



Sylvia R. Karasu M.D.  
The Gravity of Weight

## Treating the Pregnant Woman with Pernicious Vomiting

Evolution in our thinking about symptoms during pregnancy.

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### KEY POINTS

- Years ago, physicians thought pernicious vomiting in pregnancy was psychological and imposed harsh and cruel behavioral methods on women.
- The cause of pernicious vomiting is still unknown but researchers believe there is a strong genetic component and implicate the hormone GDF15.
- Intractable symptoms can be severe, occur in each subsequent pregnancy, and require hospitalization for dehydration and electrolyte imbalances.



"Fetus in placenta in utero." A plaque sculptured in wax over two centuries ago may have been used to teach students of anatomy. Opportunities to study the pregnant body were extremely rare: by law, dissections for research were often restricted to criminals. Expectant women could not be executed.

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"Having gotten the patient into the hospital, the vomit bowl is kept away from her. If she wants to vomit, she is told to vomit into the bed, and when she does vomit, the nurse is instructed not to be in too great a hurry to change her...I find that a certain curtness of manner works to advantage," wrote an obstetrician in the 1920s (Atlee, 1925). He suggested to one patient that, if she needed

to vomit, she should do so on a “particularly fine rug—a wedding present” she had brought to the hospital.

By today’s standards of care, this harsh behavioral conditioning, which may have worked for some, seems cruel treatment for pregnant women suffering from pernicious vomiting, i.e., hyperemesis gravidarum (HG), a disorder affecting up to 3% of pregnant women (London, 2017).



"Pregnancy" by American artist, Will Barnet (1911-2012), 1938.

Source: Credit: Smithsonian American Art Museum. Gift of John B. Turner, 1972. Used with permission.

There is no consensus definition for HG nor even a complete understanding of its pathogenesis. The distinction between moderate and severe symptoms can be challenging (Fejzo et al., 2019) and often rests on clinical judgment (London et al., 2017). Physicians can assess the severity of vomiting by its frequency and duration with the validated *Pregnancy-Unique Quantification of Emesis (PUQE)* scale.

Importantly, when a pregnant woman presents with severe nausea and vomiting, particularly in the second trimester, clinicians must consider other diagnoses, including *gastrointestinal* (e.g., intestinal obstruction, hepatitis, appendicitis), *genitourinary* (e.g., kidney stones, pyelonephritis), *metabolic* (e.g., diabetic ketoacidosis, Addison’s disease, hyperthyroidism), *neurological* (e.g., *migraine* headaches, CNS tumors), *other pregnancy-related* (e.g.,

preeclampsia), and even *miscellaneous* (e.g., psychological, drug toxicity) conditions.

HG, in the absence of other diseases, becomes a diagnosis of exclusion. Typically, patients have severe dehydration, electrolyte imbalance (Petry et al., 2018), and a loss of 5% of their pre-pregnancy weight (London et al., 2017).

Hyperemesis gravidarum has been called a “disease of theories”(Kemp, 1933). Over the years, physicians have speculated that toxic metabolites cause it in a patient’s blood, abnormalities of pelvic organs (Stevens, 1905), or even adrenal insufficiency (Kemp, 1933). One early 20th-century theory held that HG was purely psychological, caused by hysteria or specific neurotic conflicts (e.g., ambivalence about being pregnant), a belief damaging to some patients. It led to minimizing their distress and mistreating them with aversive techniques (Munch, 2002).

Investigators have also considered infectious origins (e.g., *H. pylori*). Recently, elevated hormone levels of GDF15 are implicated, as are genetics, since women with a family history are three times more likely to experience HG (Petry et al., 2018). Increased GDF15 levels may suppress pro-inflammatory cytokines, facilitating the development of the placenta and maintaining the pregnancy (Fejzo et al., 2018).

Treatment for nausea and vomiting of pregnancy depends on the severity of symptoms. For mild symptoms, lifestyle modifications in diet (e.g., dry crackers, avoid spicy foods, eat small, frequent meals) or non-pharmacological remedies (e.g., massage, acupuncture) may help. Ginger has benefits, but



"Throwing Up," an illustration from "Tacuinum Santiatis Codex Vindobonensis." Italian School, 14th century.

