‘Morning sickness’ in pregnancy loses psychogenic stigma

Evidence refutes past beliefs, supports organic causes and psychological sequelae

Nausea and vomiting in pregnancy (NVP) is a misunderstood disorder associated with stress, anxiety, and depression. Prejudice toward women is thought to have guided the historical psychoanalytic concept of NVP as psychogenic, but this view is being replaced by newer biologic theories.

This article examines the evidence for psychological and organic causes of NVP to inform psychiatrists treating pregnant patients. We review guidelines for pharmacologic treatment of NVP and discuss potentially useful psychotherapies and alternative approaches.

Definitive cause unknown

“Morning sickness” affects 50% to 80% of pregnant women, occurring so commonly that NVP is often considered normal. Approximately 0.5% to 2% of women experience the most severe NVP—hyperemesis gravidarum (HG)—characterized by intractable vomiting, weight loss, and electrolyte imbalance that can lead to hospitalization.

Without modern supportive care, HG can be lethal; although Charlotte Brontë’s death certificate states she died of “phthisis” (tuberculosis), the author of Jane Eyre is popularly believed to have succumbed to HG.

The search for effective NVP treatments has been disappointing, partly because no cause has been identified. After other conditions that may lead to nausea and vomiting are ruled out (Table 1, page 32), NVP medical management is supportive. Correcting dehydration and encouraging dietary and lifestyle changes (Table 2, page 33) are important adjuncts to step-wise...
Vomiting in pregnancy

Clinical Point
Stress, anxiety, and depression in women with NVP are thought to result from—rather than cause—its physical symptoms.

Medical causes of nausea and vomiting in pregnancy

<table>
<thead>
<tr>
<th>Possible cause</th>
<th>How to rule it out</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appendicitis</td>
<td>History; do physical, order imaging</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>Jaundice; order liver function tests, antibody studies, imaging</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>History of alcohol use, abdominal pain; check amylase and lipase level</td>
</tr>
<tr>
<td>Gastrointestinal obstruction</td>
<td>History of surgeries; order imaging</td>
</tr>
<tr>
<td>Peptic ulcer disease</td>
<td>History; order upper GI series/endoscopy</td>
</tr>
<tr>
<td>Thyroid disease</td>
<td>Thyroid function tests</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>Urinalysis, culture-sensitivity</td>
</tr>
<tr>
<td>Trophoblastic disease</td>
<td>Check hCG, order ultrasound</td>
</tr>
</tbody>
</table>

* Elevated human chorionic gonadotropin (hCG) has shown evidence of an association with NVP.

Pharmacologic treatment recommended by the American College of Obstetrics and Gynecology (Algorithm, page 34).7

Prejudice vs evidence

Psychological factors. Historically, psychological factors have been blamed for NVP, but support comes from a few poorly designed studies or case reports.3,4

Psychoanalytically, pregnancy and childbirth are significant events in a woman’s life and a rich environment for conflict that could lead to physical expression of symptoms. Freud believed pregnancy and childbirth involve the unconscious substitution of the penis with the child.8 Later writers viewed motherhood as woman’s most powerful wish and the primary organizer of her sexual drive and personality.8

NVP has been considered a conversion or somatization disorder in which symptoms are a “hysterical” expression of unconscious conflict. A psychoanalytic view contends that women who experience NVP are ambivalent about the pregnancy and seek to reject it.1,9 Vomiting, in this view, represents an oral abortion attempt.10 Others claim NVP is a rejection of femininity9 or that symptoms in women with overly attached maternal relationships mask unconscious aggressive feelings toward their mothers.11

Robertson11 proposed an association between NVP and a woman’s view of sexual experiences and her ability to achieve orgasm. He interviewed 100 women and found that 40 of 57 with NVP had “disturbed sexual functioning” or were “frigid” (defined as experiencing coitus as undesirable and unaccompanied by orgasm).

