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This Practice Bulletin was developed by the ACOG Committee on Practice Bulletins—Obstetrics with the assistance of T. Murphy Goodwin, MD. The information is designed to aid practitioners in making decisions about appropriate obstetric and gynecologic care. These guidelines should not be construed as dictating an exclusive course of treatment or procedure. Variations in practice may be warranted based on the needs of the individual patient, resources, and limitations unique to the institution or type of practice.



Nausea and Vomiting of Pregnancy

Nausea and vomiting of pregnancy is a common condition that affects the health of both the pregnant woman and her fetus. It can diminish the woman's quality of life and also contributes significantly to health care costs and time lost from work (1). Because "morning sickness" is common in early pregnancy, the presence of nausea and vomiting of pregnancy may be minimized by health care providers and by pregnant women (1) and, thus, undertreated. One investigator found that fewer than 50% of women who called a nausea and vomiting of pregnancy hotline and who subsequently terminated their pregnancies because of severe nausea and vomiting of pregnancy had been offered any sort of antiemetic therapy (2, 3). Of those offered treatment, 90% were offered regimens that were not likely to be effective. Furthermore, some women do not seek treatment because of concerns about safety (4). Yet, once symptoms of nausea and vomiting of pregnancy progress, treatment can become more difficult; treatment in the early stages may prevent more serious complications, including hospitalization (5). Mild cases of nausea and vomiting of pregnancy may be resolved with lifestyle and dietary changes, and safe and effective treatments are available for more severe cases. The woman's perception of the severity of her symptoms plays a critical role in the decision of whether, when, and how to treat nausea and vomiting of pregnancy. In addition, nausea and vomiting of pregnancy should be distinguished from nausea and vomiting related to other causes. The purpose of this document is to review the best available evidence about the diagnosis and management of nausea and vomiting of pregnancy.

Definition and Incidence

Nausea and vomiting of pregnancy is a common condition that affects 70–85% of pregnant women (6). Fifty percent of pregnant women have both nausea and vomiting, 25% have nausea only, and 25% are unaffected (7, 8). One study has

attempted to categorize nausea and vomiting of pregnancy into degrees of severity by assessing the duration of nausea and vomiting each day (from less than 1 hour in mild cases to more than 6 hours in severe cases) and the amount of vomiting and retching per day (up to twice for mild and moderate nausea and vomiting of pregnancy; more than 5 times in severe cases) (1). However, although these categories recognize nausea and vomiting of pregnancy as a continuum, they may not be clinically useful. The woman's perception of the severity of her symptoms and her desire for treatment are more likely to influence clinical decision making.

From an epidemiologic perspective, hyperemesis gravidarum appears to represent the extreme end of the spectrum of nausea and vomiting of pregnancy (9). The incidence of hyperemesis gravidarum is approximately 0.5–2% of pregnancies. The reported incidence varies because of different diagnostic criteria and ethnic variation in study populations. There is no single accepted definition of hyperemesis gravidarum; it is a clinical diagnosis of exclusion based on a typical presentation in the absence of other diseases that could explain the findings (10). The most commonly cited criteria include persistent vomiting not related to other causes, a measure of acute starvation (usually large ketonuria), and some discrete measure of weight loss, most often at least 5% of prepregnancy weight (11). Electrolyte, thyroid, and liver abnormalities also may be present. Hyperemesis gravidarum is the most common indication for admission to the hospital during the first part of pregnancy and is second only to preterm labor as the most common reason for hospitalization during pregnancy (12, 13).

Differential Diagnosis

The timing of the onset of nausea and vomiting is important: symptoms of nausea and vomiting of pregnancy manifest before 9 weeks of gestation in virtually all affected women. When a patient experiences nausea and vomiting for the first time after 9 weeks of gestation, other conditions should be carefully considered in the differential diagnosis (see box). A history of a chronic condition associated with nausea and vomiting that predates pregnancy should be sought (eg, cholelithiasis or diabetic autonomic dysfunction). Rare cases of hyperemesis gravidarum related to a mendelian disorder of hormone-receptor interaction (14) and mitochondrial disorders (15) suggest that at least some portion of hyperemesis is caused by discrete disease states unmasked or exacerbated in pregnancy.

