly ($p<0.01$) lower in the EH+GDM group compared to the EH group, although we did not find a signifiant difference in FI (39.91±5.27) ($p>0.01$)

PSV was significantly higher in PIH+GDM (66.01cm/s±26.03) compared to PIH (56.27cm/s±26.56) ($p<0.01$), and it was also significantly higher in EH+GDM (60.48cm/s±26.22) compared to EH (49.20cm/s±16.03) group ($p<0.01$).

The placental volume was smaller (z-score:-1.5) in EH and PIH than in NBP and higher in EH+GDM and PIH+GDM than in NBP (z-score:+0.8). Pre-gestational BMI was significantly higher ($p<0.01$) in PIH+GDM (33.46±7.11) compared to PIH (30.37±5.80) as well as in EH+GDM (32.84±3.64) compared to EH (30.55±5.68) group.

Conclusion: The 3-DPD indices combined with PSV in pregnancies complicated with EH+GDM and PIH+GDM showed that GDM aggravates EH and PIH cases significantly. Although our study proved that pre-gestational BMI and placental volume do have effect on placental vascularization, it seems that adverse pregnancy outcomes can be predicted more effectively with the help of 3-DPD indices and PSV measurements during the entire pregnancy compared to conventional uterine artery findings.

O130

Urinary congophilia in women with preeclampsia and chronic kidney disease

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Introduction: Preeclampsia remains a major cause of fetal and maternal morbidity. It has been reported recently that urinary congophilia may be a useful test in the diagnosis of preeclampsia (Buhimschi et al 2014). Congophilia has been considered to indicate the presence of amyloid protein, a marker of the unfolded protein response which has been implicated through endoplasmic reticulum stress in preeclampsia (Yung et al 2014).
Objectives: To determine whether congophilia is a specific diagnostic test for preeclampsia and superimposed preeclampsia.
Methods: Using the PEACHES (Preeclampsia And Chronic Hypertension, rEnal and SLE) cohort, samples from pregnant women with preeclampsia (n=23), gestational hypertension (n=23), Chronic Kidney Disease (CKD; n=53), CKD with superimposed preeclampsia (n=5), chronic hypertension with superimposed preeclampsia (n=12) and healthy pregnant controls (n=41) were analysed. To determine whether congophilia is seen in non-pregnant renal impairment, samples from non-pregnant women with either systemic lupus erythematosus with (n=25) and without lupus nephritis (n=14) were also analysed. Urinary congophilia was quantified by measuring Congo Red Retention (CRR) and median (interquartile range) CRR compared between groups.
Results: A significant increase in congophilia was detected in urine from women with preeclampsia (CRR median 34% [IQR 21-68]) when compared to healthy pregnant controls (CRR 15% [12-18]; $p<0.0001$) or women with gestational hypertension (CRR 17% [13-23]; $p=0.002$). Congophilia was also present in pregnant women with CKD (CRR 35% [14-62]; $p=0.23$) and was not significantly different to those with preeclampsia (CRR 34% [21-68]) or superimposed preeclampsia (CRR 46% [16-61]; $p=0.75$).
Congophilia was also present in urine from non-pregnant women with lupus nephritis (CRR 38% [17-73) when compared to those with lupus but no renal involvement (CRR 13% [11-17]; $p<0.001$).
Conclusion: This study confirms the presence of urinary congophilia, as assessed by CRR, in women with preeclampsia but demonstrates that it is similarly present in other conditions associated with renal impairment in pregnant and non-pregnant women. This suggests that congophilia is not specific to preeclampsia but is also present in women with co-existing renal disease.

O131

Pravastatin protects against glucose-induced anti-proliferative, anti-invasive and anti-angiogenic milieu in cytotrophoblasts

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Objective: An increasing level of evidence supports the utility of pravastatin in prevention against preeclampsia (preE). We previously demonstrated that hyperglycemia induces cytotrophoblasts (CTBs) dysfunction characteristic of a preE-like phenotype. We sought to demonstrate the utility of pravastatin in rescuing CTBs from hyperglycemia induced dysfunction.

Methods: Human CTBs were treated with 100, 150, 200, 300, or 400 mg/dL glucose for 48h. Some cells were pretreated with pravastatin (1ug/mL) for 2h, while others were co-treated with pravastatin (1ug/mL) prior to glucose treatment. Some cells were treated with D-Mannitol. Cell migration was performed by Matrigel migration assay kit according to manufacturer protocol. Cell lysates were utilized to evaluate the expression of urokinase plasminogen activator (uPA), plasminogen activator inhibitor 1 (PAI-1), proliferating cell nuclear antigen (PCNA) and p38 MAPK phosphorylation by western blot. Levels of vascular endothelial growth factor (VEGF), placental growth factor (PlGF), soluble fms-like tyrosine kinase-1 (sFlt-1), soluble endoglin (sEng) and interleukin 6 (IL-6) were measured in culture media using ELISA kits. Statistical comparisons were performed using analysis of variance with Duncan's post hoc test.
Results: Hyperglycemia inhibited CTBs migration, down-regulated uPA, PAI-1, PCNA and up-regulated p38 phosphorylation in CTBs treated with >150 mg/dL glucose compared to basal (100 mg/dL) (*$p < 0.05$ for each). Secretion of sFlt-1, sEng and IL-6 were increased while VEGF and PlGF were decreased in CTBs treated ≥150 mg/dl of glucose (*$p < 0.05$ for each). Both pravastatin pretreatment and co-treatment significantly rescued CTBs migration, up-regulated uPA, PAI-1, PCNA, down-regulated p38 phosphorylation, and corrected the angiogenic profile of CTBs ($p < 0.05$ for each). D-Mannitol had no effect on CTBs.
Conclusions: Pravastatin mitigates the hyperglycemia-induced dysfunction of CTBs by attenuating the glucose-induced anti-proliferative, anti-invasive and anti-angiogenic phenotype. These data should alleviate critical concerns regarding pravastatin use on CTBs development early in pregnancy and support the current research to use of pravastatin in preE prevention.

O132

Comparison of groups with and without diabetes Mellitus and preeclampsia in pregnancy: A retrospective case-control comparison

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Objective: Preeclampsia (PreE) and diabetes mellitus (DM) in pregnancy share many risk factors and consequences. Thus, the interactions between these two disease-processes need to be further examined. This study compared normal pregnancies to those complicated with preE, gestational diabetes, and/or pre-existing DM to assess the effect of elevated glucose on placental development and outcomes when this condition is complicated by the addition of preE.
Methods: Medical chart reviews were performed in an IRB approved retrospective case-control design with pregnancies resulting in live born singletons. Total 178 subjects with preE with and without diabetes in pregnancy and live born singletons were selected from deliveries in 2008 through 2011 at Scott & White Memorial hospital. These were compared to 443 without preE and with and without diabetes delivering at similar dates. Statistical analysis was performed using ANOVA and Duncan's post-hoc test.
Results: Patients who developed preE during gestation had higher blood pressures for both systolic and diastolic compared to the groups who did not developed preE during pregnancies ($p < 0.05$). Patients with either DM prior to pregnancy or developing gestational diabetes were older ($p < 0.05$). There was no difference among groups for gravidity ($p = 0.21$) with the average gravidity of 2.7 (1.8SD) for 621 subjects having a range of 1 to 14 pregnancies. Patients with preE delivered earlier in pregnancy than those without preE regardless of diabetes status. However, those with preE and pre-existing DM delivered significantly earlier at 35.0 ± 0.4 weeks than the other two preE groups ($p < 0.05$), suggesting a more severe condition. Additionally, patients with pre-existing DM who developed preE delivered smaller ($p < 0.05$) babies (correcting for gestational age at delivery)

than those with pre-existing DM without preE (1.00 ± 0.03 versus 1.16 ± 0.04, respectively). The development of gestational diabetes did not result in smaller babies for those pregnancies with preE (1.07 versus 1.09).
Conclusions: The development of preE in those with pre-existing DM led to growth restriction and more severe disease as evidenced by lower birth weights corrected for gestational age and earlier gestational ages at delivery. These differences were not seen in pregnancies where DM developed during the pregnancy. This observation supports the concept that elevated glucose levels during placental development in the first trimester may alter the placenta and lead to restriction later in pregnancy when a second stimulus triggers preE.

O133

Fetal renal vascularisation in pregnancy induced hypertension complicated by gestational diabetes or intrauterine growth restriction

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Introduction: The prevalence of pregnancy induced hypertension is 5.6 per year. The incidence of pregnancy induced hypertension increased from 2.3 per 1000 deliveries to 5.4 in the last decade. Pregnancy induced hypertension is 3-6 % of all pregnancies in Hungary. It is an important cause of feto-maternal morbidity and mortality.
Objectives: Our goal was to analyze fetal renal vascularisation in pregnancies complicated by pregnancy inducedhypertension (PIH) and gestational diabetes (GDM) or intrauterine growth restriction (IUGR) by 3-dimensional sonography using VOCAL (Virtual Organ Computer-Aided Analysis) method.
Methods: 66 pregnant women who were examined between 20 and 38 weeks of their gestations complicated by PIH (N=32), PIH+GDM (N=14), PIH+IUGR (N=20) were involved in this prospective longitudinal survey. During the study fetal kidneys were evaluated separately by 3-dimensional power Doppler technique using the VOCAL method. The following measurements were performed concerning the right and left kidneys: vascularisation index, flow index, vascularisation flow index. Wilcoxon rank-sum test was carried out to assess the relationship between fetal renal vascularisation in pregnancies complicated by PIH, PIH+GDM and PIH+IUGR. Student's t-test was utilized to reveal the concordance between fetal renal vascularisation in normal and complicated cases.
Results: The mean values of fetal renal vascularisation decreased in complicated cases. Significant difference ($p<0.01$) could be observed between pregnancies complicated by PIH (VImean±SD: 5.15±0.59%, FImean±SD: 35.75±3.77, VFImean±SD:1±0.27), PIH+GDM (VImean±SD: 2±0.32%, FImean±SD: 29±02.8, VFImean±SD: 0.5±0.12) and PIH+IUGR (VImean±SD: 2.3±0.57%, FImean±SD:31.6±6.8, VFImean±SD:0.7±0.17). The mean values (±SD) of fetal renal volume were significantly less in pregnancies complicated by PIH+GDM, and more in PIH+IUGR pregnancies compared to PIH cases (mean values (±SD): V PIH :15±7 ml, V PIH+GDM :13±4ml, V PIH+IUGR :8.5 ±2.1ml ($p<0.05$). There were no significant differences ($p<0.01$) between the right and left renal vascularisation indices.
Conclusion: Fetal renal vascularisation indices were significantly diminished in GDM and IUGR cases. Fetal downregulated vascularisation had influence on fetal renal development, thus on fetal renal volumes. PIH has a harmful effect not only on maternal, but also on fetal morbidity.

O134

Polycystic ovary syndrome as a risk factor of pregnancy induced hypertension – Review of the literature

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Indroduction: Polycystic ovary syndrome (PCO) seems to be a special form of metabolic syndrome that occurs in fertile women. It is accompanied with an increased risk for obesity, lipid- and glucose metabolism disorders, and hypertension. Beyond the hyperandrogenic state, other mechanisms, such as oxidative-nitrosative stress or vitamin D deficiency, might also have key roles in the pathogenesis of PCO and its consequences. These parameters are also involved in the development of preeclampsia. The apparent common characteristics of the two diseases might suggest their interrelation.
Methods: In this review, we list the common risk factors of polycystic ovary syndrome and preeclampsia, try to calculate the risk of preeaclampsia in patients with polycystic ovary syndrome and its possible therapeutic consequences.
Results: Most of the authors agree, that presence of polycystic ovary syndrome elevates the risk of preeclampsia, however, some of them still debated it. Vitamin D deficiency and increased oxidative-nitrosative stress that can be observed in PCOS may be at least partly responsible for the increased probability of preeclampsia development among these patients. Upon the literature we summarize the optimal preconceptional management of patients suffering from polycystic ovary syndrome for lowering the risk of preeclampsia.
Conclusion: As PCOS is accompanied by an increased risk for adverse pregnancy outcomes such as preeclampsia, these women are patients of special obstetrical care.
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O135

HELLP??? – A case

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Introduction: HELLP affects about 1% of all pregnancies and up to 20% of pregnant women with severe preeclampsia/eclampsia. Clinical symptoms are typically associated with right upper epigastric pain, headache and visual disturbance. In about 15-20% patients present without hypertension and/or proteinuria.
Objectives: After delivery symptoms and lab tests of HELLP resolve gradually within 3-4 days, in case of persistent disease awareness for other thrombotic micorangiopathies has to be raised.
Methods: We present a case of a 26 year old Primigravida, who presented in her 35+1 week of gestational age in our labour ward with epigastric pain and starting labour. Further clinical signs (mild hypertension and proteinuria) and her massively deranged lab results suggested severe HELLP with haemolytic anaemia and profound thrombocytopenia (9G/l). After ordering a thrombelastogram (TEG) and short preparation with cortison and blood products an uneventful cesarean section

was performed. A healthy boy was born (2480g/47cm length; Apgar 7/8/10; umbilical a/v pH 7,29/7,30), but unfortunately his mothers recovery took an unexpected course, continuing lab tests suggested a thrombotic microangiopathy (TTP/aHUS) and accordingly therapy was started, but nevertheless she died on day 13 after delivery.
Results: We discuss her disease, management and differential diagnosis in review of the literature.
Conclusions: In pregnant patients with severe thrombocytopenia and microangiopathic haemolytic anaemia and other symptoms suggesting severe HELLP other thrombotic microangiopathies have to be excluded.

P34

Role of high-mobility group A1 protein in trophoblast invasion

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Objectives: Early in pregnancy, abundant neovascularization at the implantation site is important for normal placentation. For placental development and reduction of uterine vascular resistance, cytotrophoblasts must migrate to the decidua and the uterine myometrium, with subsequent invasion of the spiral arteries resulting in the spiral artery remodeling. Especially, extravillous trophoblast (EVT) invades into the uterine decidual spiral arterioles and regulate the remodeling of these vessels for fetal blood supply. While, disturbed arterial remodeling can lead to the serious complications such as preeclampsia and fetal growth restriction. High-mobility group A1 protein (HMGA1) is known to play an important role in the proliferation of trophoblast; however, no specific function of HMGA1 has been reported for trophoblast invasion. The aim of this study was to evaluate the effect of HMGA1 on trophoblast invasion.
Methods: We investigated HMGA1 expressions in cytotrophoblast derived from preeclampsia model mouse, CD40-L mouse, using immunofluorescence analysis. Wound healing cell migration and matrigel invasion test was also perfomed using HTR-8/SVneo cells transfected with HMGA1 plasmid.
Results: HMGA1 was expressed in nucleus of trophoblasts derived from control mouse; in contrast, cytoplasmic expression was observed in CD40-L mouse. HMGA1 plasmid stimulated cell migration and invasion in HTR/SVneo cells; however, extranuclear translocatation of HMGA1 suppressed cell migration and invasion.
Conclusions: Cellular localization disorder of HMGA1 resulted in a lowering of its invasions and migration. Transfer of HMGA1 in cytotrophoblast is crucial for the trophoblast invasion into decidua in preeclampsia.

P35

Novel interaction of placental caveolin-1 expression with markers of oxidative stress and the renin-angiotensin system (RAS) in pre-eclampsia

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Introduction: Caveolin-1 (cav-1) is one of the major protein components of caveolae required for the coordination of some signalling pathways, including that of angiotensin II (AngII) with its Type 1 receptor (AT1R). We have previously reported decreased cav-1 and increased AT1R protein expression in placentae from women with pre-eclampsia (PE). Within the PE placenta, an increase in AngII acting via AT1R may lead to increased vasoconstriction, but possible functional effects of altered cav-1, and interactions with components of RAS and markers of oxidative stress have not been investigated.

Objective: To establish mechanistic interactions of placental cav-1 with RAS components and surrogate markers of oxidative stress and antioxidant concentrations.

Methods: Immunohistochemistry was performed on paraffin-embedded serial placental sections from 24 normotensive (NC) and 19 women with PE, using antibodies to cav-1, prorenin receptor (PRR), angiotensinogen (AGT), AT1R, AngII type 2 receptor (AT2R) and eNOS. Protein expression was semi-quantitatively assessed and also analysed with respect to previously measured maternal plasma TBARS (Thiobarbituric acid-reactive substances) concentration and placental glutathione peroxidase (GPx) activity.

Results: Positive correlations were observed between placental expression of cav-1 and the AT2R ($P = 0.003$) and PRR ($P < 0.0001$) in NC; these were lost in PE ($P>0.7$, $P>0.5$). However, cav-1 was inversely correlated with eNOS expression in both NC and PE placentae ($P<0.001$, $P = 0.003$). No significant correlations were observed with AGT or AT1R. A negative correlation was observed between maternal TBARS and cav-1 protein ($P = 0.003$), and between placental GPx activity and cav-1 protein ($P = 0.027$) only in the PE placentae.

Conclusions: A complex cascade links activation of the AT1R with NADPH oxidase activation, generation of reactive oxygen species (ROS), the uncoupling of eNOS and subsequent modification of redox-sensitive caveolar proteins in vascular smooth muscle outside pregnancy.Our findings suggest that this cascade is altered in hypertensive pregnancy, in a direction which would lead to enhanced local.vasoconstriction.

P36

Identifying a novel link between preeclampsia and chronic hypertension in the MTHFR-gene using the population based Norwegian HUNT Study

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Introduction: Preeclampsia is a complex genetic disease of pregnancy including new-onset hypertension with proteinuria. Research has demonstrated that after preeclamptic pregnancies these women are at increased risk for cardiovascular diseases (CVD) later in life. Although the link between the diseases is currently obscure, the pathophysiology of both conditions incorporates dysregulated inflammation.

Objectives: In this study we aimed to identify genetic components of the shared pathophysiology of preeclampsia and the CVD risk factor chronic hypertension.

Methods: A cohort from the Norwegian HUNT Study was selected, containing 1006 women with a history of preeclampsia and 816 women with non-preeclamptic pregnancies. From significant findings in existing genome-wide association studies on either chronic hypertension or inflammation we identified 122 candidate single nucleotide polymorphisms (SNPs). These SNPs were genotyped on the Sequenom MassArray System and tested for association with preeclampsia and chronic hypertension in the selected HUNT Study cohort in a multiple logistic regression model in PLINK software.

Results: After Bonferroni-adjustment the minor allele of the intronic SNP rs17367504 in the methylenetetrahydrofolate reductase (MTHFR) gene was significantly associated with a protective effect on preeclampsia (minor allele frequency 13%, OR 0.65, CI 95% 0.53-0.80, p=3.52x10-5). This SNP did not demonstrate a significant association with chronic hypertension in our data set.

Conclusion: Our study demonstrates a genetic link between PE and CVD. The MTHFR enzyme has been linked repeatedly to the regulation of folic acid while the minor allele of the MTHFR SNP rs17367504 is known to be associated with a protective effect on chronic hypertension in CVD-based cohorts. We have identified a novel effect of the MTHFR SNP rs17367504, finding this SNP to be associated with reduced risk of preeclampsia.

P37

Alterations in maternal and fetal plasma soluble endothelial leukocyte adhesion molecule-1 (sE-selectin) concentrations in women with pre-eclampsia

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Introduction: Pre-eclampsia (PE) is an important cause of perinatal and maternal morbidity, especially when diagnosed at or before 34 weeks' gestation (early-onset PE), and is characterised by endothelial dysfunction/inflammation. E-selectin belongs to the selectin family of adhesion molecules involved in guiding non-activated polymorphonuclear cells to areas of inflammation in the endothelial layer. sE-selectin is a sensitive and specific marker of endothelial dysfunction, thus may be important in PE.

Objective: To determine whether plasma sE-selectin concentrations differed between normotensive controls (NC) and PE, as well as sub-grouped in early- and late-onset (>34 weeks' gestation) PE in matched maternal and fetal samples.
Methods: sE-selectin was measured by ELISA in maternal and fetal umbilical venous EDTA plasma from NC (n=17) or pre-eclamptic (n=17) pregnancy. Distribution-free statistical tests were used.
Results: In PE overall, maternal sE-selectin concentrations were raised compared to normotensive controls (median [IQR]: 7.6 [6.9, 8.5] vs. 5.0 [3.5, 8.2] ng/ml; P<0.05). In contrast, fetal sE-selectin was decreased in pre-eclampsia compared to normotensive controls (8.8 [4.3, 10.5] vs. 10.6 [7.9, 15.1] ng/ml; P<0.05). Moreover, in the NC group, paired analysis revealed a significant (P<0.0001) increase of sE-selectin in fetal compared to maternal plasma, while no such difference was observed in the PE group overall. When the data were analysed as early- (n= 5) and late-onset PE (n=12), only the early-onset had higher maternal sE-selectin (P<0.05). No differences were seen for the infants.
Conclusions: The increased maternal plasma sE-selectin in pre-eclampsia reflectsthe endothelial dysfunction, possible due to oxidative stress, which is apparent only in the more severe early-onset PE. The lower levels in the fetal plasma and the lack of difference between maternal and fetal circulations from the pre-eclampsia suggest there may be a different regulatory mechanism in the fetus.

P38

Strong inhibitory effect of preeclampsia serum on angiogenesis using in vitro angiogenesis test

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Introduction: The angiogenic response of preeclampsia patient serum samples were studied by using human in vitro angiogenesis test. The hypothesis was that preeclampsia patients` serum may contain factors that disturb angiogenesis and that could explain formation of some of the adverse effects in patients.
Objective: To measure in vitro angiogenetic effects of serum samples from preeclamptic mothers and umbilical blood.
Methods: Serum samples were collected from ten primiparous preeclampsia patients and ten matched controls at gestational age of 28-38 weeks. After birth giving, also umbilical blood samples were taken. The test method consisted of a co-culture of human fibroblasts and endothelial cells in the culture medium with specific exogenous growth factors to induce formation of tubular structures and tubular networks. During the test, the co-culture was exposed to patient serum samples (dilution 1:15) and cultured for further 6 days (with one replenishment of the growth medium). After the exposure cytotoxicity was evaluated using mitochondrial viability (WST-1) assay. Tubular structures were evaluated microscopically after immunostaining with anti von Willebrand factor.
Results: There was no cytotoxicity shown with any of the samples, but the umbilical blood samples seemed to induce cell growth to some extent. There were no stimulatory effects found on tubule formation with any of the samples, but there was a strong inhibitory effect on tubule formation with serum from preeclampsia patients. Also umbilical blood from preeclamptic pregnancies showed inhibitory effect on tubule formation, but there was no clear correlation of serum from mothers compared to corresponding umbilical serum. No significant correlations to the severity of preeclampsia or any clinical features of the disease were noticed.
Conclusion: Both maternal and umbilical blood serum after established preeclampsia show inhibitory effects on angiogenesis, as tested by in vitro –model.

P39

Connection between placenta specific miRNA clusters and preeclampsia: A hypothetical miRNA-mRNA interaction network

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Introduction: Preeclampsia (PE) is the leading cause of maternal and fetal morbidity, affecting 5-8% of all pregnancies worldwide. Recent studies have shown that preeclampsia is associated with alterations in placental miRNA expression. The C19MC and C14MC miRNA clusters are specially expressed in the placenta and regulated by epigenetic mechanisms. They are believed to play important role in the modulation of placental development, however their contribution to preeclampsia is still not clear.
Objectives: We investigated the connection between placental miRNA clusters and preeclampsia by bioinformatics approaches.
Methods: We investigated 3-3 miRNAs from C14MC (hsa-miR-411, hsa-miR-377, hsa-miR-154*) and C19MC (hsa-miR-518b, hsa-miR-519e*) which were previously shown to be altered in preeclampsia. From the Gene Ontology database we acquired placenta development regulating genes (GO: 0060674, 0001890). Three prediction programs (Targetscan, microT4 and miRanda) were applied to find possible interactions between the miRNAs and the genes. We used Cytoscape bioinformatics platform for network analysis and visualization. The highly regulated genes were further investigated in order to find connections with preeclampsia.
Results: We found 162 protein coding genes in the Gene Ontology database which participate in placenta development. 24 of the 162 genes were predicted to be a target of the selected miRNAs (by at least one program). By visualizing these interactions we built a network (Fig.1.) which possesses 30 nodes (miRNAs and genes)and 54 edges (predicted interactions).11 genes were targeted by both C19MC and C14MC miRNAs ("highly regulated genes"): ANG, DCN, ITGB8, LEP, MAP2K1, PEG10, PKD2, PPARG, RXRA, SOCS and VWF. Many of these have been shown to be deregulated in preeclamptic placenta and it could be explained by abnormal miRNA regulation. Among the miRNAs, hsa-miR-519e seems to be a key regulator due to it targets 14 of the 24 genes.
Conclusion: Aberrant miRNA expression has been implicated in pregnancy-related disorders. Network analysis can help us to understand the pathomechanism of preeclampsia and reveal the functional significance of miRNAs. In this study our aim was to explore the possible effects of placenta specific miRNAs in preeclampsia. We found that genes which take part in placenta development are highly regulated by miRNAs. As DCN, LEP, PEG10, PPARG, SOCS3 and VWF have been linked to preeclampsia, the negative effect of miRNAs could give a possible explanation for developing the disease.

