CHAPTER 26: Induction and Augmentation of Labor

In other cases, if interference becomes imperative, the introduction of a bougie into the uterus, or the employment of a small Champetier de Ribes rubber bag acts as an effective uterine irritant and brings about complete dilatation.

—J. Whitridge Williams (1903)

INTRODUCTION

No effective means of labor induction were available when Williams wrote the first edition of this book. Labor augmentation methods were largely ineffective, and manual cervical dilation was performed as a last resort. Contrast with today, when several pharmacological agents permit labor induction or augmentation, and ironically the use of a "bougie" has come back into vogue.

Induction implies stimulation of contractions before the spontaneous onset of labor, with or without ruptured membranes. When the cervix is closed and uneffaced, labor induction will often commence with *cervical ripening*, a process that generally employs prostaglandins to soften and open the cervix. *Augmentation* refers to enhancement of spontaneous contractions that are considered inadequate because of failed cervical dilation and fetal descent—*inertia uteri*—as described by Williams (1903).

In the United States, the incidence of labor induction rose 2.5-fold from 9.5 percent in 1991 to 23.8 percent in 2015 (Martin, 2017). The incidence varies between practices. At Parkland Hospital, approximately 35 percent of labors are induced or augmented. By comparison, at the University of Alabama at Birmingham Hospital, labor is induced in approximately 20 percent of women, and another 35 percent are given oxytocin for augmentation—a total of 55 percent. This chapter discusses indications for labor induction and augmentation and various techniques to effect preinduction cervical ripening.

LABOR INDUCTION

Indications

Induction is indicated when the benefits to either mother or fetus outweigh those of pregnancy continuation. The more common indications include membrane rupture without labor, gestational hypertension, oligohydramnios, nonreassuring fetal status, postterm pregnancy, and various maternal medical conditions such as chronic hypertension and diabetes (American College of Obstetricians and Gynecologists, 2016).

Methods to induce or augment labor are contraindicated by most conditions that preclude spontaneous labor or delivery. The few maternal contraindications are related to prior uterine incision type, contracted or distorted pelvic anatomy, abnormally implanted placentas, and uncommon conditions such as active genital herpes infection or cervical cancer. Fetal factors include appreciable macrosomia, severe hydrocephalus, malpresentation, or nonreassuring fetal status.

Techniques

Oxytocin has been used for decades to induce or augment labor. Other effective methods include prostaglandins, such as misoprostol and dinoprostone, and mechanical methods that encompass membrane stripping, artificial rupture of membranes, extraamnionic saline infusion, transcervical balloons, and hygroscopic cervical dilators. Importantly, and as recommended in *Guidelines for Perinatal Care*, each obstetrical department should have its own written protocols that describe administration of these methods for labor induction and augmentation (American Academy of Pediatrics, 2017).

Risks

Maternal complications associated with labor induction are cesarean delivery, chorioamnionitis, uterine rupture, and postpartum hemorrhage from uterine atony. Of these, labor induction carries a two- to threefold greater risk for cesarean delivery (Hoffman, 2003; Maslow, 2000; Smith, 2003). This risk is particularly higher among nulliparas (Luthy, 2004; Wolfe, 2014; Yeast, 1999). More recently, this association has been questioned (Macones, 2009; Melamed, 2016; Miller, 2015; Saccone, 2015). Indeed, Darney and colleagues (2012) reported the cesarean delivery risk was actually lower for women with labor induction at 39 weeks' gestation compared with that in women expectantly managed. In their review, Little and Caughey (2015) found a reduced cesarean delivery rate when women undergoing labor induction were compared with women expectantly managed, as opposed to women spontaneously laboring. Currently, this is the topic of a randomized trial by the Maternal–Fetal Medicine Units (MFMU) Network—A Randomized Trial of Induction Versus Expectant Management—ARRIVE (National Institutes of Health, 2015).

Amniotomy is often selected to augment labor (Amniotomy for Induction and Augmentation). Women whose labor is managed with amniotomy have a higher incidence of chorioamnionitis compared with those in spontaneous labor (American College of Obstetricians and Gynecologists, 2016).

Rupture of a prior uterine incision during labor in women with a history of prior uterine surgery can be catastrophic (Chap. 31, Uterine Scar Rupture). The MFMU Network reported a threefold greater risk of uterine scar rupture with oxytocin, and this was even higher with prostaglandin use (Landon, 2004). The American College of Obstetricians and Gynecologists (2017b) recommends against the use of prostaglandins for preinduction cervical ripening or labor induction in women with a prior uterine incision.

Uterine atony and associated postpartum hemorrhage are more common in women undergoing induction or augmentation (Chap. 41, Risk Factors). And, atony with intractable hemorrhage, especially during cesarean delivery, is a frequent indication for peripartum hysterectomy. In a study from Parkland Hospital, labor induction was associated with 17 percent of 553 emergency peripartum hysterectomies (Hernandez, 2013). In the United States, the postpartum hysterectomy rate rose 15 percent between 1994 and 2007 (Bateman, 2012). This was largely attributed to increased rates of atony associated with more medical labor inductions and more primary and repeat cesarean deliveries. In another analysis, elective induction was also linked with a threefold higher rate of hysterectomy (Bailit, 2010).

Elective Labor Induction

Until recently, elective induction for convenience had become increasingly prevalent. Clark and coworkers (2009) described 14,955 deliveries at ≥37 weeks' gestation. They noted that 32 percent were elective deliveries, and 19 percent were elective labor inductions.

The American College of Obstetricians and Gynecologists (2016) does not endorse this once widespread practice. Occasional exceptions might include logistical and other reasons such as a risk of rapid labor, a woman who lives a long distance from the hospital, or psychosocial indications. Because of the greater risks for adverse maternal outcomes, we are also of the opinion that routine elective induction at term is not justified. Elective delivery before 39 completed weeks is also associated with significant adverse neonatal morbidity (Chiossi, 2013; Clark, 2009; Salemi, 2016; Tita, 2009). If elective induction is considered at term, inherent risks must be discussed, informed consent obtained, and guidelines followed as promulgated by the American College of Obstetricians and Gynecologists (2016), which are detailed in Chapter 31 (Labor and Delivery Considerations).

Guidelines to discourage elective inductions have been described by Fisch (2009) and Oshiro (2013) and their associates. Both groups reported significant declines in elective delivery rates following guideline initiation. In 2011, the Texas Medicaid program began to deny payment for elective induction prior to 39 weeks' gestation. This resulted in a 14-percent drop in such early-term deliveries and a rise in birthweights (Dahlen, 2017). A program in Oregon also reduced early-term deliveries, but maternal and fetal outcomes were not improved (Snowden, 2016).

Factors Affecting Induction Success

Several factors affect the ability of labor induction to achieve vaginal delivery. Favorable factors include younger age, multiparity, body mass index (BMI) <30, favorable cervix, and birthweight <3500 g (Gibson, 2015; Roland, 2017; Sievert, 2017). In many cases, the uterus is simply poorly prepared for labor. One example is an "unripe cervix." Indeed, investigators with the *Consortium on Safe Labor* reported that elective induction resulted in vaginal delivery in 97 percent of multiparas and 76 percent of nulliparas, but that induction was more often successful with a ripe cervix (Laughon, 2012).

The greater cesarean delivery risk associated with induction is likely also strongly influenced by the induction attempt duration, especially with an unfavorable cervix (Spong, 2012). In one study, labor duration to reach the active phase and to complete dilation was adversely affected by a higher BMI (Kominiarek, 2011). Similar findings were reported for women with diabetes (Hawkins, 2017). Simon and Grobman (2005) concluded that a latent phase as long as 18 hours allowed most women undergoing labor induction to achieve a vaginal delivery without a significantly increased risk of

maternal or neonatal morbidity. Rouse and associates (2000) recommend a minimum of 12 hours of uterine stimulation with oxytocin after membrane rupture, whereas Kawakita and coworkers (2016) recommend up to 15 hours for multiparas.

PREINDUCTION CERVICAL RIPENING

As discussed, the condition of the cervix—described as cervical "ripeness" or "favorability"—is important to successful labor induction. However, at least some estimates of favorability are highly subjective (Feltovich, 2017). That said, pharmacological and mechanical methods can enhance cervical favorability—also termed *preinduction cervical ripening*.