A number of physical findings point to conditions other than nausea and vomiting of pregnancy as the cause

Differential Diagnosis of Nausea and Vomiting of Pregnancy

Gastrointestinal Conditions

- Gastroenteritis
- Gastroparesis
- Achalasia
- Biliary tract disease
- Hepatitis
- Intestinal obstruction
- Peptic ulcer disease
- Pancreatitis
- Appendicitis

Genitourinary Tract Conditions

- Pyelonephritis
- Uremia
- Ovarian torsion
- Kidney stones
- Degenerating uterine leiomyoma

Metabolic Disease

- Diabetic ketoacidosis
- Porphyria
- Addison's disease
- Hyperthyroidism

Neurologic Disorders

- Pseudotumor cerebri
- Vestibular lesions
- Migraines
- Tumors of the central nervous system

Miscellaneous

- Drug toxicity or intolerance
- Psychologic

Pregnancy-Related Conditions

- Acute fatty liver of pregnancy
- Preeclampsia

Modified from Goodwin TM. Hyperemesis gravidarum. Clin Obstet Gynecol 1998;41:597–605.

of the nausea and vomiting. Abdominal pain is not a prominent characteristic of nausea and vomiting of pregnancy; abdominal pain or tenderness other than mild epigastric discomfort after retching is not seen with nausea

and vomiting of pregnancy. Fever is not present in nausea and vomiting of pregnancy but is characteristic of many other diseases associated with nausea and vomiting. Headache is not characteristic of nausea and vomiting of pregnancy. An abnormal neurologic examination suggests a primary neurologic disorder as the cause of the nausea and vomiting, although it may rarely be encountered as a consequence of severe nausea and vomiting of pregnancy (eg, thiamine-deficient encephalopathy or central pontine myelinolysis). Although biochemical hyperthyroidism may be seen with hyperemesis gravidarum, goiter is not found with nausea and vomiting of pregnancy. If a goiter is present, primary thyroid disease should be suspected.

Etiology and Risk Factors

The etiology of nausea and vomiting of pregnancy is unknown. Various theories have been proposed, including a psychologic predisposition (16), evolutionary adaptation (17), and hormonal stimulus. The question of whether certain personality types or specific psychologic disorders predispose to hyperemesis gravidarum has been raised in the literature for many years. Two general hypotheses have been proposed to explain nausea and vomiting of pregnancy as a manifestation of psychopathology: 1) psychoanalytic theories describing hyperemesis gravidarum as a conversion or somatization disorder and 2) inability of the woman to respond to excessive life stress. There have been no controlled studies to support these hypotheses.

A recent review of psychologic theories proposed to explain the etiology of nausea and vomiting of pregnancy concluded that the evidence that nausea and vomiting of pregnancy is caused by a conversion disorder or an abnormal response to stress is “questionable at best” (18). It is likely that the concept that nausea and vomiting of pregnancy reflects a psychologic disorder has impeded progress toward a greater understanding of the true etiology of the condition (19).

It also has been posited that nausea and vomiting of pregnancy is an evolutionary adaptation that developed to protect the woman and her fetus from foods that might be potentially dangerous (20). This theory may explain the temporary aversions to tastes and smells that pregnant women experience. Proponents of the adaptation theory suggest nausea and vomiting of pregnancy is a healthy, protective response to pregnancy. Clinical application of this theory, however, may lead to undertreatment of women whose quality of life is diminished by nausea and vomiting of pregnancy.

Hormones

Human Chorionic Gonadotropin

Because of the close temporal relationship between peak human chorionic gonadotropin (hCG) concentrations and peak symptoms of nausea and vomiting of pregnancy, hCG has been considered a likely candidate for the emetogenic stimulus arising from the placenta. A role for hCG also is suggested by the fact that almost all studies of thyroid hormones in pregnancy show an association between transient hyperthyroidism and nausea and vomiting of pregnancy. It has been shown conclusively that hCG is the thyroid stimulator of pregnancy (21); because hyperthyroidism itself rarely causes vomiting, this finding has focused attention back on hCG and its relationship to nausea and vomiting of pregnancy. Among the many studies comparing nonthyroidal hormone concentrations in women with and without vomiting, only hCG and estradiol have been found to have an association. The failure of some studies to show an association of nausea and vomiting of pregnancy with hCG may be related to the varying biologic activity of different hCG isoforms as well as variation in the susceptibility of the individual woman to any emetogenic stimulus. The extent of the hCG stimulus may be modified by placental conditions that increase its concentration (eg, multiple gestation, molar gestation) and by hormone-receptor interactions modifying the effect of the hormone.