P40

MIR-21 and mir-221 overexpression in placental tissue of preeclamptic patients

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Introduction: Preeclampsia is a hypertensive disorder potentially leading to severe complications in mother and the fetus. Etiology of preeclampsia is multifactorial including partially genetic and immunological pathways; the process of apoptosis is also involved in the development of

preeclampsia. MicroRNAs (miRNAs) - small noncoding molecules- are emerging as critical regulators of biological function (including apoptosis), and alterations to the miRNAome have been described in the context of pregnancy and PE.
Objectives: Goal of this work was to assess expression of pre-selected miRNAs in preeclamptic placental samples and comparison with samples from physiological pregnancies. We designed a 96-well reaction plate to analyze 21 miRNAs in duplicates described to be involved in the apoptosis regulation and expressed in placenta: pro- apoptotic miR-1, let-7c, let-7g, mir-200c, mir-143, mir-205, mir-122, mir-409-3p, mir-449, mir-708, mir-149, mir-204,mir-133 and anti-apoptotic: mir-214, mir221, mir 222, and miRNAs with both the anti-apoptotic and apoptotic targets mir29a and mir29c.
Methods: The normalization was performed against RNU44. The miRNAs were extracted from placental tissue obtained after delivery from both preeclamptic women and healthy controls. After stem-loop primer reverse transcription in one tube, the samples were analyzed on the plates and evaluated by delta Ct algorithm. The aberrantly expressed miRNAs were subsequently validated by TaqMan MicroRNA Assay by relative quantification with the standard curves.
Results: Overexpression of miRNA was observed in mir-122, mir-21, mir-221, mir-29a, mir-29c and mir-449. The validation was performed on 13 preeclamptic placental samples and 6 placental samples from physiological pregnancies; significant overexpression of mir-21 and mir-221 with $p=0.0055$ (CI95% 25.2 to 123.47) and $p=0.0047$ (CI95% 12.16 to 57.20) was observed, respectively.
Conclusion: Analysis of miRNA deregulation can help in the identification of deregulated signaling in preeclamptic placentas for detection of new, potentially usable biomarkers. Eventhough authors would like to point out the necessity of validation on a larger sample cohort.

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P41

The role of IL-10 polymorphism in pathology of hypertensive disorders in pregnancy

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Introduction: Hypertensive disorders in pregnancy are serious complications of maternal and/or fetal well being. Hypertension solely (PIH) or preeclampsia(PE), a pregnancy-associated specific disorder characterized by hypertension and excess protein excretion in the maternal urine, are important causes of maternal and fetal morbidity and mortality worldwide.
Objectives: The etiology of disorder is multi-factorial, including the imbalance between pro- and anti-inflammatory cytokines in impaired immune system. In this study we aimed to analyze the role of IL-10 592 C>A (rs1800872) in healthy pregnant women at term, women with preeclampsia and hypertension, and investigated whether this polymorphism has impact on disease risk and severity.
Methods: A 100 subjects of whom 36 were preeclamptic patients, 45 healthy pregnant controls and 19 women with PIH were involved in case-control study. Levels of proteinuria for 24 hours were measured and correlated to the IL-10 genotype. The genomic DNA was isolated from peripheral blood leukocytes and genotyping was performed by using TaqMan Universal PCR Mastermix and TaqMan SNP Genotyping Assays for rs1800872on AB7500 Fast Real-Time PCR System. Retrieved results have been correlated to clinico-pathological variables andrisk assessment of the disease. For statistical analyses, non-parametric methods were applied.

Results: There was increased risk for pregnancy induced hypertensive disorders (PE+PIH) in women with aberrant (A) allele in genotype in crude analysis showing the OR=1.25 (CI95%:0.56-2.76) for subjects carrying genotypes (C/A+A/A). The risk for PE was higher than risk for cases only with hypertension, (OR=1.31; CI95%:0.54-3.15 vs. OR=1.16; CI95%:0.39-3.40), respectively. Moreover, there was noted a positive correlation between -592A IL-10 genotype and PE with protein excretion >1g/24 hrs. (OR=1.35; 95%CI:0.34-5.43 for C/A genotype and OR=1.84; 95%CI:0.27-12.35 for A/A homozygote). Although insignificant association between IL-10 592C>A and onset of the PE was assessed, a slight trend for higher prevalence of early form (<34 g.w.) was noted in A allele carriers (OR=1.37; 95%CI:0.14-13.02).
Conclusion: The risk of hypertensive disorders in pregnancy may be elevated among Slovak women with IL-10 592C>A polymorphisms, where the A allelemay be associated with severe cases of PE.
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P42

TNF-ALPHA gene polymorphism in pathology of preeclampsia

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Introduction: Preeclampsia (PE) is a life-threatening complication of pregnancy associated with a high rate of maternal and perinatal morbidity and/or mortality worldwide. If untreated, it can progress to eclampsia, which can result in the death of mother, fetus or both.
Objectives: Etiology of PE is still uncertain, however recently the role of immune system takes on importance. Thus the role of central cytokine, tumor necrosis factor (TNF) involved in inflammation processes become widely investigated in obstetric disorders. Following this the present study is to investigate the effect of TNF-alpha gene G308A (rs1800629) polymorphism on disease risk, renal functions, microvascular permeability, endothelial cell dysfunction and organ involvement in women with preeclampsia.
Methods: Initially a 102 3rd trimester pregnant women (preeclamptic-cases and healthy controls) with singleton pregnancy were invited for participation of which 76 were genotyped for TNF-alpha G308A polymorphism, evaluated for plasma levels of sVCAM-1, fibronectin, TNF-alpha and correlated to profile of preeclampsia. The odds ratio (OR) and 95% confidence intervals obtained from unconditional logistic regression were used to set association between TNF-apolymorphism and PE risk. For continuous variables we applied Student's t-test and for categorical variables the Pearson x2 or Fisher's exact test. The two-way ANOVA with Bonferroni correction was used in multivariate analysis.
Results: The A allele was more frequent in cases than controls (22.4% vs. 13.2%) what increased disease risk (OR=2.73). Maternal serum levels of TNF-alpha, sVCAM-1 and fibronectin were significantly increased in cases (855.8±385.1 pg/mL, 1243±671 ng/mL, 0.308±0.231 g/L) compared to controls (301.1±156.1 pg/mL, 651±250 ng/mL, 0.218±0.101 g/L, p<0.0001, p<0.0001, p=0.031; respectively) and levels shoved increasing trend with mutant allele in genotype. Moderate and severe proteinuria was higher in rs1800629 allele A subjects compared to

G/G carriers (53.8% vs. 14.3%,p<0.05 and 13.0% vs. 4.7%, p<0.01; respectively). The adverse effect of rs1800629 allele A on renal functions was confirmed by increased plasma creatine levels, urinary protein excretion and lower tubular resorption rate in preeclamptic patients. Moreover, rs1800629 allele A preeclamptic carriers showed higher serum levels of fibronectin and sVCAM-1 compared to G/G homozygotes.

Conclusion: This study revealed possible association between clinical and laboratory manifestations of preeclampsia and TNF-alpha gene G308A (rs1800629) polymorphism.

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P43

Characterization of monocyte phenotype and polarization in preeclampsia and intrauterine fetal growth restriction

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Introduction: Monocytes can differentiate into various macrophage phenotypes in health and disease, however the phenotype and polarisation of monocytes in pregnancies complicated by preeclampsia and intrauterine growth retardation has not yet been fully characterised.

Objectives: To determine if monocyte phenotype and polarization is altered in pregnancy complications such as preeclampsia and fetal growth restriction.

Methods: A prospective cross-sectional case control study. Pregnant women between 24-40 weeks of gestation, were classified into four clinical groups of Normal pregnancy, Preeclampsia, IUGR and preeclampsia with IUGR (PE+IUGR). The maternal venous blood samples were collected pre-delivery/ labourusing sterile tubes containing an EDTA salt as the anticoagulant. The samples were analyzed within 2 hours of venipuncture. The whole blood sample was processed for flow cytometry. Staining was performed for expression of surface markers - CD14 used for identification of monocytes, CD16 for classification into monocyte subtypes and CD86 and CD163 for classification into phenotypes M1 and M2. The distribution of maternal monocytes subtypes (classical, intermediate and non classical) were characterized and compared for each clinical group.

Results: A total of 54 patients were recruited (normal = 24, PE = 9, IUGR = 12, PE+IUGR = 9). The intermediate monocyte percentage was significantly elevated in IUGR compared to normal pregnancy and in both PE and PE+IUGR for gestations <38 weeks. The level of CD163 expression was significantly increased in the PE+IUGR group for all three monocyte subsets compared to both the controls and PE group, as well as increased on the classical and intermediate subsets for the IUGR compared to PE group.

Conclusion: We have shown for the first time that there is a shift towards increased intermediate maternal monocyte subtype in IUGR and PE+IUGR as well as polarization of maternal peripheral monocytes (all subsets) towards M2 in pregnancies complicated by IUGR. These changes may represent the body's response to and repair of significant placental injury.

P44

Syncytiotrophoblast extracellular membrane vesicles from preeclamptic placentae show reduced abilities to guide monocyte maturation and activation as well as reduced activation of cytotoxicity of regulatory T-cells and NK-cells

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Introduction: Syncytiotrophoblast extracellular membrane vesicles (STBEV) are thought to be involved in the pathogenesis of preeclampsia (PE). They might play a role in directing the immune response and monocyte activation in PE.

Objectives: We hypothesize, that STBEV from preeclamptic placentae induced an altered activation pattern of peripheral immune cells compared to normal STBEV.

Methods: STBEV were gathered after 2 hours of ex vivo placenta perfusion and isolated from perfusion suspension by centrifugation (microvesicles, 30min 19.000g) or ultra-centrifugation (exosomes, 70min 100.000g). Peripheral blood of healthy non-pregnant women was stimulated for 24 hours with either microvesicles or exosomes. Distribution and activation of immune cell subsets were analyzed via flow-cytometry. Monocytes and granulocytes were stained for monocytes (CD115, CD14, CD16), granulocytes (CD66b) and the activation marker CD11b. Lymphocyte subsets were stained for T-cells, NK-cells and NKT-cells (CD3, CD8, CD16, CD56); T-helper cells (Th1 – Tbet, Th2 – CD294, Th17 – RoRgt); regulatory T-cells (FoxP3) and markers for activation (CD69), memory function (CD45Ro) and cytotoxicity (Perforin, GranzymeB, GranzymeK).

Results: Normal STBEV upregulated the number of intermediate monocytes (CD14++CD16+) and activated monocytes and granulocytes, while monocyte maturation and activation was reduced with PE STBEV. Also, normal STBEV promoted a Th1 phenotype whereas PE STBEV supported a Th2/Th17 phenotype. Cytotoxicity was induced in memory T-cells, NKT-cells and CD16+CD56++ NK-cells by normal STBEV. PE STBEV induced reduced cytotoxicity, especially in regulatory immune cell subsets like CD8+ memory Treg- and CD16+CD56++ NK-cells. The effects of normal placentae were induced by both STBEV types, still exosomes showed a more prominent impact. Although PE STBEV in general led to a reduced immune activation compared to normal STBEV, PE microvesicles showed increased activation abilities.

Conclusion: Incubation with normal STBEV led to activation of monocytes, granulocytes, memory T-cells, NKT-cells and CD16+CD56++ NK-cells. PE STBEV showed reduced abilities to activate these cell types, especially Treg- and NK-cells. We suggest, that this reduction of regulatory immune subsets supports an impairment of the immune system as seen for example in PE. However, PE STBEV do not induce the increased activation of monocytes apparent in PE. Concluding, our data show that placental exosomes have a more prominent effect in healthy pregnancy, while the deregulatory effect of microvesicles increases in PE.

