

Health

We finally know what causes morning sickness during pregnancy

A hormone called GDF15 has been identified as the cause of nausea and vomiting during pregnancy, which should lead to ways to prevent and treat the most severe cases

By [Michael Le Page](#)

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Around two-thirds of women experience nausea and vomiting during pregnancy. An excess level of a hormone called GDF15 is the main cause of pregnancy sickness, including the most severe cases, known as hyperemesis gravidarum. The

evidence for this has been growing for the past few years and now a study combining multiple lines of evidence should settle the issue.

Crucially, the study also shows that women's sensitivity to GDF15 depends on how much their bodies produce prior to pregnancy. The findings suggest that if those known to have a high risk of [hyperemesis gravidarum](#), which can be life-threatening, are given extra GDF15 prior to becoming pregnant, it could prevent the condition.

Around two-thirds of women experience nausea and vomiting during pregnancy. Despite being widely known as morning sickness, it can happen at any time of day. It usually declines after the first three months, but in [around 1 in 50 pregnancies](#) it can become so severe it results in hyperemesis gravidarum, in which it is impossible to eat and drink normally.

GDF15 was first discovered in 1997, but it wasn't until 2017 that several teams showed it binds to specific receptors in the brain and triggers nausea and vomiting. It is normally present in low amounts in the blood, but stresses such as illnesses can increase its level.

That led [Stephen O'Rahilly](#) at the University of Cambridge to propose that [GDF15 evolved to trigger food aversion in response to, say, poisoning](#) and that it contributes to morning sickness. Sure enough, his team found [higher levels in women with more pregnancy sickness](#).

Then, in 2018, [Marlena Fejzo](#) at the University of Southern California, Los Angeles, and her colleagues found that the risk of hyperemesis gravidarum was [associated with certain variants](#) in the gene for GDF15.

Now, an international team including Fejzo and O'Rahilly has released a preprint study describing additional evidence.

The researchers first found that GDF15 levels were significantly higher in around 60 women with hyperemesis gravidarum than in 60 pregnant women who reported little nausea and vomiting.

By looking at women and fetuses that produce different variants of GDF15, they found that most of the extra GDF15 in pregnant women comes from the fetus.

The researchers also discovered that several genetic variants linked to a higher risk of hyperemesis gravidarum have the effect of lowering GDF15 levels in non-pregnant people. They then analysed data from a previous study of 18,000 people and found that higher levels of GDF15 when not pregnant reduce the risk of the condition.

The explanation may be that women who have higher blood levels of GDF15 prior to pregnancy become desensitised to the hormone and are therefore less affected by raised levels during pregnancy, the researchers suggest.

This desensitisation effect could explain why morning sickness usually recedes after the first trimester. It might also explain why women who smoke before pregnancy, which raises GDF15 levels, are less likely to get hyperemesis gravidarum.

To test the desensitisation idea, the researchers injected some mice with a long-lasting form of GDF15 and others with a placebo. Three days later, all the mice were given a much larger dose of GDF15. Those who had initially been given the placebo ate much less and lost weight, whereas those with prior exposure were much less affected.

Because [the blood disorder beta thalassaemia](#) is known to raise GDF15 levels, the team also did a survey of 20 women with beta thalassaemia who had given birth and 20 matched controls. They found just one woman with beta thalassaemia who reported nausea and vomiting during pregnancy, compared with 13 of the control group.

“The work by Fejzo and colleagues has provided compelling evidence that alterations in GDF15 may be linked to hyperemesis gravidarum,” says [Sumona Saha](#) at the University of Wisconsin–Madison. “Based on this, I am interested to see the development of therapeutics.”

The findings suggest hyperemesis gravidarum could be prevented by desensitising those at risk prior to pregnancy. “Strategies which safely increase circulating GDF15 levels prior to pregnancy may be useful in the prevention of these conditions,” the study states.

It also suggests that lowering GDF15 levels during pregnancy will reduce nausea and vomiting. At least four companies are developing antibodies that bind to GDF15 to help treat other conditions where the hormone causes nausea, vomiting and weight loss.

For instance, a 2020 study showed that an antibody that mops up GDF15 [reduces vomiting in monkeys](#). This antibody is already being tested in early-stage clinical trials, a spokesperson for drug manufacturer Pfizer told *New Scientist*.

In the 1950s, the drug thalidomide was [used to treat morning sickness](#) before it was found to cause serious congenital conditions.

Fejzo, O’Rahilly and their colleagues don’t think anti-GDF15 antibodies will harm developing fetuses, but note that it might be safest to modify antibodies to prevent

them crossing the placenta into the fetus. “Since the tragedy of thalidomide, concerns about safety have understandably been very prominent in discussions of novel treatments for [hyperemesis gravidarum],” the team writes.

Reference

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