Estrogen

Another hormone known to influence nausea and vomiting of pregnancy is estrogen. Nausea and vomiting of pregnancy is more common when estradiol levels are increased and less common when estradiol levels are decreased (22, 23). Cigarette smoking is associated with lower levels of both hCG and estradiol (24), and numerous studies have shown that smokers are less likely to have hyperemesis gravidarum. Estrogens in the combined oral contraceptive pill were shown to induce nausea and vomiting in a dose-related fashion (25). Women with nausea and vomiting after estrogen exposure were more likely to have nausea and vomiting of pregnancy than women who did not demonstrate such sensitivity to estrogens (26).

Risk Factors

Women with increased placental mass (eg, advanced molar gestation, multiple gestation) are at risk for hyperemesis gravidarum. Other risk factors include family history (genetics) or a history of hyperemesis gravidarum in a previous pregnancy. One study found that approximately two thirds of women who described their vomit-

ing as severe in one pregnancy had similar symptoms in the next pregnancy; one half of women who described their symptoms as mild in one pregnancy found that the symptoms worsened in the next (7). Daughters and sisters of women who had hyperemesis gravidarum are more likely to have the same problem, as are women carrying a female fetus (27). Other risk factors include a history of motion sickness or migraines (26).

Maternal Effects of Nausea and Vomiting of Pregnancy

Until 60 years ago, nausea and vomiting of pregnancy was an important cause of maternal mortality. In the 1930s in the United States, 7 deaths were reported among 85 women with severe vomiting (28). Although death from nausea and vomiting of pregnancy is reported rarely today, significant morbidity, such as Wernicke's encephalopathy, splenic avulsion, esophageal rupture, pneumothorax, and acute tubular necrosis, have been reported in recent years (29–36). Thirty-three cases of Wernicke's encephalopathy (caused by a vitamin B₁ deficiency) related to hyperemesis gravidarum have been reported in the past 20 years. It often is associated with maternal death or permanent neurological disability (29–31). In addition to increased hospital admissions (37, 38), some women experience significant psychosocial morbidity caused by nausea and vomiting of pregnancy, resulting in pregnancy termination.

A number of reversible responses to subacute disease states have been described in nausea and vomiting of pregnancy, including depression, somatization, and hypochondriasis (16). Poor support by their partners was reported by 85% of women who called a hotline for nausea and vomiting of pregnancy (3).

Fetal Effects of Nausea and Vomiting of Pregnancy

The effect of maternal vomiting on the embryo and fetus depends on the severity of the condition. With mild or moderate vomiting, there is little apparent effect on pregnancy outcome. The outcome most frequently examined is the incidence of low birth weight (LBW). Seven studies have identified no increase in LBW with nausea and vomiting of pregnancy (9, 10, 39–43). Three of these studies found a higher incidence of LBW among women who did not have nausea and vomiting of pregnancy (41–43). Among women with hyperemesis gravidarum, however, a higher incidence of LBW has been reported (44–49).

Numerous studies have documented a lower rate of miscarriage among women with nausea and vomiting of pregnancy and hyperemesis gravidarum when compared with controls. This result is thought to be related to robust placental synthesis in a healthy pregnancy rather than a protective effect of vomiting. It is unlikely that hyperemesis gravidarum is associated with a significantly increased risk of malformations in offspring (50). Little is known about the long-term health of children or women after pregnancies complicated by hyperemesis gravidarum. Although some cases of fetal death are still reported, they are very rare and usually are limited to cases of extreme hyperemesis gravidarum. It is appropriate to reassure patients that the presence of nausea and vomiting of pregnancy and even hyperemesis gravidarum most often portends well for pregnancy outcome.

Clinical Considerations and Recommendations

Many studies mix patients with hyperemesis gravidarum and those with other degrees of nausea and vomiting of pregnancy. Because it is likely that hyperemesis gravidarum is part of the continuum of nausea and vomiting of pregnancy and because evidence indicates that failure to treat early manifestations of nausea and vomiting of pregnancy increases the likelihood of hospital admission for hyperemesis gravidarum (37, 38), the following discussion focuses on treatment for all stages of nausea and vomiting of pregnancy.

► *Are nonpharmacologic therapies effective for the treatment of nausea and vomiting of pregnancy?*

Treatment of nausea and vomiting of pregnancy begins with prevention. Two studies found that women who were taking a multivitamin at the time of conception were less likely to need medical attention for vomiting (51, 52). Therefore, it is reasonable to advise women with a history of nausea and vomiting or hyperemesis gravidarum in a previous pregnancy to take a multivitamin at the time of the next conception.

The woman's perception of the severity of her symptoms and her desire for treatment are influential in clinical decision making. Common recommendations to alleviate initial signs of nausea and vomiting of pregnancy include rest and avoidance of sensory stimuli that may provoke symptoms. Frequent, small meals often are recommended. Obstetrician–gynecologists often suggest avoiding spicy or fatty foods; eliminating pills with iron; and eating bland or dry foods, high-protein snacks, and

crackers in the morning before arising (53). However, there is little published evidence regarding the efficacy of dietary changes for prevention or treatment of nausea and vomiting of pregnancy. A small study showed that protein meals were more likely to alleviate nausea and vomiting of pregnancy than carbohydrate or fatty meals (54).

A study comparing powdered ginger capsules, 250 mg, with placebo in 27 women with hyperemesis gravidarum found the ginger reduced episodes of vomiting (55). Another study using a similar ginger regimen in 70 women with nausea and vomiting of pregnancy of varying severity found significant improvement in nausea and vomiting (56).

Pressure or electrical stimulation at the P6 (or Neiguan) point on the inside of the wrist has been studied for nausea and vomiting of pregnancy with conflicting results. The preponderance of the literature does show a benefit, but many of the studies had significant methodologic flaws, and the 2 largest, best-designed studies showed no benefit over sham stimulation (57). Interestingly, the findings in both of these studies were consistent with a large placebo effect. A randomized, controlled trial of acustimulation with a commercial transcutaneous electrical stimulation device for varying degrees of nausea and vomiting of pregnancy found that acustimulation improved nausea and vomiting symptoms in the first trimester (58).

► *Are pharmacologic therapies effective for treatment of nausea and vomiting of pregnancy?*

Effective pharmacologic therapy is available, but agreement on the appropriate timing of antiemetic therapy has changed in recent years. Two randomized controlled trials have evaluated pyridoxine (vitamin B₆) for treatment of varying degrees of severity of nausea and vomiting of pregnancy. One compared pyridoxine, 25 mg every 8 hours, with placebo and found a significant reduction in severe vomiting but minimal effect on mild vomiting (59). A larger study (n = 342) used pyridoxine, 10 mg every 8 hours, and found a reduction in both nausea and vomiting compared with placebo (60). When the combination of vitamin B₆, 10 mg, plus doxylamine, 10 mg, was available in the United States from 1958 to 1983, it is estimated that 25–30% of all pregnant women received this agent. Analysis of hospital admissions during this period suggests that the ready availability of vitamin B₆ and doxylamine for the treatment of the spectrum of nausea and vomiting of pregnancy was associated with fewer hospital admissions for hyperemesis gravidarum (38). After the combination was removed from the U.S. market in 1983, use of antiemetics to treat nausea and vomit-

