178 Blood pressure patterns in pregnant women with treated chronic hypertension according to the development of severe preeclampsia

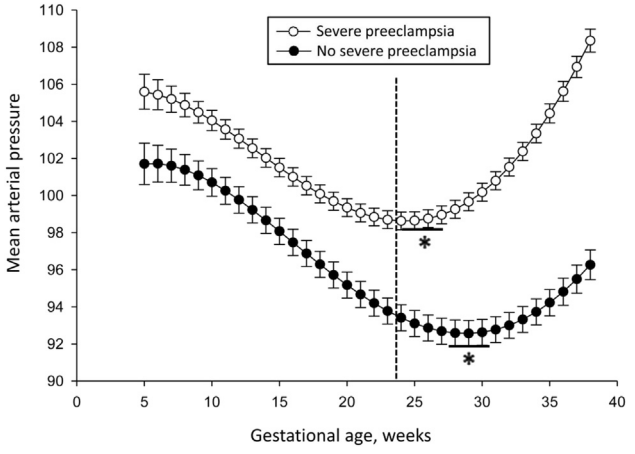
Jamie L. Morgan, David B. Nelson, Scott W. Roberts, Edward C. Wells, Donald D. McIntire, F Gary Cunningham
[1]University of Texas Southwestern Medical Center, Dallas, TX

OBJECTIVE: To examine blood pressure patterns across pregnancy in women with treated chronic hypertension according to the development of severe preeclampsia (SPE).

STUDY DESIGN: This retrospective cohort study included women who required antihypertensive therapy during the first half of pregnancy. Management of these women includes titration of prenatal antihypertensive therapies in a coordinated fashion within a dedicated high-risk pregnancy clinic. Using a random effects model, predicted means of the mean arterial pressures (MAPs) were calculated from 5 to 40 weeks gestation for women with and without SPE with gestational age entered as a fourth order polynomial.

RESULTS: Between January 2002 and December 2014, a total of 433 women met the inclusion criteria. Of these women, 67% (291/433) developed severe preeclampsia. The mean MAP was significantly higher at entry into prenatal care in women who were ultimately diagnosed with SPE in comparison those who were not (105.6 vs 101.7, p=0.002). The rate of change in MAP was similar in both the preeclamptic and non-preeclamptic cohorts until 24 weeks at which point the rates diverged significantly (p= 0.029) and continued to differ significantly until delivery. As shown in the Figure, women who developed SPE reached a blood pressure nadir at a significantly earlier gestational age than those who did not develop severe disease (25.9±7.1 vs 29.0±7.6, p <0.001).

CONCLUSION: Blood pressure patterns differ significantly in pregnant women with treated chronic hypertension who do and do not develop severe preeclampsia. The blood pressure nadir occurs approximately 3 weeks earlier in those who are destined to develop severe preeclampsia.



179 Women with chronic hypertension treated during pregnancy - perinatal outcomes related to graduated 24-hour urinary protein excretion levels measured prior to 20 weeks

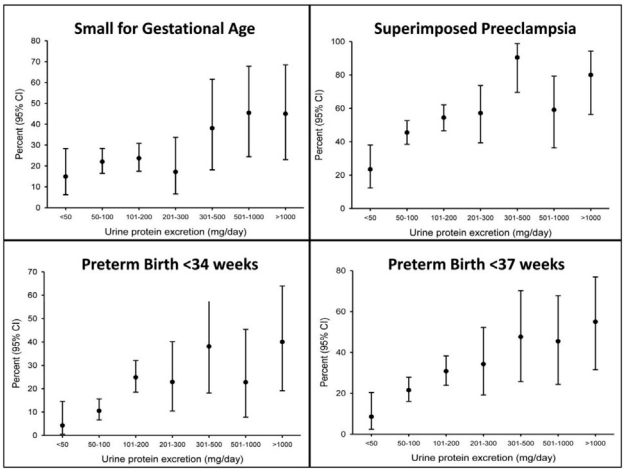
Jamie L. Morgan, David B. Nelson, Scott W. Roberts, Edward C. Wells, Donald D. McIntire, F. Gary Cunningham
[1]University of Texas Southwestern Medical Center, Dallas, TX

OBJECTIVE: To analyze the relationship between perinatal outcomes and stratified 24-hour urine protein excretion determined prior to 20 weeks in women with chronic hypertension (CHTN) treated during pregnancy.

STUDY DESIGN: This retrospective cohort study included pregnant women with CHTN for whom therapy was initiated and who completed urine protein quantification prior to 20 weeks. Management of these women is coordinated within a dedicated high-risk prenatal clinic. 24-hour urine protein excretion levels determined prior to 20 weeks were stratified as follows: <50 mg, 50-100 mg, 101-200 mg, 201-300 mg, 301-500 mg, 501-1000 mg, and >1000 mg. The frequencies of superimposed preeclampsia (SPE), preterm birth (PTB) and small-for-gestational age (SGA) infants <10th percentile were compared for each group according to these graded proteinuria levels.