Some of the techniques described may have benefits when compared with oxytocin induction alone (Table 26-1). Some are also quite successful for initiating labor. However, few data support the premise that any of these techniques lower cesarean delivery rates or lessen maternal or neonatal morbidity compared with women in whom these methods are not used.

TABLE 26-1

Some Commonly Used Regimens for Preinduction Cervical Ripening and/or Labor Induction

Techniques	Agent	Route/Dose	Comments
Pharmacological			
Prostaglandin E_2	Dinoprostone gel, 0.5 mg (Prepidil) Dinoprostone insert, 10 mg (Cervidil)	Cervical 0.5 mg; repeat in 6 hr; permit 3 doses total Posterior fornix, 10 mg	1. Shorter I-D times with oxytocin infusion than oxytocin alone 2. Insert has shorter I-D times than gel 3. 6–12 hr interval from last insert to oxytocin infusion
Prostaglandin E_1[a]	Misoprostol tablet, 100 or 200 µg (Cytotec)[b]	Vaginal, 25 µg; repeat 3–6 hr prn Oral, 50–100 µg; repeat 3–6 hr prn	1. Contractions within 30–60 min 2. Success comparable to oxytocin for ruptured membranes at term and/or favorable cervix 3. Tachysystole common with vaginal doses >25 µg
Mechanical			
Transcervical 36F Foley catheter	30-mL balloon		1. Improves Bishop scores rapidly 2. 80-mL balloon more effective 3. Combined with oxytocin infusion is superior to PGE_1 vaginally 4. With EASI, results improved and possible decreased infection rate
Hygroscopic dilators		Laminaria, hydrogel	1. Rapidly improves Bishop score 2. May not shorten I-D times with oxytocin 3. Uncomfortable, requires speculum and placement on an examination table

[a]Off-label use.

[b]Tablets must be divided for 25- and 50-µg dose, but drug is evenly dispersed.

EASI = extraamnionic saline infusion at 30–40 mL/hr; I-D = induction-to-delivery.

Cervical "Favorability"

One quantifiable method used to predict labor induction outcomes is the score described by Bishop (1964) and presented in Table 26-2. As favorability or Bishop score declines, the rate of induction to effect vaginal delivery also decreases. A *Bishop score* of 9 conveys a high likelihood for a successful induction. For research purposes, a Bishop score of 4 or less identifies an unfavorable cervix and may be an indication for cervical ripening.

TABLE 26-2

Bishop Scoring System Used for Assessment of Inducibility

	Cervical Factor				
Score	**Dilatation (cm)**	**Effacement (%)**	**Station (–3 to +2)**	**Consistency**	**Position**
0	Closed	0–30	–3	Firm	Posterior
1	1–2	40–50	–2	Medium	Midposition
2	3–4	60–70	–1	Soft	Anterior
3	≥5	≥80	+1, +2	—	—

From Bishop, 1964.

Laughon and coworkers (2011) attempted to simplify the Bishop score by performing a regression analysis on 5610 singleton, uncomplicated deliveries between $37^{0/7}$ and $41^{6/7}$ weeks' gestation in nulliparas. Only cervical dilation, station, and effacement were significantly associated with successful vaginal delivery. Thus, a simplified Bishop score, which incorporated only these three parameters, had a similar or improved positive- or negative-predictive value compared with that of the original Bishop score. Other investigators have reported similar findings when consistency and position are omitted (Ivars, 2016; Raghuraman, 2016).

Transvaginal sonographic measurement of cervical length is the only biophysical marker that has been evaluated as a Bishop score alternative (Feltovich, 2017). In one metaanalysis of trials in which cervical length was used to predict successful induction, study criteria heterogeneity precluded the authors from reaching a summary answer (Hatfield, 2007). A subsequent metaanalysis of 31 trials found overall low sensitivity and specificity and limited predictive utility for sonographic cervical length and "wedging" to predict successful labor induction (Verhoeven, 2013).

Pharmacological Techniques

Unfortunately, women frequently have an indication for induction but also have an unfavorable cervix. Several techniques are available, and these can also stimulate contractions and thereby aid subsequent labor induction or augmentation. Methods most commonly used for preinduction cervical ripening and induction include several prostaglandin analogues.