P45

Target cells of pregnancy-associated extracellular vesicles

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Introduction: Extracellular vesicles (EVs) produced by living cells are abundant in body fluids. They have a significant role in the intercellular cross-talk. The cellular origin of circulating EVs is characteristic for pregnancy complications and may determine their regulatory effects on maternal immune system.
Objectives: The aim of our study was identification of the target cells of circulating EVs isolated from the blood plasma of both healthy pregnant women and patients with pregnancy complications. The cell binding ability of isolated EVs of preeclamptic patients and pregnant women with gestational hypertension or chronic hypertension were compared.
Methods: EVs were isolated by differential centrifugation from ACD anticoagulated plasma samples (6 samples per group). Multicolor flow cytometry was used for the recognition of EV-lymphocyte interaction. PKH26 stained isolated EVs were incubated with immunophenotyped human peripheral blood lymphocytes. T cell subsets were defined on the basis of their CD3, CD4 and CD8 expressions, while B lymphocytes were identified by CD19 labelling.
Results: Although circulating EVs bound to T lymphocytes in all groups, their binding ability to T cell subsets differed substantially. EVs isolated from healthy pregnant women or from the plasma of women in the chronic hypertension group, showed more pronounced binding to Th than to Tc cells. In contrast, EVs isolated from preeclamptic patients had preferential binding to Tc cells. Equal binding to Tc and Th cells could be detected in the case of gestational hypertension. Although we could detect the binding of circulating EVs to B cells in each group, the most characteristic binding was observed in preeclampsia.
Conclusion: We identified T and B lymphocytes as target cells of pregnancy-associated circulating EVs. The differences in the EV binding may have been caused by both the diverse surface molecular patterns of EVs and the functionality associated immunophenotypes of circulating lymphocytes. Although we have to further characterise the molecular relationships between EVs and lymphocytes, our findings indicate that pregnancy-associated EVs have a role in the systemic regulation of maternal immune system.

P46

Dysregulated levels of novel circulating autoantibodies in preeclampsia

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Introduction: The contributions of the T-cell population and Natural Killer cells have been extensively studied in relation to pregnancy and adverse pregnancy outcomes. Less attention has been given to the B-cell population although maternal levels of circulating autoantibodies against the angiotensinII type 1(AT1)-receptor and antiphospholipid antibodies (aPLs) have been shown to be associated with preeclampsia. Members of the PAR (protease activated receptor) family and VEGF (vascular endothelial growth factor) family have previously been shown to be implicated in preeclampsia.
Objectives: The aim of this exploratory study was to study levels of IgG autoantibodies against these families of PAR and VEGF proteins in pregnant women with and without preeclampsia.

Methods: We developed novel immunoassays detecting levels of IgG autoantibodies against PAR-1, PAR-2, PlGF (Placental Growth Factor), VEGF-A, VEGF-B, VEGF-receptor 1 (VEGFR-1) and VEGF receptor 2 (VEGFR-2).
Results: We found that levels of autoantibodies against PAR-1, PAR-2, VEGF-A, VEGF-B, PlGF, VEGFR-1 and VEGFR-2 were lower ($p<0.05$) in preeclamptic pregnancies ($n=42$) compared to normotensive pregnancies ($n=46$). Clinical features associated with augmented risk for the preeclampsia syndrome (such as primigravidity, primiparity, obesity and a small for gestational age fetus) were also associated with lower levels of the autoantibodies we investigated, although not always reaching statistical significance.
Conclusion: We speculate that these autoantibodies may play a protective role in the development of preeclampsia and are involved in the dysregulation of the PAR and VEGF pathways.

P47
First trimester urine and serum metabolomics to predict preeclampsia and gestational hypertension

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Introduction: New methods are required for improved prediction of preeclampsia. Metabolomics is the study of low molecular weight metabolites in tissues or biofluids.
Objectives: To evaluate early prediction of preeclampsia and gestational hypertension by 1H nuclear magnetic resonance (NMR) metabolomics.
Methods: 1H NMR spectra of urine and serum samples from 599 women with medium-to high risk of preeclampsia in weeks 11-14 of pregnancy were analyzed by principal component analysis and partial least squares discriminant analysis. Variable selection was applied on the metabolic profiles to find the best markers of prediction. Preeclampsia developed in 26 of the women and gestational hypertension in 21 women. Selected metabolites were combined with maternal characteristics in a logistic regression model.
Results: Using urine metabolomic profiles, preeclampsia could be predicted at 51.3% sensitivity, gestational hypertension at 40% sensitivity and both combined at 37% sensitivity at 10% false positive rate (FPR). Increased creatinine and decreased hippurate were the main discriminating metabolites in urine. Using serum metabolomic profiles, preeclampsia could be predicted at 15% sensitivity, gestational hypertension at 33% sensitivity and both combined at 30% sensitivity at 10% FPR. Women who later developed preeclampsia or gestational hypertension had increased serum VLDL and decreased HDL. Combining maternal markers (age > 35 or < 20, and mean arterial blood pressure) and selected urinary metabolite ratios (hippurate and creatinine) in a logistic regression model, preeclampsia could be predicted with a sensitivity of 42% at 10% FPR.
Conclusion: First trimester metabolomic profiles in urine and serum can independently predict hypertensive disorders of pregnancy. A panel of metabolites measured in urine in the first trimester may improve prediction rates for preeclampsia in combination with maternal biophysical markers.

P48
Possible laboratory markers and anthropometric women with preeclampsia – Preliminary results

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Introduction: Preeclampsia (PE) affects 5- 8% of pregnant women, it is a multi-systemic damage which obesity is a predisposing factor and may be recognized by anthropometric measurements. The increased adiposity results in tissue necrosis and release of fatty acids, promoting metabolic changes known as lipotoxicity that causes endothelial damage. This immune disorders causes: vascular reactivity, vasospasm, alterations in capillary permeability and coagulation system. Resulting in anatomical / functional damage such as brain, cardio-pulmonary, renal, hepatic, hematological and utero-placental. This research project is part of a line of research that will assess the long-term values of the selected indicators in the remote postpartum period, thus seeking to observe the behavior of these effectors in the mother's body.

Objective: To evaluate possible laboratory and anthropometric markers in selected mothers with PE in the immediate postpartum compared to women without this complication.

Methods: Case-control study developed at the Hospital Guilherme Álvaro, Santos / Brazil. Blood samples and anthropometric data from 15 mothers were collected in the period from January to May / 2015 in the immediate postpartum and analyzed selected laboratory and nutritional markers, possibly related to PE. Case group: women with PE according to the NHBPEP (2000). **Control group:** women with vaginal birth and newborn full-term, without hypertension and other comorbidities. Variables analyzed: maternal age, gestational age at birth, body mass index (BMI), neck, arm and abdominal circumferences, total cholesterol, HDL (high density lipoprotein), LDL (low-density lipoprotein), VLDL (very low- density lipoprotein), triglycerides, fasting glucose and insulin levels to calculate HOMA-IR index, C-reactive protein. Exclusion terms: collagen disease, smoking, twin pregnancy and fetal malformations.

Results: The total of 15 blood samples (09 - study group and 06 - control group).

Comparing the results analyzed the potential laboratory and anthropometric markers. (*=$p < 0,05$)

Variable	Control Group	Study Group	Variable	Control Group	Study Group
Maternal age (average/years)	28,5	29,11	Insulin (uIU/mL)	2.43	5.76*
Gestation age	39 5/7	37 3/7*	HOMA - RI	0.39	1,17*
Cholesterol (mg/dL)	206	195	CRP (mg/dL)	4.72	9.02*
VLDL (mg/dL)	32	37.67*	Neck circ. (cm)	33.25	37.19*
LDL (mg/dL)	122.33	105.67	Arm circ. (cm)	23.25	31.06*
HDL (mg/dL)	51.67	52	Abdominal circ. (cm)	89.50	111.25*
Triglyderides (mg/dL)	160	188.22*	BMI	23.61	39.24*

Conclusion: This study showed that potential markers lipotoxicity and anthropometric data can relate to the PE, possibly indicating probable risk factors, contributing to the understanding of certain clinical expressions and possibly correlate with prognostic factors. More studies are needed to expand the preliminary information of the present study.

P50

Microalbuminuria is a predictor of adverse pregnancy outcomes including preeclampsia

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Introduction: Abnormal urinary protein loss is a marker associated with a diverse range of renal diseases including preeclampsia. Current measures of urine protein used in the diagnostic criteria for the diagnosis of preeclampsia includes urine protein:creatinine ratio and 24-hour urine protein. However very little is known about the value of urine albumin:creatinine ratio (uACR) in pregnancy.
Objectives: In this study we examined the prognostic value of microalbuminuria detected antepartum to predict adverse pregnancy outcomes.
Methods: This is a single-centre retrospective analysis of 84 pregnant women over the age of 16 attending a tertiary 'high-risk' pregnancy outpatient clinic between July 2010 and June 2013. Utilising medical records, antepartum peak uACR level and pregnancy maternal and fetal outcomes were recorded. To be included in the study, the participant had to have at least one uACR measurement performed during pregnancy (excluding measurements performed at or near to delivery). uACR measurements were obtained at various time points in the pregnancy, from gestational periods 0-19+6 weeks, 20-27+6 weeks, 28-33+6 weeks. As not all participants had uACR measurements at each of these time points, the peak uACR measurement prior to 34 weeks gestation (and prior to delivery date, to ensure that the uACR was not measured at the time of an adverse pregnancy outcome such as preeclampsia) was chosen for the final analysis. Patient characteristics, medications (particularly the use of aspirin and calcium), blood pressure, urinalysis, serum creatinine, fetal and maternal outcomes of the pregnancy were collected from patient medical records and electronic databases. Those patients who did not have at least one uACR performed prior to <34wks or did not have data on the pregnancy outcomes of interest were excluded from the study.
Results: Out of 116 patients attending the renal pregnancy clinic between July 2010 and June 2013, 33 patients were excluded due to absence of at least one uACR performed prior to <34wks or missing data on the pregnancy outcomes, leaving 83 patients for the final analysis. The women had a mean age of 33.1 (±5.4) years. Mean BMI was 29.4 (±8.1) kg/m2. Almost half the population (47.6%) had a previous history of hypertension, one fifth (20.2%) had a previous history of preeclampsia, and more than a third (36.9%) had chronic kidney disease. Over a third of the population (36.9%) had diabetes mellitus (DM) either in the form of gestational diabetes mellitus (GDM), Type 2 DM or Type 1 DM. The primary outcome was a composite of poor maternal and fetal outcomes including preeclampsia, maternal death, eclampsia, stillbirth, neonatal death, IUGR, premature delivery and placental abruption. As the antepartum peak uACR level (in mg/mmol) increased from normoalbuminuria (uACR <3.5) to microalbuminuria (uACR 3.5-35) to

macroalbuminuria (>35), the percentage of women with the primary composite outcome increased in a stepwise fashion (13.8% to 24.1% to 62.1% respectively, p <0.001). After adjusting for covariates including history of hypertension, chronic kidney disease and aspirin therapy during pregnancy, micro- and macroalbuminuria remained significant predictors of the primary outcome.
Conclusion: We have shown that antepartum peak uACR is a useful simple marker to help predict adverse maternal and fetal outcomes. Further prospective studies are required to assess uACR as a prognostic tool in pregnancy before it can be applied in clinical practice.

P51
Screening for preeclampsia in the first trimester: A reduced fat mass increases the risk in normo BMI patients

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Introduction: Maternal cardiovascular system adapts to pregnancy thanks to complex physiological mechanisms that involve cardiac output, total vascular resistance (TVR) and water body distribution. Abnormalities of this adaptive mechanisms are connected with hypertensive disorders and foetal growth restriction. Moreover, maternal serum PAPP-A is considered a biochemical marker extensively used for the first trimester screening of PE.
Objective: To identify patients at high risk of developing hypertensive complications of pregnancy during the first trimester through the use of non-invasive methods such as USCOM (Ultrasonic Cardiac Output Monitor), bioimpedance and biochemical marker.
Materials and Methods: We enrolled 96 healthy normotensive women with normal Body Mass Index during the first trimester of pregnancy (from 11+0 to 13+6 weeks of gestation) obtaining all measurements with the USCOM system, Bioimpedance and collecting MoM values of PAPP-A
Results: Patients were divided into two groups: Group A (n = 54) with TVR <1200 dynes.sec.cm-5, Group B (n = 42) with TVR> 1200 dynes.sec.cm-5. 10% (n=10) of our study population developed pregnancy complications as IUGR and hypertensive disorders. In this group 81% of patients presented high TVR values and 37% PAPP-A<0,4 MoM. Higher values of the Cardiac Output and Stroke Volume have been highlighted in the group A (p<0,05). No statistically significant difference was identified in terms of water distribution, mean arterial pressure (MAP), heart rate, inotropy index and flow time corrected between the two groups (Table 1). Moreover,as shown in table 2, we found a statistically significant lower Fat Mass percentage in complicated pregnancies with higher TVR values with respect uncomplicated pregnancies in Group B (23% vs 26% of Fat Mass)
Conclusions: High TVR and lower Fat Mass during the first weeks of gestation may be an early marker of cardiovascular maladaptation more than the evaluation of PAPP-A values and blood pressure assessment.