RESULTS: Between January 2002 and December 2014, a total of 514 women met inclusion criteria and selected outcomes are shown in the Figure. The rates of SPE, PTB <34 weeks, PTB <37 weeks, and SGA were all significantly increased as 24-hour protein excretion levels increased (p-value for trend <0.001). The frequency of SGA infants was unrelated to co-existent rates of SPE when compared across strata of proteinuria levels (p=0.30). When outcomes of women with protein excretion levels <300mg/day were analyzed separately, there remained a significant association between increasing proteinuria strata and rates of SPE and PTB (Figure).

CONCLUSION: As the quantity of baseline proteinuria increased in pregnant women with treated CHTN, the frequencies of SPE, PTB, and SGA all significantly increased. This relationship remained significant for SPE and PTB at proteinuria levels heretofore considered to be within normal range (<300 mg/24 hours).



180 Do genetic and environmental influences on abnormal metabolic profile in pregnancy continue to second generation offspring?

Fangxian Lu, Francesca Ferrari, Alejandra E. Ontiveros, Yongsheng Lan, Bahaeddine M. Sibai, Sean Blackwell, Jerrie S. Refuerzo, Monica Longo
[1]UT Health - University of Texas Medical School at Houston, Houston, TX

OBJECTIVE: Fetal programming contributes to metabolic and cardiovascular disease in offspring even during their adult life. Whether fetal programming increases the risks for disease in subsequent generations remain unknown. Our aim was to evaluate the effect of genetic and environmental inheritance on the metabolic profile in a transgenerational mouse model.

STUDY DESIGN: In order to study the effects of fetal programming on 2nd generation offspring we conducted three breeding schemes, all with wild type (WT) males. WT males were bred to heterozygous $eNOS^{+/-}$ females fed a high fat diet (HFD) manifesting metabolic-like syndrome (MLS) phenotype (Group 1), heterozygous $eNOS^{+/-}$ females fed a control diet (CD) manifesting hypertension (HTN) (Group 2), or WT female fed CD use as control (Group 3). WT male

offspring from these groups (2nd generational animals) were then fed control diet from weaning to until 3 months of age after weaning. Offspring weight was measured from 3 weeks to 8 weeks of age to obtain weight gain trajectory. Systolic blood pressure (SBP), glucose tolerance test (GTT) and lipid profile (cholesterol, HDL, LDL and triglycerides) were measured at 3 months of age.

RESULTS: WT offspring born from MLS mother had similar postnatal weight gain at 8 weeks of age (MLS, group 1: 8.8 ± 0.7 g) compared with offspring born from HTN and control mother (HTN, group 2: 12.3 ± 2.3 g; control, group 3: 11.3 ± 0.5 g)(p=0.172). Among the three groups, similar glucose levels were obtained by GTT at each time-point of the curve. There was no difference in SBP among all the WT male offspring groups (MLS, group 1: 156.9 ± 5.5; HTN, group 2: 134.2 ± 11.9 and control, group 3: 138.9 ± 6.3, p=0.137). Also no difference was seen in the lipid profile between groups (Table, p=0.994 for cholesterol; p=0.984 for HDL; p=0.980 for LDL; p=0.998 for TG).

CONCLUSION: This is one of the first studies to evaluate the effects of fetal programming on 2nd generation offspring. Abnormal metabolic profiles resulting from genetic and environmental exposures in first generation female during pregnancy do not appear to increase the risk of passage of metabolic or cardiovascular dysfunction to the 2nd generation animals fed a normal diet.

Figure. Trans-generational breeding scheme
Three groups of 2nd generation wild-type male offspring were obtained: heterozygous eNOS-KO$^{+/-}$ females fed a high fat diet (HFD) manifesting MLS (Group 1), heterozygous eNOS-KO$^{+/-}$ females fed a control diet (CD) manifesting HTN (Group 2), or WT female fed control diet (CD) used as control (Group 3)

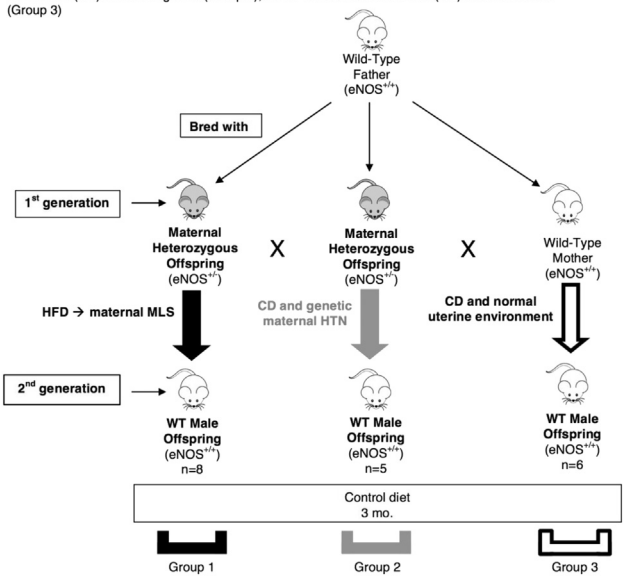


Table. Lipid profiles in WT male offspring from each trans-generational breeding scheme. Values are reported as Mean ± SEM.

