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The Hospital Physician Obstetrics and Gynecology Board Review Manual is a peer-reviewed study guide for residents and practicing physicians preparing for board examinations in obstetrics and gynecology. Each quarterly manual reviews a topic essential to the current practice of obstetrics and gynecology.

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INTRODUCTION

In the past, operative vaginal delivery was used to shorten the second stage of labor, as early biomedical literature demonstrated maternal and fetal benefit when the second stage was less than 2 hours. Currently, diligent fetal monitoring during the second stage allows identification of fetuses unable to tolerate labor. In addition, the maternal risks of a prolonged second stage, including hemorrhage and lacerations, appear to be mainly related to operative delivery. These factors have led the American College of Obstetricians and Gynecologists (ACOG) to now emphasize that the length of the second stage of labor is not an absolute indication for operative delivery. The rate of operative vaginal deliveries in the United States has steadily declined in recent years, from a peak of 9.5% in 1994 to 5.9% in 2002. Furthermore, the use of forceps has decreased while use of vacuum-assisted delivery has increased. For example, in 1997, when the total number of operative vaginal deliveries was 9%, 6% were by vacuum extraction and 3% by forceps. Most recently, both forms of operative vaginal delivery are giving way to cesarean section, the rate of which climbed to 26.1% in 2002 in the United States.

The following discussion addresses the appropriate situations in which operative vaginal delivery should be considered. Two case patients are presented to illustrate appropriate use of vacuum devices and forceps for operative vaginal delivery. Factors that influence the choice of instrument include the clinician’s level of training, maternal analgesia, and the risks and benefits of each instrument.

INDICATIONS AND PREREQUISITES FOR OPERATIVE DELIVERY

CASE PRESENTATION

A 28-year-old woman who is gravida 1, para 0, at 41 weeks gestation presents in active labor. After artificial rupture of membranes, epidural placement, and oxytocin augmentation, the patient progresses to complete cervical dilation. She pushes for 3 hours and is too tired to push any longer. Her cervix has remained completely dilated and completely effaced; she has been at station +2 cm for the entire second stage of labor.

The patient appears to have an adequate pelvis by examination. The estimated fetal weight is 3500 g by Leopold’s maneuvers. The position is right occiput anterior, with no asynclitism. The patient has had ineffective analgesia from her epidural despite a recent bolus to see if it would help her push more effectively.

• Is a trial of operative delivery indicated in this patient?
• What preoperative conditions must be met before proceeding with operative delivery?

INDICATIONS AND CONTRAINDICATIONS FOR OPERATIVE DELIVERY

ACOG recommends that a trial of operative vaginal delivery is warranted only if the chance of success is high, because the risks are greater with cesarean section after a failed attempt at operative delivery when compared with cesarean section without attempting operative delivery. ACOG has specified several indications and contraindications for operative delivery based on the assumption that the fetal head is engaged and the cervix is fully dilated (Table 1). However, no indication for operative delivery is absolute.

ACOG does not list macrosomia as a contraindication for operative delivery but does recommend caution when macrosomia is suspected. This recommendation is based on studies demonstrating that shoulder dystocia and significant neonatal injury are higher in macrosomic infants delivered by vacuum or forceps. Unfortunately, most methods to detect macrosomia are inaccurate. Cases of increased fetal bleeding with vacuum extraction after recent fetal scalp sampling have been reported. This is a rare event, and a history of fetal scalp sampling or electrode placement is not a contraindication for vacuum extraction. Many authorities consider vacuum extraction contraindicated in pregnancies before 34 weeks gestation secondary to the risk of intraventricular hemorrhage.

PREOPERATIVE PREREQUISITES

Before operative vaginal delivery can proceed, certain
Operative Vaginal Delivery

conditions must be met. The fetus must be in cephalic presentation, the head must be engaged, and the position of the head must be exactly known. Face presentation with mentum anterior is acceptable for forceps delivery. In regards to the mother, the cervix must be completely dilated, the membranes must be ruptured, and the pelvis must be adequate (ie, no suspicion of cephalopelvic disproportion [CPD]). In addition, analgesia must be appropriate, and the operator must have experience with the chosen technique for operative delivery. With the bladder empty, the delivery can be performed with constant reassessment of the fetal and maternal condition to optimize outcomes and minimize morbidity. Finally, preparations must be made so that immediate cesarean delivery can be performed if operative delivery fails.

The case patient meets the recommended criteria for consideration of an attempt at operative delivery. The definition of a prolonged stage 2 of labor in a nulliparous patient is lack of continuing progress for 3 hours with regional anesthesia. In addition, analgesia must be appropriate, and the operator must have experience with the chosen technique for operative delivery. With the bladder empty, the delivery can be performed with constant reassessment of the fetal and maternal condition to optimize outcomes and minimize morbidity. Finally, preparations must be made so that immediate cesarean delivery can be performed if operative delivery fails.

The case patient meets the criteria for prolonged stage 2 of labor, because she has been pushing the entire time. In addition, clinical pelvimetry reveals no suspicion of CPD, the estimated fetal weight is not excessive, and the fetal position is known. If a decision is made to proceed with operative vaginal delivery, the patient’s suboptimal level of analgesia will be an important consideration in choosing the instrument. Of note, epidural analgesia has been associated with an increased length of the first and second stages of labor, an increase in malrotation, and an increased rate of operative delivery.

MATERNAL AND FETAL OUTCOMES WITH OPERATIVE DELIVERY

CASE CONTINUED

A decision is made to proceed with operative delivery. Because of the patient’s suboptimal analgesia level and the physician’s greater comfort level with vacuum devices, vacuum-assisted delivery is recommended.

The physician explains that she would like to assist delivery with the use of a vacuum extractor because the patient’s labor is not progressing. She advises the patient of potential negative outcomes to herself and to her baby. However, she notes that the chance of success is high (ie, no macrosomia, adequate pelvis, no CPD suspected). The patient gives her consent to proceed with vacuum-assisted delivery.

What maternal and fetal outcomes have been associated with operative vaginal delivery?

MATERNAL OUTCOMES

A 2000 Cochrane systematic review of 10 trials found that vacuum extraction was associated with less maternal trauma and less anesthesia than forceps delivery but also was less likely to result in successful vaginal delivery than use of forceps. Another meta-analysis of these trials showed less anal sphincter trauma in vacuum deliveries than in forceps deliveries. It is safe to assume that the use of forceps has decreased because the vacuum is easier to apply, requires less anesthesia, and causes less maternal trauma.

Long-term data on bowel and bladder function after operative vaginal delivery are inconsistent and lack adequate studies. In a follow-up of a cohort of women randomly assigned to forceps or vacuum delivery 5 years postpartum, 47% of respondents reported some degree of urinary incontinence and 20% reported occasional or frequent loss of bowel control; no significant differences were observed between the 2 modes of delivery. In a review of 906 women, forceps and vacuum were the only
independent risk factors identified for fecal incontinence; of interest, emergency cesarean section during labor was not protective against incontinence. Some studies suggest that cesarean section is protective against urinary and fecal incontinence. These studies are inconclusive regarding the increase in protective effect of a cesarean section prior to labor versus cesarean section during labor.

NEONATAL OUTCOMES

The Cochrane systematic review found that delivery by vacuum extractor was associated with an increase in neonatal cephalhematoma and retinal hemorrhages when compared with forceps. ACOG also states that retinal hemorrhage is more common with vacuum devices than with forceps. These conditions usually are not associated with long-term sequelae.

Towner et al conducted the largest study to date on neonatal risks with operative vaginal delivery, which involved a retrospective look at 583,340 infants born to nulliparous women. The authors found that, compared with spontaneous delivery, the vacuum and forceps were associated with higher rates of subdural or cerebral hemorrhage, brachial plexus injury, and mechanical ventilation. Importantly, this study also showed that the risk for intracranial hemorrhage was higher among infants delivered by vacuum, forceps, or cesarean section during labor than among infants delivered spontaneously or during scheduled cesarean section before labor. The authors were careful to point out that abnormal labor is a risk factor for the above complications, not operative delivery. Vacuum-assisted delivery also was associated with an increase in convulsions and central nervous system (CNS) depression when compared with spontaneous delivery. Forceps were significantly associated with facial nerve injury when compared with spontaneous delivery or vacuum-assisted delivery.

INFORMED CONSENT

Whether the risks involved with operative vaginal delivery result from the difficult labor or from the operation itself is controversial. Regardless, the patient must be made aware that operative vaginal delivery is associated with an increased risk for certain maternal and neonatal sequelae. The use of vacuum devices carries approximately a 5% risk of significant complications.

When compared with spontaneous delivery, vacuum delivery has been associated with an increased risk for scalp marks, bruising, cephalhematoma, subgaleal hematoma, retinal hemorrhage, intracranial hemorrhage, shoulder dystocia and brachial plexus injury, convulsions, CNS depression, and mechanical ventilation. In discussing options, the risks of vacuum devices versus forceps include an increased rate of cephalhematoma and retinal hemorrhage.

Most of these risks do not carry long-term complications. An exception is subgaleal hematoma, which occurs when blood collects in a large potential space between the galea aponeurotica and the periosteum. A large amount of blood loss may occur, leading to shock and death. Intracranial hemorrhage and neurologic injury could potentially have long-term sequelae; however, these complications are rare. Finally, operative delivery has been associated with an increase in perineal lacerations, with vacuum having less of a risk than forceps for significant tears.

VACUUM-ASSISTED DELIVERY

CASE CONTINUED

The patient is prepared for operative vaginal delivery, and her bladder is drained. A soft cup vacuum extractor is selected and is applied correctly. However, minimal to no descent is noted.

• How should patients be prepared for operative delivery? Is episiotomy recommended?

PREPARATION FOR OPERATIVE DELIVERY

Preparation for operative delivery includes obtaining adequate analgesia and emptying the bladder. The use of episiotomy remains controversial; no randomized controlled trials have compared operative delivery with and without episiotomy. Some retrospective studies demonstrate an increase in perineal trauma during operative delivery with episiotomy. Ecker et al reported a decrease in episiotomy use during a 10-year period with both vacuum and forceps, with a concurrent decrease in fourth-degree lacerations and no change in third-degree lacerations. Robinson et al noted that the use of episiotomy with forceps did not influence the amount of perineal trauma, but the use of episiotomy with vacuum devices increased perineal trauma. Adequate biomedical literature demonstrates that liberal use of midline episiotomy in spontaneous labor increases the risk of perineal trauma, and mediolateral episiotomy does not prevent anal sphincter injury. Applying these findings to vacuum deliveries is probably reasonable, because the mechanics of vacuum delivery and spontaneous delivery are similar.

• What is the correct use of vacuum devices for operative delivery?
Operative Vaginal Delivery

CORRECT USE OF VACUUM DEVICES

The vacuum device should be applied on the sagittal suture, with the center of the vacuum 2 to 3 cm in front of the posterior fontanelle (Figure 1). Care should be taken not to trap maternal tissue between the fetal vertex and the suction cup and to avoid the anterior fontanelle. Traction is applied in the axis of the birth canal. Pressure should not exceed 550 to 600 mm Hg, a level that can be rapidly attained. Pressure does not need to be increased in a stepwise fashion. Rocking movements and torque should be avoided. Bofill et al20 demonstrated that traction maintained between contractions to prevent loss of fetal station did not influence time to delivery, method failure, maternal lacerations, episiotomy extension, incidence of cephalhematoma, or neonatal outcome. Lastly, the pediatrician should be made aware that the infant was delivered via vacuum extraction.6

Although the biomedical literature is inconsistent, most authorities support using the vacuum for no longer than 15 minutes.6 Some vacuum device manufacturers recommend a 10-minute time limit. The vacuum should not be used after a maximum of 2 to 3 cup detachments or “pop-offs.” Many authorities recommend that some descent with the first traction should occur; otherwise, the situation should be reassessed.6

Newer vacuum devices have been created to try to improve efficacy for vaginal delivery and to decrease maternal and neonatal trauma. A Cochrane systematic review of 9 trials found that soft cups were more likely to fail to achieve vaginal delivery but were associated with less scalp injury when compared with hard cup devices; for maternal injury, no difference was observed between the 2 devices.21 The reviewers concluded that hard or metal cups were preferable when more traction is required, such as for occiput posterior, occiput transverse, and asymmetrical positions, whereas the soft cups were preferred for straightforward, occiput anterior positions.21

• If an attempt at vacuum-assisted delivery fails, what is the most appropriate next step?

FAILURE OF VACUUM DELIVERY

If the vacuum fails to assist delivery, it is controversial whether forceps should be used. Use of sequential vacuum then forceps to assist delivery carries a higher rate of potential fetal and maternal morbidity. Before attempting the other method after an initial failed attempt at traction, one should reassess the option of cesarean delivery.

Towner et al14 found significantly higher rates of subdural or cerebral hemorrhage, subarachnoid hemorrhage, facial nerve injury, and brachial plexus injury in infants delivered by vacuum and forceps compared with infants delivered by vacuum alone. In particular, the risk for intracranial hemorrhage was 3.4 times greater with vacuum and forceps than with vacuum alone (95% confidence interval, 1.7–6.6). Other studies have confirmed an increase in neonatal trauma with the combination of vacuum and forceps compared with vacuum alone, forceps alone, or spontaneous delivery. Gardella et al15 also observed that the risk associated with sequential use of vacuum and forceps was higher than the risk for the individual components combined. The authors concluded that the risk of neonatal and maternal morbidity associated with combined use of a vacuum extractor and forceps was greater than expected and suggested the presence of a synergistic effect.15 Some studies state that
sequential use of these instruments is safe in certain situations. These data have led ACOG to discourage multiple attempts at vaginal delivery with different instruments, except when there is a “compelling and justifiable reason.”

CESAREAN SECTION AFTER FAILURE OF OPERATIVE VAGINAL DELIVERY

Towner et al. found that neonatal outcomes were significantly worse after cesarean section with a trial at operative vaginal delivery versus cesarean section in labor without a trial of operative vaginal delivery. Overall, this study found an increased rate of intracranial hemorrhage in infants delivered by cesarean section after a failed attempt at operative delivery; the rate was 2.6 times that associated with vacuum extraction and 2.9 times that associated with cesarean delivery during labor with no attempt at operative delivery. Other studies have found no adverse effects of a trial of operative vaginal delivery if cesarean section could promptly follow. Taken together, these data have led ACOG to recommend that a trial of operative vaginal delivery is warranted only if the chance of success is high.

CASE CONCLUSION

A decision is made to proceed with a cesarean section. The patient undergoes the procedure without complications and delivers a viable male infant weighing 3350 g. Apgar scores are 9 + 9. The mother and infant do well and are discharged on postpartum day 3.

FORCEPS DELIVERY

CASE PRESENTATION

A 24-year-old gravida 2 para 1001 at 40 and 4/7 weeks gestation presents in active labor. The patient undergoes artificial rupture of membranes for clear fluid, epidural placement, and oxytocin administration. She reaches complete cervical dilation, complete effacement, and station +2 cm. She begins pushing, but with each push, the fetal heart rate tracing shows variable decelerations to the 60s, with slow return noted.

The estimated fetal weight is 3500 g, and clinical pelvimetry does not support CPD. The fetal vertex is direct occiput anterior, without asynclitism. The patient has good pain relief from her epidural. The physician decides to proceed with forceps delivery because it is her preference in cases where there is an adequate level of analgesia. The patient’s bladder is drained.

The patient’s delivery is classified as a low forceps delivery. Because the patient’s labor progress has not been protracted, the estimated fetal weight is not excessive, and the patient has not pushed for a long period of time, her fetus is unlikely to have a significant amount of caput or molding. Overestimation of the station is thus not probable and it appears safe to assist the delivery.

- How are forceps deliveries classified?

CLASSIFICATION OF FORCEPS DELIVERY

ACOG’s most recent criteria for forceps-assisted vaginal delivery were issued in 2000. In this document, station is defined as the number of centimeters that the leading bony part of the fetal head is below the ischial spines, ranging from 0 to 5 cm. Several other factors have been specifically defined to ensure areas of risk are precisely understood. Using these common definitions, ACOG has defined the criteria for forceps deliveries (Table 2). Despite these straightforward definitions, the use of forceps in practice is further complicated by several clinical factors unique to each parturient.

The most common confounding factor is molding. The intent when determining station is to delineate when the biparietal diameter (BPD)—the largest diameter that must pass through the maternal pelvis—has become engaged at the pelvic inlet—truly 0 station. When molding occurs, the longitudinal axis of the head is lengthened; thus, the distance between the BPD and the spines is greater. Therefore, one may palpate the station as +3 cm; however, the BPD may be only 1 cm beyond the inlet, creating a problem. When molding occurs, a delivery that initially is believed to be a low forceps delivery is actually a much more difficult midpelvic delivery. Figure 2 shows an example of extreme molding on a fetus in the occiput posterior presentation, making the station seem lower than it really is. Similar to molding, caput succedaneum (or the edema formed from labor and stage 2 pushing at the leading portion of the fetal vertex) also can be erroneously perceived as a lower station than in reality is the case. Combining both of these clinical factors can lead to situations where an apparently straightforward outlet forceps delivery is in fact a difficult low or even midpelvic delivery.

- What types of forceps are available, and how should they be applied?

FORCEPS TYPES

Classic Forceps

Forceps can loosely be divided into 2 main categories, classic and specialized. In the classic grouping, the main
difference is in the style for the shank. For the Elliot-type forceps, the shanks overlap. Thus, in order to traverse the same cephalic diameter or cephalic curve, these forceps have a sharper angle and thus a rounder curve. In contrast, the Simpson-type forceps have a parallel shank and, therefore, take a less round configuration to create the cephalic curve. The Simpson-type forceps are more elongated and are better for the more molded fetal head, whereas the classic Elliot-type forceps have a rounder cephalic curve and are better for the unmolded fetal head. Variations in these classic forceps have occurred, and some are listed in Table 3.

**Table 3. Classic Forceps**

<table>
<thead>
<tr>
<th>Types/Variations</th>
<th>Cephalic Curve</th>
<th>Shank</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elliot, Tucker-McLane</td>
<td>Rounder</td>
<td>Overlapping</td>
</tr>
<tr>
<td>Simpson, DeLee, Irving, Dennen</td>
<td>More oblong</td>
<td>Parallel</td>
</tr>
</tbody>
</table>


Specialized Forceps

Specialized forceps have been developed to increase the success with vaginal delivery in particular clinical situations where the forceps design affords a distinct advantage. There are many different types of specialized forceps—too many to list in this brief review. The 2 most commonly used specialized forceps and their specific clinical applications are briefly noted below.

**Kielland’s forceps.** Introduced in 1915, Kielland’s forceps have a specialized design to use for rotating the fetal head. Originally used for deep transverse arrest, use of Kielland’s forceps now includes occiput posterior presentations as well. The modification that makes these forceps so unique is the flatter pelvic curve. Unlike the cephalic curve, which is the portion of the blade that goes around the fetal skull, the pelvic curve refers to the portion of the forceps that curves along the axis of the birth canal—much like a bent stovepipe. In the Kielland’s forceps, the pelvic curve is flat, with a slight downward slope. The advantage is that when placed on the fetal head and rotated, the ends or toes of the Kielland’s forceps subtend a very small radius. Thus, these forceps are less likely to cause harm and are more likely to be successful.

**Piper forceps.** Introduced in 1924, the Piper forceps are used for breech delivery. The Piper forceps consist of very long shanks that are curved in the middle in a reverse fashion. Thus, the handles go much lower and allow the fetus to be held above them without hyperextending the neck. In addition, after they are placed to the aftercoming head in a breech delivery, the blades have very little pelvic curve so that as the fetal head is delivered in concert with the body of the fetus, movement through the perineum is

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Figure 2. Extreme molding in mid-occiput posterior presentation. (Reprinted with permission from Dennen EH, Hale RW. Dennen’s forceps deliveries. 4th ed. Hale RW, editor. Washington [DC]: American College of Obstetricians and Gynecologists; 2001:15.)

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Table 2. Criteria for Forceps-Assisted Vaginal Deliveries

<table>
<thead>
<tr>
<th>Condition</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outlet forceps</td>
<td>Scalp visible at the introitus without separating the labia. Fetal skull has reached the pelvic floor. Sagittal suture is in anteroposterior diameter or in right or left occiput anterior or posterior position. Fetal head is at or on perineum. Rotation does not exceed 45 degrees.</td>
</tr>
<tr>
<td>Low forceps</td>
<td>Leading point of fetal skull is at station +2 cm or above and not on the pelvic floor. Rotation 45 degrees or less (left or right occiput anterior to occiput anterior, or left or right occiput posterior to occiput posterior). Rotation exceeds 45 degrees.</td>
</tr>
<tr>
<td>Midforceps</td>
<td>Station is above +2 cm, but head is engaged.</td>
</tr>
</tbody>
</table>

slowed. This feature also is the one disadvantage of Piper forceps, because it may cause more distal vaginal and perineal injury if an episiotomy is not performed.

**Applying Forceps**

Forceps should be applied with the following 3 checks in mind:

- The posterior fontanelle is midway between the sides of the blades, and the posterior fontanelle is one finger’s breadth above the plane of the shank.
- The sagittal suture is perpendicular to the plane of the shanks throughout its length.
- The fenestrations of the blades are barely felt, if at all. No more than the tip of a finger should be able to be inserted between the fenestration and the head.

**CASE CONCLUSION**

Tucker-McLean forceps are selected, and the patient undergoes forceps-assisted vaginal delivery without complication. A viable female is delivered, weighing 3470 g. Apgar scores are 8 + 9. The mother suffers a second-degree laceration that is repaired without incident. The mother and infant both do well and are discharged on postpartum day 2.

**REFERENCES**

Hyperthyroidism and Pregnancy
Kathleen Cook, MD, Michelle L. Matthews, MD, and Bradley S. Hurst, MD

INTRODUCTION
Thyroid hormone is secreted from the thyroid gland in the tetra-iodinated form (thyroxine; T₄) and is peripherally deiodinated to the active triiodothyronine (T₃) form. T₃ plays a critical role in maintaining normal metabolic function, including the regulation of calorigenesis, oxygenation, and other metabolic processes. It is unsurprising, therefore, that thyroid hormone is integral to the physiologic changes that occur in a woman’s body during pregnancy and the postpartum period.

Thyroid disorders are 5 to 10 times more prevalent in women than in men.¹ Hyperthyroidism in particular is an important consideration in women of childbearing age because it can lead to infertility,² although spontaneous pregnancies often occur in women with thyroid hyperactivity. In fact, women often are first diagnosed with hyperthyroidism in pregnancy, as this may be one of the few times young, otherwise healthy females come in contact with the health care system.

Hyperthyroidism complicates 0.2% of pregnancies in the United States, with Graves’ disease accounting for 85% to 95% of all cases of true hyperthyroidism in pregnancy.² Transient hyperthyroidism caused by inappropriate secretion or action of human chorionic gonadotropin, such as occurs in gestational trophoblastic disease or hyperemesis gravidarum, is recognized as the most common cause of decreased levels of thyroid-stimulating hormone (TSH) early in pregnancy. Less common causes of hyperthyroidism include single toxic thyroid adenoma (Plummer’s disease), multinodular toxic goiter, subacute thyroiditis, and iatrogenic hyperthyroidism. Rarely, hyperthyroidism is caused by a TSH-producing pituitary tumor or struma ovarii, is induced by iodine unmasking pretoxic thyroid disease, or results from exposing a previously normal thyroid or euthyroid goiter to iodine.³

The following case-based discussion addresses the approach to diagnosis and management of hyperthyroidism in women who are pregnant or attempting to conceive. Hyperthyroidism in pregnancy can increase the rate of miscarriages and result in significant maternal and fetal morbidity, emphasizing the importance of preconceptual control of hyperthyroid states. In addition, hyperthyroidism often occurs or worsens in the first year postpartum.³ Therefore, the obstetrician/gynecologist is in a unique position to both diagnose and treat hyperthyroidism in women. The case that follows focuses on Graves’ disease, as it accounts for the majority of true hyperthyroidism in women.

PREPREGNANCY DIAGNOSIS AND MANAGEMENT

CASE PRESENTATION
A 33-year-old woman with slightly irregular cycles presents to her gynecologist for prepregnancy counseling and evaluation. The patient’s medical history is negative, but review of systems reveals a 10-lb weight loss in the last 6 months, dry eyes, occasional palpitations, and a preference for cold rooms. Physical examination reveals a temperature of 99.0°F, pulse of 102 bpm, respiratory rate of 20 breaths/min, and blood pressure of 130/70 mm Hg. Mild bilateral proptosis is evident. The thyroid gland is symmetrically enlarged, to 2 to 3 times the normal size. A slight hand tremor is noted. The examination is otherwise normal. Initial laboratory studies are normal, with the exception of a TSH of 0.01 mIU/L (normal, 0.27–4.2 mIU/L) and an elevated free T₄ (FT₄) of 4.0 ng/dL (normal, 0.9–1.7 ng/dL).

• Does this patient’s prepregnancy evaluation reveal sufficient clinical evidence to make a diagnosis of hyperthyroidism?
• Are further tests required at this time?

DIAGNOSIS OF HYPERTHYROIDISM
Signs and Symptoms
The initial symptoms of hyperthyroidism usually develop over several months. The most common complaints include nervousness, irritability, palpitations, fatigue, heat intolerance, weight loss, change in menstrual patterns, and a decrease in tolerance to usual physical activities. Oligomenorrhea is not uncommon and is sometimes followed by amenorrhea. An increase in the number of bowel movements is common, but frank diarrhea is rare. Palpitations may be continuous or episodic. Weight loss despite a good appetite is common. However, up to 10% of patients may experience weight gain and a

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decreased appetite. Itching is commonly reported.

A careful physical examination is essential in the diagnosis of hyperthyroidism. A symmetrical, diffuse, nontender goiter is present in almost every young patient with Graves’ disease, with enlargement of the thyroid gland to about 2 to 4 times the normal size,

as was found in the case patient. If a single nodule is felt in the presence of a diffusely enlarged gland, this should be documented for additional follow-up, as it increases the potential for malignancy. A thrill may be felt over the gland, or a bruit may be heard. The skin usually is warm and moist, especially on the hands. The face may be flushed, and palmar erythema may be present. A rash on skin exposed to the sun is commonly observed. The hair may be fine and fragile. A separation of the distal margin of the nail from the nail bed may be seen, with irregular recession of the junction (onycholysis).

The most prominent manifestations of thyrotoxicosis are cardiovascular. Tachycardia (pulse > 90 bpm) almost always is present, as was noted on examination of the case patient. The pulse pressure usually is widened. Systolic and even presystolic murmurs are often heard at the apex. The beat at the apex usually is forceful and diffuse, suggestive of cardiac enlargement. However, the cardiac silhouette appears normal on chest radiographs. About 10% of patients present with atrial fibrillation. Heart failure also may be present in severe cases or with underlying cardiac disease.

The characteristic ophthalmopathy of Graves’ disease (ie, prominent, bulging eyes, stare, and injected conjunctiva) occurs in about 20% to 50% of all patients and is diagnosed by the presence of periorbital edema and injected conjunctiva. In general, eye signs are very common and may be independent of the characteristic ophthalmopathy. Patients may have a bright-eyed stare secondary to retraction of the upper lid, known as proptosis. They often manifest lid lag or globe lag when asked to look slowly upward or downward.

The dermopathy of Graves’ disease is seen in only about 5% of patients. It is characterized by pretibial myxedema, which usually appears as a violaceous induration of the skin or, occasionally, as localized nodules.

Nervous system abnormalities may be noted with hyperthyroidism and include restlessness, short attention span, or the need for constant movement despite a feeling of exhaustion. Hand or tongue tremor may be noted. The patient also may manifest proximal muscle weakness, which can be tested by asking the patient to rise from a sitting or lying position without using her arms.

During pregnancy, symptoms of hyperthyroidism may be difficult to identify, since both conditions may cause palpitations, heat intolerance, and warm skin. However, the presence of a goiter, proptosis, tachycardia (pulse > 90 bpm), proximal muscle weakness, and weight loss despite good appetite are more characteristic of Graves’ disease during pregnancy.

Laboratory Findings

Serum FT₄ is elevated in almost every patient with hyperthyroidism. The TSH level is suppressed or undetectable with third-generation TSH assays. Both of these laboratory abnormalities were found in the case patient. These test results combined with the characteristic physical findings confirms the diagnosis of Graves’ disease. Occasionally, a patient may have a low TSH and a normal FT₄, but an elevated free T₃, will confirm the diagnosis. Of note, about 15% of normal pregnant women have a suppressed TSH in the first trimester.

In Graves’ disease, TSH receptor antibodies, also referred to as thyroid-stimulating immunoglobulins (TSIs), have a stimulating effect. TSI testing is not required to diagnose Graves’ disease in nonpregnant women, although finding elevated TSIs can provide additional supportive information if the diagnosis is uncertain. During pregnancy, TSI testing may be helpful in the following specific situations: 1) fetal or neonatal hyperthyroidism in a prior pregnancy; 2) active hyperthyroidism; 3) current treatment with antithyroid drugs; or 4) maternal euthyroidism after treatment or remission in the presence of fetal tachycardia, intrauterine growth restriction, or the presence of fetal goiter on ultrasonography.

Other laboratory abnormalities may include hypercalcemia and lymphocytosis. Patients with Graves’ disease have an increased incidence of other autoimmune disorders, such as rheumatoid arthritis and Sjögren syndrome.

- What prepregnancy counseling and management would be appropriate for this patient?

PREPREGNANCY MANAGEMENT

In women with confirmed Graves’ disease, it is ideal to achieve a euthyroid state before pregnancy to reduce the risk of miscarriage. Treatment options before pregnancy include antithyroid medications (thionamides), radioactive ablation of the thyroid gland, or thyroidectomy.

Antithyroid Medications

Long-term therapy (12–24 months) with antithyroid medications (ie, propylthiouracil [PTU] or methimazole) produces remission in 20% to 50% of patients. Remission is most likely to occur in women with a short duration of disease, small goiter, and no ophthalmopathy. The usual initial dosage of PTU is 100 to 150 mg administered 3 times daily (TID) for a total daily dose of
300 to 450 mg, and the typical initial dose of methimazole is 15 to 40 mg given once daily, with higher doses of either drug prescribed to control more severe symptoms. The initial dose is reduced after symptoms have been fully controlled for 2 months. The usual total maintenance dose of PTU is 100 to 150 mg per day in 3 divided doses and for methimazole is 5 to 15 mg per day.\(^8\)

**Radioactive Ablation**

Radioactive ablation of the thyroid is the treatment of choice in nonpregnant women because it is simple and highly effective and causes no life-threatening complications. This approach would be most appropriate for the case patient. A single dose of radioactive iodine (iodine \(131^I\)) permanently controls hyperthyroidism in the majority of patients with Graves’ disease. A 24-hour \(131^I\) uptake is measured and used to calculate the dose, which for most patients is 8 to 10 mCi. It takes several months to achieve a euthyroid state. Patients are evaluated clinically and with FT\(_4\) levels every 4 to 6 weeks until thyroid function stabilizes. If a patient remains symptomatic 6 months following therapy, another dose of \(131^I\) may be given.

Thirty percent of women develop permanent hypothyroidism within a year of radioactive ablation, followed by 3% per year thereafter. Hypothyroidism is treated with thyroid replacement medication. Because \(131^I\) uptake by the thyroid is highly selective, radiation exposure to the ovaries is equivalent to that of common diagnostic plain film radiography. \(131^I\) ablation does not increase the risk of future malignancies; the risk of congenital anomalies in the offspring also is not increased after \(131^I\) ablation. A pregnancy test should be performed before giving \(131^I\), and reliable contraception should be prescribed.\(^8\) Women should avoid pregnancy for at least 6 months following \(131^I\) administration.\(^2,13\) \(131^I\) crosses the placenta and can cause fetal hypothyroidism and cretinism, so ablation is contraindicated during pregnancy.

**Thyroidectomy**

Surgery is used only when \(131^I\) ablation fails or when side effects preclude thionamide therapy. If undertaken, surgery should be performed in the second trimester or delayed during the postpartum period.

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**TREATMENT DURING PREGNANCY**

**CASE CONTINUED**

The patient was diagnosed with Graves’ disease based on her clinical profile and results of laboratory testing, and radioactive iodine was recommended as the best long-term treatment option. However, the patient conceives while awaiting radioactive ablation. She is concerned about the risk of using thionamides during pregnancy and initially refuses treatment. Her hyperthyroid symptoms progress, and by 16 weeks she reports worsened anxiety, palpitations at rest, and heat intolerance. Physical examination reveals a pulse of 116 bpm, respiratory rate of 24 beats/min, and a blood pressure of 120/60 mm Hg. The patient is afebrile, and her weight is unchanged from her pre-pregnancy weight. She is anxious and has sweaty palms. Fundal height is appropriate, and fetal heart rate is 170 bpm. The examination is otherwise unchanged.

- Are any of the maternal or fetal findings in this patient important concerns and, if so, how should they be addressed?

**MANAGEMENT OF GRAVES’ DISEASE DURING PREGNANCY**

**Definitive Treatment**

Control of hyperthyroidism from early pregnancy can prevent serious maternal and fetal complications, such as preterm delivery, toxemia, congestive heart failure, thyroid crisis (also called thyroid storm), and placental abruption (Table).\(^9\) During pregnancy, medical therapy is the treatment of choice for Graves’ disease. The goal of medical therapy during pregnancy is to keep the FT\(_4\) level in the upper one-third limit of normal with the lowest dose of drug possible.\(^9\) Symptoms of Graves’ disease generally worsen in the first half of pregnancy, improve in the second half, and recur postpartum, even while on treatment.\(^3\) The amelioration of the symptoms may be so pronounced that treatment can be discontinued during the last few weeks of gestation.

Two thionamides currently are used in the United States for medical treatment of Graves’ disease in pregnancy: PTU and methimazole. Both drugs block the synthesis of T\(_4\) by preventing the iodination of tyrosine residues. Both medications are equally effective in normalizing thyroid dysfunction.\(^2,13\) PTU must be administered every 8 hours (TID), whereas methimazole may be administered once or twice daily. Therefore, patient compliance is better with methimazole. However, congenital aplasia cutis has been reported with in utero exposure to methimazole, making PTU the drug of choice in pregnancy.\(^7\) Congenital aplasia cutis is characterized by scalp defects, esophageal atresia, tracheoesophageal fistula, choanal atresia, and absent or hypoplastic nipples.\(^2,12\) Methimazole is a pregnancy category D agent (ie, adequate well-controlled or observational studies in pregnant women have demonstrated a risk to the fetus; however, the benefits of therapy may outweigh
the potential risk). Methimazole can be used for pregnant patients who are unable to comply with a TID regimen or have an allergy to PTU.

Excessive doses of thionamides may produce fetal goiter and hypothyroidism. The starting dose of PTU is 150 mg per day. TSH and FT4 should be determined in 2 weeks. If improvement is seen, the dosage is cut in half. The dosage is progressively reduced as the thyroid tests improve. Once the patient has been euthyroid for a few weeks on 50 mg per day, the medication is discontinued. However, thyroid function testing every 2 to 3 weeks should continue. Tests of fetal well-being (eg, non-stress tests, biophysical profiles) are reserved for women who have persistent third trimester hyperthyroidism. Ultrasonography may assess fetal growth and detect fetal goiter. Long-term studies of children exposed in utero to thionamides have shown no intellectual or somatic defects compared with nonexposed siblings or age-matched controls.

Toxic reactions occur in about 5% of patients taking either PTU or methimazole and include skin rashes, arthralgias, fever, nausea, and pruritis. Most of these problems resolve without needing to discontinue the drug. However, substitution for the other drug is recommended, since cross-sensitivity rarely occurs. One serious side effect, agranulocytosis, has been reported with both drugs in 1 in 300 patients. Symptoms usually have an acute onset and consist of fever, sore throat, malaise, and gingivitis. Patients should be warned of these symptoms and advised to discontinue the medication and report to their physician if such symptoms occur. Hospitalization is required for administration of antibiotics, glucocorticoids, and supportive therapy. Other serious but rare adverse effects include hepatitis and vasculitis. Switching to the alternative drug after a serious toxic reaction is not recommended.

Minimal amounts of PTU are secreted in breast milk. If a mother using PTU decides to breast-feed, the infant should be monitored with frequent thyroid function tests. Breast-feeding is not advised when using methimazole, because the drug is secreted in higher concentrations in breast milk.

Symptomatic Therapy

β-Blockers may be prescribed to control hyperthyroidism symptoms (tachycardia, tremor, sweating) when thionamides are initiated. Propranolol and atenolol are the agents of choice. The dose is titrated to keep the maternal pulse between 70 and 90 bpm. β-Blockers should be used for a few weeks only, until symptoms abate, since long-term use has been associated with neonatal morbidity and increased incidence of miscarriage.

### Table. Pregnancy Complications of Uncontrolled Hyperthyroidism

<table>
<thead>
<tr>
<th>Maternal complications</th>
<th>Fetal complications</th>
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</thead>
<tbody>
<tr>
<td>Pregnancy–induced hypertension</td>
<td>Hyperthyroidism</td>
</tr>
<tr>
<td>Preterm delivery</td>
<td>Neonatal hyperthyroidism</td>
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<tr>
<td>Congestive heart failure</td>
<td>Intrauterine growth restriction</td>
</tr>
<tr>
<td>Thyroid storm</td>
<td>Small for gestational age</td>
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<tr>
<td>Miscarriage</td>
<td>Prematurity</td>
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<tr>
<td>Placental abruption</td>
<td>Stillbirth</td>
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<tr>
<td>Infection</td>
<td></td>
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</tbody>
</table>

Adapted from Mestman JH, Goodwin TM, Montoro MN. Thyroid disorders of pregnancy. Endocr Metab Clin N Am 1995;24:41–71 with permission from Elsevier.

### THYROID CRISIS

#### CASE CONTINUED

The case patient agrees to begin PTU therapy to control her symptoms. Treatment is initiated at a dose of 50 mg TID, with plans to taper and stop the PTU before delivery. Her pregnancy goes to term without complication. Her intrapartum course, however, is complicated by chorioamnionitis. Following arrest of cervical dilation at 6 cm, a cesarean section is performed, and the patient gives birth to a healthy baby boy. On postoperative day 2, the patient suddenly develops chills and vomiting.

Physical examination reveals a temperature of 103.2°F, pulse of 144 bpm, respiratory rate of 28 breaths/min, and blood pressure of 150/60 mm Hg. The patient is diaphoretic and appears confused. New findings include tachycardia, a 2/6 systolic ejection murmur, rales in the lower third of the lungs bilaterally, and mild uterine fundal tenderness. The fundus is firm at the umbilicus, and the incision is clean, dry, and intact. There is 2+ pitting edema of the extremities bilaterally.

Laboratory studies reveal an elevated white blood cell count of 22,000/mm³, with 75% neutrophils and 14% bands. Sodium is mildly decreased at 132 mEq/L,
and potassium is 3.1 mEq/L. Glucose is 189 mg/dL, and calcium is increased at 10.2 mEq/L. Aspartate aminotransferase and alanine aminotransferase are elevated at 94 IU/L and 106 IU/L, respectively. TSH is low at 0.01 mIU/L, and FT₄ is elevated at 9.5 ng/dL.

- Is this presentation consistent with thyroid storm?
- How is thyroid storm diagnosed and managed?

### DIAGNOSIS AND TREATMENT OF THYROID STORM

This patient presents with signs and symptoms typical of postpartum thyroid crisis (ie, sudden chills, vomiting, fever, tachycardia, tachypnea, elevated systolic blood pressure, mental status changes, elevated white blood cell count, metabolic abnormalities, and laboratory evidence of hyperthyroidism). The dramatic worsening of this patient’s Graves’ disease probably was exacerbated by chorioamnionitis.

Thyroid crisis is a severe manifestation of hyperthyroidism, which usually develops following a severe stress such as infection, anesthesia, labor, or surgery, all of which occurred in the case patient. It also may be triggered by preeclampsia, gestational trophoblastic disease, or placenta previa. This is a life-threatening condition that requires early recognition and aggressive treatment.

Thyroid crisis is diagnosed clinically in the presence of severe symptoms of hyperthyroidism. Fever is present, with temperatures often exceeding 103°F. Nervous system symptoms include irritability, agitation, and severe tremor. Mental status is always altered and can range from disorientation to psychosis or coma. Cardiovascular symptoms are pronounced and include tachycardia, often with a pulse greater than 140 bpm, atrial fibrillation, and congestive heart failure. Gastrointestinal symptoms include nausea, vomiting, and diarrhea.

Laboratory tests are not diagnostic. Thyroid function tests are consistent with hyperthyroidism, but the degree of elevation of FT₄ has no meaning. Often there is leukocytosis, elevated hepatic enzymes, hypokalemia, and hypercalcemia. Glucose and cortisol may be elevated.

Once a clinical diagnosis is made, the patient should be admitted (if not already hospitalized) and treated in an intensive care unit (ICU). Thyroid crisis requires aggressive treatment with acetaminophen, β-blockers, thionamides, iodine, and glucocorticoids. Acetaminophen is the drug of choice to control fever; aspirin is contraindicated in thyroid crisis because it displaces T₃ and T₄ from binding proteins. Precipitating causes, such as infection, should be corrected. Heart failure may require large doses of digoxin. Oral propranolol, 60 to 80 mg, should be given every 4 hours to control tachycardia. Theoretically, such high doses of β-blockers could worsen heart failure. If this is a concern, short-acting esmolol may be used. PTU, 300 mg every 6 hours, also should be started immediately. If the patient is unable to take oral medications, a nasogastric tube should be placed. An hour after the first dose of PTU, oral iodine should be administered to block thyroid hormone release. Finally, dexamethasone 2 mg intravenously (IV) every 6 hours should be given to reduce the peripheral conversion of T₃ to T₂.

### CASE CONCLUSION

A clinical diagnosis of thyroid crisis is made and the patient is transferred to the ICU for supportive therapy, correction of electrolyte abnormalities, and control of fever. Acetaminophen 650 mg is given every 4 to 6 hours to control fever. Since mild uterine tenderness was noted, IV cefoxitin 2 g every 8 hours plus doxycycline 100 mg every 12 hours is initiated to treat presumptive endomyometritis. The patient also is given nasal oxygen and IV fluids of dextrose 5% normal saline with half potassium chloride 40 mEq 50 mL/hr. Echocardiography reveals adequate left ventricular function. Oral propranolol 80 mg is given every 4 hours to control tachycardia. PTU, 300 mg every 6 hours, is started immediately. An hour after the first dose of PTU, oral iodine (Lugol’s solution) 10 drops TID is initiated. Finally, IV dexamethasone 2 mg every 6 hours is prescribed.

The patient’s hypermetabolic signs and symptoms are greatly improved by the next day. After an additional 24 hours observation, she is transferred back to the postpartum unit. Three days later, she is discharged but continues on PTU 300 mg TID. Six months after delivery, the patient successfully undergoes radioactive ablation of the thyroid.

### REFERENCES