Table 1

	GROUP A	GROUP B	p
SBP	118,1±10,5	120,8±5,7	ns
DBP	72±15,5	77,3±6,5	ns
CO	7,0±1	5,8±0,3	<0,05
TVR	1023±77,2	1349,8±124	<0,05
SV	88,4±10,6	72,8±18,7	<0,05
HR	80,9±9,4	75,6±10,9	ns
TFC	370,5±32,5	371,7±29,1	ns
INO	2,01±0,2	2,00±0,3	ns

Table 2

	GROUP A	GROUP B	p
TBW	34,6±2,2	35,9±2,2	ns
ICW	13,6±2,4	16,6±2,6	ns
ECW	16,9±3,4	14,8±2,7	ns
FM	26,3±1,0	23±0,5	<0,05
FFM	44,4±4,4	42,6±3,1	ns

P52

Prevalence of preeclampsia in patients of pre-gestational diabetic pregnancy in Bangladesh

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Background: Preeclampsia, sometimes referred to as toxemia or pregnancy-induced hypertension, is a disorder that occurs during pregnancy and affects both the mother and the fetus. It is a rapidly progressive condition characterized by elevated blood pressure, swelling and protein in the urine. The cause of preeclampsia is still not fully understood, though the disease was recognized and described nearly 2000 years ago. Pre-eclampsia and eclampsia is a cause of high morbidity and mortality for both mother and fetus especially in developing countries.

Objective: Preeclampsia (preE) is a pregnancy disorder characterized by the de novo development of hypertension and proteinuria with multiple path physiologic triggers and mechanisms. Approximately 20% of the diabetic pregnant women develop preE. The mechanisms contributing to this effect is not well characterized. In a recent study, we have shown that hyperglycemia impairs cytotrophoblast (CTB) function via stress signaling. Several researchers demonstrate a direct link between preE and diabetes. The objective of the study was to evaluate potential linkage between the risk of developing preE and the presence of diabetes in pregnant patients in Bangladesh.

Methods: This is a cross-sectional study of 270 pregnant women performed to evaluate the prevalence of PreE with respect to different risk factors such as previous pregnancy, presence of Antiphospholipid antibodies, pre-existing diabetes (before this pregnancy), multiple gestation / singleton, family history of preE in first degree relative (mother, sister and daughters; most commonly mother), maternal age of 40 or greater. The study was conducted in selected hospitals of Dhaka city, Bangladesh during October 2012 to December 2013. We gave special emphasis on the occurrence of PreE in pre-gestational diabetic patients. This study was approved by the Ethical review committee of Bangladesh Medical Association.
Results: The key study findings revealed that the rate of development of PreE in Bangladeshi pre-gestational diabetic patients is 27%.
Conclusions: There is an association has been found between the risk of developing preE and the presence of diabetes in pregnant patients in Bangladesh.

P53
Body mass index before pregnancy and hypertensive disorders in following pregnancy

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Introduction: Hypertensive disorders (HD) burden 5-10% of all pregnancies and are the most frequent complication in pregnancy after anemia. HD are associated with high rates of maternal and fetal mortality and morbidity. Recent studies show that the systemic and local inflammatory response to pregnancy amplified in women who were obese before conception.
Objective: The aim of this study was to estimate the association between range of body mass index (BMI) before pregnancy and type of hypertensive disorders in following pregnancy.
Materials and Methods: The study was conducted as a prospective study. The study included 179 women older than 18 years with singleton following pregnancies which have chronic hypertension or have developed some form of hypertensive disorders (gestational hypertension, preeclampsia, chronic hypertension with superimposed preeclampsia and others) in following pregnancy, 82 in the study group with a BMI ≥ 25 and control group (97) with BMI < 25. Study group was divided into subgroups: S1 with BMI 25-27, S2 with BMI 28-29 and S3with BMI ≥ 30. Blood samples from women were collected for analysis of hematological and biochemical parameters before pregnancy and in the first trimester of following pregnancy. Complete blood count is determined on an automated analyzer. On the same device, were determined CRP values, by nephelometric method. The amount of uric acid was measured by enzymatic colorimetric method with uricase and peroxidas. The determination of serum urea and creatinine has been done by U.V. kinetic method.
Results: The study group (31/82) had statistically significantly higher incidence of hypertensive disorders in pregnancy compared to the control group (7/97). The subgroup S3 (18/31) had a higher incidence of hypertensive disorders in relation to S2 (9/31) and S1 (4/31), and subgroup S3 had the higher incidence of preeclampsia (7/17) than S2 (1/10) and S1 (0/4). There was no statistically significant difference in hematological and biochemical parameters (CBC, C-reactive protein, uric acid, urea and creatinin) before pregnancy and in the first trimester of following pregnancy between study and control group.
Conclusion: The results of this study suggest that the body mass index significantly affects the occurrence and severity of hypertensive disorders in pregnancy.

P33

Decreasing of placental progesterone induced blocking factor expression and spiral artery remodeling disturbance in mice preeclampsia model

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Introduction: Preeclampsia is a major cause of morbidity and mortality in our developing country. The biggest obstacle in the high prevalence of preeclampsia and its management is due to lack of knowledge in preeclampsia pathologic mechanism. Progesterone is an important pregnancy hormone that has immunomodulatory effect by inducing Progesterone induced Blocking Factor (PIBF) release, due to binding of progesterone with its receptor in lymphocyte. PIBF inhibits cytolytic NK cells activity and inducing T-helper 2 cytokine dominant while on contrary, preeclampsia has a condition of T-helper 1 cytokine dominant and increase of NK cells cytolytic activity. This was the first study to evaluated PIBF expression directly on the placenta when the pathogenesis of preeclampsia occurred after completion of vascular remodeling in animal models.

Objective: The objectives of this study were to compare placental PIBF expression, spiral artery wall thickness as characteristic of vascular remodeling disturbace and investigated correlation between both in mice preeclampsia model.

Methods: This experimental study used 32 pregnant mus musculus mice and randomly divided to normal group and preeclampsia model group. Our preeclampsia model was created by injecting anti - Qa2 (anti HLA - G) 10 ng from 1st until 4th day of pregnancy, to reduced HLA - G expression. Termination of both groups were performed after completion of spiral artery remodeling in mice by day 16th of pregnancy followed by immunohistochemistry examination for PIBF expression using immunoreactive score and spiral artery wall thickness measurement. Ethical clearance was taken from Medical Veterinary Faculty ethics commission. Difference and correlation were analysed using SPSS 20. Probability values < 0.05 were considered statistically significant.

Result: In the result, PIBF were expressed in trophoblast, decidual and lymphocyte cells in placental tissue. The placental PIBF expression on preeclampsia model (2.01 ± 1.14) was significantly reduced ($p < 0.01$) compared with control (3.99 ± 2.53). There was a significant increased of spiral artery wall thickness ($p < 0.001$) in preeclampsia model (20.70 ± 5.93 micrometers) compared with control (9.98 ± 3.36 micrometers). There was a significant association ($p < 0.001$) with negative correlation (rho / pearson correlation = - 0.623) between placental PIBF expression and the spiral artery wall thickness.

Conclusion: We concluded a decreased expression of placental PIBF and the increase of spiral artery wall thickness as a characteristic of spiral artery remodeling disturbance in mice model of preeclampsia, with negative correlation between placental PIBF expression and spiral artery wall thickness.

P87

Alteration of Delta-like ligand 1 and Notch 1 receptor in various placental disorders with special reference to early-onset preeclampsia

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Introduction: Notch signaling pathway has been shown to be dysregulated in placentas with preeclampsia, but there has been a lack of studies on methylation of Notch family genes in this disorder. Objectives: To investigate the methylation status of DLL 1 and Notch 1 and expression of those proteins in placenta with preeclampsia.

Methods: We therefore executed methylation-specific polymerase chain reaction and immunostaining for Notch 1 receptor and the activating ligand,Delta-like (DLL) 1, with placental tissues from cases of preeclampsia (early-onset, n = 18; late-onset, n = 19) and other placental disorders, including maternal complications such as diabetes mellitus and collagen disease (n = 10), fetal growth restriction (n = 17), fetal anomaly (n = 23), pretermbirth (n = 15),miscarriage (n = 25), and hydatidiform moles (n = 9) as well as term births (n = 12).

Results: The frequency of DLL1 methylation was higher in early-onset preeclamptic placentas (61%) than the other subjects (0%-36%; $P \leq 0.016$). Appreciable samples (36%) of miscarriage also represented DLL1 methylation. None of the samples studied showed Notch 1 methylation. On gestational period-matched analysis, the rate of DLL1 methylation was higher in early-onset preeclampsia (83.3%) than preterm birth (13.3%; $P < 0.001$), with no significant differences in clinical backgrounds between the two. In this analysis, increase of syncytial knots and accelerated villous maturation were most prominent in DLL1-methylated placentas with early-onset preeclampsia. Notch 1 and DLL1 expressions in villous trophoblasts and endothelial cells were significantly lower in early-onset preeclamptic placentas as compared with preterm birth controls.

Conclusion: Altered Notch signaling via methylation of DLL1 is likely involved in possible disease-related mechanisms of early-onset preeclampsia. Alternatively, DLL1 methylation in early-onset preeclampsia could be a manifestation of a lack of placental maturation, similar to miscarriage.

P88

Pre-eclampsia risk stratification for low risk 1st pregnancies: First results of a new LC-MS based multiplex metabolite assay

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Introduction: Screening for pre-eclampsia is a focus of prenatal care and is largely based on the use of clinical risk factors. However, current screening protocols are unfit to determine pre-eclampsia risk in 1st time pregnant women; biomarkers have the potential to address this unmet need. As single biomarkers have insufficient predictive accuracy, unbiased biomarker discoveries have been performed to identify panels of markers which when combined, have the potential pre-eclampsia prediction. Metabolite based solutions using mass spectrometry have gained significant interest as they have the potential to readily translate to clinical practice.

Objectives: To translate the discovery that blood-borne metabolite biomarkers stratify pregnant women early in pregnancy (~15 weeks) to their risk of pre-eclampsia1 into a commercial LC-MS based clinical assay.
To pursue fit-for-purpose testing of the first version of the developed LC-MS pipeline, followed by independent verification through a case:control study.
Methods: The analysis pipeline incorporated 1) a single step metabolite extraction, 2) multiplex LC-QqQ –MS assays for 40+ metabolites and 3) a dedicated data processing protocol. Case:control study testing utilised 15 weeks' plasma samples of from 50 pregnant women who subsequently developed pre-eclampsia and 500 random control pregnancies. All participants are part of the SCOPE study2 and were recruited in Cork, Ireland.
Results: For the 40+ metabolite assays: 62% had a %CV £ 15% and 82% had a %CV £ 25%. Univariate analyses using the ROC statistic showed that 7 of the metabolites tested had significant predictive power (lower limit 95% CI ROC-AUC ³ 0.5). Multivariate logistic regression analysis revealed particular combinations of metabolites which identified groups of women either at increased risk or at decreased risk for pre-eclampsia.
Conclusion: These findings underpin the potential of metabolite-centric multimarker panels to encapsulate a complex syndrome such as pre-eclampsia considerably in advance of any clinical manifestation. Further development steps will include performing additional case:control studies and subsequent clinical validation of this metabolite based test in the large scale European, multicentre phase IIa clinical study IMproved Pregnancy Outcomes by Early Detection (IMPROvED) which is currently recruiting 1st time pregnant women in 5 European countries3.
1Kenny, L. C. et al. Hypertension 56, 741–9 (2010);2North, R. A. et al. BMJ 342, d1875 (2011); 3Navaratnam, K. et al. 13, 226 (2013).
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Biochemical parameters of the first trimester in preeclampsia

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Introduction: Preeclampsia is a multisystem disorder with complex and incompletely understood etiopathogenesis.
Objective: The aim of this study is to determine is there a statistically significant difference in the values of biochemical markers in serum of pregnant women between 11-14. weeks of gestation, between pregnant women with preeclampsia and the control group of pregnant women with physiological pregnancy.
Methods: This researchis conducted as a prospective study in the period 2013.-2014 at the Department of Obstetrics and Gynecology and the Center for Laboratory Medicine, Clinical Center

of Vojvodina. The study included a total of 183 pregnant women who were outpatients between 11. to 14. weeks of gestation, because of screening for fetal and chromosomal abnormalities of the fetus. The women were followed until the end of pregnancy when they were divided into study group (n = 72) who developed preeclampsia in current pregnancy and control group (n = 111) with physiological pregnancy. All pregnant women in the period from 11. to 14. weeks gestation, blood samples were taken for determination of laboratory parameters (CBC, urea, creatinine, uric acid, C- reactive protein and pregnancy associates plasma protein PAPP-A).
Results: Pregnant women who developed pre-eclampsia in current pregnancy had significantly higher values of CRP and PAPP-a than in control group, while the values of leukocytes, platelets, red blood cells, urea, creatinin and uric acid were not significantly different between groups.
Conclusion: The results of this study suggest that in pregnancy with preeclampsia, reactions of maternal endothelium on the placental factors of ischemia starts already in early pregnancy with consequent increase in marker of acute inflammatory reaction (CRP) and PAPP-A, that much earlier precede the manifestation of clinical symptoms of multiorgan dysfunction in preeclampsia.