Higgins15 in 1887 proposed that the cause of NVP “is sexual intercourse, the husband too eager for it and the wife too adverse.” Additionally, NVP and HG have been associated with infantile, childish, immature, and hysterical personalities.12-14

Psychiatric comorbidities. Attempts have been made to associate NVP with other psychiatric disorders such as depression, bipolar disorder, schizophrenia, and anxiety disorders, including posttraumatic stress disorder (PTSD). No definitive association has been found between NVP and depressive illness, bipolar disorder, or schizophrenia15 or the use of antidepressants before or during early pregnancy.16 Studies reporting an association with depression have not established a cause-effect relationship.17 Seng18 reported increased NVP risk in women with PTSD. High levels of stress, anxiety, and depression found in women with NVP are thought to result from—rather than cause—NVP’s physical symptoms, however.3,19,20

Psychosocial stressors have been implicated, with higher NVP rates reported in unmarried women, those with unwanted or unplanned pregnancies, immigrants, and those living in crowded situations.13 NVP also is more frequent among women who experience emotionally disturbing events or interpersonal, economic, or occupational difficulties during pregnancy.22 Physical symptoms may provide secondary gain in attention and sympathy and a time-out from stressful home events.14

These psychosocial theories are poorly supported by data, but some clinicians...
may still believe NVP has a psychogenic cause. Lennane and Lennane\textsuperscript{23} proposed in 1973 that this perception may result from gender bias because:

- most conditions believed to have psychogenic causes affect women more than men
- the belief that NVP is psychogenic has been perpetuated primarily by male authors.

They argued that sexual prejudice may prevent women from receiving necessary symptomatic treatment and impede research into the cause of NVP\textsuperscript{23}.

Gender bias continues to be found in the diagnosis of women with physical complaints. In 2006, Chiaramonte and Friend\textsuperscript{24} found strong, consistent gender bias among medical students and residents when evaluating women who reported coronary disease symptoms during stressful life events.

**Organic theories**

Organic theories view NVP as multifactorial, with contributions from evolution and multiple organ systems. Endocrine, vestibular, and gastrointestinal systems may all be involved. Women may have additional hormonal changes that may contribute to the symptoms of NVP.

**Table 2**

**Advice for patients: Strategies to manage NVP**

**Correct dehydration**

- Drink small amount of fluids frequently

**Dietary changes**

- Eat frequent, small meals
- Avoid high-fat foods
- Snack before getting out of bed and before going to sleep
- Don’t force yourself to eat
- Use candy and salty snacks to combat nausea
- Avoid strong odors and scents; try cold foods, which may have less odor than hot foods
- Take advantage of good days or good hours of the day for eating

**Lifestyle changes**

- Get out of bed slowly
- Lie down when nauseated
- Avoid stressful situations

NVP: nausea and vomiting in pregnancy

Source: Reference 6

Adults with ADHD were 3X more likely to be unemployed\textsuperscript{*1}

The consequences may be serious.

Screen for ADHD.

Find out more at [www.consequencesofadhd.com](http://www.consequencesofadhd.com) and download patient support materials, coupons, and adult screening tools.

\*Data compiled from a study comparing the young adult adaptative outcome of nearly 140 patients (ADHD and non-ADHD control) followed concurrently for at least 13 years.

Vomiting in pregnancy

Clinical Point

Human chorionic gonadotropin shows a clear association with NVP and is thought by some researchers to be the most likely cause.

