ACOG 59th Annual Clinical Meeting, April 30 - May 4, 2011, Washington, DC
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# Diagnosing PROM with Combination Monoclonal/Polyclonal Immunological Protein Detection

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## Introduction

This study is designed as a prospective, observational study comparing the accuracy of the "new test" vs. conventional clinical tests of ROM (Clin-Assess). This study is designed to assess the reliability, sensitivity, and specificity of a new point of care test for rupture of membranes. The test we are using is a rapid qualitative immuno-chromatographic test for the detection of in-vitro amniotic fluid in cervico-vaginal secretions of women with suspected rupture of membranes (ROM).

Our hypothesis is that this new point of care test will be more sensitive and specific than current methods of detecting rupture of membranes.

## Objectives

Premature rupture of membranes (PROM), defined as spontaneous ROM before the onset of labor, is a common diagnostic dilemma in obstetrical practice today. Early and accurate diagnosis of PROM would allow for appropriate gestational interventions designed to optimize perinatal outcome and minimize serious complications including preterm delivery and infections such as chorioamnionitis and neonatal sepsis.

Conversely a false-positive diagnosis of PROM may lead to unwarranted obstetric interventions including hospitalization, administration of medications and even labor induction. Hence accurate and timely diagnosis of ROM is of critical importance to clinicians.

This test detects a specific combination of proteins present in amniotic fluid of pregnant women during all trimesters of pregnancy. This combination is unique to amniotic fluid, and is not found in significant concentrations in blood, urine or semen, and it may prove to be a valuable biomarker of ROM. Our objective is to assess the reliability of this point of care test and its ability to detect this unique combination of proteins.

## Methods

This study was designed as a prospective, observational study comparing the accuracy of the "ROM Plus" vs. conventional clinical tests of ROM. Conventional clinical testing is positive for ROM if: 1) amniotic fluid is seen leaking from the cervical os on speculum examination, 2) if at least two of the following three clinical signs are present: (a) visual pooling of fluid in the posterior fornix, (b) positive nitrazine test, (c) microscopic evidence of ferning.

After informed consent and a detailed history were obtained, the patient underwent standard clinical examination, and a sample of the cervico-vaginal fluid was collected using a vaginal swab to perform the "ROM Plus." The reading of the "ROM Plus" was to be performed by a different investigator blinded to the results of the standard examination. If two of the three control procedures were positive for ROM, this was considered positive for the control.

After an initial assessment for ROM all patients were managed by standard gestational age-specific clinical algorithms.

Once the patient delivered, the clinical record was reviewed to assess whether the patient had ROM, PROM, or PPROM (PROM prior to 37 weeks of gestation). The study data was collected, analyzed, and stored by study personnel in a fashion which ensured patient anonymity and confidentiality.

The "ROM Plus" specimens were individually assessed for sensitivity, specificity, and positive and negative predictive values rates for ROM, PROM, and PPROM. Any discrepancies between the "ROM Plus" and the control method were addressed in a thorough review of the patients clinical course by the local investigator.

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## Results

| Total Subjects | Clin-Assess | |
|---|---|---|
| "ROM Plus" | Positive | Negative |
| Positive | 86 | 2 |
| Negative | 0 | 24 |

Sensitivity: 86/(86+0)= 100%
Specificity: 24/(24+2)= 92%
PPV: 86/(86+2)= 98%
NPV: 24/(24+0)= 100%

| Term Subjects | Clin-Assess | |
|---|---|---|
| "ROM Plus" | Positive | Negative |
| Positive | 73 | 1 |
| Negative | 0 | 10 |

Sensitivity: 73/73=100%
Specificity: 10/(10+1)= 91%
PPV: 73/(73+1)= 99%
NPV: 0/(10+0)= 100%

| Preterm Subjects | Clin-Assess | |
|---|---|---|
| "ROM Plus" | Positive | Negative |
| Positive | 13 | 1 |
| Negative | 0 | 14 |

Sensitivity: 13/13=100%
Specificity: 14/(14+1)= 93%
PPV: 13/(13+1)= 93%
NPV: 14/14 =100%

## Conclusion

Based on our data "ROM Plus" proved to have a higher sensitivity and specificity than nitrazine testing, to be equally as sensitive as ferning, yet more specific, and more robust in positive predictive value than either nitrazine or ferning.

"ROM Plus" has demonstrated itself to be an excellent test for consistently and accurately determining ROM at all gestational ages, while being easy to understand, convenient, simple, and safe to use in a clinical setting.

## References

Arthur, James. Anatomy Blue. Web. 25 Apr. 2011. http://www.anatomyblue.com/illus_16.html

Chen, Frank, and Joachim Dudenhausen. "Comparison of Two Rapid Strip Tests Based on IGFBP-1 and PAMG-1 for the Detection of Amniotic Fluid." American Journal of Perinatology 25.4 (2008): 243-46. Print.

Di Renzo, Gian Carlo, and Lluis Cabero Roura. "Guidelines for the Management of Spontaneous Preterm Labor." Journal of Perinatal Medicine 34.5 (2006): 359-66. Print.

"Expressing Self Wordpress.com." Expressing Self | Just Another WordPress.com Site. Web. 25 Apr. 2011. <http://exprself.wordpress.com/

Lee, Seung Mi, Joonho Lee, Hyo Suk Seong, Si Eun Lee, Joong Shin Park, Roberto Romero, and Bo Hyun Yoon. "The Clinical Significance of a Positive Amnisure Test™ in Women with Term Labor with Intact Membranes." The Journal of Maternal-Fetal & Neonatal Medicine 22.4 (2009): 305-10. Print.