P90
Effect of angiotensin II receptor subtype2 stimulant on the pathogenesis of preeclampsia
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Objective: Early in pregnancy is a critical period for preeclampsia pathogenesis. We already succeeded in developing a new breed of preeclampsia model mouse using CD40L gene-transfection at implantation. Renin-angiotensin system is reportedly activated in preeclampsia. Angiotensin II (AII) receptor subtype 1 antagonist is a major antihypertensive agent; however, the drug cannot be used during pregnancy because of the fetal nephrotoxic action. Then, we evaluated the effect of AII receptor subtype 2 agonist (C21) on preeclampsia-phenotype expressed mice.
Methods: Blastocysts were collected from pregnant ICR mice and incubated with adenovirus including CD40L gene and transferred into the uterine horns of pseudopregnant ICR mice. An osmotic pump was placed subcutaneously on the dorsal side with C21 or saline. Blood pressure was measured using the tail cuff method and urine samples were collected using metabolism cage for measuring albumin concentration. On e17.5, uterus and placenta was retrieved from the mice and investigated the structure.
Results: In CD40L mice, blood pressure was significantly increased from the mid pregnancy and was decreased by C21 during mid pregnancy; however, blood pressure was increased on e17.5 again. The concentration of albuminuria was also significantly increased from the mid pregnancy and slightly decreased by C21 during mid pregnancy; however, the concentration was increased on e17.5 again. The weight of neonates and placentas was also increased by C21.
Conclusion: C21 influenced renal function, blood pressure only in mid pregnancy. Placental and neonatal weight was improved by C21. It is thought that C21 exerts a favorable influence on preeclampsia. However, the effects do not last for a long time. We should further examine to decide the detail of the amount of C21 for longer and stronger effects.

P91

Possible therapeutics for preeclampsia: Drug repositioning by In Vitro screening via induction of placental growth factor

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Introduction: We have established a model of the maternal vascular endothelium using human umbilical vein endothelial cells (HUVECs), and shown that nicotine restores endothelial dysfunction caused by excess soluble fms-like tyrosine kinase 1 (sFlt1) and soluble endoglin (sEng) via induction of placental growth factor (PlGF).
Objectives: In this study, we screened a library of 528 approved drugs to identify candidate compounds with therapeutic potential as preeclampsia treatments via their proangiogenic properties.
Methods: We assessed whether the screened drugs induced PlGF and restored damaged endothelial cell function using HUVECs. Enzyme-linked immunosorbent assays (ELISAs) were carried out to measure levels of PlGF in conditioned media treated with each drug (100 μmol/L) in the drug library. Tube formation assays were performed using HUVECs to evaluate the angiogenic effects of drugs that induced PlGF. We also performed ELISA, quantitative reverse transcription polymerase chain reaction, and tube formation assays after treatment with a range of concentrations of the candidate drug and with various combinations of sFlt1 (100 ng/mL), sEng (100 ng/mL).
Results: Of the drugs that induced PlGF, vardenafil was the only compound that significantly facilitated tube formation in comparison with the control cells ($P < .01$). Treatment with vardenafil at concentrations of 50, 100, and 250 μmol/L increased expression of PlGF in a dose-dependent manner. Vardenafil (250 μmol/L) significantly improved tube formation which was inhibited in the presence of sFlt1 and/or sEng. Production of PlGF from HUVECs in the presence of sera derived from patients with preeclampsia was significantly elevated by administration of vardenafil (250 μmol/L).
Conclusion: By assessing drug repositioning through screening a library of approved drugs, we identified vardenafil as a potential protective agent against preeclampsia. The therapeutic mechanism of vardenafil may involve inhibition of the systemic maternal antiangiogenic state that leads to preeclampsia, in addition to its vasodilating effect. As concentrations used are high and unlikely to be useful clinically, further work is needed before testing it in humans.

P92

When there is a lack of magnesium during pregnancy

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Introduction: The most frequent use of magnesium in cardiology is the adjuvant treatment of arterial hypertension, supraventricular and ventricular premature beats and in the heart failure. During pregnancy is even in the physiological statement higher magnesium consumption.In the therapeutic approaches in cardiovasular diseases in pregnancy is extremely important the influence of the mother's and child's hemodynamics. Furthermore is also relevant the placental transfer of the medication. The most frequent usage of magnesium during pregnancy from cardiologist's

indications is arterial hypertension of the mother.In the prenatal period the conductive heart system is very sensitive to the ione imbalance. The most frequent manifestations are fetal premature supraventricuar beats

Objectives: The aim of the the study was to analyse the efficacy of the treatment of arterial hypertension during pregnancy and premature fetal atrial contractions.

Methods: The retrospective analysis of the pregnant females during the period 1 year. 1 We examinated 4 patients in the age 32-38 years (median 34,6). In the 22th-28th gestational week (GW) (median 27,1) the new diagnosis of the arterial hypertension was confirmed. 2. We analysed 14 pregnant patients with the diagnosis of fetal arrhythmia. Mother's age at the time of diagnosis was 22-38 years (median 31,5). The fetal arrhytmia was detected at the 20th-38th GW (median 26,5). Patients were examinated by ECHO and prenatal ECHO.

Results: 1. Analysis of the arterial hypertension during pregnancy:the average blood pressure (BP) at the entrance to the study was 146,7± 5,8 mmHg, heart rate (HR) 96,3±5,8/min. Patients were treated with the maximum tolerated dose of magnesium with the BP reduction to 112,4±5,8 mmHg ($p<0,001$) and HR 76,5±9,4/min. ($p=0,05$). In 1 patient (twins) was the magnesium treatment insufficient. The treatment with alphametyldopa was initiated. All patients tollerated the treatment with magnesium very good. In all patient was the reduction of the blood pressure after the delivery. Without further treatment of arterial hypertension. 2.Analysis of the fetal arrhythmias: In 10 patients (71,4%) was arrhythmia detected in the 20th-30th GW, in 1 patient (7,1%) in the 31st-35th GW and in 3 patients (21,4%) in the 36th-38th GW. In all patients were very frequent premature supraventricular beats- majority were isolated, in 2 patients was bigeminy present, in 1 patient trigeminy was present. The maximum tolerated dosage of magnesium was started. In 11 patients (78,6%) was reduction of the premature beats during the period less than 4 weeks. In 3 patients (detected in 36th-38th week) was the maintenance of the arrhythmia until the end of the pregnancy. After the delivery were presented only isolated premature beats with the spontaneous termination within 1 month after delivery.

Conclusion In the case of adequate magnesium substitution is the new diagnosis of arterial hypertension and premature fetal supraventricular beats reversible in both: in the mother and fetus as well. However after the magnesium substitution is the disease non sustained even after the delivery. So it is very important to substitute magnesium during pregnancy. The adequate magnesium substitution during pregnancy could lead to the reduction of the stress for the mother and baby.

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Early-onset eclampsia with intrauterine fetal death after placental abruption at 22 weeks gestation : a case report and literature review

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Background: Eclampsia is one of the complications of preeclampsia, and associated with increased risks of maternal and prenatal mortality and morbidity. The incidence of eclampsia varies worldwide, and ranges from 4/10,000 0.04% deliveries to 7.4/10,000 0.07% deliveries in Japan. The time of eclamptic episode can be antepartum, intrapartum, or postpartum. However, report of eclampsia occurs at<28 weeks gestation is relatively rare. We report a case of eclampsia occured on 22 weeks gestation, with miserable outcome after placental abruption.

Case Report: A 37-year-old primiparous Japanese woman who had no history of hypertension suddenly developed convulsion attack in local clinic at 22 weeks and 2 days gestation, was transported to our tertiary center. On admission, she was recovered from convulsions, and blood pressure was 136/88mmHg with proteinuria and oliguria. After the decision of course observe, she had a magnetic resonance imaging (MRI) of the brain which showed features consistent with posterior reversible encephalopathy syndrome (PRES). Whlile being maneged with magnesium sulface and antenatal corticosteroid therapy, she developed placental abruption confirmed with retroplacental hematoma with transabdominal ultrasound and intrauterine fetal death at 22 weeks and 4days gestation. After the patient and her husband's choice of vaginal delivery, uterine cervical dilation was performed. However, she presented an increase of blood pressure up to 170/90mmHg, immediate cesarean section eith general anethesia was performed. On postpartum, she was given intensive care with nicardipine and magnesium sulface infusions, and she made improvement significantly. Eight days later, her brain showed an improvement of PRES in follow-up MRI. She was discharged from hospital on 8days post-operation without recurrence of eclampsia.

Discussion: This case highlights the occurrence of eclampsia and rapidly progressed placental abruption at very early gestation as 22 weeks gestation. Mattar F. and Sibai B.M. showed case series of eclampsia including early onset cases in the last century[1]), but confirmation with MRI of the brain were not performed. It must be noted that some cases reported formally as eclampsia include cerebral hemorrhage in pregnancy, since cerebrovascular disorders occurs more frequently than we expected[2]). Clinicians should care both eclampsia and brain stroke to all pregnant course.

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P94

Preeclampsia in pregnancies with and without diabetes; the associations with placental weight. A population study of 655 842 pregnancies.

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Introduction: Women with diabetes are at increased risk of preeclampsia, and women with diabetes tend to deliver placentas and offspring that are large for gestational age. Therefore, it is reasonable to suggest that large placentas in preeclamptic pregnancies may be attributed to concomitant maternal diabetes.

Objectives: We studied whether the placental weight in preeclamptic pregnancies differs in women with and without diabetes.

Methods: Information on all singleton births from 1999 through 2010 (n = 655 842) were obtained from the Medical Birth Registry of Norway. We used z-scores of placental weight to adjust for differences in gestational age between deliveries, and compared the distribution of placental weight z-scores in tenths in preeclamptic pregnancies with and without diabetes, and in normotensive pregnancies with and without diabetes.

Results: When comparing z-scores, there was no difference in mean placental weight in pregnancies with diabetes with or without preeclampsia (ANOVA-test; $p = 1.00$.). However, mean placental weight was significantly higher in pregnancies with diabetes as compared to pregnancies with preeclampsia only or in pregnancies with none of these conditions (ANOVA-test; $p < 0.01$).

Among preeclamptic pregnancies, having a placental weight in the highest tenth of placental

weight was nearly three times more frequent (28.8%) in pregnancies with diabetes compared to pregnancies without diabetes (9.8%). In the lowest tenth of placental weight, preeclamptic pregnancies with diabetes were underrepresented (7.5%), and preeclamptic pregnancies without diabetes were overrepresented (13.6%). Thus, among women with diabetes, more pregnancies with high as compared to low placental weight developed preeclampsia.
Conclusion: These results suggest that women with diabetes who develop preeclampsia have larger placentas than other women with preeclampsia. Thus, the placental involvement in preeclampsia may differ by diabetes status.