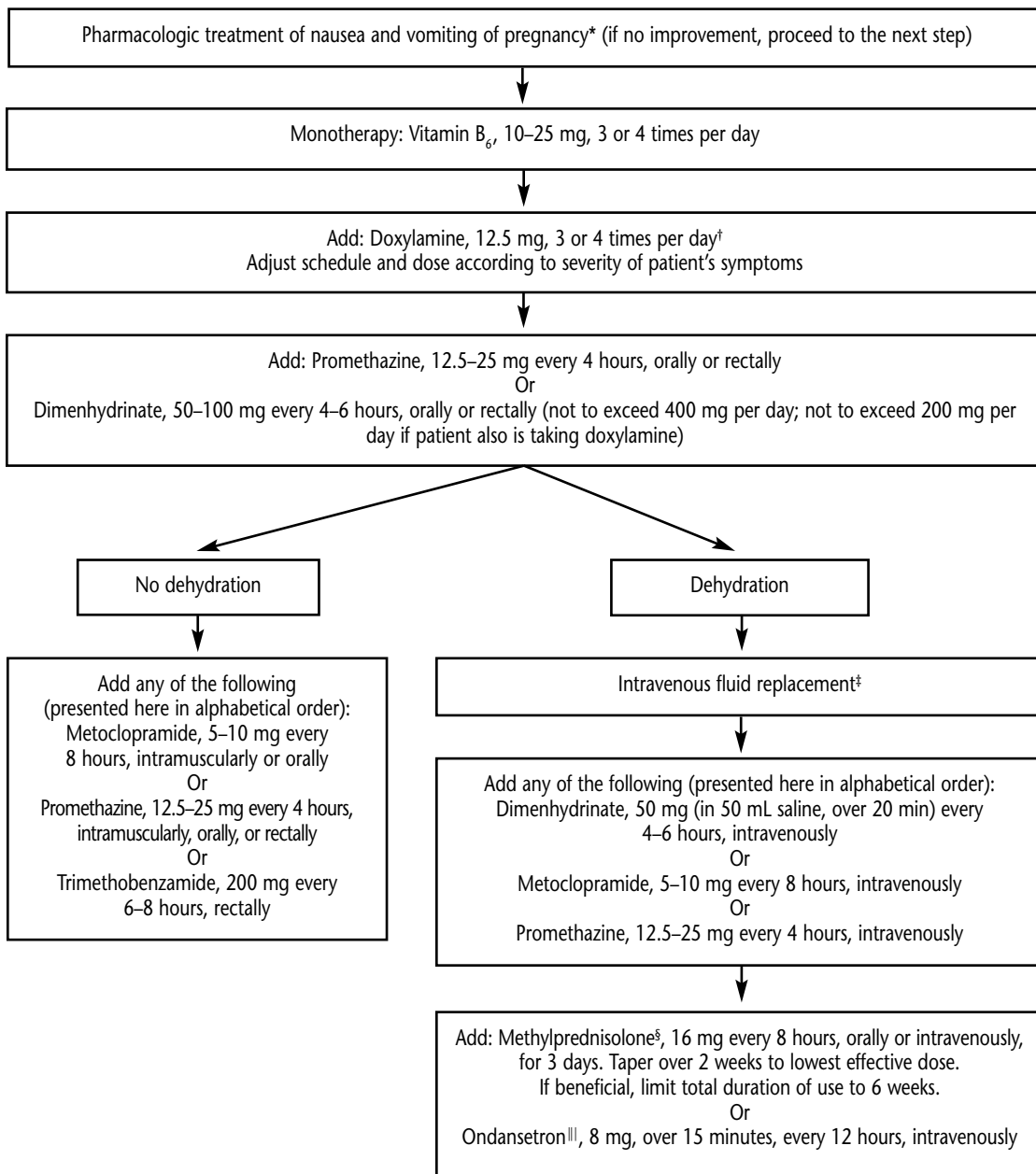
ing of pregnancy diminished considerably, and hospitalization rates for nausea and vomiting of pregnancy increased (38).

Figure 1 depicts a hierarchy of therapeutic interventions that balances safety and efficacy. Despite the fact that the combination of doxylamine and vitamin B₆ is no longer commercially available in the United States, it remains among the first-line therapies. Individual compounding pharmacies in many communities will make up the combination of 10 mg of pyridoxine and 10 mg of doxylamine on request. The only randomized, placebo-controlled trials have shown a 70% reduction in nausea and vomiting (61–63). Several case-control and cohort studies involving more than 170,000 exposures have found the combination to be safe with regard to fetal effects (64).

Many other conventional antiemetics have been described in the literature for treatment of nausea and vomiting of pregnancy (Table 1). Data that suggest safety and efficacy are available on several classes of these medications. The safety of antihistamine H₁ receptor blockers (eg, doxylamine) is supported by a review of more than 200,000 first-trimester exposures (65). Phenothiazines were identified as a possible cause of malformations in one study (66), but the aggregate of studies attest to their safety (67). Three studies attest to the safety of trimethobenzamide (68–70).

