13 THE DIAGNOSTIC AND PROGNOSTIC VALUE OF MMP-8 PTD CHECK IN WOMEN WITH PRETERM PREMATURE RUPTURE OF MEMBRANES KUN WOO KIM[1], HYUN SOO PARK[1], SOON-SUP SHIM[1], JONG KWAN JUN[1], ROBERTO ROMERO[2], BO HYUN YOON[1], [1]Seoul National University College of Medicine, Department of Obstetrics and Gynecology, Seoul, South Korea, [2]Grosse pointe, Grosse pointe, Michigan

OBJECTIVE: To examine if the MMP-8 PTD Check™, a rapid bedside test which can be performed in 15 minutes, is of value in the identification of intra-amniotic infection/inflammation(IAI) and in the assessment of the likelihood of adverse pregnancy outcome in patients with PPROM.

STUDY DESIGN: Amniotic fluid (AF) was retrieved by transabdominal amniocentesis in 105 women with PPROM (GA<35 weeks). Fluid was cultured for aerobic and anaerobic bacteria and Mycoplasmas and analyzed for matrix metalloproteinase-8 (MMP-8), white blood cell (WBC) count and MMP-8 PTD Check™ test. IAI was defined as a positive AF culture and/or elevated AF MMP-8 concentration (>23ng/ml). Nonparametric and survival analysis were used.

RESULTS: The prevalence of IAI was 45% (47/105) and that of proven AF infection was 17% (18/105). Patients with a positive MMP-8 PTD Check™ test have a significantly higher rate of IAI (85% [44/52] vs 6% [3/53]; p<.001), proven AF infection (31%[16/52] vs 4%[2/53], p<.001) and adverse outcome than those with a negative MMP-8 PTD CheckTM test. Adverse outcome included shorter interval to delivery and higher rate of preterm delivery, histologic chorioamnionitis, funisitis, low Apgar scores and significant neonatal morbidity. A positive MMP-8 PTD Check™ test had a sensitivity of 94%, a specificity of 86%, a positive predictive value of 85% and a negative predictive value of 94% in the identification of IAI and was an independent predictor of interval to delivery (hazards ratio 4.1; 95% CI, 2.4–6.9) and significant neonatal morbidity (OR 8.2; 95% CI, 2.1–31.4).

CONCLUSION: The MMP-8 PTD Check™ test is a rapid, simple, sensitive bedside test to detect IAI and predict adverse outcome including short latency, chorioamnionitis and significant neonatal morbidity in patients with preterm PROM. The results of this study bring the rapid detection of intra-amniotic inflammation to the bedside in clinical obstetrics.

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14 4-YEAR FOLLOW-UP OF CHILDREN EXPOSED TO 17ALPHA HYDROXYPROGESTERONE CAPROATE (17P) IN UTERO ALLISON NORTHEN[1], [1]NICHD MFMU Network, Bethesda, Maryland

OBJECTIVE: We have previously found 17P treatment to prevent recurrent preterm birth and infant morbidity when given to women with prior spontaneous preterm births. The purpose of this long-term follow-up evaluation was to determine if there are evident adverse effects of 17P after in-utero exposure.

STUDY DESIGN: We attempted to locate and evaluate surviving children of mothers who participated in a multicenter placebo-controlled trial of weekly intramuscular 17P with a 2:1 allocation to 17P and Placebo, respectively. The guardian was interviewed about the child's general health. Children underwent a physical exam and developmental screen with the Ages and Stages developmental questionnaire (ASQ). Gender specific play was assessed with the Preschool Activities Inventory (PSAI).

RESULTS: Of 348 eligible surviving children, 278 (80%) were available for evaluation (194 17P, 84 Placebo). The mean age at follow-up was 48 months. No significant diffferences were seen in health status and conditions, or physical exam, including genital anomalies between 17P and Placebo children. Scores for gender-specific play (PSAI) were within the normal range and similar between 17P and Placebo groups.

CONCLUSION: In-utero exposure to 17P was not associated with adverse health outcomes in surviving children.

