

The Cervical Microbiome & Parturition

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Background

- The human microbiome is composed of fungi, viruses, archaea and bacteria.
- Estimated to be 10x as many microbial cells as human cells.
- Microbiota may function as *mutualists* (symbiotically beneficial), *commensals* (neither harm nor benefit), or *pathogens* (of host detriment) (Qin et al, 2010).
- Microbes that reside in and on the human body are increasingly recognized for the action they carry out, influencing human health, behavior, and disease through immunologic, endocrine, and neural pathways (Zhang et al, 2015).
- Human Microbiome Project – mapping the microbiota which reside in varied parts of the body was completed in 2012 (NIH, 2012) and are now engaged in the integrative Human Microbiome Project 2 which will examine changes in the microbiome and human health.
- One site that has not yet been examined is the human cervix during pregnancy, as well as other key reproductive tissues such as the myometrium.
- Understanding the resident cervical microbiota, and how those microbes relate to those found in the myometrium holds promise for understanding mechanism of labor onset and significant perinatal problems, such as preterm birth.

Research Purpose

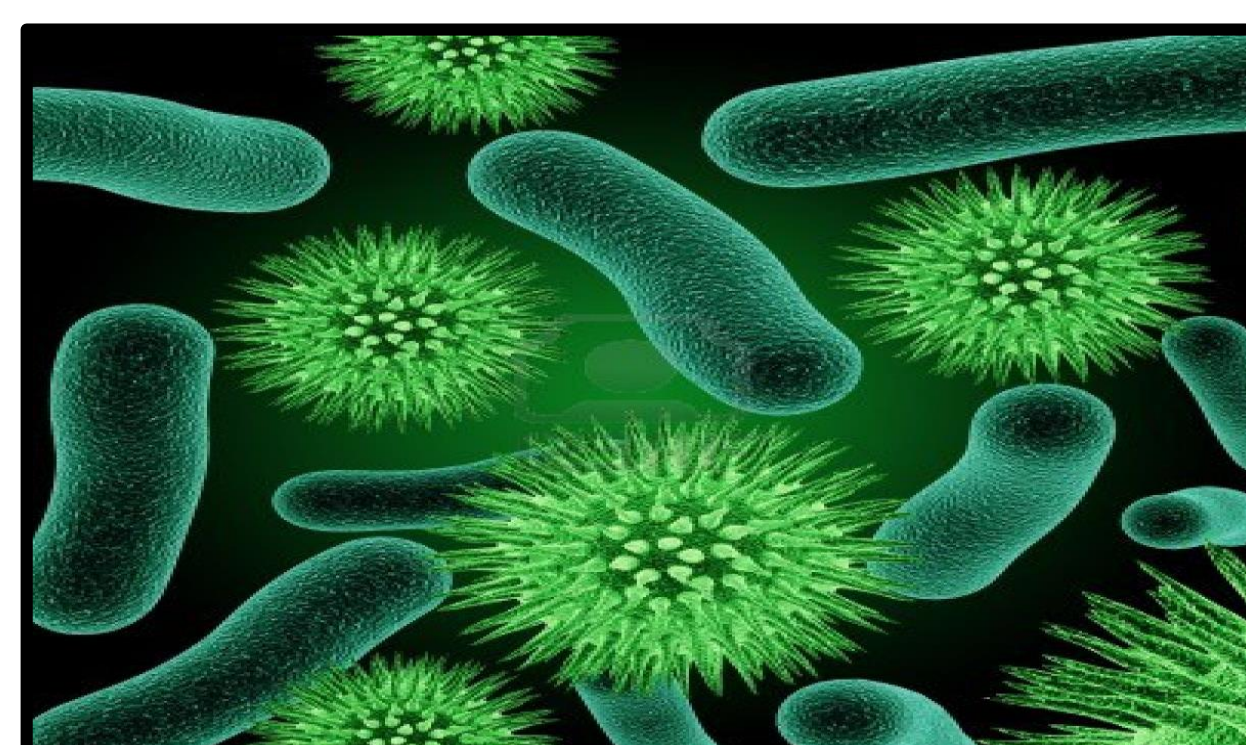
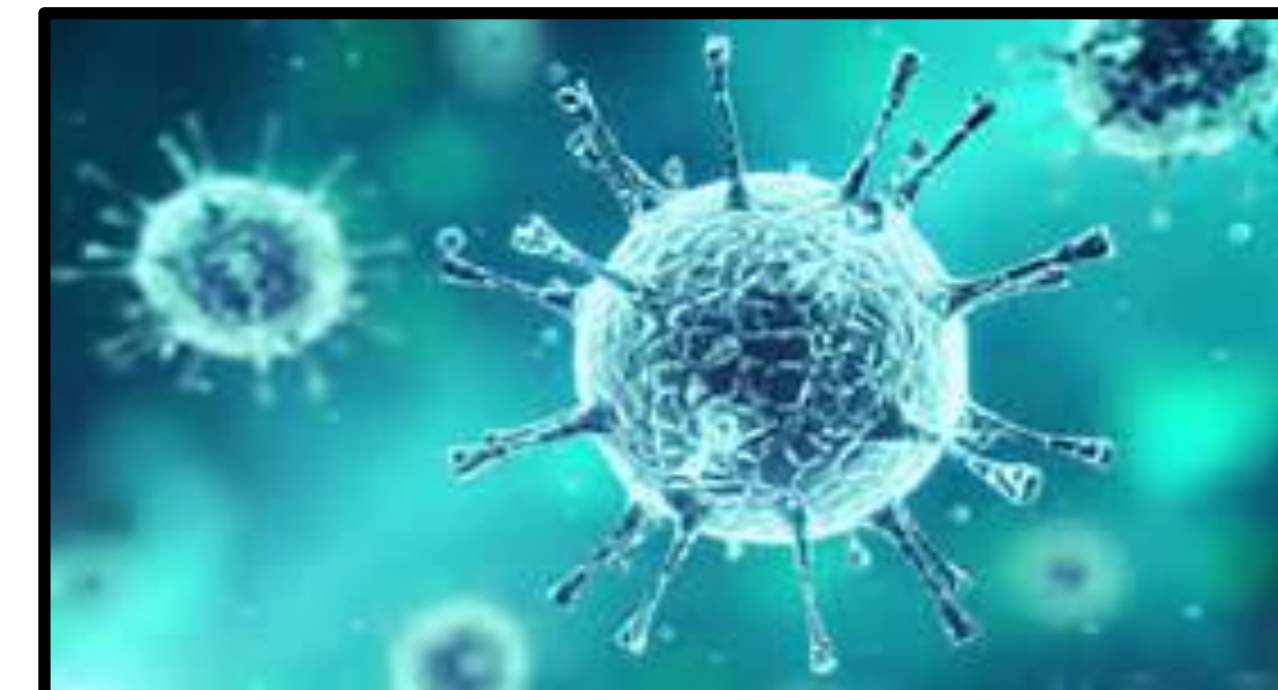
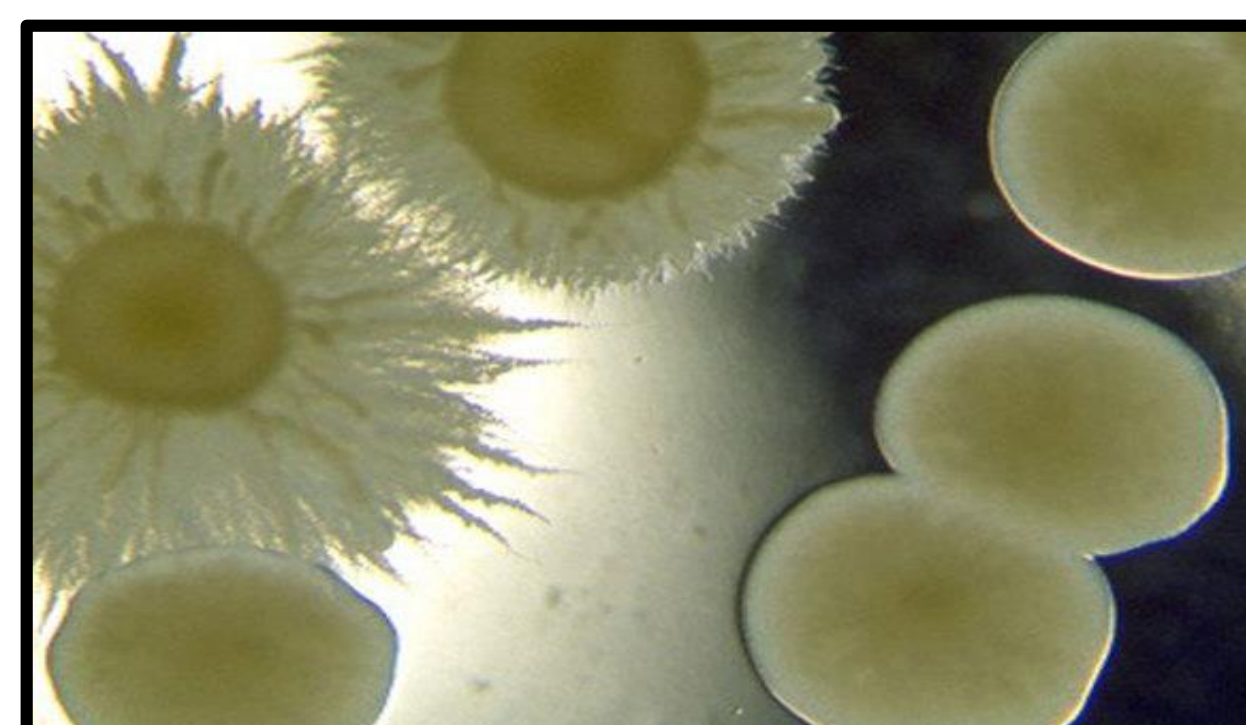
The purpose of this exploratory research is three-fold:

