Reducing Perinatal Infection Risks Caused by Sexually Transmissible Microorganisms in the Reproductive Tract through Parental Behavior Changes: a CROWDSOURCED-Inspired Analysis
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Background:
Using internet “commons” or direct contact sources Group B Strep International has heard from women/families who have suffered consequences of pregnancy-associated infections, most commonly ascribed to group B Streptococcus (GBS), as far back as the 1990’s and 1980’s.

Common concerns have been:
1) How did I/we get GBS or other pathogen colonization?
2) How do we prevent this from happening?
3) How do we prevent harm to our baby?

Other Common Prenatal Infections
• Parents also wanted to have comprehensive information about means to prevent other common perinatal infections, such as E. coli which is a significant bacterial cause of perinatal infection and CMV which is the most common congenital viral infection in the US
Goal
Respond appropriately to these parent inquiries to:
1) provide information for their closure and any subsequent pregnancies
2) identify gaps in knowledge or care
3) formulate strategies to prevent future perinatal loss or damage from vertical infections
4) guide perinatal infection research

Common Gap in Knowledge
Parents were unaware that microorganisms not considered to cause sexually-transmitted infections could still be sexually transmissible.

Framework:
“Overall, by a number of mechanisms, it appears that in developed countries, between 1 and 2 pregnancies in 1000 end in a stillbirth caused by a bacterial infection. In developing countries, where the stillbirth rates may be 10 times those in developed countries, it appears that a much larger proportion of stillbirths is related to bacterial intrauterine infection.”

Many common vertical infections, such as those caused by types of bacteria such as group B strep (GBS) and E. coli, and also by viruses such as the cytomegalovirus (CMV), are not considered to be sexually transmitted infections (STIs) by pregnancy care providers or public health officials.
Definition of STIs

According to the CDC, sexually transmitted infections (STIs) are passed from one person to another through sexual activity including vaginal, oral, and anal sex. They can also be passed from one person to another through intimate physical contact, such as heavy petting, though this is not very common.

STIs commonly considered important:
- Herpes
- Chlamydia
- Gonorrhea
- Mycoplasmas

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However, many microorganisms occur naturally in the body or are in the environment and are therefore not considered STIs, but are still sexually transmissible and capable of harming unborn babies.

Note: Common and important reproductive tract-derived infections originate from the endogenous genitourinary and/or oral/gastrointestinal/skin microbiome (male or female).


Why is GBS not considered an STI?

GBS is not considered an STI because it is naturally-occurring or commensal in the gastrointestinal and reproductive tracts. Someone with no prior sexual experience may carry GBS.

However, GBS as well as other microorganisms can be transmissible by sexual contact including oral sex or through diet or other environmental sources.


The Burden of Prenatal Infection Caused by GBS

3,500,000 preterm births (each year) may be attributable to GBS which can cause preterm labor and a woman's water to break too soon. Being born too soon can cause lifelong health challenges for a baby. (1)

57,000 possibly even up to 314,600 unborn babies die in their mother's womb or are born very sick due to GBS (each year). (1,2,3)

Why is E. coli not considered an STI?

Escherichia coli (E. coli) is not considered an STI because these bacteria normally live in the intestines of people and animals.

E. coli can spread to the reproductive and urinary tracts of both men and women.

The Burden of Prenatal Infection Caused by E. coli

"In developed countries, ascending bacterial infection, both before and after membrane rupture, with organisms such as Escherichia coli, group B streptococci, and Ureaplasma urealyticum is usually the most common infectious cause of stillbirth."

According to the World Health Organization, "An estimated 2.6 million stillbirths occur annually."

In one study, "E. coli was found in 25% of stillborn heart blood samples."

References:
3) www.who.int/reproductivehealth/topics/maternal_perinatal/stillbirth/en/ "An estimated 2.6 million stillbirths occur annually."

References:
Why is CMV not considered an STI?

CMV is not generally considered a STI because CMV is commonly spread through saliva and urine, often of toddlers, transplanted organs, blood and breast milk.

However, CMV can also be spread by direct contact with semen and vaginal fluid. In studies, CMV has been isolated from the cervix of 13% to 23% of women attending clinics for suspected venereal disease.


NOTE:

CMV can be spread through blood transfusions so pregnant women should alert medical providers if pregnant BEFORE any transfusions since not all blood is tested for CMV.


The Burden of Perinatal Infection Caused by CMV

In one study, "Evidence of CMV infection—viral DNA and foci of replication—was detected in fetal tissues and placentas from 15% of stillborn infants, greatly outnumbering other pathogens."

Congenital cytomegalovirus (CMV) infection in developed countries occurs with an incidence between 0.3% and 2.4% of all live births.

Cytomegalovirus infection is the most prevalent congenital infection in the world and is the leading infectious cause of mental retardation and sensorineural deafness.


Lenore Pereira; Have We Overlooked Congenital Cytomegalovirus Infection as a Cause of Stillbirth?, The Journal of Infectious Diseases, Volume 203, Issue 11, 1 June 2011, Pages 1510–1512.
Figure 1. Chart of the five phyla of the intrauterine bacteria of 349 women with intra-amniotic infection who gave birth preterm (Mendez et al. 2013)

This study indicates that microorganisms are from more than one phyla

Results:
1. Inquiring parents readily comprehended (microbe-host) pathophysiological principles including necessity to "screen and treat" commonly accepted STIs which are recommended to be screened during pregnancy by CDC, ACOG, or other agencies

Results:
2. Parents of affected children frequently express frustration and dismay that pregnant women are not screened for recognized bacterial, viral, fungal, or pathologic vaginal microflora such as "BV" or dysbiosis because of "cost," or operational complexity, or tradition, or lack of proven benefit
Results:
3. Parents of affected children frequently express frustration and dismay that although GBS is routinely screened for at 35-37 weeks gestation in many countries, treatment is not received for positive test results until labor and delivery even though GBS is known to cross intact membranes and cause stillbirth.