P95
Perinatal outcome of pregnant with severe preeclampsia and gestational diabetes mellitus in Rondônia, Brazil: Case report

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Introduction: The appropriate management of pregnant women with comorbidities is a routine challenge, requiring efforts to obtain a favorable outcome. Gestational diabetes mellitus (GDM) is associated with increased perinatal mortality and perinatal morbidity, with high rates of macrosomia, birth trauma, metabolic, hematologic and respiratory complications. The risk reduction for patients with preeclampsia requires rigorous clinical control of blood pressure (BP) (BRAZIL, 2011).
Case report: Patient F.R.A. 34 years old, brown, multiparous (5 pregnancies, 2 vaginal deliveries and 2 miscarriages), with a history of GDM and abortion in previous pregnancy without comorbidities, accompanied by pre-natal high-risk service, held 9 queries, presented at the tenth week of gestation one fasting blood glucose of 105 mg / d, conducted the oral glucose tolerance test with 75 mg, which submitted the relevant values: 96 mg / dL, 146mg / dL, 131mg / dL. She made use of NPH insulin, but have abandoned use in the last month of pregnancy, and there were no other changes in the other prenatal tests. She was admitted in a tertiary center at 30 weeks and 3 days pregnancy (calculated in ultrasonography exam) due to hypertensive frame (150 x 100 mmHg), referring pain in the epigastric region, fetal movements present and without uterine activity. The patient underwent ultrasonography obstetric showed intrauterine growth restriction (IUGR), oligohydramnios and small placenta. Furthermore, the umbilical artery Doppler presented diastole zero and middle cerebral artery with decreased vascular resistance. The ductus venosus presented wave "A" positive above the baseline. During hospitalization was monitored for blood pressure and blood glucose without amendments. It was pointed out by cesarean section DMG, IUGR and zero diastole. The newborn (NB), male, weight 830 g, cried, presented tone and did not require resuscitation. The Capurro calculated was 34 weeks and five days, with no malformations. The NB evolved with respiratory distress, requiring intubation and intensive care. Postpartum was not performed glycemic control of the patient and the same was discharged after two days.
Relevance and Comments: The risk of preterm birth and perinatal mortality are added in association significant obstetric pathologies. The quality of care is critical to minimize adverse outcomes and maternal effects as pre-eclampsia and polyhydramnios, in addition to fetal repercussions example of prematurity and perinatal mortality.

P96

Neonatal outcome in women after kidney transplantation: Effect of immunosuppressive therapy on the risk of preeclampsia

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The number of women with a renal transplant within the fertile phase of their life has increased over the last decades. Pregnancy in these women is associated with an increased risk of maternal and fetal complications such as pre-eclampsia (PE) and preterm birth (PTB). Azathioprine (AZA) and calcineurin inhibitor (CNI), two different immunosuppressive drugs, are frequently used in these patients. Their precise effect on pregnancy is unclear. Therefore, our objective was todescribe the maternal and fetal outcomes in women with a renal transplant and to compare these outcomes according to their immunosuppressive treatment.
We performed a retrospective analysis of pregnant patients with a renal transplant between 1997 and 2013 in the Radboud University Medical Centre Nijmegen. We collected data on maternal and neonatal characteristics by checking medical records. Patients were divided in two groups according to their immuno¬suppressive regimen (CNI or AZA) used during pregnancy for which pregnancy outcomes were com¬pared. Statistical analyses were performed with Mann-Whitney-U test, Fisher's exact test and Wilcoxon rank signed test.
We identified 40 pregnancies of 26 renal transplant recipients. The patients' mean age was 31 (±4 SD) years and the mean interval between transplantation and conception was 7 (± 5 SD) years. The live birth rate was 75%. Pregnancies were complicated by PE (40%), PTB (46.7%) and low birth weight (43.3%). Patients using CNI developed PE earlier as compared to patients using AZA (gesta¬tional age at onset respectively 32 weeks and 37 weeks, p=0.009). Mean protein levels rose during pregnancy for our total study population (AZA 0.50 g/L, p=0.008; CNI 0.84 g/L, p=0.002). No statistical differences were found in the course of renal function with respect to immunosuppressive regimens. Patients using CNI showed a higher diastolic blood pressure within 6 months post-delivery (p=0.005). Foetal outcomes were similar, although new¬borns of patients using CNI tend to have a lower birth weight.
Our data suggest that AZA is a better immunosuppressive choice for pregnant renal transplant patients. Antenatal awareness for early onset PE in CNI treated patients, and close follow-up post-delivery in these women is important to control blood pressure and to review the anti-hypertensive management. For renal transplant recipients using CNI gaining preconceptional counselling, we advise a switch to AZA.

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Chronic kidney disease and pregnancy – A case report

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Introduction: Chronic kidney disease (CKD) is classified in five stages. Perinatal complications, such as preterm labor, preeclampsia and fetal growth restriction (FGR) are increased for all stages. In women with serum creatinine (sCr) above 2.5mg/dL, the rate of preterm delivery is as high as 86%, mainly due to preeclampsia, which occurs in over 40%.

The degree of renal insufficiency, rather than the underlying etiology, is the primary determinant of outcome. Women who become pregnant with high sCr level, are more likely to have a decline in renal function, than women who do not become pregnant, for the same sCr level. Hypertension and degree of proteinuria are also among the most important predicting factors.
Fifty percent of women with sCr >1.5 mg/dL have a significant decline in glomerular filtration rate (GFR) in late pregnancy or early postpartum, with 20% of them progressing to end-stage renal disease (ESRD) within 6 months after delivery.
Methods: Review of literature about CKD and pregnancy and presentation of a clinical case.
Results: A 37-year-old african female, G3P1, engaged prenatal care at our hospital at 13 weeks gestation, with CKD - stage 4 (estimated GFR of 20.2mL/min), for a baseline sCr level of 3.3 mg/dL. She had had a nephrotic syndrome at 9 years old. Renal biopsy revealed diffuse mesangial proliferative glomerulonephritis, and was treated with prednisolone and cyclophosphamide. It progressed to CKD with secondary hypertension, treated with enalapril and amlodipine. During pregnancy she was medicated with methyldopa, amlodipine, darbepoetin, vitamin D, vitamin B, ferrous sulfate and calcium.
Routine workup at 26 weeks revealed sCr 3.57 mg/dL, uric acid 9.4 mg/dL, without proteinuria. Pregnancy was uneventful until 34 weeks gestation, when she was admitted to with preeclampsia and worsening renal function.
At admission, sCr 5.11 mg/dL, urea 174 mg/dL, uric acid 9.55 mg/dL and spot urine protein level of 200. Ultrasound revealed FGR (1stpercentile), with altered Doppler velocimetry, that motivated urgent cesarean delivery. The newborn weight was 1340g, female, Apgar score 10/9/10.
At day 7 postpartum, she was discharged from the hospital, with sCr 5.34 mg/dL, urea 211 mg/dL and proteinuria 4+. Hemodialisys was programmed, as she awaits a donor for renal transplant.
Conclusion: Although pregnancy in women with CKD is associated with a high rate of live births, it is usually complicated by preeclampsia and fetal growth restriction. The higher the stage of CKD, the greater the probability of postpartum deteriorated renal function, with a significant proportion of women progressing to ESRD.

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Maternal lipid- and steroid hormone concentrations during the course of pregnancy and in pregnancy pathologies

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Introduction: Lipids and steroid hormones are closely and interactively linked. While cholesterol is substrate for (placental) steroid hormone synthesis, steroid hormones regulate hepatic lipid production.
Objective: We aimed to estimate the interaction between lipid metabolism and steroid hormones in normal and diseased pregnancy with emphasis on those with hepatic and/or placental pathologies.
Methods: A total of 217 serum samples were analyzed. In group A 33 patients with uncomplicated pregnancies were analyzed at three different time points (first through third trimester) and post partum. Group B consisted of 42 patients (24 to 42 weeks of gestation) with pregnancy pathologies (IUGR n=14, preeclampsia n=14, HELLP n=7, intrahepatic cholestasis n=7) and 42 gestational age matched controls. Steroid profile including estradiol, progesterone, and dehydroepiandrosterone was measured by GC-MS and related to cholesterol and triglyceride concentrations.
Statistics: Spearman's rank coefficient and Kruskal-Wallis test with Dunn's multiple comparisons.

Results: Group A: Positive correlations were found for triglycerides and cholesterol with correlation coefficients for estradiol, progesterone ranging from $\rho=0.50$ to $\rho=0.57$. Negative correlations were found for trigylcerides and cholesterol with dehydroepiandrosterone ($\rho=-0,38$ and $\rho=-0,48$). Group B: As compared to controls cholesterol levels were lower in IUGR ($p<0.05$) whereas triglyceride levels were higher in preeclampsia ($p<0.05$). The steroid hormone concentrations of estradiol ($p<0.01$) and progesterone ($p<0.01$) all were found to be lower in IUGR. No other significant differences have been observed.
Conclusion: We found lipid and steroid levels to be affected in pregnancy pathologies with placental insufficiency but not in pregnancy-associated hepatic diseases. Our data suggests that placental rather than hepatic function strongly determines lipid and steroid concentrations in pregnancy.

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Use of high dose cortisosteroids in HELLP syndrome

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Introduction: Several reports have shown high levels of pro-inflammatory agents in maternal plasma in HELLP syndrome. Corticosteroids, as potent anti-inflammatory agents are maybe able to ameliorate inflammatory response and thereby positively influence the deterioration of disease. Even if several studies have showed a beneficial effect of corticosteroids in patients with HELLP syndrome, the possible effect of corticosteroids in HELLP syndrome is still under discussion.
Objectives: Corticosteroids in the management of HELLP syndrome has been introduced to our department in 2006. The therapeutic concept includes high-dose prednisolone administered one to three times. Background of this therapy is maximum impact; high dose; connectedto the minimum of negative effects; no adrenal suppression and minimum of placental transfer. To evaluate the corticosteroid use at our department we analyzed the HELLP syndrome cases of the last 10 years.
Methods: Maternal and neonatal outcome in HELLP syndrome cases was analyzed in a retrospective study between 1st Jan 2005 and 31st Dec 2014. Data were presented in absolute numbers and percentages; statistic was performed using Chi square, Fisher's exact test, independent T test and ANOVA calculation. A two-sided p-value of less than 0.05 was considered as significant.
Results: Pregnancies complicated by HELLP syndrome (n=91) were divided in 3 groups: 1) PRED treated by high prednisolone administered one to three times (n=61, 67.1 %), 2) NO, receiving no corticosteroids (n=18, 19,7 %) and 3) MIX, received more than three doses and different types of corticosteroids (n=12, 13,2 %). The characteristics of the MIX group were different compared to the other groups: earlier gestational age at diagnosis, additional diseases and reasons with need of corticosteroid administration. The NO and PRED groups were similar regarding group distribution. Comparing NO with PRED group, there was a tendency (n. s.) to shorter intensive care and hospitalization times, decreased incidence of cesarean section and increased ratio of complete fetal lung maturation cycle in the PRED group. There were no differences between maternal morbidity or neonatal asphyxia.
Conclusion: The management of HELLP syndrome with a high dose prednisolone should be evaluated in a further prospective study. However, it seems that the use of high dose corticosteroids could improve the outcome of pregnancies complicated by HELLP syndrome. Adjustment of the therapy regime may be necessary in cases with very early HELLP syndrome before 25th week of gestation or additional morbidity. Due to the low placental transpass of prednisolone it can be advantageous over other corticosteroids in the use as HELLP syndrome therapy.

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Differences in depression scores between women with a history of term hypertensive pregnancy disorders and women with a history of uncomplicated pregnancies

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Introduction: Depression is among the leading causes of disability adjusted life years. For women in their fertile ages the occurrence of depression is of great impact for their selves and families. We analyzed the association between termhypertensive pregnancy disordersand depression scores.
Methods: Two to six years after pregnancy, women with a history of term preeclampsia or gestational hypertension were included in the hypertensive pregnancy cohort (HTP cohort) (n=257). Controls were women who had an uncomplicated pregnancy (n=83) (NTP cohort).The Edinburgh Postnatal Depression Scale (EPDS score) (Cox et al 1987) was used to determine individual depression scores. Depression was defined as an EPDS score > 12 or the use of antidepressants. Potential differences between groups were compared using the Student's T test, the Chi- squared test (X2 test), or the Mann-Whitney U test when appropriate. We used logistic regression analyses to adjust for potential confounders.
Results: Women in the HTP cohort had higher depression scores than women in the NTP cohort (table 1) and were more often depressed (OR 5.8 (1.4-24.6)). After correction for parity (adjusted OR 1.3 (0.8-2.0), BMI (adjusted OR 1.2 (1.1-1.2) and antihypertensive medication use (adjusted OR 1.1 (0.3-3.8), no significant differences were found in depression rates with an adjusted OR 4.2 (0.9-18.8).
Conclusion: More than three years postpartum women with a history of term hypertensive pregnancy disorders are more often depressed compared to women with a history of a normotensive pregnancy.