- Describe the indigenous cervical microbiota in late pregnancy and parturition.
- Provide preliminary data regarding the corresponding indigenous myometrial microbiota.
- Characterize the cervical microbiotic pattern contributing to normal physiologic birth outcomes.

Sample

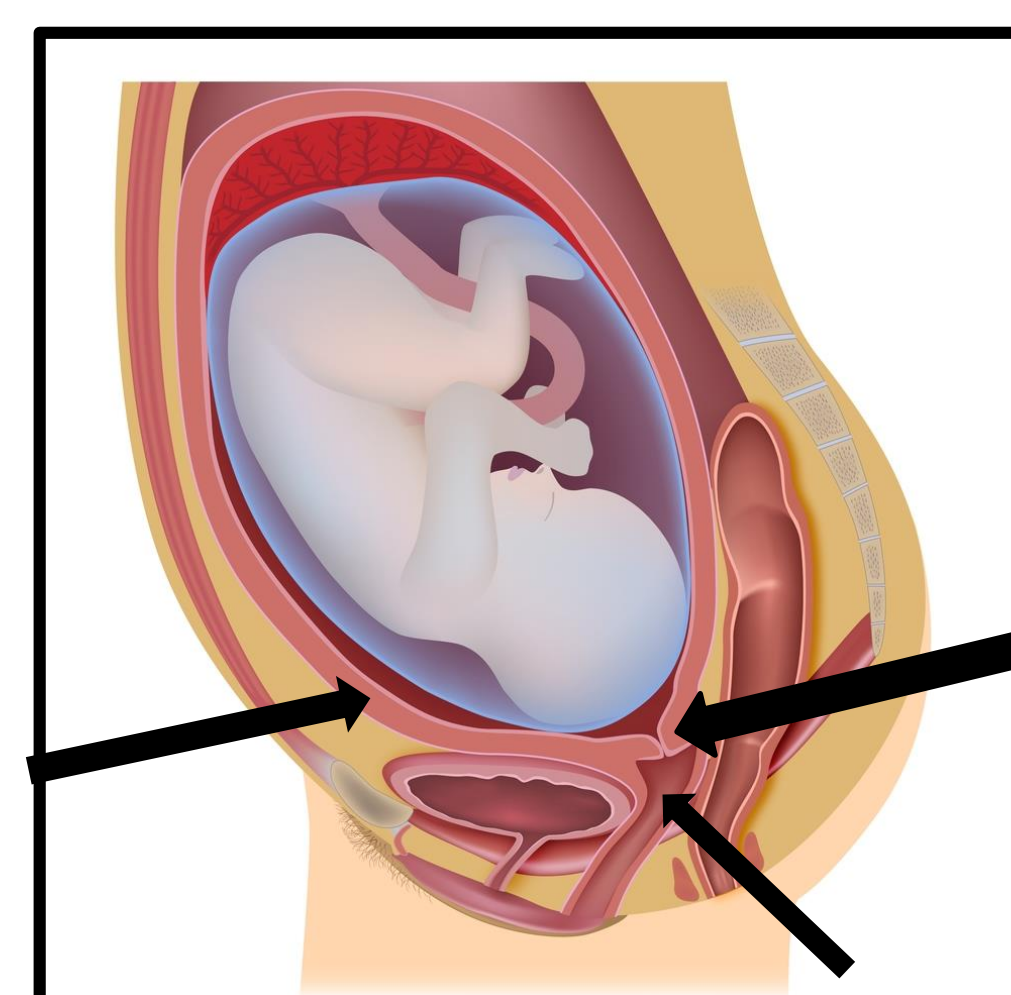
- N = 20 healthy pregnant women with singleton pregnancy
- Inclusion Criteria
 - 18-35 years of age
 - ≥ 35 weeks' gestation by early ultrasound/dating
 - Caucasian
 - Normal BMI (18.5-24.9 kg/m²)
 - Receiving care at an out-of-hospital birth center
- Exclusion Criteria
 - Currently on antibiotics
 - Current vaginal or cervical infection
 - Multiple gestation
 - Chronic disease
 - Intercourse in prior 48 hours
- Written informed consent prior to enrollment

Human Microbiome Composition



Methods

- Data collected at two points: 35-37 weeks, onset of labor
- **DATA COLLECTION**
 - Demographic/Background Data
 - Baseline Clinical Characteristics/Select Perinatal Outcomes
 - Dietary intake (24 hour recall) prior to specimen collection
 - REAPS (Rapid Eating Assessment for Participants)
(Segal-Isaacson, Wylie-Rosett & Gans)
 - Standardized specimen collection at 3 potential sites by same provider
 - cervix: swab of endocervix
 - myometrium: swab where cesarean occurs
 - vagina: swab of posterior fornix



- **WORKFLOW PROCESS**
 - Immediate preservation of samples at -80° C
 - Aliquots of samples for DNA extraction
 - Sample quantification
