Recognition of Pathogenic Pathways to Intrauterine Infection: Keys to Identifying Testable Primary Prevention Strategies

James A. McGregor 1, Marti Perchac 1, Josh Jones 1, Janice I. French 2
1 Group B Strep International, 2 La Best Babies Network

Background: Research shows that various microbes (bacteria, viruses, yeasts/fungi, parasites) arising from endogenous sources (vagina, cervix, and gastrointestinal, genitourinary, others) are frequently present in the upper reproductive tract and gestational (decidua, placenta, membranes, amniotic fluid, meconium) tissues. These molecules (their toxins, metabolic products, breakdown products) may stimulate or moderate inflammatory/coagulation “host” (mother, fetus, trophoblast) responses.

Goals:
1. We sought to perform a logic analysis and literature review.
2. To identify and characterize how microbes and their products may be transported to
   a. upper genital tract organs and tissues, and
   b. gestational organs and tissues, e.g., decidua, Fallopian tubes, trophoblast, placenta and fetal structures.
3. We speculate how to mitigate or prevent potentially injurious substances from reaching the female upper tract and gestational tissues and organs.
4. To identify possibly primary preventive strategies to reduce risks of transport of potentially damaging substances to reproductive tract organs and tissues.

Methods:
1. We conducted an updated English language PubMed and Medline computerized literature search.
2. We used search terms as “uterine transport,” “uterine transmission,” and “uterine activity.”
3. We constructed a logic analysis matrix in order to identify personal and public health and policy recommendations to reduce risks of microbial transport to reproductive tract structures.

Results:
1. Multiple pathways identified:• Uterine peristalsis in non-pregnant (i.e., sperm, talc) and pregnant• Hematogenic, i.e., oral, periodontal, UTI, bacteremia, bacteriuria)• Lymphatic• Translocation, i.e., intestinal, GI tract• COUNTER CURRENT mechanism• Locally spreading, i.e., STI, surgical• Hygienic practices i.e., perineal talc powder, douching• IATROGENIC, i.e., membrane “stripping,” labor induction, amniocentesis• Breastfeeding• Placenta phagy
2. No systematic, comprehensive studies

Discussion:
1. We noted multiple pathways for microbes or their toxins, metabolites, breakdown products and other small/nano substances to have access to upper reproductive tract tissues.
2. Rather than being “protected” or “sterile,” it appears that upper tract tissues are endowed with considerable host defenses to deal with the multiple microbes in their environments.
3. Of the multiple pathways, we note that FIRST PASS or direct translocation and COUNTER CURRENT mechanisms are priority research areas.

Conclusions:
1. There is RAPID TRANSPORT of fluids, LARGE/SMALL MOLECULES from the vagina/cervix via MULTIPLE PHENOMENA:
   • Uterine peristalsis (“upsuck”)• Local diffusion• FIRST PASS• Lymphatics/venous plexus• COUNTER CURRENT processes
2. These observations prompt consideration of NEW APPROACHES intrauterine and transvascular therapeutics.
3. These may include NANOTECHNOLOGY and immune therapies.
4. UNKNOWN if similar mechanisms occur in GU and GI tracts

References: