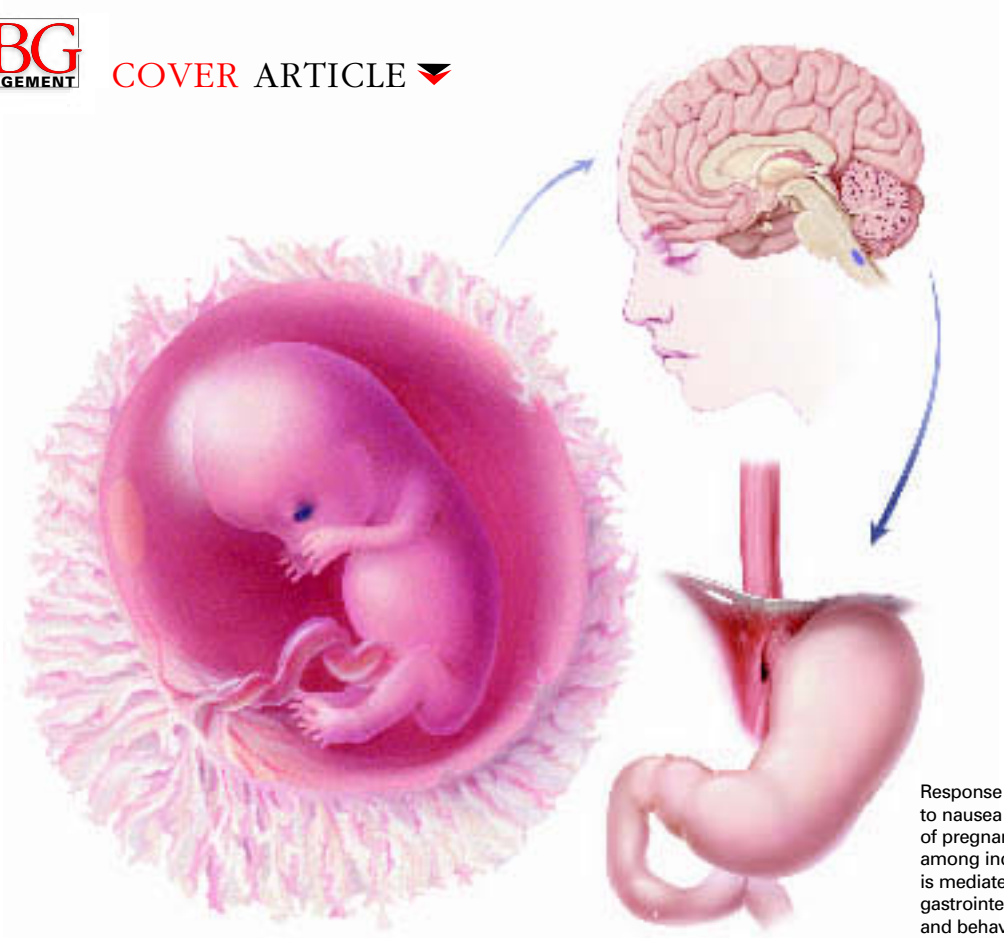

Response to the stimulus to nausea and vomiting of pregnancy varies among individuals and is mediated by vestibular, gastrointestinal, olfactory, and behavioral pathways.

Nausea and vomiting of pregnancy

Q&A with T. Murphy Goodwin

An expert tells why this common condition is undertreated, and what can help, including how to formulate the effective drug formerly marketed as Bendectin.

BY JANELLE YATES, SENIOR ASSOCIATE EDITOR

T. Murphy Goodwin, MD, a contributor to the new American College of Obstetricians and Gynecologists practice bulletin on nausea and vomiting of pregnancy (NVP),[1] tells why it is important to ask every patient about nausea and vomiting, when to intervene, and what the best treatments are—including a substitute compound for the no-longer-available drug Bendectin.

Dr. Goodwin is professor of obstetrics and gynecology at the Keck School of Medicine, University of Southern California, Los Angeles.

Many patients assume they must endure nausea, vomiting

■ **Women do not always mention nausea and vomiting, believing they must "live with it." Prompt intervention can stave off more severe NVP, so it makes sense for Ob/Gyns to raise the subject early.**

OBG MANAGEMENT: What new information in the American College of Obstetricians and Gynecologists (ACOG) practice bulletin should the Ob/Gyn be aware of?

