13 IIMPROVED SENSITIVITY (SEN) & POSITIVE PREDICTIVE VALUE (PPV) FOR THE DETECTION OF PRE-TERM LABOR (PTL): A NEW MULTIVARIATE QUANTITATIVE PROTEIN MICROARRAY SERUM PANEL

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OBJECTIVE: Interventions for PTL have been very unsuccessful in part because of inadequate identification of candidates for therapy. Available markers have high negative predictive values (NPV) but poor SEN and PPV. We have investigated a new set of protein markers to achieve a much higher SEN while maintaining high specificity (SPEC) and NPV

STUDY DESIGN: Serum specimens were obtained from 318 gravidas (152 in imminent/early labor and 166 NIL). First, we used high-resolution mass spectrometry and proteome enrichment kits (the prOTOF2000TM and ProEXPRESSION Protein Fractionation kits, PerkinElmer; ProteinChip® Bio-Rad) for peptide and protein biomarkers that correctly discriminated patients for imminent labor; second, several bioinformatic platforms were then employed to discern potential markers. Third, several of the most predictive candidates called RAL 1,2,& 3 (IP in progress) were selected for sequence identification and, fourth, we then validated markers on our in-house, quantitative protein microarray platform in a panel with several other putative markers and compared with published FFN data. Specificity (SPEC) was set at 95%+ for PBEF and multivariate analyses.

RESULTS: Components PBEF, RAL 1,2,3, both in univariate analyses and multivariate analysis showed much higher SEN and PPV for PT than FFN.

CONCLUSION: PBEF, per se, and RAL 1,2,& 3 in univariate and multivariate combinations produce dramatically higher SEN and PPV for similar SPEC and NPV to FFN (IOM report 2006). Accurate identification of pts at imminent high risk may allow for targeted interventions to reduce the sequelae of pre-term birth without requiring unnecessary, expensive treatment of large numbers of low risk patients. Serum testing also has considerable advantages over cervical swabs.

Multivariate quantitative protein microarray serum panel

	SENS	SPEC	PPV	NPV
RAL Multivar	88%	95%	72%	98%
PBEF	39%	96%	75%	98%
RAL 1	81%	84%	40%	97%
RAL 2	78%	77%	32%	91%
RAL 3	83%	77%	33%	97%
FFN (IOM)	39%	95%	30%	92%

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14 CIRCULATING ANGIOGENIC FACTORS IN SPONTANEOUS PRETERM LABOR AND DELIVERY

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OBJECTIVE: To determine whether spontaneous preterm (SPT) labor and delivery (L&D), like preeclampsia, is accompanied by elevated maternal serum concentrations of soluble fms-like tyrosine kinase 1 (sFlt1) and soluble endoglin (sEng) and reduced levels of free placental growth factor (PlGF).

STUDY DESIGN: 2200 nulliparas were randomly selected from the CPEP trial. After excluding women with gestational hypertension or preeclampsia, 1609 remained of whom 125 delivered before 37 wks (preterm) after spontaneous labor and 1463 delivered at 37 wks or later (term) . Serum angiogenic factor concentrations were measured in all 4055 specimens obtained before delivery. Significance was acertained on log-transformed data after adjustment for GA and race.

RESULTS: Compared with women delivered at term following spontaneous labor, women with SPT L&D had higher sEng at 21-32 wks (5.6 vs 5.3 ng/ml, $P<0.01$); higher sFlt1 (10948 vs 7248 pg/ml, $P<0.01$) and sEng (12.0 vs 9.8, $P<0.01$) at 33-36 wks; and lower PlGF at 33-36 wks (281 vs 613 pg/ml, $P<0.001$). In analyses by wks before SPT delivery, comparing angiogenic factors in specimens obtained from women with SPT L&D to GA-matched specimens from women with term delivery, sEng was elevated beginning 6-8 wks before SPT delivery (6.1 vs 5.2 ng/ml, $P<0.01$); sFlt1 was elevated (5333 vs 4457 pg/ml, $P<0.05$) 2-5 wks before and PlGF reduced (305 vs 680 pg/ml, $P<0.01$) the week before SPT delivery.