Breeding Scheme	Maternal MLS (Group 1)	Maternal HTN (Group 2)	Maternal Control (Group 3)
	Second generation WT Male Offspring		
Cholesterol (mg/dl)	185.4 ± 92.7	178.5 ± 32	174.6 ± 78
HDL (mg/dl)	182.9 ± 91.4	166.8 ± 27.2	177.5 ± 79.4
LDL (mg/dl)	31.4 ± 15.7	28.3 ± 11.5	27.9 ± 12.4
TG (mg/dl)	142.2 ± 71.1	146.1 ± 59.7	148.5 ± 66.4

181 Administration of 17-hydroxyprogesterone caproate in mid-gestation improves fetal growth possibly by reducing sFlt-1 and placental cytolytic NK cells in the Reduced Uterine Perfusion Pressure (RUPP) rat model of Preeclampsia

Jamil T. ElFarra, Lorena M. Amaral, Denise C. Cornelius, Jessica L. Faulkner, Mark W. Cunningham Jr, Taia R. Mcafee, D'andrea S. Thomas, Babbette LaMarca
[1]University of Mississippi Medical Center, Jackson, MS

OBJECTIVE: Preeclampsia (PE) is characterized by elevated anti-angiogenic factor soluble fms-like tyrosine kinase (sFlt-1), cytolytic natural killer (NK) cells and placental ischemia predicted with increased uterine artery resistance (UARI) which are likely culprits for decreased fetal weight during PE pregnancies. Cytolytic NK have been shown to be increased in PE women compared to those with normal pregnancy (NP). Currently, there is no effective treatment for PE except for delivery, making PE the leading cause for premature births worldwide. Administration of 17-hydroxyprogesterone caproate (17-OHPC) is used for prevention of spontaneous preterm labor, but is not included in the current management for PE. This study was designed to test the hypothesis that early administration of 17-OHPC could improve pregnancy outcomes in response to placental ischemia.

STUDY DESIGN: 17-OHPC (3.32mg/kg) was administered intraperitoneally on gestation day 15 to reduced uterine perfusion pressure (RUPP) rats, UARI was measured using Doppler ultrasound and carotid catheters were inserted on day 18. Blood pressure (MAP), sFlt-1, and placental cytolytic NK cells were measured on GD 19.

RESULTS: MAP in normal pregnant (NP) rats (n=12) was 94 + 2, 126 + 2 in RUPP (n=27) and 111+1 mmHg in RUPP+17-OHPC (n=15), p <0.05. Pup weight was 2.3+0.09 in NP, 1.9+ 0.04 in RUPP rats, which improved to 2.1+0.06 grams in RUPP+17-OHPC p <0.05. UARI was 0.6+0.01 in NP (n=3), 0.8+0.03 in RUPP rats (n=4), which improved to 0.6+0.04 in RUPP+17-OHPC (n=5), p<0.05. Total number of placental NK cells was 8.6 + 3.1 in NP, 20.2 +2.4 in RUPP rats, which decreased to 1.6 + 0.54 % in RUPP+17-OHPC, p<0.05. Activated placental NK cells was 3.8 + 2.2 in NP, 11.9+2.01 in RUPP, which improved to 0.4 + 0.2 % in RUPP+17-OHPC, p <0.05. Plasma sFlt-1 was 36.1+7.5, 385.9+141 in RUPP rats (n=5), which was blunted to 110.2+11.1 pg/mL in RUPP+17-OHPC, p<0.05.

CONCLUSION: Mid-term administration of 17-OHPC improves sFtl-1, UARI, activated cytolytic NK cells, pup weight and hypertension in response to placental ischemia and could be considered for addition to the management of PE.

182 Signature placental and kidney-specific transcripts in the urinary misfoldome of women with preeclampsia (PE)

William E. Ackerman, Hongwu Jing, Guomao Zhao, Antonis Rokas, Taryn Summerfield, Vicki Wysocki, Catalin S. Buhimschi, Irina A. Buhimschi
[1]The Ohio State University, College of Medicine, Columbus, OH, [2]The Ohio State University, Department of Chemistry and Biochemistry, Columbus, OH, [3]Nationwide Children's Hospital, Center for Perinatal Research, Columbus, OH, [4]Vanderbilt University, Department of Biological Sciences, Nashville, TN

OBJECTIVE: The mechanisms responsible for development of PE remain to be elucidated. Using proteomics, we discovered unique amyloid-like aggregation signatures (misfoldome) in the urine of women with PE. Yet, the tissue origin of proteins composing the PE misfoldome is not known. This study was undertaken to examine