Pharmacologic treatment of nausea and vomiting in pregnancy*

**Algorithm**

**Pharmacologic treatment of nausea and vomiting in pregnancy**

<table>
<thead>
<tr>
<th>Monotherapy: Vitamin B6, 10 to 25 mg, 3 or 4 times daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>Add: Doxylamine, 1 12.5 mg, 3 or 4 times daily</td>
</tr>
<tr>
<td>Adjust schedule and dose according to symptom severity</td>
</tr>
<tr>
<td>Add: Oral or rectal promethazine, 12.5 to 25 mg every 4 hours OR</td>
</tr>
<tr>
<td>Oral or rectal dimenhydrinate, 50 to 100 mg every 4 to 6 hours</td>
</tr>
<tr>
<td>(not to exceed 400 mg/d; not to exceed 200 mg/d if patient also is taking doxylamine)</td>
</tr>
<tr>
<td>No dehydration</td>
</tr>
<tr>
<td>Dehydration</td>
</tr>
<tr>
<td>Add any of the following:</td>
</tr>
<tr>
<td>IM or oral metoclopramide 5 to 10 mg every 8 hrs OR</td>
</tr>
<tr>
<td>IM, oral, or rectal promethazine 12.5 to 25 mg every 4 hours OR</td>
</tr>
<tr>
<td>Rectal trimethobenzamide 200 mg every 6 to 8 hours</td>
</tr>
<tr>
<td>IV fluid replacement</td>
</tr>
<tr>
<td>Add any of the following:</td>
</tr>
<tr>
<td>IV dimenhydrinate, 50 mg (in 50 mL saline, over 20 min) every 4 to 6 hrs OR</td>
</tr>
<tr>
<td>IV metoclopramide 5 to 10 mg every 8 hrs OR</td>
</tr>
<tr>
<td>IV promethazine 12.5 to 25 mg every 4 hours</td>
</tr>
<tr>
<td>Add: Oral or IV methylprednisolone, 16 mg every 8 hrs, for 3 days. Taper over 2 weeks to lowest effective dose. If beneficial, limit use to total of 6 weeks OR</td>
</tr>
<tr>
<td>IV ondansetron, 8 mg over 15 minutes, every 12 hrs</td>
</tr>
</tbody>
</table>

* Assumes other causes of nausea and vomiting have been ruled out. Consider parenteral nutrition if dehydration or persistent weight loss occurs. Alternative therapies may be added at any time; consider P6 acupressure with wristbands or ginger capsules, 250 mg 4 times daily. 
† Available as the active ingredient in some nonprescription sleep aids; one-half of a scored 25-mg tablet can be used to provide a 12.5-mg dose of doxylamine. 
‡ IV thiamine, 100 mg/d for 2 to 3 days (followed by IV multivitamins), is recommended for every woman who requires IV hydration and has vomited for >3 weeks. 
§ Corticosteroids appear to increase risk for oral clefts in the first 10 weeks of gestation. 
¶ Safety, particularly in the first trimester of pregnancy, not yet determined; less effect on nausea than on vomiting.


ular, gastrointestinal, and CNS contributions have been described, but none have solved NVP’s etiologic mystery.

**Evolutionary.** NVP may provide an evolutionary advantage by protecting the embryo and mother. This theory states that potential toxins are present in many foods, especially if eaten in large quantities. NVP prevents the pregnant woman from eating very much and harming the embryo. Below-average miscarriage rates are seen in women with NVP.12,25

And because a woman’s immune system is depressed during pregnancy, NVP may be advantageous for the mother by limiting her ingestion of potential toxins.25

**Endocrine.** Human chorionic gonadotropin (hCG), estrogens, progesterone, and leptin, as well as adrenal cortex insufficiencies have been investigated for a role in NVP. Only hCG has shown clear evidence of an association, and some researchers believe it is the most likely cause of NVP.20
NVP rates are higher in pregnancies with elevated hCG. Molar and multiple-gestation pregnancies—each associated with elevated hCG—are complicated more frequently with the severest form of NVP. Conversely, NVP is less common in women who smoke, which is associated with lower hCG.

During pregnancy, actions of hCG stimulate the thyroid. Hyperstimulation, leading to transient hyperthyroidism, has been implicated in NVP development. Symptom severity and the degree of thyroid stimulating hormone (TSH) suppression are closely correlated.

Elevated hCG levels, hypersensitive TSH receptors, and the presence of a hyperactive hCG isoform have been proposed.

Gastrointestinal disorders are believed to be involved in the pathogenesis of persistent NVP. Women with NVP usually lack structural or mucosal abnormalities and have normal endoscopic upper GI evaluations. They may, however, have disorders of the stomach’s neuromuscular function. Severe cases of gastric dysrhythmias and abnormalities of gastric tone may lead to gastroparesis.