Prostaglandin E_2

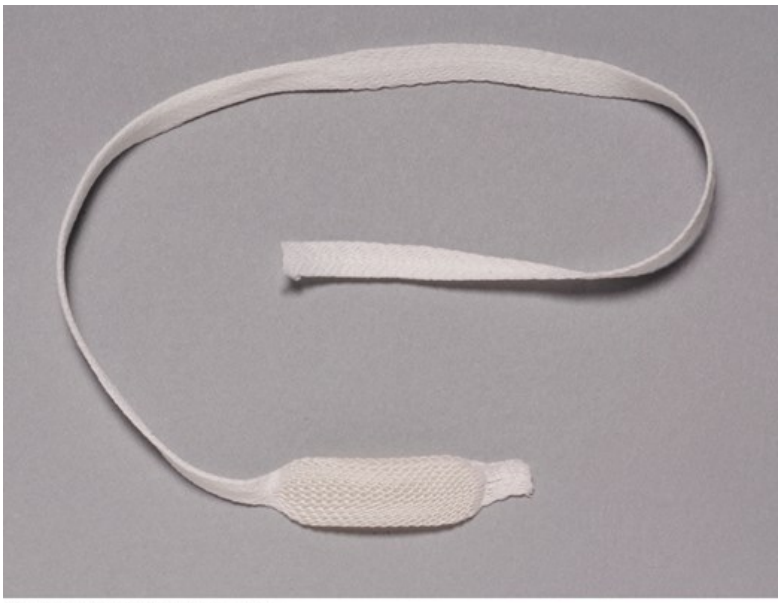
Dinoprostone is a synthetic analogue of prostaglandin E_2 (PGE_2). It is commercially available in three forms: a gel, a time-release vaginal insert, and a 20-mg suppository (Table 26-1). The gel and time-release vaginal insert formulations are indicated only for cervical ripening before labor induction. However, the 20-mg suppository is not indicated for cervical ripening. It instead is used for pregnancy termination between 12 and 20 weeks' gestation and for evacuation of the uterus after fetal demise up to 28 weeks.

Local application of its gel form—*Prepidil*—is available in a 2.5-mL syringe for an intracervical application of 0.5 mg of dinoprostone. With the woman supine, the tip of a prefilled syringe is placed intracervically, and the gel is deposited just below the internal cervical os. After application, the woman remains reclined for at least 30 minutes. Doses may be repeated every 6 hours, with a maximum of three doses recommended in 24 hours.

A 10-mg dinoprostone vaginal insert—*Cervidil*—is also approved for cervical ripening. This is a thin, flat, rectangular polymeric wafer held within a small, white, mesh polyester sac (Fig. 26-1). The sac has a long attached tail to allow easy removal from the vagina. The insert provides slower release of medication—0.3 mg/hr—than the gel form. Cervidil is used as a single dose placed transversely in the posterior vaginal fornix. Lubricant is used sparingly, if at all, because it can coat the device and hinder dinoprostone release. Following insertion, the woman remains recumbent for at least 2 hours. The insert is removed after 12 hours or with labor onset and at least 30 minutes before the administration of oxytocin.

FIGURE 26-1

Cervidil vaginal insert contains 10 mg of dinoprostone designed to release approximately 0.3 mg/hr during a 10-hour period.



Most metaanalyses of dinoprostone efficacy report a reduced time-to-delivery within 24 hours, however, they do not consistently show a reduction in the cesarean delivery rate. Thomas and colleagues (2014) provided a Cochrane review of 70 trials and 11,487 women given vaginal prostaglandins or either placebo or no treatment. They noted a higher vaginal delivery rate within 24 hours when prostaglandins were used. They also reported a threefold greater risk of tachysystole accompanied by fetal heart rate changes, but cesarean delivery rates were not significantly decreased. Similar results were noted in another Cochrane review of intracervical dinoprostone gel (Boulvain, 2008). Compared with placebo or no treatment, a reduced risk of cesarean delivery was found only in a subgroup of women with an unfavorable cervix and intact membranes. Finally, the Foley catheter versus vaginal PGE_2 gel for induction of labor at term—PROBAAT-P and -M trials—were unblinded, randomized trials comparing these two options (Jozwiak, 2011, 2013, 2014). The cesarean delivery rate did not differ, a finding consistent with accompanying metaanalyses.

