

Premature births linked to changes in mother's bacteria

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Changes to the communities of microbes living in the reproductive tract of pregnant women could help to spot those at risk of giving birth prematurely.

A study of hundreds of [women](#), carried out at Imperial College London,

found that subtle changes to the [bacteria](#) present in the vagina were strongly associated with the mother's waters breaking early and preterm birth - the baby being born before 37 weeks.

According to the researchers, the findings show that a shift away from the usual healthy balance of vaginal bacteria was associated with waters breaking early, and could have an impact on the health of mother and baby, including increasing the risk of sepsis for newborns.

In a paper, published today in the journal *BMC Medicine*, the researchers also highlight that while the standard [antibiotic treatment](#) (prescribed in accordance with national guidelines) given to women whose waters break early can help to reduce infection, for a small subset of women it may actually be detrimental.

They explain that for a small proportion of women the treatment, administered as a protective measure in hospital, can disrupt the balance of the mother's microbes by eradicating the 'good' bacteria and allowing more harmful bacteria to take their place in the vagina - with potentially devastating consequences for the baby. The team suggests alternative treatments should be used for these women to mitigate their risk.

During pregnancy babies are protected inside the amniotic sac, with the surrounding membrane rupturing as part of the normal birthing process when the mother's 'waters break' as a precursor to labour.

However, when this occurs before 37 weeks, termed [premature rupture](#) of membrane (PPROM), the baby is likely to be born prematurely. After the membranes rupture, the baby remains without the protective membrane and is at increased risk of infection - as the vaginal bacteria spread upwards to the placenta and uterus. In order to reduce this risk, the women whose waters have broken early are given intravenous antibiotics as standard practice on the NHS.

Researchers from the Institute of Reproductive and Developmental Biology (IRDB) at Imperial looked at the impact of premature rupturing of the membrane and antibiotic treatment on the vaginal microbiota, taking swabs from the vaginas of pregnant women at different points during their pregnancy and analysing them to reveal the types of bacteria present, their proportions and any changes.

Samples were collected from a prospective group of 250 pregnant women with and without risk factors for giving birth prematurely - such as having a history of [preterm birth](#) or miscarriage - of which 27 did in fact have a premature birth. They also collected samples from a second, smaller group of 87 women who presented to hospital with premature membrane rupture. All patients were seen at Queen Charlotte's and Chelsea Hospital and Chelsea and Westminster Hospital.

Previous research has shown that over the course of pregnancy the bacteria that colonise the vagina become less diverse and are dominated chiefly by *Lactobacillus* species, the same type of bacteria found elsewhere in the body including the gut and mouth.

Analysis of the team's samples revealed that premature membrane rupture was associated with a shift in microbiota, with a drop in *Lactobacillus* and an increase in other types of bacteria, including potentially harmful bugs such as *Staphylococcus* and *Streptococcus*.

The team also analysed samples from the small group of women with premature rupture before and after the preventative antibiotic treatment - oral erythromycin, four times a day for 10 days. Swabs were taken before treatment and then at 48 hours, one week and two weeks.

For those women whose microbial makeup was dominated by *Lactobacillus* before the treatment, the antibiotics resulted in a decline in *Lactobacillus* and a greater diversity of bugs. However, in those women

with reduced Lactobacillus to begin with, the treatment was beneficial in some, reducing the amount of potentially [harmful bacteria](#) as well.

The study also revealed associations between specific vaginal bacteria and newborns who developed sepsis following delivery. While the mothers of healthy babies were dominated by Lactobacillus, samples from the mothers of newborns with sepsis revealed a greater diversity of bacteria, including the presence of *Streptococcus* and *E. coli*.

Dr David MacIntyre, from the Imperial IRDB, said: "This study is one of the first to show that around almost a half of [pregnant women](#) may have an unbalanced [vaginal microbiota](#) before premature rupture, providing further evidence of the role of bacteria in some cases of premature births.

"Crucially, our findings identify two different groups of women with premature rupture - one group in which targeted antibiotics may be beneficial and the other in which this same treatment may actually be detrimental."

The group adds that further studies are needed to assess current clinical guidelines for women with premature rupture and that developing alternative ways to treat women, such as using more selective antibiotics, could potentially improve outcomes for women and their babies.

Professor Phil Bennett, a Professor of Obstetrics and Gynaecology at Imperial, said: "All of the women in this study were treated in accordance with national and hospital guidelines, which suggests more focus is urgently needed to see if these guidelines are appropriate and effective.

"Our findings could have important implications for the use of antibiotics as a preventative measure for these women, which is the

recommended course of action in the UK and other countries, including Canada, Germany, Australia and New Zealand."

Dr Richard Brown, a Clinical Research Fellow at Imperial and first author of the study, added: "The aim of antibiotic treatment in PPRM is to reduce the risk of ascending infection. Our results suggest that a more personalised approach targeting only those women likely to benefit from [antibiotics](#) may prove more beneficial than the current 'one [treatment](#) fits all' approach."

More information: 'Vaginal dysbiosis increases risk of preterm fetal membrane rupture, neonatal sepsis and is exacerbated by erythromycin' is published in the journal *BMC Medicine*

Provided by Imperial College London

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