Results:
4. Once informed, parents readily understood that various microbes (GBS, CMV, HSV) may be transmitted or inoculated during sexual contact.

   Parents offered behaviorally-based recommendations for future research or immediate implementation including:
   a. avoidance of new or multiple sex contacts before or during pregnancy
   b. routine use of condoms or other “safe sex” barriers or abstinence to prevent microbiologic change during pregnancy
   c. avoidance of rectal/anal contact and possibly oral/genital contact

Results:

   d. routine screening and treatment of abnormal urogenital microflora (ASB, UTI, vaginal dysbiosis)
Results:
e. Serologic testing for common relevant viral infections (HIV, HSV, CMV) so that serodiscordant couples can be identified and modify their behaviors.
f. Give advice to avoid douching which can disrupt normal, established microbiome-host relationships.

Douching is not recommended. Douching can lead to many health problems, including problems getting pregnant. Douching is also linked to vaginal infections and STIs. In addition, the process of inserting fluid intravaginally can help to push harmful bacteria further up into the reproductive tract.

https://www.womenshealth.gov/a-z-topics/douching

g. Pursue evidence-based prevention research.
Table 1. Parental Behaviors which May REDUCE Spread of Perinatal Infections Implicated in Stillbirth

<table>
<thead>
<tr>
<th>Behavior</th>
</tr>
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<tbody>
<tr>
<td>Be selective with all personal contacts/enjoy monogamy!</td>
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<tr>
<td>Avoid SALIVA contacts in daycare/religious/other settings</td>
</tr>
<tr>
<td>Designate hygiene items (toothbrush, etc.) for personal use</td>
</tr>
<tr>
<td>Avoid contact with possible HERPES sores</td>
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<tr>
<td>Avoid rectal/anal contact and possibly oral/genital contact</td>
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<tr>
<td>Follow recommended strategies to help prevent infection during sexual contact, e.g., condom usage, other barriers</td>
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<tr>
<td>Avoid douching which can disrupt normal vaginal flora</td>
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<tr>
<td>Alert medical providers if you are pregnant BEFORE any transfusions (not all blood is tested for CMV)</td>
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Further Questions about GBS

- Can concurrent antibiotics interfere with my GBS test result? Maybe
- Can feminine products interfere with my GBS test result? Maybe

Further questions about GBS

- Can GBS colonization return after testing? Yes
- Can my partner be colonized and inoculate me through contact after testing negative? Yes
- Does safe sex prevent GBS colonization? Has not been studied

Note: “CMV is often present in semen, so it may be prudent to include condom use as part of the hygienic precautions given to seronegative pregnant women.”

Further questions about GBS

- Do herbal cures work? None have been proven

- Would a GBS maternal vaccine reduce risks of prenatal infection? Yes. Although some babies would likely still be unprotected such as babies of anti-vaccine mothers, babies <28 weeks gestation, partial protection for babies before term, babies affected by GBS strains not covered by the vaccine and babies in populations without access to a GBS vaccine

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Table 2. Possible candidates for “perinatal pathogen” vaccination* development/implementation strategies

| Group B Streptococcus (GBS) |
| Haemophilus influenzae, unencapsulated |
| Cytomegalovirus (CMV) |
| Herpes simplex virus-1 (HSV-1) |
| Herpes simplex virus-2 (HSV-2) |
| Human parvovirus B-19 (HPV-B19) |
| Neisseria gonorrhoeae |
| Chlamydia trachomatis |
| Ureaplasma parvum |
| Syphilis |
| Others (“BV” and E. coli) |

*vaccinations already developed: Hepatitis E virus (HEV), Hepatitis B virus (HBV), Human papilloma virus (HPV)

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Recap

Parents of babies affected by perinatal infection are eager to know and understand how to help protect their babies from the wide variety of microorganisms that can cause perinatal infection.

Parents often feel blindsided that they did not know that many microorganisms are sexually transmissible even if not considered STIs.

They want to know and understand the various ways these microorganisms can possibly be acquired to change their behaviors as needed to help ensure a healthy baby.
Discussion
How to best inform parents to be aware that:

1. Microorganisms are often not considered to be STIs, but still may be sexually transmissible CAUSING INOCULATION OF NON-COLONIZED PARTNERS (further research is needed to determine how often this occurs)

2. Even if test results are negative, caution in behavior choices may still be warranted as:
   a. microorganisms can be transient so status can change, and
   b. test results can show a false negative, and
   c. some microorganisms can cross intact membranes and infect babies prior to possible expected treatment during labor and delivery

Conclusions:
Best ways to inform parents need to be tested and optimized.
Parents and providers and others are "ready and willing" to provide positive prevention directed suggestions.

Recommendations:
1. Encourage providers, parents, and perinatal organizations through the internet "commons" and personal conversations to inform parents as to what they need and want to know to be able to help reduce the risk of perinatal infections
2. Actively support evidence-based research
3. Evaluate educational materials (appropriate education of common parent questions remains a challenge and needs to be improved)
4. Translation of educational materials into common languages
For more information, please email info@gbst-intl.org or visit www.groupbstrepinternational.org