Medications for which there are some safety data but no conclusive evidence of efficacy include anticholinergics and metoclopramide. Additionally, evidence is limited on the safety or efficacy of the 5-hydroxytryptamine 3 inhibitors (eg, ondansetron) for nausea and vomiting of pregnancy; however, because of their effectiveness in reducing chemotherapy-induced emesis, their use appears to be increasing. Although the evidence is not strong, doses of droperidol greater than 25 mg were associated with a prolonged Q-T interval that in some cases has led to the potentially fatal arrhythmia torsades de pointes. This drug should be used with caution.

Several case series in the past 10 years have suggested a benefit of corticosteroids in the treatment of hyperemesis gravidarum. A randomized trial comparing methylprednisolone (16 mg, 3 times per day for 3 days, followed by a 2-week taper) with oral promethazine showed equal rates of improvement among hospitalized patients; however, readmission to the hospital within 2 weeks of discharge occurred significantly less frequently in those taking steroids (71). In contrast, a later randomized controlled trial of intravenous methylprednisolone followed by a tapered dose of an oral prednisone among women hospitalized for hyperemesis gravidarum found the use of corticosteroids did not reduce the need for rehospitalization (72).



*This algorithm assumes other causes of nausea and vomiting have been ruled out. At any step, consider parenteral nutrition if dehydration or persistent weight loss is noted. Alternative therapies may be added at any time during the sequence depending on patient acceptance and clinician familiarity; consider P6 acupressure with wrist bands or acustimulation or ginger capsules, 250 mg 4 times daily.

†In the United States, doxylamine is available as the active ingredient in some over-the-counter sleep aids; one half of a scored 25-mg tablet can be used to provide a 12.5-mg dose of doxylamine.

‡Thiamine, intravenously, 100 mg daily for 2–3 days (followed by intravenous multivitamins), is recommended for every woman who requires intravenous hydration and has vomited for more than 3 weeks. No study has compared different fluid replacements for nausea and vomiting of pregnancy.

§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.

Figure 1. Pharmacologic treatment of nausea and vomiting of pregnancy. (Adapted from Levichek Z, Atanackovic G, Oepkes D, Maltepe C, Einarson A, Magee L, et al. Nausea and vomiting of pregnancy. Evidence-based treatment algorithm. *Can Fam Physician* 2002;48:267–8, 277.)

Table 1. Summary of Drugs Used to Treat Nausea and Vomiting of Pregnancy

Agent	Randomized Controlled Trial*	Comments on Efficacy	Comments on Safety
H ₁ blockers		Effective in reducing nausea and vomiting of pregnancy	No increased risk of malformations
Doxylamine	√		
Dimenhydrinate	√		
Cetirizine			
Meclizine	√		
Buclizine	√		
Hydroxyzine	√		
Diphenhydramine			
Anticholinergics		No effectiveness trials for nausea and vomiting of pregnancy	No increased risk of malformations
Scopolamine			
Dopamine Antagonists			
Benzamides			
Trimethobenzamide	√	Effective in reducing nausea and vomiting of pregnancy	No known malformations
Metoclopramide		No trials regarding efficacy	No known malformations
Butyrophenones			
Droperidol			One study of limited power identified no known malformations Maternal risk of prolonged Q-T interval
Haloperidol			
Phenothiazines			
Promethazine	√	Effective in reducing nausea and vomiting of pregnancy	Bulk of evidence indicates no teratogenicity (isolated case report [†] discounted in meta-analysis)
Prochlorperazine			
Chlorpromazine			
Perphenazine			
Benzodiazepines			
Diazepam			
5-Hydroxytryptamine 3 receptor agonists			
Ondansetron	√	One trial found equal effectiveness to promethazine	No malformations noted
Steroids		Pooled results do not suggest benefit in decreasing nausea and vomiting of pregnancy	
Adrenocorticotrophic hormone	√		
Corticosteroids	√		Small increased risks of clefts

*The drug has been evaluated in at least 1 randomized, controlled trial.

[†]Rumeau-Rouquette C, Goujard J, Huel G. Possible teratogenic effect of phenothiazines in human beings. *Teratology* 1977;15:57-64.

