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اسم المحاضرة السابعة عشر باللغة الإنكليزية : Vomiting during pregnancy

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Vomiting during pregnancy

Nausea and vomiting occur in up to 74% of pregnant women, and 50% experience vomiting alone. Although the term morning sickness is commonly used to describe nausea and vomiting of pregnancy, the timing, severity, and duration of symptoms vary widely. Approximately 80% of women report that their symptoms last all day, whereas only 1.8% report symptoms that occur solely in the morning.

Women who are less educated, older, and those who have lower incomes, multiple gestations, or increasing gravidity (including miscarriages) are at greater risk of nausea and vomiting of pregnancy. A personal history of motion sickness, migraine headaches, or nausea associated with the use of estrogen-containing contraceptives also increases the risk.

Hyperemesis gravidarum describes nausea and vomiting that is severe enough to cause fluid and electrolyte disturbances, and often requires hospitalization. It affects up to 1% of pregnant women and is associated with persistent vomiting (more than three episodes per day) that results in severe dehydration, ketonuria, electrolyte abnormalities such as hypokalemia, and weight loss of more than 5%. A personal history of hyperemesis gravidarum, gestational trophoblastic disease, fetal triploidy, fetal trisomy 21, hydrops fetalis, and multiple gestations increases the risk of this condition. The risk may be increased by as much as 50% if the fetus is female.

# Etiology and Pathophysiology

The causes of nausea and vomiting of pregnancy and of hyperemesis gravidarum are unknown. However, observational data indicate that these conditions correlate with levels of human chorionic gonadotropin (hCG) and the size of the placental mass, which suggests that placental products may be associated with the presence and severity of nausea and vomiting. Some women with complete hydatidiform molar pregnancies, in which no fetus is present, have significant nausea and vomiting, which indicates that placental factors, particularly hCG, are responsible. Women with higher hCG levels, such as those with multiple gestations, hydatidiform moles, or fetuses with Down syndrome, are at increased risk of nausea and vomiting.

Levels of estrogen and progesterone may also be involved. Other potential etiologies include placental prostaglandins, serotonin levels, thyroid dysfunction, increased leptin levels, immune system dysregulation, *Helicobacter pylori* infection, and gastrointestinal dysmotility.

# Differential Diagnosis

In most pregnancies, nausea and vomiting is mild and self-limited. It usually starts within four weeks of the last menstrual period and peaks at nine weeks' gestation. An estimated 60% of cases resolve by the end of the first trimester, and 87% resolve by 20 weeks' gestation. Women who have atypical presentations (e.g., onset of symptoms after nine weeks' gestation, symptoms beyond the first trimester, severe symptoms, hyperemesis gravidarum) should be evaluated to exclude potentially serious causes.

**Table 1. Differential Diagnosis of Nausea and Vomiting of Pregnancy**

**Common causes**

Cholecystitis

Gastroenteritis

Gastroesophageal reflux

Migraine headaches

**Less common causes**

Biliary tract disease

Drug toxicities or intolerances

Hepatitis

Hyperthyroidism

Kidney stones

Molar pregnancy

Pancreatitis

Peptic ulcer disease

Preeclampsia/HELLP syndrome  
(hemolysis, elevated liver  
enzymes, and low platelet count)

Pyelonephritis

**Uncommon causes**

Acute fatty liver of pregnancy

Addison disease

Appendicitis

Central nervous system tumors

Degenerating uterine leiomyoma

Diabetic ketoacidosis

Hypercalcemia

Intestinal obstruction

Meniere disease

Ovarian torsion

Porphyria

Pseudotumor cerebri

Uremia

Vestibular lesions



In women with straightforward nausea and vomiting of pregnancy, physical examination findings are generally unremarkable. Abnormal findings (e.g., abdominal tenderness, peritoneal signs, fever) suggest another cause. In the absence of other physical findings, significant dehydration, with or without orthostasis, is consistent with hyperemesis gravidarum.

No laboratory tests are necessary in patients with normal examination findings and no evidence of dehydration. If not already performed, ultrasonography may be used to evaluate for the presence of a molar pregnancy or multiple gestation if there is clinical suspicion or abnormally elevated hCG levels.

If laboratory tests are ordered because of clinical suspicion that symptoms are not caused by straightforward nausea and vomiting of pregnancy, a basic approach should include a complete blood count; urinalysis; metabolic panel including transaminase levels; and measurement of thyroid-stimulating hormone, quantitative hCG, and amylase levels. An abnormally high hCG level suggests a multiple gestation, molar pregnancy, or, in rare cases, a twin pregnancy with both a normal fetus and a molar gestation.

# Maternal and Fetal Outcomes

In pregnancies with uncomplicated nausea and vomiting, there is a decreased risk of miscarriage, as well as lower rates of preterm delivery, fetal death, and growth restriction. However, infants of women who lost weight early in the pregnancy, particularly in the setting of hyperemesis gravidarum, are at increased risk of growth restriction or low birth weight. Women with nausea and vomiting that is refractory to treatment or complicated by weight loss have increased risks of fetal growth restriction and fetal death, as well as preeclampsia and maternal complications associated with vomiting (e.g., esophageal rupture, retinal hemorrhage, Mallory-Weiss syndrome, pneumothorax).

