13 **THE EFFECT OF FETAL PROGRAMMING ON THE EXPRESSION OF GENES INVOLVED IN ADULT VASCULAR FUNCTION** MONICA LONGO[1], FANGXIAN LU[1], VENU JAIN[1], RADEK BUKOWSKI[1], GARY HANKINS[1], GARLAND ANDERSON[1], GEORGE SAADE[1], [1]University of Texas Medical Branch, Obstetrics and Gynecology, Galveston, Texas

OBJECTIVE: Endothelial nitric oxide synthase (NOS3) is involved in the vascular adaptations to pregnancy. We have previously reported that mice born to mothers lacking NOS3 gene have fetal growth abnormalities and abnormal vascular function in later life. This study investigate the potential mechanisms involved in the fetal programming of adult vascular function by evaluating expression of relevant genes in this animal model of fetal programming induced by an unfavorable uterine environment.

STUDY DESIGN: Homozygous NOS3 knockout (C57BL/6J-$NOS3^{-/-KO}$) and wild type mice ($NOS3^{+/+WT}$) were cross-bred to produce litters grown in a maternal environment lacking NOS3 ($NOS3^{-/-KO}$] and maternally-heterozygous ($NOS3^{+Pat/-Mat}$) and litters grown in normal maternal environment, paternally-derived heterozygous ($NOS3^{+Mat/-Pat}$) and wild type ($NOS3^{+/+WT}$). Female offspring at 7-8 weeks of age (n = 4-5/group) were sacrificed. The aorta was isolated and total RNA extracted. TaqMan and appropriate probes for neuronal (NOS1), inducible (NOS2), and cyclooxygenases 1 and 2 (COX1 and COX2), and for pre-developed 18S rRNA probe were used for real-time RT-PCR. mRNA quantification was expressed as relative value (ratio to its own 18s rRNA). One-way ANOVA followed by post-hoc test was used for statistical analysis.

RESULTS: In the aorta, the NOS1, NOS2, and COX1 mRNA expressions were significantly lower in $NOS3^{-/-KO}$ and $NOS3^{+Pat/-Mat}$ female mice compared with $NOS3^{+/+WT}$ ($P < .005$). COX2 expression was not different between the groups (Table).

CONCLUSION: Fetal programming and altered vascular function in adult offspring developing in an unfavorable uterine environment are associated with downregulation of genes active in maintaining normal vascular function.

Relative value

	NOS1	NOS2	COX1	COX2
$NOS3^{-/-KO}$	1.43 ± 0.001	1.27 ± 0.01	1.16 ± 0.01	1.49 ± 0.002
$NOS3^{+Pat/-Mat}$	1.35 ± 0.02	1.24 ± 0.004	1.11 ± 0.009	1.42 ± 0.01
$NOS3^{+Mat/-Pat}$	1.49 ± 0.03	1.28 ± 0.005	1.18 ± 0.01	1.40 ± 0.03
$NOS3^{+/+WT}$	1.50 ± 0.03	1.30 ± 0.005	1.23 ± 0.02	1.46 ± 0.02

14 **EFFICACY OF ENOXAPARIN FOR IMPROVING PREGNANCY OUTCOMES AND UTEROPLACENTAL BLOOD FLOW IN WOMEN WITH THROMBOPHILIA AND RECURRENT PREGNANCY LOSS** ISRAEL THALER[1], BENJAMIN BRENNER[2], [1]Technion-Israel Institute of Technology, Obstetrics & Gynecology, Haifa, Israel, [2]Rambam Medical Center, Hematology, Haifa, Israel, Israel

OBJECTIVE: Maternal thrombophilia is associated with recurrent pregnancy loss (RPL). Prophylaxis with low-molecular-weight heparin can benefit women with thrombophilia and RPL. There is little information about the effect of such treatment on uteroplacental blood flow. The purpose of this study was to evaluate the efficacy of two doses of enoxaparin for improving pregnancy outcomes and to invesigate the effect on uteroplacental blood flow.

STUDY DESIGN: This multicentre, prospective, randomised, open-label study compared pregnancy outcome in women with thrombophilia and recurrent pregnancy loss (3 losses in first trimester, 2 losses in second trimester or 1 loss in third trimester) receiving enoxaparin 40 mg/day or 80 mg/day (40 mg twice daily). Women were enrolled at 5–10 weeks gestation and received enoxaparin throughout pregnancy and post-partum. The primary efficacy endpoints were the delivery of a live, healthy infant and Doppler indices in the uterine and umbilical arteries.

RESULTS: Prophylaxis with enoxaparin significantly increased the rate of live birth (84.3% vs 28.2% for 40 mg/day, 78.3% vs 28.3% for 80 mg/day; $P = .001$), decreased the rate of pre-eclampsia (3.4% vs 6.7% for 40 mg/day, 4.4% vs 14.3% for 80 mg/day; $P = .001$) and decreased the rate of placental abruption (4.5% vs 13.5% for 40 mg/day, 3.3% vs 8.8% for 80 mg/day; $P = .002$) compared with patientś historical rates. The pulsatility index was significantly lower in the uterine arteries of women who received 80 mg/day compare to those receiving 40 mg/day, between 30-34 weeks (1.2 ± 0.08, vs 1.5 ± 0.15, respectively $P < .05$). No other significant differences in efficacy or safety were observed between the two enoxaparin groups.