Side Effects

Uterine tachysystole follows vaginally administered PGE_2 in 1 to 5 percent of women (Hawkins, 2012). Although definitions of abnormal uterine activity vary among studies, most use the definition recommended by the American College of Obstetricians and Gynecologists (2017a):

1. *Uterine tachysystole* is defined as >5 contractions in a 10-minute period. It should always be qualified by the presence or absence of fetal heart rate abnormalities.
2. *Uterine hypertonus, hyperstimulation,* and *hypercontractility* are terms no longer defined, and their use is not recommended.

Because uterine tachysystole associated with fetal compromise may develop when prostaglandins are used with preexisting spontaneous labor, such use is not recommended. If tachysystole follows the 10-mg insert, its removal by pulling on the tail of the surrounding net sac will usually reverse this effect. Irrigation to remove the gel preparation has not been shown to be helpful.

The manufacturers recommend caution when these preparations are used in women with ruptured membranes. This concern is also extended to women with glaucoma or asthma. However, in a review of 189 women with asthma, dinoprostone was not associated with asthma worsening or exacerbation (Towers, 2004). Other contraindications listed by the manufacturers include a history of dinoprostone hypersensitivity, suspicion of fetal compromise or cephalopelvic disproportion, unexplained vaginal bleeding, women already receiving oxytocin, those with six or more previous term pregnancies, those with a contraindication to vaginal delivery, or women with a contraindication to oxytocin or who may be endangered by prolonged uterine contractions, for example, those with a history of cesarean delivery or uterine surgery.

Administration

PGE_2 preparations should only be administered in or near the delivery suite. Moreover, uterine activity and fetal heart rate should be monitored (American College of Obstetricians and Gynecologists, 2016). These guidelines stem from the risk of uterine tachysystole. When contractions begin, they are usually apparent in the first hour and show peak activity in the first 4 hours. According to manufacturer guidelines, oxytocin induction that follows prostaglandin use for cervical ripening should be delayed for 6 to 12 hours following PGE_2 gel administration or for at least 30 minutes after removal of the vaginal insert.

Prostaglandin E_1

Misoprostol—*Cytotec*—is a synthetic prostaglandin E_1 (PGE_1) that is approved as a 100- or 200-µg tablet for peptic ulcer prevention. It has been used "off label" for preinduction cervical ripening and may be administered orally or vaginally. The tablets are stable at room temperature. Although widespread, the off-label use of misoprostol has been controversial (Wagner, 2005; Weeks, 2005). Specifically, G. D. Searle & Company notified physicians that misoprostol is not approved for labor induction or abortion (Cullen, 2000). Still, the American College of Obstetricians and Gynecologists (2016) reaffirmed its recommendation for use of the drug because of proven safety and efficacy. It currently is the preferred prostaglandin for cervical ripening at Parkland Hospital. In one review of 234 women administered misoprostol, no instances of asthma exacerbation were associated with its use, and the risk of this was calculated to be <2 percent (Rooney Thompson, 2015).

Vaginal Administration

Compared with intracervical or intravaginal PGE_2, vaginally administered misoprostol tablets offer equivalent or superior efficacy for cervical ripening or labor induction. A metaanalysis of 121 trials also confirmed these findings (Hofmeyr, 2010). Compared with oxytocin or with intravaginal or intracervical dinoprostone, vaginal misoprostol increased the vaginal delivery rate within 24 hours. In this review, although the uterine tachysystole rate rose, this did not affect cesarean delivery rates. Moreover, compared with dinoprostone, misoprostol lowered the need for oxytocin induction, but it increased the frequency of meconium-stained amnionic fluid. Higher doses of misoprostol are associated with a decreased need for oxytocin but with more uterine tachysystole, with and without fetal heart rate changes. The American College of Obstetricians and Gynecologists (2016) recommends a 25-µg vaginal dose—a fourth of a 100-µg tablet. The drug is evenly distributed among these quartered tablets.

Wing and colleagues (2013) described use of a vaginal polymer insert containing 200 µg of PGE_1. They compared its efficacy with 10-mg dinoprostone inserts, and preliminary observations are favorable.