Stomach motility in pregnancy is influenced by neurohormonal changes, specifically in estrogen and thyroid hormones. Gastric motility abnormalities—evaluated by electrogastrography (EGG)—have been associated with NVP symptoms and normal EGGs with the absence of symptoms. Some women who had NVP and abnormal EGGs were retested after delivery when symptom-free and found to have normal myoelectric EGG patterns.

Heliobacter pylori also may be involved in NVP, and at least 1 study found active H pylori infection and HG to be highly correlated. Pregnancy is not believed to predispose to H pylori infection, but active infection compounded by pregnancy’s hormonal changes may exacerbate NVP.

Want to know more?
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Treating anxiety during pregnancy:
Just how safe are SSRIs?
FEBRUARY 2008
continued
Vomiting in pregnancy

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Mirtazapine exhibits an antiemetic effect and has been reported to ameliorate NVP symptoms, usually within 24 hours.

NVP and motion sickness share many features, suggesting that NVP treatment could be targeted if a vestibular disorder could be discovered. Abnormal electroencephalography—particularly generalized slowing—that is not present in asymptomatic pregnant women has been reported in women with NVP.

CNS contributions. Persistent NVP may be a learned behavior, a view based on findings of anticipatory nausea and vomiting in chemotherapy patients. Through conditioning, a pregnant woman may associate her physical symptoms with elements in her life that maintain the cycle of nausea and vomiting.

Treating psychological symptoms
Brief psychotherapy to identify and correct sources of anxiety in pregnancy may alleviate a patient’s nausea and vomiting. Progressive muscle relaxation training, often combined with guided imagery, can decrease nausea and vomiting associated with chemotherapy and may prevent anticipatory symptoms by decreasing anxiety. Systematic desensitization is successful in most chemotherapy patients who try it. In this technique, relaxation is counterconditioned as a response to stimuli known to elicit symptoms.

Hypnosis allows patients to achieve a physiologic state incompatible with nausea and vomiting and can terminate vomiting after 1 to 3 sessions.

Medication. Similar to ondansetron, the antidepressant mirtazapine exhibits an antiemetic effect by blocking the 5-HT3 receptor. In treatment-resistant cases, mirtazapine, 30 mg/d, has been reported to ameliorate NVP symptoms, usually within 24 hours. Patients were able to return to normal diets and discontinue treatment after 6 to 10 days. Mirtazapine appears to be safe during pregnancy, based on animal studies using 17 and 20 times the maximum recommended human dose.

For patients with anxiety symptoms, consider other medications—including selective serotonin reuptake inhibitors and benzodiazepines—only after counseling the patient about potential risks and benefits to her and the fetus.

Alternative treatments. In traditional Indian medicine, a mixture of powdered ginger and honey is given to women with NVP. At least 2 studies demonstrate ginger’s efficacy.

In traditional Chinese medicine, stimulating the Neiguan point (P6) on the wrist is believed to relieve nausea and vomiting. Although results are inconclusive, studies suggest that P6 stimulation can help control NVP. The FDA has approved wristbands that stimulate the P6 site, either electrically or by acupressure (Figure).

Consider thiamine supplementation for women with severe symptoms, as Wernicke’s encephalopathy is a rare complication of prolonged NVP.

References

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Related Resources


Drug Brand Names

Dimenhydrinate - Dramamine
Mirtazapine - Remeron
Doxylamine - Unisom
Ondansetron - Zofran
Methylprednisolone - Medrol
Promethazine - Phenergan
Metoclopramide - Reglan
Trimethobenzamide - Tigan

Disclosure

The authors report no financial relationship with any company whose products are mentioned in this article or with manufacturers of competing products.


Bottom Line

Severe nausea and vomiting in pregnancy is no longer viewed as psychogenic but as arising from biopsychosocial factors. Rule out medical causes of vomiting and correct dehydration. Consider mirtazapine for treatment-resistant cases. To reduce stress, anxiety, and anticipatory vomiting, consider brief psychotherapy, progressive muscle relaxation, systematic desensitization, or hypnosis.