CONCLUSION: Enoxaparin increased the rate of live births in thrombophilic women with recurrent pregnanchy loss. A dose of 40 mg/day was sufficient to significantly improve pregnancy outcome. Improved uteroplacental blood flow in the group receiving the higher dose of enoxaparin suggests that this dose should be considered in women with multiple thrombophilic defects.

15 **THE INFLUENCE OF PRIOR ROUTE OF DELIVERY: POSTPARTUM MATERNAL AND NEONATAL OUTCOMES** ANNA MCKEOWN[1], DAVID LAGREW[2], MELISSA BUSH[2], JAMES KURTZMAN[2], [1]University of California, Irvine, OB/Gyn Maternal Fetal Medicine, Orange, California, [2]Saddleback Memorial Medical Center, Maternal Fetal Medicine, Laguna Hills, California

OBJECTIVE: Accurate risk/benefit information is needed to counsel an increasing number of women requesting elective cesarean section. The purpose of this study was to assess maternal and neonatal postpartum outcomes associated with previous method of delivery.

STUDY DESIGN: We analyzed prospectively collected singleton maternal and neonatal data from 7/2002-12/2003 in four MemorialCare hospitals. Birth data were collected into a dedicated perinatal database and combined with coded data from a MedAI® database of postpartum maternal and neonatal procedures and outcomes. Patients were subdivided in four groups: (1) Nulliparous; (2) Prior vaginal; (3) Prior Cesarean (CS) without trial of labor (TOL); and (4) Prior Cesarean with TOL. Results were compared by chi square analysis with significance at $P < .05$.

RESULTS: During the study period there were 17,406 births fitting the above criteria. Compared to prior vaginal delivery, patients with prior CS had significantly increased risks of morbidity. The subgroup of prior CS patients without a TOL were more likely to require blood transfusion ($P < .001$, OR 3.1), ICU admission ($P < .001$, OR 4.5), and readmission within 30 days ($P < .025$, OR 1.7) than patients with prior vaginal deliveries. Prior CS with TOL patients did not have these increased risks but were more likely to receive aminoglycosides for postpartum infection ($P < .01$, OR 1.81). Term neonates born to mothers with previous CS were more likely to have prolonged hospitalization (>7 days) in both groups: no TOL ($P < .001$, OR 6.69) and TOL ($P < .05$, OR 2.51). There were no significant differences based on prior delivery route for neonatal mortality within the first 28 days of life, neonatal seizures or encephalopathy.

CONCLUSION: Prior cesarean delivery is a significant risk factor for important postpartum morbidities of the mother and neonate. These risks and benefits should be carefully discussed with women considering elective primary cesarean section.

16 **ABSENCE OF ASSOCIATION OF INHERITED THROMBOPHILIA WITH UNEXPLAINED THIRD TRIMESTER INTRAUTERINE FETAL DEATH** RON GONEN[1], NOA LAVI[2], DINA ATTIAS[3], LILIANA SCHLIAMSER[3], ZVI BOROCHOWITZ[4], ELIAS TOUBI[5], [1]Technion- Israel Institute of Technology, Obstetrics & Gynecology, Bnai Zion Medical Center, Haifa, Israel, Israel, [2]Technion- Israel Institute of Technology, Haifa, Israel, [3]Technion- Israel Institute of Technology, Division of Hematology, Bnai Zion Medical Center, Haifa, Israel, Israel, [4]Technion-Israel Institute of Technology, Institute of Genetics, Bnai Zion Medical Center, Haifa, Israel, Israel, [5]Technion- Israel Institute of Technology, Division of Clinical Immunology, Haifa, Israel, Israel

OBJECTIVE: To investigate the alleged association between thrombophilia and unexplained third trimester stillbirth.

STUDY DESIGN: Case subjects were 37 women with a history of a third trimester unexplained stillbirth. The inclusion criteria were a singleton non malformed fetus, without signs of infection and the absence of any significant maternal risk factors for fetal death. Controls were 46 volunteers, matched for ethnic origin, who have had at least one uncomplicated live birth, and no history of stillbirth, recurrent fetal loss or thrombo-embolism. The exclusion criteria were a pregnancy in the last two months and current hormonal or anticoagulant treatment. The thrombophilia work-up included: Factor V Leiden G1691A, prothrombin G20210A, MTHFR C667T, Protein C, Protein S, antithrombin III, Factor VIII, Factor XI, lupus anticoagulant, anticardiolipin and β2-glycoprotein 1 antibodies. The pathology report of 34/37 placentas of case subjects was reviewed.

RESULTS: The mean (SD) gestational age and birth weight among case subjects were 33.7 wk (4.4) and 1987 g (1013) respectively. The prevalence of at least one inherited thrombophilia among case subjects was 37.8% (14/37) compared with 41.3% (19/46) among controls. (OR = 0.87; 95% CI 0.32, 2.29). Combined inherited thrombophilia was present in 8.1% (3/37) of case subjects compared with 8.7% in controls. (OR = 0.93; 95% CI 0.13, 5.89). Moreover, there was no significant difference between case subjects and controls with respect to the prevalence of any single inherited thrombophilia. There was, however, a significantly higher prevalence of lupus anticoagulant and/or anticardiolipin antibodies, among case subjects compared with controls, 47.2% (17/36) versus 8.7 (4/46) respectively. (OR = 9.4; 95% CI 2.5, 42.3) Infarcts were present in 21/34 (61.7%) of case placentas, however, no significant difference was noted in the prevalence of thrombopilia among subjects with or without placental infarcts.

CONCLUSION: We did not find an association between unexplained third trimester stillbirth and inherited thrombophillia.