Data from Jewell D, Young G. Interventions for nausea and vomiting in early pregnancy (Cochrane Review). In: *The Cochrane Library*, Issue 4, 2003. Chichester, UK: John Wiley & Sons, Ltd.; and Magee LA, Mazzotta P, Koren G. Evidence-based view of safety and effectiveness of pharmacologic therapy for nausea and vomiting of pregnancy (NVP). *Am J Obstet Gynecol* 2002;186:S256-61.

Three recent studies have confirmed an association between oral clefts and methylprednisolone use in the first trimester (73-75). The teratogenic effect is weak, probably accounting for no more than 1 or 2 cases per 1,000 treated women (76). Nevertheless, in view of this probable association, corticosteroid use for hyperemesis gravidarum should be used with caution and avoided before 10 weeks of gestation.

Corticosteroids may be considered as a last resort in patients who will require enteral or parenteral nutrition because of weight loss. The most commonly described regimen is methylprednisolone, 48 mg daily for 3 days, given orally or intravenously. Patients who do not respond within 3 days are not likely to respond, and treatment should be stopped. For those who do respond, the dose may be tapered over a period of 2 weeks. For

recurrent vomiting, the tapered dose may be stopped and the patient continued on the effective dose for up to 6 weeks. To limit serious maternal side effects, corticosteroids should not be continued beyond this period for the treatment of hyperemesis gravidarum (77).

► ***Is there a role for laboratory or radiologic assessment in the diagnosis of hyperemesis gravidarum?***

Most patients with nausea and vomiting of pregnancy do not require laboratory evaluation, but in those with nausea and vomiting of pregnancy that is severe, prolonged, or extended, laboratory assessment may help in the differential diagnosis of hyperemesis gravidarum and to assess the severity of the condition. Common laboratory abnormalities in hyperemesis gravidarum include increased liver enzymes (usually <300 U/L), serum bilirubin (<4 mg/dL), and serum amylase or lipase concentrations (up to 5 times greater than normal levels). Primary hepatitis as a cause of nausea and vomiting of pregnancy results in increased liver enzyme levels, often in the thousands; bilirubin concentrations usually are greatly increased as well. Acute pancreatitis may cause vomiting and elevated amylase concentrations, but serum amylase concentrations usually are 5–10 times greater than the elevations associated with nausea and vomiting of pregnancy. A hypochloremic metabolic alkalosis can be seen with severe vomiting of any cause. Serum concentrations of hCG are not helpful in determining whether vomiting is caused by hyperemesis gravidarum. Urinalysis may show elevated specific gravity or ketonuria or both. Patients with persistent hyperemesis gravidarum that is unresponsive to standard therapy may have an ulcer; treatment with antibiotics and H₂ receptor antagonists is safe (78, 79) and has been reported to be beneficial in case reports (80).

Up to 70% of patients with hyperemesis gravidarum will have suppressed thyroid-stimulating hormone levels or elevated free thyroxine concentrations (81). For the patient who has no history of hyperthyroidism before pregnancy and no goiter, the hyperthyroidism of hyperemesis gravidarum can be expected to resolve by 20 weeks of gestation without specific antithyroid therapy. Hyperthyroidism itself rarely may present with significant vomiting (82), but in the patient who has no goiter, thyroid tests are not needed routinely to clarify the differential diagnosis. To confirm the diagnosis of hyperthyroidism in the setting of nausea and vomiting of pregnancy, measurement of free thyroxine and free triiodothyronine concentrations should be obtained.

An ultrasound evaluation may be useful in cases of severe presumed nausea and vomiting of pregnancy. It

may identify a predisposing factor, such as multiple gestation or molar gestation.

► ***When is enteral or parenteral nutrition recommended?***

The principal criterion for introducing additional nutritional strategies is persistent weight loss. Serious complications of hyperemesis gravidarum for the woman and fetus arise in the group of women who cannot maintain their weight despite antiemetic therapy. Intravenous hydration should be used for the patient who cannot tolerate oral liquids for a prolonged period or if clinical signs of dehydration are present. Correction of ketosis and vitamin deficiency should be strongly considered. Dextrose and vitamins, especially thiamine, should be included in the therapy when prolonged vomiting is present.