# Treatment

Treatment should be directed toward reducing symptoms while posing the least amount of risk to the fetus and mother. Various modalities have been used, some without evidence of benefit.

# Nonpharmacologic Therapies

Traditional first-line therapy for nausea and vomiting of pregnancy and for hyperemesis gravidarum includes dietary modifications such as avoidance of large meals and consumption of low-fat, bland foods (e.g., breads, crackers, cereals, eggs, lean meat, peanut butter, fruits, vegetables). Avoidance of foods with strong smells and those with increased protein and liquid content is often recommended. However, there is little evidence to support these recommendations.

Although nausea and vomiting of pregnancy and hyperemesis gravidarum have been linked with a variety of psychological conditions, including depression and stress-related disorders, more recent data have not shown a definitive association. Evidence shows that women appreciate acknowledgment of the distress caused by nausea and vomiting of pregnancy and hyper-emesis gravidarum.

A variety of other nonpharmacologic therapies for nausea and vomiting of pregnancy. Although commonly used by patients and recommended by health care professionals, most of these treatments have only limited evidence supporting their benefit.e.g.

P6 Acupressure

Ginger extract 125-150mg every 6 hours found to be effective.

# Pharmacologic Therapies

*Vitamin B<sub>6</sub> and Doxylamine.* Vitamin B<sub>6</sub> (10 to 25 mg every eight hours) is more effective than placebo in improving symptoms of nausea, although the reduction in vomiting is less clear. Combination therapy with vitamin B<sub>6</sub> and doxylamine reduces nausea and vomiting by 70%. Although there have been concerns about teratogenicity, a large meta-analysis showed that combination therapy with vitamin B<sub>6</sub> and doxylamine is safe for use in the first trimester, and it is recommended for treatment of nausea and vomiting of pregnancy by the American College of Obstetricians and Gynecologists. In 2013, the U.S. Food and Drug Administration approved a delayed-release formulation of doxylamine and pyridoxine hydrochloride.



*Antiemetics.* Chlorpromazine and prochlorperazine have been shown to reduce symptoms of nausea and vomiting of pregnancy and of hyperemesis gravidarum. Buccal administration of prochlorperazine is associated with less sedation than oral administration. Promethazine is commonly used, but is sedating. It is available as a rectal suppository and can be compounded as a topical agent that is applied to the wrist. Its safety in the first trimester has been established.

Small studies have shown comparable effectiveness between ondansetron (Zofran) and promethazine in treating nausea and vomiting, although patients receiving ondansetron had less sedation. Ondansetron is significantly more expensive than promethazine. The use of ondansetron in pregnancy has not been shown to increase the risk of miscarriage, major malformations, or low birth weight.

*Antihistamines and Anticholinergics.* Antihistamines decrease stimulation of the vomiting center by affecting the vestibular system. Diphenhydramine, meclizine , and dimenhydrinate have been shown to be safe and more effective than placebo in reducing the symptoms of nausea and vomiting of pregnancy. Although scopolamine is likely effective, its use in the first trimester is not recommended because of the potential for limb and trunk defects.

*Promotility Agents.* Metoclopramide is often used alone and in combination with other agents, such as vitamin B<sub>6</sub>, for the treatment of nausea and vomiting of pregnancy. As a promotility agent, it increases gastric transit and lowers esophageal sphincter pressure. It is as effective as promethazine, but has fewer adverse effects. Metoclopramide in combination with vitamin B<sub>6</sub> is more effective than prochlorperazine or promethazine, although all three therapies improve symptoms. Because metoclopramide is associated with tardive dyskinesia, the U.S. Food and Drug Administration has issued a boxed warning. The risk of this rare complication increases with total dosage and duration of treatment; therefore, it should not be used for longer than 12 weeks.

*Corticosteroids.* A study involving 40 women found that methylprednisolone is superior to promethazine in reducing symptoms of nausea and vomiting in patients with hyperemesis gravidarum. However, a meta-analysis of four studies found that the use of glucocorticoids before 10 weeks' gestation is associated with a three- to fourfold increased risk of cleft lip. Therefore, glucocorticoids should be used only after 10 weeks' gestation.

*Intravenous Fluids.* Fluid replacement is safe and effective in restoring volume and electrolytes in women who have hyperemesis gravidarum and are unable to tolerate oral intake. Lactated Ringer solution or normal saline is acceptable. Because of the risk of Wernicke encephalopathy, intravenous thiamine should be added if dextrose-containing fluids are administered, if vomiting has lasted longer than three weeks, or if fluid replacement lasts longer than three days.

*Enteral and Parenteral Nutrition.* Patients who have refractory nausea and vomiting may require hospitalization. In these patients, enteral tube feeding in addition to routine intravenous fluids may be helpful. If patients do not respond to this therapy, parenteral nutrition may be necessary. Administration of parenteral nutrition is associated with significant risk during pregnancy, including a 25% risk of line sepsis, as well as steatohepatitis if lipid emulsion is used. Therefore, it should be reserved for extreme cases that have been refractory to enteral nutrition.

*Acid-Reducing Medications.* Recent data indicate that pregnant women who have acid reflux have more severe nausea and vomiting. Histamine H<sub>2</sub> antagonists and proton pump inhibitors are safe and effective for use in pregnant women and may improve nausea and vomiting.



Thank you