

PLOS Science Wednesday: Hi reddit, my name is Anirban Banerjee and I discovered tiny sacks of toxins may increase the risk of premature delivery in pregnant mice, with implications for preterm birth in humans – Ask Me Anything!

PLOSScienceWednesday<sup>1</sup> and r/Science AMAs<sup>1</sup>

<sup>1</sup>Affiliation not available

April 17, 2023

### Abstract

Hi Reddit, My name is Anirban Banerjee and I am an Assistant Professor at the Department of Biosciences & Bioengineering, Indian Institute of Technology Bombay, INDIA. I am a microbiologist and my research primarily focuses on the identification of various methods adopted by pathogens to breach different barriers in our body, such as the blood-brain barrier or feto-maternal barrier etc. We hope to learn from the smart tactics employed by these tiny creatures and apply them to deliver drugs across these barriers which are hard to penetrate. We recently published an article titled “Membrane Vesicles of Group B Streptococcus Disrupt Feto-Maternal Barrier Leading to Preterm Birth” in PLOS Pathogens. It is a well established fact that colonization of vagina and cervix of pregnant women with Group B Streptococcus (GBS), an opportunistic pathogen, significantly increases the probability of preterm birth. However, in fairly large number of cases the bacteria has not been detected in the feto-maternal interface and/or amniotic fluid. This led us to wonder how GBS sitting in the vagina can orchestrate events at the feto-maternal barrier. We were of the opinion that since rupture of amniotic membrane which is a prerequisite for preterm birth involves a complex series of events; this can only be augmented by a host of bacterial factors and not just simply one. Our findings suggest GBS produces membrane bound vesicles (MVs) that are loaded with multiple toxic proteins and enzymes of the bacteria. These MVs are capable of traveling up through the reproductive tract and lead to a series of deleterious effects resulting in extensive damage of the feto-maternal barrier (amniotic membrane) and subsequently preterm birth. This work was primarily done by four doctoral students in my lab (Manalee Surve, Anajali Anil, Kshama Kamath and Smita Bhutda) in collaboration with Dr. Deepak Modi, from National Institute for Research in Reproductive Health (NIRRH), Mumbai, INDIA. I will be answering your questions at 1pm ET – Ask Me Anything!

[REDDIT](#)

# **PLOS Science Wednesday: Hi reddit, my name is Anirban Banerjee and I discovered tiny sacks of toxins may increase the risk of premature delivery in pregnant mice, with implications for preterm birth in humans -- Ask Me Anything!**

PLOSSCIENCEWEDNESDAY [R/SCIENCE](#)

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I find this an interesting topic as I am a former midwife and a woman who gave birth at 31 weeks due to PROM. I tested negative for GBS as did the placenta cultures, and my suspicion is that I had polyhydramnios that was not diagnosed.

I'm curious if GBS was the only isolated bacteria? Would gardnerella or chlamydia have a similar effect? Any foreign bacteria to the vagina?

Do you see vaginal/rectal screening of GBS earlier in pregnancy and treatment antenatally coming from further research?

[cats-quilts](#)

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I assume Gardnerella or chlamydia would have similar effects. Our study proposes that women should be screened antenatally for GBS and if found positive then treated accordingly. Vaccination can also be a viable option to prevent colonization.

Hi, Dr. Banerjee!

What are the implications of this research on future treatment of GBS+ mothers? Would earlier detection and antibiotic treatment reduce the likelihood of preterm birth in these women?

Does damage to the fetomaternal barrier occur just before birth or is it a slower process? Is there evidence that this increases passage of, for instance, medication the mother is taking to the fetus?

[divvyflax](#)

We believe that earlier detection and prevention of GBS colonization is the way forward to prevent this adverse outcomes. Rupture of the fetomaternal barrier happens just before birth, but rupture is the consequence of slow damage.

Hi Anirban, thanks for the AMA

What are typical sources of these toxins and how can people (pregnant women) avoid exposure to them?

[DMann420](#)

Bacteria produces them. the only way to not get exposed to them is to eradicate them using antibiotics.

I recently had my second child. I was GBS positive my first birth and Negative for my second. I was on a heavy regime of probiotics my second pregnancy. Do you think there is a link between taking probiotics and treatment-prevention of GBS in pregnant women? I was part of a study at the Bastyre institute for my midwives assistants thesis. She seems to think there is a connection. Thank you for your AMA! This a fascinating and much needed area of study. It could save so many women and babies at risk for pre term labor/birth.

[LeGrandeBadger](#)

Your probiotics may have helped you. Generally the lactobacillus bacteria present in the vagina keeps a check on the number of other harmful bacteria such as GBS. However, due to unknown reasons if the lactobacillus counts go down the GBS counts will go up and that creates the disbalance.

The current treatment for GBS is IV antibiotics during labor. In what way does your research impact that treatment protocol?

Additionally, studies have indicated that a very large proportion of the population is colonized by GBS, yet the proportion of preterm birth is much smaller. Does your research indicate why only some pregnant women with GBS would have preterm labor and not others?

[2manymans](#)

IV antibiotics are given only during labor, we believe that colonization is equally detrimental and

therefore must be prevented. One reason may that for women who were positive for GBS but still did not have preterm labor, the degree of colonization would be much less that what is required for damage to the membrane.

Could you give us a simplified explanation of what this means? Like for a 5 year old?

