

# **Dispelling severe morning sickness myths: It's not normal or harmless, but prevention and treatment might be on the way**

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Late 2023, geneticist Marlena Fejzo and colleagues made the discovery that morning sickness's most serious presentation, hyperemesis gravidarum (HG), is caused by the hormone GDF15, not human

chorionic gonadotropin as previously thought. In an opinion article published May 22 in the journal *Trends in Molecular Medicine*, Fejzo dispels common morning sickness myths and discusses potential treatments, including sensitizing people to GDF15 prior to pregnancy, similar to the way we treat allergies.

"HG can be life threatening and is associated with adverse outcomes that need to be taken seriously," says Fejzo of the Keck School of Medicine of the University of Southern California. "Now that we know that GDF15 is the most likely cause of HG, we are on the cusp of having treatments that target this hormonal pathway and end the suffering."

## **Myth 1: Severe morning sickness is harmless and normal**

Pregnant people with HG are essentially starving, Fejzo says, and an increasing number of studies have demonstrated that this has serious short- and long-term clinical implications for both the parent and child. HG is a top predictor of postnatal depression, and 26% of pregnant people with HG report suicidal ideation while 18% meet the full criteria for post-traumatic stress disorder.

For the child, HG is associated with [preterm birth](#), [low birth weight](#), and later in life, [autism spectrum disorder](#), ADHD, depression, social problems, in addition to an increased risk of childhood cancer and respiratory and cardiovascular disease. Still, pregnant people with the condition are often dismissed by their clinicians and families.

"It really is like a teratogen in [pregnancy](#), a factor which interferes with normal fetal development, but it's still not taken seriously by a lot of medical professionals," Fejzo says. "A lot of people are brushed off and told, 'oh that's normal, it's okay, just don't take your pre-natal vitamins;

you don't need them."

At its most extreme, individuals with HG can develop Wernicke encephalopathy, a life-threatening swelling of the brain due to thymine (vitamin B1) deficiency. Since individuals with HG can have trouble even swallowing vitamins, the American College of Obstetricians and Gynecologists currently recommends that they replace broad spectrum prenatal vitamins with [folic acid](#), but Fejzo warns that this is likely insufficient, and that thiamine supplementation is also warranted for individuals with HG.

"I believe all women who have hyperemesis should be given vitamin B1 to avoid this serious brain swelling that can lead to permanent brain damage and often leads to fetal death," Fejzo says.

## **Myth 2: Morning sickness is caused by human chorionic gonadotropic hormone (hCG) or is psychosomatic**

Though it was long thought that morning sickness is caused by hCG, the recent breakthrough has shown that HG's main cause is actually the hormone GDF15, which is part of a normal stress response. Usually, GDF15 is expressed only in very small amounts, but during early pregnancy it spikes by a huge amount, then wanes, and finally rises again during the third trimester.

A recent *Nature* [study co-authored by Fejzo showed](#) that individuals who suffer from HG can have genetic variants that causes them to have lower levels of circulating GDF15 prior to pregnancy, which makes them extra sensitive when they become pregnant and are suddenly exposed to high levels.

This finding has clinical implications for preventing and treating HG, since preliminary research suggests that it might be safe to manipulate GDF15 during or even prior to pregnancy.

"GDF15 may be safe to manipulate in pregnancy or even prior to pregnancy," says Fejzo. "If we can increase levels of GDF15 before someone becomes pregnant, that might desensitize them, similar to how we try to desensitize people to allergens who have severe allergies," says Fejzo. "And during pregnancy, we may be able to minimize or get rid of symptoms by blocking GDF15 or its receptors in the brain stem."

### **Myth 3: Only humans experience morning sickness**

Nausea and appetite loss during gestation is not a uniquely human trait—these symptoms have been observed throughout the animal kingdom, from monkeys, dogs, and cats, to chickens, vipers, and octopuses.

"I always think it's interesting that the recommendation for cats is that if they're unable to eat for a day, you should contact your veterinarian, but we don't have that recommendation out there for women with hyperemesis," says Fejzo. "If you call your doctor's office and say you haven't eaten for a day, they'll say, 'that's normal' and won't do anything. There's more proactive care for cats than humans."

In addition to preventing ingestion of harmful foods, Fejzo speculates that pregnancy-induced nausea likely evolved to prevent dangerous foraging trips.

"This condition likely evolved because it was probably beneficial to avoid going out searching for food during pregnancy," says Fejzo. "That may still be true for animals, but people don't need this anymore, so let's end the suffering once and for all if we can."

Now, Fejzo is working toward developing and testing the proposed GDF15-based treatments. She also plans to investigate other genes and variants of GDF15 that might contribute to HG.

**More information:** Hyperemesis gravidarum theories dispelled by recent research: A paradigm change for better care and outcomes, *Trends in Molecular Medicine* (2024). DOI: [10.1016/j.molmed.2024.04.006](https://doi.org/10.1016/j.molmed.2024.04.006)

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