



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.

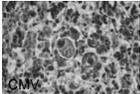
Common concerns have been:

- 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.



McClure, E. M., & Goldenberg, R. L. (2009). Infection and stillbirth. *Seminars in fetal & neonatal medicine*, 14(4), 182-9.

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



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).

Dan M. et al. Sexually transmitted Escherichia coli urethritis and orchiepididymitis. Sexually Transmitted Diseases. 39(1):16-17, JAN 2012



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.

SD Manning et al. Determinants of co-colonization with group B streptococcus among heterosexual college couples. Epidemiology. 2002 Sep;13(5):533-9.

S Kallimuddin, S Chen, T Barkham et al. B2015 epidemic of severe Streptococcus agalactiae sequence type 283 infections in Singapore associated with the consumption of raw freshwater fish: a detailed analysis of clinical, epidemiological, and bacterial sequencing data. Clinical Infectious Diseases. Vol. 64, No. suppl_2, 15.05.2017, p. S145-S152.

J Morinis et al. Horizontal transmission of group B streptococcus in a neonatal intensive care unit. Paediatr Child Health. 2011 Jun-Jul; 16(6): e48-e50.



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)

1) Estimates of the Burden of Group B Streptococcal Disease Worldwide for Pregnant Women, Stillbirths, and Children. Anna C. Seale et al. *Clinical Infectious Diseases*, Volume 65, Issue suppl_2, 6 November 2017, Pages S200-S219.
2) Maternal group B Streptococcus-related stillbirths: a systematic review. C Nan et al. *BJOG*. 2015 Oct;122(11):1437-45.
3) www.who.int/reproductivehealth/topics/maternal_perinatal/stillbirth/en/ "An estimated 2.6 million stillbirths occur annually."



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.

<https://www.cdc.gov/ecoli/general/index.html>



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..."

McClure, E. M., & Goldenberg, R. L. (2009). Infection and stillbirth. *Seminars in fetal & neonatal medicine*, 14(4), 18.
www.who.int/reproductivehealth/topics/maternal_perinatal/stillbirth/en/
Goldenberg, R. L., McClure, E. M., Saleem, S., & Reddy, U. M. (2010). Infection-related stillbirths. *Lancet (London, England)*, 375(9724), 1482-90.



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.

Ziemann, M., & Hennig, H. (2013). Prevention of Transfusion-Transmitted Cytomegalovirus Infections: Which is the Optimal Strategy?. *Transfusion medicine and hemotherapy : offizielles Organ der Deutschen Gesellschaft für Transfusionsmedizin und Immunhamatologie*, 41(1), 40-4.
Drew, LW. *Condoms and the Transmission of Cytomegalovirus*. Sexually Transmitted Diseases. October 1996 - Volume 25 - Issue 9 - p 481-482



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.

Ziemann, M., & Hennig, H. (2013). Prevention of Transfusion-Transmitted Cytomegalovirus Infections: Which is the Optimal Strategy?. *Transfusion medicine and hemotherapy : offizielles Organ der Deutschen Gesellschaft für Transfusionsmedizin und Immunhamatologie*, 41(1), 40-4.



The Burden of Perinatal Infection Caused by CMV



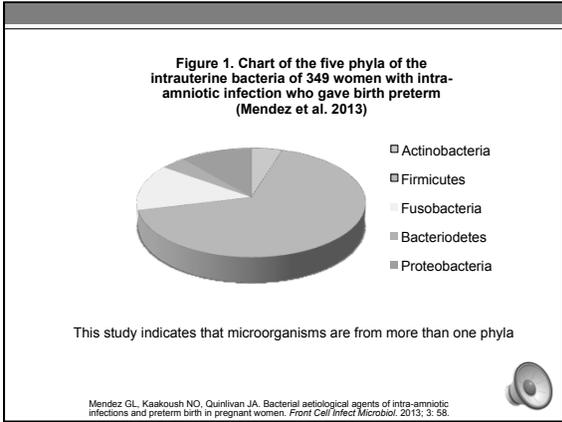
In one study, "Evidence of CMV infection—viral DNA and foci of replication—was detected in fetal tissues and placentas from 15% of stillborn infants, greatly outnumbering other pathogens."

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.

Bonalumi, S., Trapanese, A., Santamaria, A., D'Emidio, L., & Mobil, L. (2011). Cytomegalovirus infection in pregnancy: review of the literature. *Journal of prenatal medicine*, 5(1), 1-8.
Lenora 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.





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



Results:

f. Give advice to avoid douching which can disrupt normal, established microbiome-host relationships.

In the United States, almost one in five women 15 to 44 years old douche

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>
<https://www.asha.org/policies-and-advocacy/public-health-policy-statements/policy-database/2014/07/29/13/09/vaginal-douching-and-adverse-health-outcomes>



Results:

g. pursue evidence-based prevention research



Table 1. Parental Behaviors which May REDUCE Spread of Perinatal Infections Implicated in Stillbirth	
Be selective with all personal contacts/enjoy monogamy!	
Avoid SALIVA contacts in daycare/religious/other settings	
Designate hygiene items (toothbrush, etc.) for personal use	
Avoid contact with possible HERPES sores	
Avoid rectal/anal contact and possibly oral/genital contact	
Follow recommended strategies to help prevent infection during sexual contact, e.g., condom usage, other barriers	
Avoid douching which can disrupt normal vaginal flora	
Alert medical providers if you are pregnant BEFORE any transfusions (not all blood is tested for CMV)	

Further Questions about GBS	<ul style="list-style-type: none"> • Can concurrent antibiotics interfere with my GBS test result? Maybe • Can feminine products interfere with my GBS test result? Maybe <p><small>RM Ostroff, JW Slaaffens. Effect of specimen storage, antibiotics, and feminine hygiene products on the detection of group B Streptococcus by culture and the STREP B OIA test. Diagn Microbiol Infect Dis. 1995; Jul;22(3):253-9.</small></p>
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Further questions about GBS	<ul style="list-style-type: none"> • 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 <p>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."</p> <p><small>Adler, SP, Nigro G. Prevention of Maternal-Fetal Transmission of Cytomegalovirus. Clinical Infectious Diseases, Volume 57, Issue suppl_4, 15 December 2013, Pages S189-S192.</small></p>
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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



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

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

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



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@gbs-intl.org or visit
www.groupbstrepinternational.org
