- Polycystic Ovary Syndrome (PCOS)

News

Health

Gut linked to PCOS fertility issues

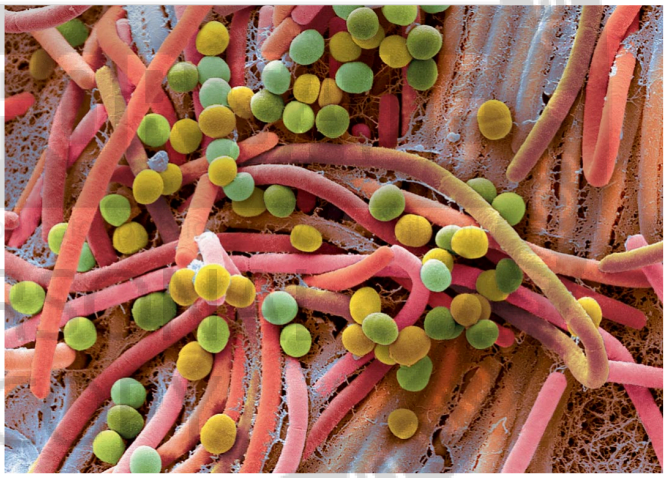
An altered gut microbiome may explain why those with polycystic ovary syndrome experience a higher risk of miscarriage, finds **Grace Wade**

WOMEN with polycystic ovary syndrome (PCOS) have lower levels of a gut microbe, which appears to raise the risk of pregnancy complications.

PCOS is the most common hormonal condition in women of reproductive age and is a leading cause of infertility. Yet relatively little is understood about what causes it or how to best treat it. For instance, it isn't clear why those with PCOS who are able to get pregnant have a higher risk of complications like miscarriage, preterm birth and gestational diabetes.

Aixia Liu at Zhejiang University in China and her colleagues monitored pregnancy outcomes in 220 women across 44 cities in China, half of whom had PCOS. All of them were under 35 years old and provided blood, stool and tissues samples of their endometrium, or the inner lining of the uterus.

Despite similar pregnancy rates, those with PCOS were nearly twice as likely to experience a pregnancy complication, such as miscarriage, preterm birth, gestational diabetes or a child with low birth weight. The researchers also found that those with PCOS had about half the amount of a gut bacterium called *Parabacteroides merdae* than those without the condition and that this was associated with pregnancy outcomes.



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Levels of certain gut microbes could be linked with pregnancy outcomes

"It is nice to have a potential target to treat because we don't really have specific treatments for PCOS"

P. merdae helps convert certain nutrients, such as the amino acid isoleucine, into beneficial compounds called short-chain fatty acids that play an important role in reproductive health. This probably explain why participants with PCOS had, on average, about 39 per cent more isoleucine and 10 per cent lower levels of short-chain fatty acids in blood samples than those without it. They also had higher levels of isoleucine in endometrial tissues.

When the researchers cultured the participants' endometrial cells and exposed them to isoleucine in a dish, they saw an increase in markers of cellular senescence, where cells become so worn or damaged that they cease to function.

The isoleucine also hindered the process endometrial cells undergo in preparation for, and during, pregnancy.

"These findings indicate ageing-like changes in the uterus," said Liu in a press release from an annual meeting of the European Society of Human Reproduction and Embryology, where she presented these findings. "Our data suggest that high isoleucine levels and the loss of *P. merdae* may impair endometrial health, even in women under 35."

While this suggests that changes to the gut microbiome may contribute to fertility issues in PCOS, Andrea Dunaif at the Icahn School of Medicine at Mount Sinai in New York state is sceptical. Her own research suggests that reproductive ageing in PCOS is delayed, rather than accelerated. "Their reproductive abnormalities tend to improve in their 30s," says Dunaif. "That makes me sceptical about how significant the endometrial findings are, and if they are really what is responsible for these alterations and pregnancy outcomes."

Still, these findings could lead to improved fertility treatments for PCOS. "The microbiome is something [where] you could intervene with different probiotics to alter the [bacteria]," says Dunaif. "So that is nice to have a potential target to treat because we don't really have any specific treatments for PCOS." ▮

We may know how PCOS is passed on

POLYCYSTIC ovary syndrome (PCOS) often runs in families, but it isn't clear how it is inherited.

Studies in mice suggest changes in epigenetic marks, the chemical tags that turn genes on and off without altering DNA sequences, may play a role. It is thought most such marks are erased when eggs form, but some could remain.

To see if this occurs in connection with PCOS in humans, Qianshu Zhu at Chongqing Medical University in China and his colleagues analysed epigenetic marks in eggs and 3-day-old embryos donated by 133 people with PCOS and 95 people without.

This revealed a link between PCOS and changes in three types of epigenetic marks in the eggs and embryos. Two of these marks turn genes off by making DNA coil more tightly around proteins called histones, which help package it within cells. This makes the genetic code in DNA less accessible to molecules that transcribe it into RNA, a key step in making proteins. The third mark activates genes by loosening DNA coils.

Together, these changes altered the metabolism of eggs and embryos, suggesting they may raise the risk of PCOS in offspring.

Zhu presented the results at the annual meeting of the European Society of Human Reproduction and Embryology. Carissa Wong

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