Percent of children failing developmental screen

Area	17P	Placebo	p
Communication	11%	11%	0.9
Gross motor	3%	4%	0.7
Fine motor	21%	18%	0.6
Problem solving	10%	11%	0.9
Personal-social	4%	1%	0.4
At least one area	28%	28%	0.9

Characteristics of study children

Characteristic	17P	Placebo	p
Mean height %ile	54	57	0.5
Mean weight %ile	55	57	0.7
Mean head circumf %ile	50	54	0.4
Mean systolic BP	92	93	0.6
Mean diastolic BP	56	58	0.2
Mean PSAI- boys	67	67	0.3
Mean PSAI- girls	32	33	0.5

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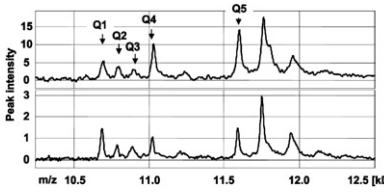
15 PROTEOMICS ANALYSIS OF AMNIOTIC FLUID. A NOVEL METHODOLOGY TO PROVIDE INSIGHT INTO THE MECHANISMS OF IDIOPATHIC PRETERM BIRTH IRINA A. BUHIMSCHI[1], VICTOR A. ROSENBERG[1], SONYA S. ABDEL-RAZEQ[1], STEPHEN F. THUNG[1], CATALIN S. BUHIMSCHI[1], [1]Yale University, Ob./Gyn.& Reprod.Sci., New Haven, Connecticut

OBJECTIVE: Identification of relevant disease biomarkers that may impact prediction of preterm birth (PTB) and fetal outcome is critical. Recent advancement in proteomics has provided a valuable perspective related to several complex functional and molecular mechanisms (inflammation, bleeding) leading to PTB. Still, the etiology of most PTB remains elusive. A comprehensive analysis of the amniotic fluid (AF) proteome was conducted to identify disease biomarker patterns related to PTB in the absence of infection/inflammation or bleeding.

STUDY DESIGN: A proteomic fingerprint was generated from fresh AF using SELDI-TOF mass spectrometry in a total of 268 consecutive samples retrieved from women who presented with signs or symptoms of preterm labor or PPROM. Intra-amniotic inflammation and bleeding were excluded based on previously validated proteomic profiles and biomarker identification. Hierarchical clustering algorithms based on novel descriptors quantifying similarity/dissimilarity among tracings allowed identification of mass areas of interest.

RESULTS: The prevalence of PTB <34 wks was 77%. A novel discriminatory profile was identified in the 10-14 kDa area of interest and consisted of 5 proteomic peaks (Q1-5; Figure). The abnormal profile was associated with PTB in the absence of intra-amniotic infection, inflammation or bleeding. Women displaying the novel profile were at 27.1 [16.3-36.1] wks GA at amniocentesis and most often presented with intact membranes. The novel profile appeared alone and all other tests of AF were normal in 85% (17/20) of cases.



Biomarker	Average mass [Da]
Q1	10689.5
Q2	10791.0
Q3	10892.9
Q4	11025.7
Q5	11597.2

CONCLUSION: Proteomic profiling of the AF coupled with novel mathematical algorithms can be used to identify patients at risk for PTB in the absence of intra-amniotic inflammation or bleeding.

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16 THE EFFECT OF ESTERASES ON 17-HYDROXYPROGESTERONECAPROATE RU YAN[1], TATIANA NANOVSKAYA[1], GARY HANKINS[1], MAHMOUD AHMED[1], [1]University of Texas Medical Branch at Galveston, Obstetrics and Gynecology, Galveston, Texas

OBJECTIVE: Recent clinical trials demonstrated the role of 17α-hydroxyprogesterone caproate (17-HPC) in preventing spontaneous pre-term labor. However, the underlying mechanism is still unclear. This study was undertaken to determine whether 17-HPC is hydrolyzed to 17α-hydroxyprogesterone (17-HP) and caproate and hence a role for 17-HP in the therapeutic effect of the parent drug.

STUDY DESIGN: The hydrolysis of 17-HPC by the following three preparations and recombinant esterases was determined: Human plasma, S9 fraction obtained from human liver and placentas as well as recombinant esterases that included porcine liver carboxylesterase, rabbit liver carboxylesterase and equine cholinesterases. The reaction solution contained dual labeled radioactive 17-HPC (substrate), one of the above preparations (enzyme) and other components then incubated for 60 minutes at 37°C. The amounts of 17-HP and caproate formed were determined using an HPLC instrument equipped with a detector for radioactivity. The enzymatic activity of the above preparations and recombinant esterases for hydrolysis of p-nitrophenyl acetate (pNPA), p-nitrophenyl butyrate (pNPB) and butyrylthiocholine (BTC) was determined under the same reaction conditions and served as positive controls.

RESULTS: The activity of hepatic and placental preparations as well as recombinant esterases in hydrolysis of pNPA, pNPB and BTC were high. However, when 17-HPC was used as a substrate neither caproate nor 17-HP were detected. The detection limits of 17-HP and caproate under our conditions were in the femto mole range.

CONCLUSION: 17-HPC is not hydrolyzed in vitro by enzymes of human plasma, liver and placenta. If true in vivo, it is unlikely that the role of 17-HPC in treatment of preterm labor is due to either caproate or 17-HP. Supported by the Obstetric Pharmacology Research Network, NICHD.

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