Table 1.

	HTP cohort (n=257)	NTP cohort (n=83)	P-value
Maternal age at follow- up, years	36 (5.1)	35 (4.8)	.39
Follow-up period (years)	4.1 (3.6-4.6)	3.6 (3.1-4.1)	<.001
Parity at follow-up	1.9 (0.7)	2.1 (0.8)	.01
Body mass index at follow-up, kg/m2	26.2 (23.7-29.7)	23.2 (21.7-25.1)	<.001
Smoking at follow up	29 (11%)	12(14%)	.44
Hypertension at 2.5 years follow-up	91 (35%)	1 (1%)	<.001
Antihypertensive medication use at 2.5 years follow-up	22 (9%)	0 (0%)	.006
Antidepressants use	10 (4%)	1 (1%)	.23
EPDS score	2.0 (1.0-6.0)	1.0 (0.0-3.0)	.001
EPDS > 12	25 (10%)	2 (2%)	.03
Depression	32 (12%)	2 (2%)	.008

Data are presented mean (SD), median (interquartile range) or numbers (percentages)

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Cardiac function and ventriculo-arterial interaction 11 years after preeclampsia complicated pregnancy

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Introduction: Preeclampsia (PE) is associated with left ventricular systolic and diastolic dysfunction. Studies demonstrated a relationship between PE and cardio-vascular disease (CVD) later in life, however there is little evidence of disturbances in cardiac function at long-term follow-up after PE.

Objective: The aim of this study was to assess cardiac function and ventriculo-aterial coupling (VAC) in middle-aged women more than 10 years after a pregnancy complicated by PE.

Material and Methods: Cardiac function in 15 women with history of PE (mean age 39±4 years) and 16 matched healthy controls (41±3 years) was evaluated 11 years following the index pregnancy. Medical and family history was assessed, echocardiography including Tissue Doppler Imaging (DTI) and two-dimensional speckle-tracking echocardiography (2D STE) for myocardial strain imaging were performed. Systolic and diastolic function, left and right ventricular (LV and RV) size and function, LV global strain, LV wall thickness and atrial size as well as stroke volume (SV) and cardiac output (CO), indices of VAC and levels of NT-pro- BNP were analyzed. 24-h ambulatory blood pressure measurement was performed. Indices of VAC were measured as effective arterial elastance(EA), EA=LV end-systolic pressure(LVESP)/SV; LV end systolic elastance (ELV),ELV=LVESP/LVESV(LV end –systolic volume), VAC =ratio EA/ELV; Compliance=SV/(SBP-DBP) and total peripheral resistance (TPR)=[DBP+(SBP-DBP)/3]/CO .

Results: We could not show any significant difference in systolic (111±11 vs 117±14 mmHg) or in diastolic blood pressure (70±2 vs 75±2 mmHg, P=0.16) between the groups at 11 year follow-up. However there was a significant difference in the night /day SBP and DBP ratios (0.81±0.06 vs 0.76±0.05,and 0.88±0.04 vs 0.84±0.04;both $p<0.05$).There were no significant differences in LV and RV dimensions, systolic function or global LV strain. Indices of diastolic LV function, left and right atrial size or NT-pro- BNP levels did not differ between our study groups. EA/ELV was 0.53(0.45-0.6) in PE and 0.52(0.48-0.61) in controls, p=0.60.None of the VAC variables differed between the groups.

Conclusion: We could not demonstrate alterations in systolic or diastolic left or right ventricular function, or in ventriculo-arterial interaction in women 11 years after a pregnancy complicated by PE, despite sensitive echocardiographic techniques. Pre-existing risk factors may be more important for future cardiovascular complications than myocardial and vascular damage apparent during pregnancy in women with PE.

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Placental weight in the first pregnancy and risk for preeclampsia in second pregnancy: A population cohort study of 186 859 women

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Introduction: Underlying maternal factors associated with placental growth in first pregnancy may predispose for the development of preeclampsia in a second pregnancy. Such underlying factors may differ according to preeclampsia status in the first pregnancy.
Objective: Thus,in women with and in women without previous preeclampsia, we studied whether placental weight in the first pregnancy was associated with the risk for preeclampsia in the second pregnancy.
Methods: In a population-based cohort study, we included all women with two singleton births in Norway during the period 1999-2012(n = 186 859).We calculated placental weight z-scores in the first pregnancy and divided the distribution into five groups of equal size (quintiles). We estimated odds ratios (OR) with 95% confidence intervals (95% CI) for preeclampsia in the second pregnancy according to quintiles of placental weight z-scores in the first pregnancy.
Results: Among women without previous preeclampsia, 1.5% (2597/177 239) developed preeclampsia in second pregnancy as compared to 15.7% (1522/9710) among women with previous preeclampsia. In women without previous preeclampsia, there was a u-shaped association between placental weight z-scores in first pregnancy and the risk for preeclampsia in second pregnancy; crude OR 1.30 (95% CI 1.14-1.47) for pregnancies in the lowest quintile, and crude OR 1.20 (95% CI 1.06-1.36) in the highest quintile, using pregnancies in the 3rd quintile of placental weight as the reference. In separate analyses of pregnancies with previous preeclampsia, pregnancies with placental weight in the first quintile had the highest recurrence risk, crude OR 1.30 (95% CI 1.10-1.55) using the 3rd quintile of placental weight as the reference. A large placenta was not associated with recurrence risk; crude OR 0.99 (95% CI 0.83-1.18).
Conclusions: In women without previous preeclampsia, we found that both high and low placental weight in the first pregnancy was associated with increased risk for preeclampsia in the second pregnancy. In women with previous preeclampsia, the overall risk was increased and low placental weight further increased the risk for preeclampsia in the second pregnancy.

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Relationship between severe preeclampsia onset with IUGR incidence at dr. Soetomo General Hospital in 2013

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Introduction: Intrauterine growth restriction can be a serious problem in neonates because it is associated with increased morbidity and mortality and long-term sequel in the future. One of the main maternal risk factors of Intrauterine growth restriction is severe preeclampsia in pregnancy. As we know preeclampsia has two tipe, first is ealy onset of severe preeclampsia that caused by failed of trofoblast invasion to the spiral artery and the second is late onset of severe preeclampsia that caused by such as chronic hypertension, diabetes melitus, obese, tuberculoses, SLE (systemic lupus erythematosus) and other autoimmune disease.

Objectives: We are curious about relationhip onset of severe preeclampsia with Intrauterine growth restriction. This study analyzed the relationship between the onset of severe preeclampsia and the incidence of Intrauterine growth restriction in Dr. Soetomo General Hospital Surabaya. The aim of this study was to prove whether early onset severe preeclampsia is a risk factor for Intrauterine growth restriction compared with late-onset severe preeclampsia.
Methods: This was an analytic observational cross-sectional study. Sampling technique we used in this study was random sampling. The data in this study were taken from the medical records at the Department of Obstetrics and Gynecology Dr. Soetomo General Hospital Surabaya in January 2013 until december 2013, which include in these data are gestational age, preeclampsia onset, sex, birth weight, and Intrauterine growth restriction incidence. The Onset of severe preeclampsia were divided into two categories: first, early onset (≤ 34 weeks) and second, late onset (> 34 weeks). Data analysis was performed in two stages, the univariate and bivariate analysis. Data analysis used was cross tabulation and chi-square test with level of significance of 95 % ($p < 0.05$). This study identifies the relationship between the severe preeclampsia onset as independent variable on the IUGR incidence as dependent variable and the estimation of the prevalence ratio of the causes of incidence of Intrauterine growth restriction There were 120 patients in this study.
Results: Results showed that prevalence rate of IUGR in early-onset severe preeclampsia was 1.32 times higher compared with late-onset severe preeclampsia,. However, there was no statistically significant association between early-onset preeclampsia and the incidence of IUGR. ($p = 0.53$; PR = 0.71 ; 95 % CI = 0.25 to 2.07). Late-onset severe preeclampsia also had no effect on the incidence of Intrauterine growth restriction ($p = 0.53$; PR = 1.40 ; 95 % CI = 0.48 to 4.08).
Conclusion: It can be concluded that the onset of severe preeclampsia had no effect on the incidence of Intrauterine growth restriction.

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Stromal derived factor-1α is a key to improving neonatal brain injuries

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Background: With perinatal medical progress, the survival rate of the newborn baby was improved, but in late years , cerebral palsy is increase increasing with abortive the increase of preterm birth. The Hypoxic ischemicischemia (HI) encephalopathy is known as a main cause of the cerebral palsy, but; however, the effective medical therapy is has not been established. Stromal derived factor-1α (SDF-1α) is known reported to control regulate the migration of cells derived from bone marrow into the ischemic lesion for of damaged tissuesregeneration. In this study, we evaluated the effect of SDF-1α on brain damage in of neonatal rats.
Method: The lLeft common carotid artery arteries of seven-day-old Wistar rat pups was were ligated with 6–0 silk threads. The pups were subsequently exposed to hypoxic gas mixture (8% oxygen, 92% nitrogen) for 120 min. The pups were divided into 4 groups, 1) control, 2) HI and seline saline intracranial injection , 3) HI and SDF-1α (60μg/kg) intracranial injection, 4) HI and SDF-1α (600μg/kg) intracranial injection, and 5) SDF-1α intracranial injection only. Seven days later, brain damage in of pups was evaluated with magnetic resonance imaging. 11 to 15 days later, neurocognitive outcomes were evaluated using the Morris water maze (WM). Four weeks later, Motor coordination

ability was assessed with an accelerated rotarodusing the accelerating rotarod assay. After the rotarod test, the pups were sacrificed and the brains were dissected. Brain injury was assessed using TTC staining.

Result: WM showed that there was an improvement of spatial perception ability in the SDF-1α (600 μg/kg) injection group. On the other hand, in the rotarod examination, meaningful improvement of the motor coordination ability was not observed by the rotarod assay. I did notFurthermore, accept meaningful improvement to the size of the brain injury was not changed eitherby SDF-1α.

Conclusion: In neonatal hypoxic ischemicHI encephalopathy, the possibilityit is possible that SDF-1α might be influential on the improved spatial perception ability without the physical improvement of the brain injury was suggested.Background: With perinatal medical progress, the survival rate of the newborn baby was improved, but in late years , cerebral palsy is increase increasing with abortive the increase of preterm birth. The Hypoxic ischemicischemia (HI) encephalopathy is known as a main cause of the cerebral palsy, but; however, the effective medical therapy is has not been established. Stromal derived factor-1α (SDF-1α) is known reported to control regulate the migration of cells derived from bone marrow into the ischemic lesion for of damaged tissuesregeneration. In this study, we evaluated the effect of SDF-1α on brain damage in of neonatal rats.

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ROCHE LUNCH SYMPOSIUM

24 AUGUST, 2015 • PLENARY ROOM

Preeclampsia testing with sFlt-1/PlGF ratio:
Clinical implementation and health economic impact
Chairs: Holger Stepan – Manu Vatish

Angiogenic biomarkers in preeclampsia: Ready for primetime
Holger Stepan
Leipzig University, Department of Obstetrics, Leipzig, Germany

The Health Economics perspective on preeclampsia testing
Manu Vatish
University of Oxford, Nuffield Department of Obstetrics and Gynaecology, Oxford, UK

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Short-term prediction and diagnosis

ROCHE LUNCH SYMPOSIUM
Thursday, Sept 24th, 13:00 – 13:45, Plenary Room

Preeclampsia testing with sFlt-1 / PlGF ratio: clinical implementation and health economic impact

Angiogenic biomarkers in preeclampsia: ready for primetime
Prof. Holger Stepan, Leipzig University, Department of Obstetrics, Germany

The Health Economics perspective on preeclampsia testing
Dr. Manu Vatish, University of Oxford, Nuffield Department of Obstetrics and Gynaecology, UK

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