CONCLUSION: Modest increases in maternal serum sFlt1 and sEng and decreases in free PlGF are associated with spontaneous preterm labor and delivery.

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15 PROGESTERONE REDUCES THE RATE OF CERVICAL SHORTENING IN WOMEN AT RISK FOR PRETERM BIRTH: SECONDARY ANALYSIS FROM A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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OBJECTIVE: To determine whether progesterone supplementation alters the rate of cervical shortening in a cohort of women at increased risk for preterm birth.

STUDY DESIGN: A secondary analysis was performed of women enrolled into a preterm prevention trial utilizing 90mg intravaginal, daily progesterone gel, Procheive®. Participants in this trial had a singleton and a history of spontaneous preterm birth between 20-35 weeks gestation or a history of midtrimester cervical shortening. Patients were randomized 1:1 drug versus placebo. Transvaginal cervical length measures were obtained at randomization (18^{+0}-22^{+6} weeks' gestation) and at 28 weeks' gestation. The difference in cervical length between these time points was compared. In a subpopulation identified as having a treatment effect by prior secondary analysis, those subjects with a cervical length 30mm at randomization, the rate of cervical change was also assessed.

RESULTS: 668 women were enrolled with data available for 611 participants (309 progesterone, 302 placebo). Demographic characteristics were similar between groups. Initial mean baseline cervical length was 3.7 ± 0.7 cm for both groups, $P=.97$. At the 28 week exam, the mean cervical length had decreased significantly in both groups, progesterone 3.3 ± 0.9 cm, $P<.001$, and placebo 3.1 ± 0.9, $P<.001$. The progesterone group had significantly less cervical shortening than the placebo group during this interval (−0.2 cm; 95% CI of the difference −0.31 to −0.01; $P=.038$). In the 116 subjects with cervical shortening at randomization, the difference in cervical length over time was also significant with the treatment group preserving 0.33 cm more cervical length compared to the placebo group (95% CI 0.62 to 0.03), adjusted for the covariate of cervical length at screening.

CONCLUSION: Progesterone supplementation reduces the rate of cervical change when given as a prophylactic therapy in women at higher risk for preterm birth. Whether this effect is a mechanism that contributes to progesterone's efficacy to prevent preterm birth requires further study.

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16 CAN MYOMETRIAL ELECTRICAL ACTIVITY IDENTIFY PRETERM LABOR?

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OBJECTIVE: We hypothesized that false and active labor in preterm pregnancy can be differentiated using myometrial electrical activity.

STUDY DESIGN: In a prospective study (IRB approved) patients with gestational age <37 reporting to Labor and Delivery for premature labor were recruited (with signed consent). Myometrial electrical activity of the uterine muscle was measured using a proprietary multi-channel EMG amplifier and a 3-dimensional non-invasive position sensor (EUM-100) with non-significant patient risk. Subjects were monitored for 30 minutes. Spontaneous premature delivery was defined as delivery within 2 weeks from time of test. An index score (1-5) for prediction of premature labor was developed: average period between contractions (in seconds); average power of contraction peaks (in watts) [The higher the energy, the higher the grade]; average movement of "center of gravity" (in mm). The computerized data that generated the index score were analyzed with the evaluator blinded to the clinical outcome. For further comparison to the EUM score, transvaginal cervical length, fetal fibronectin (FFN), and time interval from test to delivery were collected.

RESULTS: 64 patients consented to the study. Of tests performed, 18% scored 1 (0-2.9 watts), 27% scored 2 (3-6.9watts), 33% scored 3 (7-13.9watts), 11% scored 4 (14-19.9watts) and 9% scored 5 (20-high watts). An EUM score ≥4 identified 75% of patients delivering within 2 weeks regardless of tocolytic therapy. A score of ≤3 identified 72% of patients who failed to deliver within two weeks ($p=0.002$). Data on patients with gestational age ≤34 for single/combination of prediction tests is displayed below.

CONCLUSION: Our data suggests that measuring myometrial electrical activity may enhance identification of patients in true premature labor.

	Sensitivity	Specificity	PPV	NPV
EUM	47	90	75	72
FFN	34	70	46	64
CL	40	48	27	63
EUM + CL	67	80	50	89
EUM + FFN	80	75	67	86

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