[Ch33sys0cks](#)

GBS residing in the vagina can produce these MVs, which can travel up the reproductive tract, just like sperms and then damages the membrane holding the baby. The membrane therefore ruptures before schedule and the baby is born prematurely.

Hi Dr. Banerjee, these are interesting results. My wife was unfortunate enough to experience PPROM with our son, who was born at 34 weeks (healthy, and a year old now). She ended up testing negative for GBS but positive for Ureaplasma urealyticum. There doesn't seem to be much institutional knowledge about whether this could be a factor or now.

Do your findings have any bearing on whether other bacterial strains could produce MVs that also would have damaging effects to the amniotic membrane?

[leontrout00](#)

Ureaplasma is another common bacteria found in female vagina. We do not know whether they produce similar structures, but one of my collaborator studies *Gardnerella vaginalis* which is responsible for bacterial vaginosis and he has seen that they also produce MVs.

So maybe my question is not completely related to the main subject but here i go, how true is that making experiments with mice being a male affects the results that you would get being female, i heard that female scientists make the mice more comfortable.

Thanks , very interesting work

[Z2DION](#)

Vary from person to person

Are there any practical steps women can take based on your research to prevent pre-term births, or is it too early to extrapolate to that?

[Empigee](#)

Its too early to extrapolate. The research probably shows that even colonization is as bad as an invasive disease. So may be the route to prevent this is to stop GBS colonization.

Since the MVs are produced by GBS is it possible to find and remove GBS early in pregnancy to prevent preterm birth? Or does this process only occur later in the pregnancy?

[Sevran](#)

Presence of GBS is only screened late in the pregnancy. Our research shows that colonization is

equally detrimental and so preventing GBS from colonizing the vagina can be a real good strategy.

Hello Dr. Banerjee.

This is certainly very interesting research. I realize that the linked paper is al in vitro, however, to what extent do you think a GBS infection would have to be present in the vagina before these membrane vesicles significantly affect the pregnancy?

I ask this because having lower levels of several different Streptococci is quite common in women.

[Pokeme101](#)

Well we have done some in vivo experiments in mouse model. We do not know what degree of colonization one needs to have such an effect, but our current experiments plans to answer this.

You see an increased number in macrophage infiltration, did you look at the potential of their production of MMPs contributing to the loss of collagen strength?

[devdude30](#)

We have not, but the macrophages can also produce MMPs and that may augment the damage. However, our ex vivo studies show that even the proteases present in MVs are also capable of degrading the collagen by themselves.

Some of our current explanations for preterm rupture and preterm delivery include infections with other organisms like Ureaplasma urealyticum and Mycoplasma hominis. Do you think that a significant portion of recurrent preterm births may instead be attributable to GBS and it's "poison packets"?

[Yousirareagod](#)

Ureaplasma and Mycoplasma are also responsible for causing vaginal infections which is directly related to preterm birth. However, GBS resides in the vagina asymptotically and under these conditions these MVs can cause this adverse effect.

Hello, as twins me and my brother were born more than 2 months early, most twins i know had a premature birth, so my question is, can it be the toxin you mentioned more likely to appear on twin births?

[pintazpt](#)

possibly no.

Hello and thank you, Dr. Banerjee! Does GBS has a specialized traveling mechanism for going up the vaginal canal--what triggers this ascent? If the presence of GBS isn't found in amniotic fluid, what is the time frame of the damage caused by GBS, relatively immediate?

[nobodylikespants](#)

We do not what triggers its upward movement, may be chemotaxis, but not sure. Its difficult to predict the time frame also as that will depend on the amount of MVs secreted by GBS. In mouse howevr, we

have found that with 24h the damage is extensive. Whether the same time frame applies to human is ofcourse debatable.

Do these infections ever lead to sepsis?

Can the bacteria be discovered and treated with antibiotics before they cause premature birth?

[IdCallthePolice](#)

If the neonate get exposed to live GBS and the bacteria some gets access to the blood then it can cause sepsis. Infact that's exactly why pregnant women who are found to be GBS positive are given antibiotics during delivery. But unfortunately that can't prevent preterm birth.

Not necessarily is a women GBS+ At each pregnancy,

[yukel](#)

approximately 20-30% women are GBS positive.

[deleted]

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No

What kind of premature labor does this bring on? How would it look and when does it typically happen? Spontaneous rupture of membranes and contractions? Infection of the placenta? Bleeding? Cervical insufficiency?

I had my son at 27 weeks because of complete placenta previa and had catastrophic bleeding. I was also GBS +. Would that situation possibly be related to your research?

[IHaveAFunnyName](#)

Its generally thought that placenta is a sterile site. However, present research shows that its wrong. In your case there may have been that GBS would have traveled up and caused the damage, but it is also possible that GBS could do it with the aid of the MVs. In both cases there will extensive damage of the fetal membrane leading to preterm birth.

Why would GBS produce toxic vesicles? Is there an evolutionary advantage to causing premature birth?

[coronavitae](#)

As of now we don't know why GBS produces MVs. May be it produces MVs when it is under stress, or may be to compete with other bacteria, but not sure. We have started experiments to understands this.

Being an Indian scientist, what are your thoughts on our country being so behind in research? Apart

from the general public attitude towards science and choosing a profession in general, what do you think might be the reasons?

[RexGalilae](#)

I guess the general attitude towards scientific research is not up to the mark. Most research is award centric and less exploration centric. The funding is also an issue.