

Measures of Maternal and Fetal Infection and Inflammation in the National Children's Study

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for the participants of the National Children's Study Infection and Inflammation Workshops

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Introduction

Two workshops brought together experts to review the role of maternal and fetal infection and inflammation in adverse perinatal and childhood outcomes such as cerebral palsy, autism, and preterm birth and to explore opportunities and challenges for measuring these infectious and inflammatory risk factors.

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Measures of Maternal and Fetal Infection and Inflammation in the National Children's Study

August 22, 2005

Assessment of Fetal Exposure to Infection and Inflammation for the National Children's Study

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Objectives of Workshops

- Determine optimal and feasible measurements of maternal infection and inflammation.
- Identify potential assessments of fetal infection and inflammation or fetal response to maternal infection and inflammation.

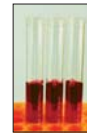
Measurement Strategies

- **Before pregnancy:** Establish a baseline measure of a woman's "inflammatory state" as well as capture evidence of past or chronic infectious or inflammatory conditions.
- **During pregnancy:** Attempt to capture timing of maternal infection or inflammatory response.
- **Birth:** Identify maternal or fetal/infant infection at or shortly preceding birth; assess fetal exposure to variation in maternal temperature.



Selected Measurements Before Pregnancy

- Questionnaire – Assessment of prior, recurrent, or persistent infections (e.g., UTI, STD)
- Vaginal swabs – Gram stain for BV; assessment of cytokines and "inflammatory profile"
- Urine – Process and store for PCR identification of specific organisms, proteomic analysis of additional markers
- Saliva – Potential use for periodontal disease assessment (via specific IgA, PCR)
- Blood (serum or plasma) – Immunoglobulins; "inflammatory profile" including general acute phase reactants (CRP, heat shock proteins)
- Blood (cells) – T-cell subtypes for Th-type



Selected Measurements During Pregnancy

First Trimester Visit:

- Questionnaire – History of infections, antibiotic use; assessment of elevations in body temperature
- Vaginal swab, urine, blood, saliva – Same collections as for pre-pregnancy visit

Second and Third Trimester Visits:

- Vaginal, urine, blood, saliva – Same collections as for pre-pregnancy visit
- Physical exam – Periodontal/dental assessment (once during pregnancy)



Selected Measurements at Birth

- Chart review (mother, infant) – Maternal temperature during labor; antibiotic therapy during pregnancy and L&D; anesthesia received
- Maternal blood – Storage (all inflammatory markers will be high due to labor, potential use for assessment of seroconversion)
- Cord blood (collected both in tubes and as blood spots to compare with infant samples) – "Inflammatory profile"; immunoglobulins; T-cell subtypes for Th-type; possible blood gas or pH
- Placenta – Digital photo; block and hold for histology; possible PCR for infectious agents
- Infant blood spot – "Inflammatory profile" and possible proteomics
- Colostrum – Immunoglobulins and T-cells
- Other (if available) – Amniotic fluid for "inflammatory profiles" and PCR; CVS decidual material for inflammatory histology



Workshop Conclusions Summary

- Important to use multiple data sources.
- Imperative to make serial measurements, particularly of biologic samples, to capture timing and extent of exposure.
- Methods that need pilots include
 - Serial maternal temperature assessment
 - Use of filter paper collection method for cytokine and inflammatory marker assessment.
- Interest in specific infectious agents and inflammatory markers will likely evolve as planning progresses. Biologic samples should be collected to maximize analytic flexibility.