GOODWIN: Rather than "new information," I would call it a change in emphasis. Previously, the focus was almost exclusively on life-threatening hyperemesis gravidarum, while lesser degrees of nausea and vomiting of pregnancy went untreated or undertreated. In reality, approximately 35% of gravidas have NVP severe enough to interfere with their daily routine. Fortunately, effective therapy is available.

OBG MANAGEMENT: Some authorities believe NVP is a continuum between mild upset and hyperemesis gravidarum. How would such a continuum affect patient care?

GOODWIN: Epidemiologic studies suggest that women with mild NVP and those with hyperemesis are significantly similar, strongly supporting the notion of a continuum.[2] This fact underscores the importance of treating NVP in its early stages, before it advances to hyperemesis.

My own sense is that a small group of women with hyperemesis are predisposed to it because of rare genetic disorders such as mitochondrial mutations.

OBG MANAGEMENT: Since so many women experience NVP, should obstetricians routinely ask about it, including its psychosocial effects?

GOODWIN: Yes. This is important because of the continuum we mentioned—and because many women consider NVP "normal" and may not mention it unless they are asked.

OBG MANAGEMENT: Do you think some physicians share this mindset?

GOODWIN: Undoubtedly. Studies have shown that as many as 50% of women with severe NVP are not offered antiemetic therapy.[3,4] But the days of letting the condition "run its course" are past. Now the best strategy is asking about it—and intervening early.

What causes NVP?

- **The factors at play in each patient help determine the best treatment. NVP is more likely with high levels of hCG and estrogen.**

OBG MANAGEMENT: In a 2002 study,[5] you concluded that NVP is actually a syndrome rather than a single condition.

How would this concept affect management of NVP?

GOODWIN: Women who are susceptible to NVP because of a vestibular mechanism might respond to a medical regimen that works at that site. Still other women may have "background" gastrointestinal motility dysfunction that makes them more susceptible to NVP; in that case, therapies to treat motility abnormalities would be appropriate. Others may have a strong behavioral overlay and would be expected to respond to the kinds of treatment used for anticipatory nausea and vomiting associated with chemotherapy.

These are theoretical scenarios at present, but a new paradigm will allow new ways of thinking about therapy.

OBG MANAGEMENT: In the early 1990s, you and your colleagues[6] reported your study on the link between human chorionic gonadotropin (hCG) and NVP. What is the association?

GOODWIN: A temporal association has attracted the attention of obstetricians for years. In addition, biochemical hyperthyroidism and NVP are strongly associated. Fifty percent to 70% of women with hyperemesis gravidarum have transient hyperthyroidism, with no goiter.[7] (If a goiter is present, suspect primary thyroid disorder.) Because hCG causes the bio-

KEY POINTS

- About 35% of gravidas have nausea and vomiting severe enough to disrupt their daily routine. As many as 50% of women with severe NVP are not offered antiemetic therapy, studies show.
- At any level of severity, nausea and vomiting cause psychosocial morbidity.
- Multivitamin use at the time of conception reduces the severity of nausea and vomiting.
- When drug therapy is necessary, start with 10 to 25 mg pyridoxine (vitamin B_6) 3 or 4 times daily.
- If nausea and vomiting continue, add 12.5 mg doxylamine (by halving the over-the-counter sleep aid Unisom) to each dose of pyridoxine. The pyridoxine-doxylamine combination is the same formulation as the highly effective drug Bendectin, which is no longer available in the US.

chemical hyperthyroidism related to pregnancy, and because hyperthyroidism by itself rarely causes vomiting, hCG is implicated. However, it remains unclear how hCG would cause NVP—perhaps by stimulating the ovary to produce more estrogen, which causes emesis, or through some other, unknown step.

Interestingly, a number of "high-hCG" conditions are associated with increased NVP: molar pregnancy, multiple gestation, and Down's syndrome. Conversely, trisomy 18 is a "low-hCG" condition anecdotally associated with reduced NVP.

OBG MANAGEMENT: What is estrogen's role?

GOODWIN: Estradiol and hCG are the only 2 hormones ever found to differ when women with NVP are compared to controls. Women who get sick with estrogen exposure are much more likely to develop NVP. Some studies have found increased estradiol levels in women with NVP, compared with controls.[6,8] Conversely, low estradiol levels may reduce the risk of NVP. Take smoking, for example. It is associated with lower hCG and estradiol levels, and smokers are less likely than nonsmokers to have NVP.

Studies also have focused on a possible link between cytokines and hyperemesis, and between hyperemesis and tumor necrosis factor alpha.

OBG MANAGEMENT: Do these findings alter clinical management?

GOODWIN: No. The findings about etiology do not affect management at present.

NVP can be protective or perilous

▪ Some degree of nausea and vomiting affects the vast majority of pregnancies. Unless it is severe, however, NVP appears to have a protective effect on the fetus.

OBG MANAGEMENT: What is the prevalence of NVP, and what are its characteristics?

GOODWIN: About 70% to 85% of gravidas experience it.[9] In the spectrum of NVP, about 50% of women experience both nausea and vomiting, 25% experience nausea alone, and 25% are unaffected.[10]

Hyperemesis gravidarum affects roughly 3 to 20 of every 1,000 pregnancies.

It generally is categorized according to the level of intervention required:

- Mild NVP does not affect daily life.
- Moderate NVP interferes with daily life.
- Severe NVP, or hyperemesis, requires fluid and/or nutritional support. Hyperemesis is further defined as persistent vomiting, weight loss exceeding 5% of prepregnancy weight, and significant ketonuria, with or without electrolyte disturbances. Hospitalization usually is required.

OBG MANAGEMENT: What is the clinical course?

GOODWIN: NVP almost always appears before 10 weeks' gestation. If it begins any later, it is likely the patient has a different condition associated with nausea and vomiting.

One study found that most women develop NVP at about 4 to 7 weeks' gestation, and that it resolves at less than 10 weeks in about 30% of women, at 10 to 12 weeks in another 30%, and at 12 to 16 weeks in another 30%.[10]

As for diurnal changes, symptoms tend to occur with greater frequency early in the day.

OBG MANAGEMENT: Is NVP ever harmful for the fetus?

GOODWIN: It is associated with improved fetal outcomes unless hyperemesis supervenes. Then it is associated with mild fetal growth delays and rare cases of fetal death.

We lack studies of the long-term effects of severe NVP on the fetus, but starvation and weight loss in women during famine have been shown to cause many diverse problems in offspring later in adult life.

OBG MANAGEMENT: What do you make of evidence that suggests NVP plays a protective role in pregnancy?

GOODWIN: If true, it likely represents a vestigial response that is no longer beneficial—similar to thrombophilias in pregnancy, which played an important role protecting women against bleeding at childbirth but

NVP at a glance: Pervasive, disabling, and undertreated

Prevalence. 70% to 85%.[1]

Presentation. About 50% of women have both nausea and vomiting, 25% have nausea only, and 25% are not affected.[10]

Hyperemesis gravidarum. 3 to 20 of every 1,000 pregnancies. Marked by persistent vomiting, weight loss exceeding 5% of prepregnancy weight, and significant ketonuria.

Clinical course. If NVP is going to occur, it is present before 10 weeks' gestation. It resolves at less than 10 weeks' gestation in about 30% of women, at 10 to 12 weeks in another 30%, and at 12 to 16 weeks in another 30%.[10]

Predisposing factors. History of illness with estrogen exposure, motion sickness, migraine, or hyperemesis; mother or sister with hyperemesis; female fetus; mitochondrial disorders; multiple gestation; gestational trophoblastic disease; and fetal anomalies such as Down's syndrome and triploidy.

Undertreatment. As many as 50% of women with severe NVP are not offered therapy.[3,4]

Physical discomfort. Intensity and character similar to nausea and vomiting induced by cancer chemotherapy, even at milder levels of severity.[11]

Social and psychological impact. Reduced job efficiency, lost work time, negative impact on family relationships and mental health, decision to terminate an otherwise desired pregnancy. Women with hyperemesis are more likely to have anxiety, depression, somatization, psychoticism, and obsessive-compulsive symptoms, but return to normal after delivery.[21]

Fetal effects. Improved fetal outcomes unless hyperemesis supervenes. Hyperemesis with maternal weight loss is associated with mild fetal growth delays and rare cases of fetal death.

Maternal effects. Not linked to adverse effects except for hyperemesis gravidarum, in which Wernicke's encephalopathy, Mallory-Weiss tears, splenic avulsion, esophageal rupture, pneumothorax, acute tubular necrosis, or peripheral neuropathy (due to vitamins B_6 and B_{12} deficiencies) can result.

now are more of a clinical problem because of the associated thrombosis.

Effects on the mother and predisposing factors

■ **Even at milder levels, physical discomfort is considerable. Predisposing factors include a female fetus, history of hyperemesis, migraine headaches, and a tendency to develop motion sickness.**

OBG MANAGEMENT: How does NVP affect the mother?

GOODWIN: Serious sequelae are limited to hyperemesis, in which case Mallory-Weiss tears, splenic avulsion, esophageal rupture, pneumothorax, acute tubular necrosis, peripheral neuropathy (due to deficiencies of vitamins B_6 and B_{12}), or Wernicke's encephalopathy can result. This last condition is the most serious potential complication, and it can be difficult to recognize. Look for signs of confusion, memory loss, and blunted affect.

Even at milder levels of NVP, however, physical discomfort can be considerable. One prospective study using the McGill Nausea Questionnaire found the nausea experienced by pregnant women to be similar in character and intensity to that experienced by cancer patients on chemotherapy.[11]

OBG MANAGEMENT: Are there predisposing factors?

GOODWIN: Yes. They include a history of illness upon exposure to estrogen (for example, oral contraceptives), as well as a history of motion sickness and migraine.

Hyperemesis is more likely when the fetus is female. Women who had hyperemesis in a

Bendectin: The sad saga of a useful drug

The most widely prescribed drug for nausea and vomiting of pregnancy (NVP), Bendectin, was voluntarily withdrawn from the US market in 1982, after numerous, unsuccessful lawsuits alleged it had caused birth defects.

After its withdrawal, hospitalization rates for NVP doubled while solid evidence of Bendectin's safety continued to accumulate. In the years since, researchers have found no difference in major malformations between infants in the general population and those born to women who took Bendectin. Nor has there been any decrease in specific malformations. As the *New England Journal of Medicine* pointed out, a decrease in the number of malformations "would be expected for a truly teratogenic drug estimated to have been used by up to 40% of pregnant women at one time."[18]

The drug is still available in Canada, where it is marketed as Diclectin. In the US, its ingredients—pyridoxine (vitamin B_6) and doxylamine—can be compounded by a pharmacy, or the patient can be instructed to take 10 to 25 mg of pyridoxine and 12.5 mg of Unisom (half a tablet) 3 or 4 times daily. (Unisom is an over-the-counter sleep aid containing doxylamine succinate.)

previous pregnancy are likely to experience it again in their next gestation, and their daughters and sisters also are more likely to develop it.

We also know that inherited and acquired disorders of mitochondria commonly manifest as migraine and/or gastrointestinal disease, including nausea and vomiting.[12]

Predisposing factors also include pregnancy-related conditions: multiple gestation; gestational trophoblastic disease; and fetal anomalies such as triploidy, Down's syndrome, and hydrops fetalis. Overall, the chance of fetal defects associated with hyperemesis is extremely small.

The work-up: Key signs and tests

■ In severe cases, look for Wernicke's encephalopathy, dehydration, weight loss, other causes of nausea and vomiting, and abnormal lab values.

OBG MANAGEMENT: Let's say you have a patient at 8 weeks' gestation who complains of persistent nausea and vomiting. What is an appropriate work-up?

GOODWIN: Physical assessment is necessary only in severe cases. If nausea and vomiting last more than 3 weeks, signs of Wernicke's encephalopathy should be sought (this condition is never reported as early as 8 weeks).

Other important signs to look for are dehydration and evidence of other diseases that can cause nausea and vomiting (**TABLE**). If the patient has experienced vomiting throughout her pregnancy, but it suddenly becomes acute, another condition may be responsible.

It also is important to be aware that abdominal pain, fever, and headache do not represent NVP, but usually reflect other conditions associated with nausea and vomiting.

I ask about the duration and severity of NVP, and whether the woman has lost weight as a result. Weight loss is very important: Women who can't sustain their weight need nutritional therapy.

OBG MANAGEMENT: Do you order lab tests?

GOODWIN: Yes. In severe cases, I get a liver panel and check amylase, lipase, and electrolytes. A number of abnormalities have been documented when hyperemesis is present. They include elevated liver enzymes, serum bilirubin, and serum amylase or lipase measurements, as well as increased free thyroxine and suppressed thyroid-stimulating hormone.

Serum hCG measurements are generally not useful, however, in exploring whether the

patient's vomiting is caused by hyperemesis gravidarum.

Imaging is necessary only to check for predisposing causes such as twins or molar gestation.

Do vitamins, rest, diet, ginger, or acupuncture help?

■ **Vitamins may help prevent NVP. For mild NVP, simple lifestyle changes or alternative remedies may suffice.**

OBG MANAGEMENT: Would your first step with the patient described earlier be lifestyle and dietary adjustments?

GOODWIN: The first step in this case should have been prevention. Two studies have found that multivitamins given at conception help reduce the severity of NVP.[13,14]

As for lifestyle changes, I would recommend rest and instruct the patient to avoid foods, activities, and other stimuli that exacerbate symptoms. Small, frequent meals are usually suggested to take the place of 3 large daily meals.

Scientifically, however, almost nothing is known about these common recommendations, though 1 study showed protein liquid meals reduced nausea and gastric-motility abnormalities more than carbohydrate or fatty meals with the same caloric content.[15]

OBG MANAGEMENT: Do you ever recommend alternative remedies such as ginger powder or stimulation of the P6 acupuncture point (eg, via acupuncture, Sea-Band, or ReliefBand)?

GOODWIN: As the ACOG guidelines point out, they are worth a try. When the patient wants to take ginger, I recommend 250 mg by mouth 3 to 4 times daily.

When to start drug therapy

■ **Pyridoxine (vitamin B_6) is the first choice, followed by a combination of pyridoxine and doxylamine, which together form the drug Bendectin (no longer available in the US).**

OBG MANAGEMENT: When do you opt for drug therapy?

TABLE

Differential diagnosis of nausea and vomiting of pregnancy

Gastrointestinal disorders
Appendicitis
Biliary tract disease
Esophagitis
Gastroenteritis
Gastroparesis
Hepatitis
Intestinal obstruction
Pancreatitis
Peptic ulcer disease
Genitourinary disorders
Acute renal failure
Degenerating fibroid
Nephrolithiasis
Pyelonephritis
Torsion
Metabolic disorders
Addison's disease
Diabetic ketoacidosis
Hyperparathyroidism
Hyperthyroidism
Porphyria
Pregnancy-related
Acute fatty liver of pregnancy
Preeclampsia
Pregnancy-induced hypertension
Miscellaneous
Central nervous system lesions
Drug toxicity/side effects
Eating disorder
Migraine
Pseudotumor cerebri
Vestibular lesions

Adapted from Goodwin TM[21]

GOODWIN: When symptoms interfere with daily life and the remedies already mentioned fail or patients choose not to use them. In such cases, pyridoxine (vitamin B_6) is my first choice. I recommend 10 to 25 mg 3 or 4 times daily. In 1 randomized, controlled trial,[16] 25 mg of pyridoxine every 8 hours led to a significant reduction in severe vomiting. In another, 10 mg of pyridoxine every 8 hours

decreased both nausea and vomiting compared to placebo.[17]

When pyridoxine alone fails to ease NVP, I add doxylamine (see "Stepwise drug treatment of nausea and vomiting of pregnancy" on page 65). When it was commercially available, Bendectin contained the pyridoxine-doxylamine combination (10 mg of each) in 1 pill and was the most commonly prescribed agent, but it is no longer offered in the US. In Canada, it is sold as Diclectin.

The teratogenicity of Bendectin has never been proven despite extensive study, and a 1998 review described the agent's safety.

Although the manufacturer voluntarily removed the drug in the early 1980s because of lawsuits alleging birth defects, teratogenicity has never been proven despite extensive study. A 1998 review described Diclectin's safety.[18]

Fortunately, the combination of pyridoxine and doxylamine is still available—though not in a single pill. Some pharmacies will compound it, or the patient can be given pyridoxine in combination with the over-the-counter sleep aid Unisom, which contains 25 mg doxylamine succinate per tablet.

If pyridoxine alone is ineffective, I generally add 12.5 mg of doxylamine (half a Unisom tablet) to each dose. The patient should be instructed to buy Unisom in tablet form, rather than gel caps, as the active ingredient in the latter is not doxylamine.

Adding other drugs

■ **When pyridoxine is insufficient (alone or in combination with doxylamine), add promethazine, dimenhydrinate, or another agent.**

OBG MANAGEMENT: How safe are antiemetics in pregnancy?

GOODWIN: The safety of antihistamines for use in pregnancy is well established. There are fewer data for phenothiazines, but they also appear to be quite safe.

As for 5-HT3-receptor antagonists, no teratogenicity has been found for ondansetron, which is used to treat nausea and vomiting associated with chemotherapy. However, in the only randomized trial, it did not appear to offer benefit over promethazine (a drug with characteristics of both antihistamines and phenothiazines and a good safety profile). Another drug, granisetron, has not been studied in regard to NVP.

OBG MANAGEMENT: What drugs do you prescribe besides pyridoxine and doxylamine?

GOODWIN: If the combination of pyridoxine and doxylamine fails to provide relief, I add 12.5 to 25 mg of promethazine every 4 hours (orally or rectally) or 50 to 100 mg of dimenhydrinate every 4 to 6 hours (orally or rectally, but not exceeding 200 mg daily when the patient is also taking doxylamine).

If this regimen fails to ease the patient's symptoms, other combinations can be suggested. (See page 65.)

OBG MANAGEMENT: Any caveats?

GOODWIN: I never give droperidol, a butyrophenone, because the US Food and Drug Administration has warned of an association with cardiac arrhythmias. This linkage may be overstated, but since there are safe alternatives, I avoid this agent.

Last resort: Corticosteroids

■ **Corticosteroids may help resolve refractory hyperemesis gravidarum.**

OBG MANAGEMENT: What about corticosteroids? What is their safety profile for NVP?

GOODWIN: They do not appear to be teratogenic unless they are given during the first 10 weeks of gestation; then they are associated with a slightly increased risk of oral clefts.[19] Even so, they should be a last resort—and then only in refractory cases involving weight loss and the need for enteral or parenteral nutrition.The literature is mixed on the effi-

Stepwise drug treatment of nausea and vomiting of pregnancy

Before starting drug therapy, rule out other causes of nausea and vomiting.

STEP 1

Try monotherapy. Start with **pyridoxine (vitamin B6),** 10 to 25 mg, 3 or 4 times daily.

STEP 2

Add doxylamine (Unisom tablet), 12.5 mg, 3 or 4 times daily, and adjust dosage as necessary according to severity of symptoms. (Note: Half of a 25-mg Unisom tablet = 12.5 mg.)

STEP 3

Add promethazine (Phenergan), 12.5 to 25 mg every 4 hours, orally or rectally,
or **dimenhydrinate (Dramamine),** 50 to 100 mg every 4 to 6 hours, orally or rectally. Not to exceed 400 mg/day; if the patient is taking doxylamine, limit to 200 mg/day.

STEP 4

If the patient is sufficiently hydrated, add any of the following (listed alphabetically):
metoclopramide (Reglan), 5 to 10 mg every 8 hours, intramuscularly or orally,
or **promethazine,** 12.5 to 25 mg every 4 hours, intramuscularly, orally, or rectally,
or **trimethobenzamide (Tigan),** 200 mg every 6 to 8 hours, rectally.
If the patient is dehydrated, give intravenous fluids. For women who require intravenous hydration and have been vomiting for 3 or more weeks, intravenous thiamine, 100 mg daily for 2 to 3 days, followed by intravenous multivitamins, is recommended. (No study has compared different fluid replacements for NVP.)
and add any of the following intravenous agents (listed alphabetically):
dimenhydrinate, 50 mg (in 50 mL saline over 20 minutes) every 4 to 6 hours,
or **metoclopramide,** 5 to 10 mg every 8 hours,
or **promethazine,** 12.5 to 25 mg every 4 hours.

STEP 5

In refractory cases: Add methylprednisolone (Medrol), 16 mg every 8 hours, orally or intravenously, for 3 days. Taper over 2 weeks to the lowest effective dose. Limit total therapy to 6 weeks. (If given in the first 10 weeks of gestation, corticosteroids may increase risk for oral clefts.)
or **add ondansetron (Zofran),** 8 mg over 15 minutes, every 12 hours, intravenously. Safety, particularly in first trimester, not determined. (Used mainly for emesis; less effect on nausea.)

AT ANY STEP

- Consider parenteral nutrition for dehydration or persistent weight loss. Stop nutrition once the patient achieves relief.
- Consider alternative therapies such as ginger capsules (250 mg 3 times daily) and stimulation of the P6 acupuncture point (via wrist bands or acustimulation).

Adapted from Goodwin TM and American College of Obstetricians and Gynecologists[1]

cacy, but I find that a subset of patients have a dramatic response to corticosteroids.

The usual regimen is 16 mg methylprednisolone 3 times daily for 3 days, followed by tapering over 2 weeks, declining in 4-mg increments. If vomiting occurs during the taper, increase the dose by 4 mg for 1 week, then continue tapering. If vomiting recurs after tapering, restart the drug at 8 to 12 mg/day. All told, therapy should be limited to 4 to 6 weeks.

If there is no improvement during the initial 3 days of therapy, stop the drug altogether.

The steroid can be given orally or intravenously. It also is important to give 1,200 mg daily of calcium throughout the regimen.

CONTINUED

Hydration and nutrition for hyperemesis

■ **Give fluids and nutritional support to maintain weight.**

OBG MANAGEMENT: Do you hydrate the patient? What about enteral or parenteral nutrition?

The most extreme psychosocial effect of NVP is the decision to terminate an otherwise desired pregnancy.

GOODWIN: Yes. If she is dehydrated, I replace fluids, taking care to give intravenous thiamine before dextrose if she has been vomiting longer than 3 weeks. Otherwise, Wernicke's encephalopathy may develop.

I prefer enteral nutrition, provided the patient can tolerate it and a good nutrition team is available to support both physician and patient.

Generally, hospitalization is warranted for women who cannot maintain hydration or nutrition or when the patient and her family cannot cope with the condition. However, depending on community resources, outpatient hydration/nutrition may be a feasible option.

When she is able to tolerate oral hydration and maintain weight—with or without nutritional support—she can be discharged.

Crippling psychosocial effects

■ **Acknowledging NVP's disruptive effect—at all levels of severity—is critical. Let her know you aren't minimizing its impact, and that a range of options are at her disposal.**

OBG MANAGEMENT: One aspect of NVP often overlooked is the psychosocial impact. Would you say it is considerable?

GOODWIN: Yes. In some cases, it can be crippling. Unfortunately, this dimension is rarely addressed by the physician. Effects can include reduced job efficiency, lost work time (in 1 study, a mean of 62 hours[10]), and a negative impact on family relationships and mental health. The most extreme effect, of course, is the decision to terminate an otherwise desired pregnancy.

These effects are not limited to hyperemesis; NVP involves psychosocial morbidity at all levels of severity.[3] One study concluded that the severity of NVP fails to adequately reflect the distress it causes.[3]

The patient's sense of her condition is critical. It is important to find out what effects NVP is having on her daily routine and let her know you aren't minimizing its impact—also that a range of options are at her disposal.

OBG MANAGEMENT: In the past, haven't a number of psychodynamic causes been proposed for NVP?

GOODWIN: Yes. These included speculation that the woman was subconsciously rejecting the pregnancy, "hysterical," maternally dependent or too independent, or denying her femininity. Fortunately, these ideas have been discredited.

Severe NVP does have psychological effects, however. Simpson et al[20] found that women with hyperemesis gravidarum were more likely to experience anxiety, depression, somatization, psychoticism, and symptoms of obsessive-compulsive disorder. After delivery, however, they returned to normal and were no more likely than other nonpregnant women to experience these conditions.

NVP is not more likely to occur during an unwanted pregnancy. The rates are about the same as for desired gestations.

OBG MANAGEMENT: Is NVP ever the result of a psychologic condition?

GOODWIN: Very rarely, although a behavioral component may be involved—eg, vomiting as a conditioned response. However, this does not mean that the patient has a disease or is responsible for her own condition.

That kind of thinking is one reason women hesitate to raise the subject. ■

REFERENCES

1. American College of Obstetricians and Gynecologists. *ACOG Practice Bulletin: Nausea and Vomiting of Pregnancy*. Clinical management guidelines for obstetrician-gynecologists. No. 52. Washington, DC: ACOG: April 2004.
2. Klebanoff M, Koslone P, Kaslow R, Rhoads G. Epidemiology of vomiting in early pregnancy. *Obstet Gynecol*. 1985;66:612–616.
3. Mazzotta P, Stewart D, Atanackovic G, Koren G, Magee LA. Psychosocial morbidity among women with nausea and vomiting of pregnancy: prevalence and association with anti-emetic therapy. *J Psychosom Obstet Gynaecol*. 2000;21:129–136.
4. Mazzota P, Magee L, Koren G. Therapeutic abortions due to severe morning sickness. Unacceptable combination. *Can Fam Physician*. 1997;43:1055–1057.
5. Goodwin TM. Nausea and vomiting of pregnancy: an obstetric syndrome. *Am J Obstet Gynecol*. 2002;186:S184–S189.
6. Goodwin TM, Montoro M, Mestman JH, Pekary AE, Hershman JM. The role of chorionic gonadotropin in transient hyperthyroidism of hyperemesis gravidarum. *J Clin Endocrinol Metab*. 1992;75:1333–1337.
7. Goodwin TM, Hershman JM. Hyperthyroidism due to inappropriate production of human chorionic gonadotropin. *Clin Obstet Gynecol*. 1997;40:32–44.
8. Depue RH, Bernstein L, Ross RK, et al. Hyperemesis gravidarum in relation to estradiol levels, pregnancy outcome, and other maternal factors: a seroepidemiologic study. *Am J Obstet Gynecol*. 1987;156:1137–1141.
9. Vellacott ID, Cooke EJ, James CE. Nausea and vomiting in early pregnancy. *Int J Gynaecol Obstet*. 1988;27:57–62.
10. Gadsby R, Barnie-Adshead AM, Jagger C. A prospective study of nausea and vomiting during pregnancy. *Br J Gen Prac*. 1993;43:245–248.
11. Lacroix R, Eason E, Melzack R. Nausea and vomiting during pregnancy: a prospective study of its frequency, intensity, and patterns of change. *Am J Obstet Gynecol*. 2000;182:931–937.
12. Boles RG, Williams JC. Mitochondrial disease and cyclic vomiting syndrome. *Dig Dis Sci*. 1999;44:103S–107S.
13. Czeizel AE, Dudas I, Fritz G, Tecsoi A, Hanck A, Kunovits G. The effect of periconceptional multivitamin-mineral supplementation on vertigo, nausea and vomiting in the first trimester of pregnancy. *Arch Gynecol Obstet*. 1992;251:181–185.
14. Emelianova S, Mazzotta P, Einarson A, Koren G. Prevalence and severity of nausea and vomiting of pregnancy and effect of vitamin supplementation. *Clin Invest Med*. 1999;22(3):106–110.
15. Jednak MA, Shadigian EM, Kim MS, et al. Protein meals reduce nausea and gastric slow wave dysrhythmic activity in first trimester pregnancy. *Am J Physiol*. 1999;277:G855–G861.
16. Sahakian V, Rouse D, Sipes S, Rose N, Niebyl J. Vitamin B6 is effective therapy for nausea and vomiting of pregnancy: a randomized, double-blind, placebo-controlled study. *Obstet Gynecol*. 1991;78:33–36.
17. Vutyavanich T, Wongtrangan S, Ruangsri R. Pyridoxine for nausea and vomiting of pregnancy: a randomized, double-blind, placebo-controlled trial. *Am J Obstet Gynecol*. 1995;173:881–884.
18. Koren G, Pastuszak A, Ito S. Drugs in pregnancy. *N Engl J Med*. 1998;338:1128–1137.
19. Park-Wyllie L, Mazzotta P, Pastuszak A, et al. Birth defects after maternal exposure to corticosteroids: prospective cohort study and meta-analysis of epidemiological studies. *Teratology*. 2000;62:385–392.
20. Simpson SW, Goodwin TM, Robins SB, et al. Psychological factors and hyperemesis gravidarum. *J Womens Health Gend Based Med*. 2001;10:471–477.
21. Goodwin TM. Hyperemesis gravidarum. *Clin Obstet Gynecol*. 1998;41:597–605.

Dr. Goodwin reports no financial relationships relevant to this article.