Source: Credit: Osterreichische Nationalbibliothek, Vienna. Austria Alinari/Bridgeman Images. Used with permission.



there is no standardization of dose as with any plant or herbal preparation. Cannabis has been used for its anti-emetic properties, but the American College of Obstetricians and Gynecologists recommends against it. Though the mechanism is unknown, administering a multivitamin B complex at the time of conception (in those women who have planned their pregnancy) may decrease symptoms (Fejzo et al., 2019).



"The urine examination." German School, 18th century, Museo Nazionale Dell' Arte Sanitaria, Rome. The analysis of urine has been used for centuries, but it is only in the 20th century that clinicians tested for the hormone hCG. The first home pregnancy test became available in 1978, according to the Science Museum, London.

Source: Bridgeman Images. Used with permission.

For more serious, intractable symptoms, clinicians must first assess the need for hospitalization. Recently, the media reported that Kate Middleton, Duchess of Cambridge, suffered from hyperemesis gravidarum during all three of her pregnancies (not uncommon), severe enough to require hospitalization. Before accurate methods to diagnose pregnancy and before intravenous hydration, women did die from HG. See my previous blog for a discussion of the *speculation* that 19th-century novelist Charlotte Brontë died due to hyperemesis gravidarum.

Medications are available, but only nine drugs have been approved officially for use in pregnancy. Only one for nausea and vomiting not responding to lifestyle changes: Diclegis, an extended-release combination of an antihistamine and

the B<sub>6</sub> vitamin pyridoxine (Wesley et al., 2021). Many other medications are used "off-label." Between 40% to 60% of pregnant women reportedly take one or more prescription medications for either pre-existing conditions (e.g., diabetes, asthma) or pregnancy-related conditions (Ren et al., 2021).

In 2014, the *Pregnancy and Lactation Labeling Rule* eliminated the previous drug classifications *ABCDX*. The label now contains a *risk summary of available evidence* for use during pregnancy. However, clinical interpretation is still required, and in most cases, safety and dosing information is not available or “embarrassing scant” (Caritis and Venkataramanan, 2021).

Many physicians understandably remain reluctant to prescribe, and their pregnant patients reluctant to take, medications during pregnancy, particularly in the wake of the thalidomide tragedy of the early 1960s. It took five years for clinicians to connect thalidomide and the severe congenital disabilities, including the shortened, flipper-like limbs of phocomelia, that resulted. At least 10,000 babies were affected worldwide.

FDA advisor Frances Kelsey, M.D., Ph.D., resisted considerable pressure to approve the drug for use in the U.S. (Loughlin, 2017), even though it had been marketed to treat nausea and vomiting in pregnancy in 49 countries. Even a single 50 mg tablet during a “time-sensitive window” led to congenital disabilities in up to 50% of pregnancies (Vargesson, 2015).

This tragedy changed the entire drug-approval process: no longer could animal testing alone be sufficient (London Science Museum, 2019).



"The Arnolfini Portrait," 1434, by Jan van Eyck. National Gallery, London. There is some mystery surrounding this painting, and scholars have wondered whether this woman was actually pregnant. Painted centuries before there were accurate means of determining pregnancy,

Source: Wikimedia Commons/Public Domain



One of the effects of the drug Thalidomide, which affected over 10,000 babies in the early 1960s. Fortunately, through the efforts of FDA advisor Dr. Kelsey, the drug was never released in the U.S.

Source: Wikimedia Commons/ Creative Commons Attribution 2.0 Generic. Originally from the Otis Historical Archives National Museum of Health and Medicine.

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Investigators emphasize that pregnant women be protected *by research* rather than *from research* (Ren et al., 2021). However, clinicians are right to ask, “What level of evidence is required before exposing the first pregnant woman?” (Bahmanyar et al., 2021). Unfortunately, we don't always have the answer.

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