No randomized trials compare enteral with parenteral nutrition in women with nausea and vomiting of pregnancy who continue to lose weight despite antiemetic therapy. Several case reports and a small series (83) suggest that enteral tube feeding is well tolerated in pregnancy. Because life-threatening complications of parenteral nutrition have been described (35, 36, 84), it is reasonable to attempt enteral tube feeding initially. Peripheral parenteral nutrition using a high-lipid formula can be used for patients whose calorie requirements are not great and those whose length of treatment is anticipated to be no more than several days. For women who need longer-term support and who cannot tolerate enteral tube feedings, the use of total parenteral nutrition has been described for hyperemesis gravidarum in case reports and 2 small series (35, 85). A peripherally inserted central catheter can be used to avoid some of the complications of central access (86), but it is still associated with significant morbidity (87).

► ***When is hospitalization indicated?***

No controlled trials compare hospitalization with outpatient management of hyperemesis gravidarum. When a woman cannot tolerate liquids without vomiting and has not responded to outpatient management, hospitalization for evaluation and treatment is recommended. After the patient has been hospitalized on one occasion and a workup for other causes of severe vomiting has been undertaken, intravenous hydration, nutritional support, and modification of antiemetic therapy often can be accomplished at home. Nevertheless, the option of hospitalization for observation and further assessment should be preserved for patients who experience a change in vital signs or a change in affect or who continue to lose weight.

► ***Is there a role for psychotherapy in treatment?***

There is little evidence for a therapeutic effect of traditional psychotherapy in hyperemesis gravidarum. No controlled trials have evaluated behavioral therapy in nausea and vomiting of pregnancy, but there are data to indicate that delayed and anticipatory nausea and vomiting after chemotherapy is diminished by systematic desensitization (88) and relaxation therapy (89).

It has been suggested that hypnotized women with severe nausea and vomiting of pregnancy are more easily influenced by suggestion than controls, and at least one controlled study supports this hypothesis (90). In a limited number of studies, all lacking controls, hypnosis has been shown to decrease vomiting in patients undergoing chemotherapy (91, 92) and those with hyperemesis gravidarum (93, 94).

Summary of Recommendations

The following recommendations are based on good and consistent scientific evidence (Level A):

- Taking a multivitamin at the time of conception may decrease the severity of nausea and vomiting of pregnancy.
- Treatment of nausea and vomiting of pregnancy with vitamin B₆ or vitamin B₆ plus doxylamine is safe and effective and should be considered first-line pharmacotherapy.
- In patients with hyperemesis gravidarum who also have suppressed thyroid-stimulating hormone levels, treatment of hyperthyroidism should not be undertaken without evidence of intrinsic thyroid disease (including goiter and/or thyroid autoantibodies).

The following recommendations are based on limited or inconsistent scientific evidence (Level B):

- Treatment of nausea and vomiting of pregnancy with ginger has shown beneficial effects and can be considered as a nonpharmacologic option.
- In refractory cases of nausea and vomiting of pregnancy, the following medications have been shown to be safe and efficacious in pregnancy: antihistamine H₁ receptor blockers, phenothiazines, and benzamides.
- Early treatment of nausea and vomiting of pregnancy is recommended to prevent progression to hyperemesis gravidarum.

- Treatment of severe nausea and vomiting of pregnancy or hyperemesis gravidarum with methylprednisolone may be efficacious in refractory cases; however, the risk profile of methylprednisolone suggests it should be a treatment of last resort.

The following recommendations are based primarily on consensus and expert opinion (Level C):

- Intravenous hydration should be used for the patient who cannot tolerate oral liquids for a prolonged period or if clinical signs of dehydration are present. Correction of ketosis and vitamin deficiency should be strongly considered. Dextrose and vitamins, especially thiamine, should be included in the therapy when prolonged vomiting is present.
- Enteral or parenteral nutrition should be initiated for any patient who cannot maintain her weight because of vomiting.

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The MEDLINE database, the Cochrane Library, and ACOG's own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 1985 and December 2003. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles. When reliable research was not available, expert opinions from obstetrician-gynecologists were used.

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force:

- I Evidence obtained from at least 1 properly designed randomized controlled trial.
- II-1 Evidence obtained from well-designed controlled trials without randomization.
- II-2 Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than 1 center or research group.
- II-3 Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.
- III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A—Recommendations are based on good and consistent scientific evidence.

Level B—Recommendations are based on limited or inconsistent scientific evidence.

Level C—Recommendations are based primarily on consensus and expert opinion.

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