 - NanoDrop™ spectrophotometer (sample purity)
 - Metagenomic sequencing
 - 16S sequencing (Sanger sequencing)
 - Sequencing random fragments of whole genome DNA (Illumina platform)

Preliminary Results (n=8)

Demographics

- 100% Caucasian, married
- 75% with commercial insurance
- 88% multigravidas
- Education (years completed): 16 years average (range 13-17)
- BMI (pre-pregnant): 23.5 kg/m² (range 18.5-24.9)
- 100% taking daily prenatal vitamins with folic acid
- 100% vaginal births

Key Preliminary Findings

- Microbial abundance and diversity appears to differ in the pregnant state.
- Diet may well alter the cervical and myometrial microbiota signature.
- Resident microbiota appear to differ between the cervix and vagina.
- Diversity and richness of the cervical microbiome appears to diminish from 35-37 weeks gestation to term.



Implications

- Profiling the “healthy” cervical and myometrial microbiota in pregnancy may reveal the comparative diversity and richness of species and subsequent impact on birth outcomes.
- Cervical microbiome-pregnant host interactions likely determine the significant differences in the timing of labor onset, as well as account for adverse outcomes such as preterm birth.
- Understanding the cervical microbiome and the relationship with other reproductive tissues (i.e., myometrium) may foster targeted interventions which improve perinatal outcomes.

Acknowledgements

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