Oral Administration

PGE_1 tablets are also effective when given orally. One Cochrane metaanalysis of 76 trials reported that oral misoprostol compared with placebo significantly raised the rate of vaginal birth within 24 hours, while decreasing the need for oxytocin and lowering the cesarean delivery rate. Comparisons of oral misoprostol and oxytocin and of oral misoprostol and dinoprostone also found significantly reduced rates of cesarean delivery with misoprostol. Similar efficacy was noted between oral misoprostol and vaginal administration, although oral administration was associated with significantly higher Apgar scores and less postpartum hemorrhage (Alfirevic, 2014). Thorbiörnson and associates (2017) also reported lower rates of cesarean delivery for oral misoprostol compared with vaginal dinoprostone.

Nitric Oxide Donors

Several findings have prompted a search for clinical agents that stimulate nitric oxide (NO) production locally (Chanrachakul, 2000). First, NO is likely a mediator of cervical ripening. Also, cervical NO metabolite concentrations are increased at the beginning of uterine contractions. And, cervical NO production is very low in postterm pregnancy (Väisänen-Tommiska, 2003, 2004).

Bullarbo and colleagues (2007) reviewed rationale and use of two NO donors, *isosorbide mononitrate* and *glyceryl trinitrate*. Isosorbide mononitrate induces cervical cyclooxygenase 2 (COX-2), and it also initiates cervical ultrastructure rearrangement similar to that seen with spontaneous cervical ripening (Ekerhovd, 2002, 2003). Despite this, NO donors are less effective clinically than prostaglandins, either PGE_2 or misoprostol, for cervical

ripening. In one large metaanalysis, the rate of cesarean delivery was not reduced in those given NO donors compared with those given placebo, intravaginal or intracervical prostaglandins, intravaginal misoprostol, or intracervical catheter (Ghosh, 2016). However, NO donors were associated with significantly more headaches, nausea, and vomiting.

Mechanical Techniques

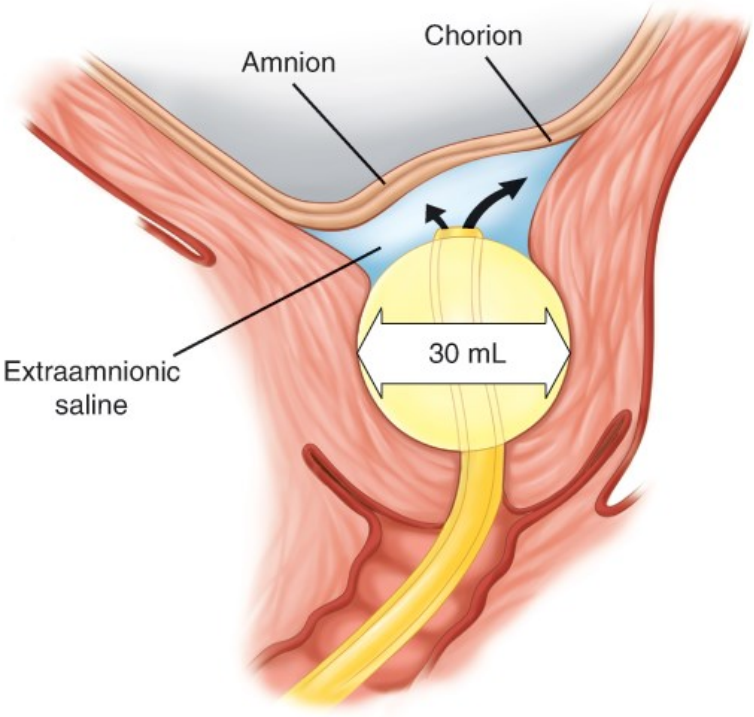
These include transcervical placement of a Foley catheter, with or without extraamnionic saline infusion; hygroscopic cervical dilators; and membrane stripping. In their metaanalysis, Jozwiak and associates (2012) reported that mechanical techniques reduced the risk of uterine tachysystole compared with prostaglandins, although cesarean delivery rates were unchanged. Trials comparing mechanical techniques with oxytocin found a lower rate of cesarean delivery with mechanical methods. Trials comparing mechanical techniques with dinoprostone found a higher rate of multiparas undelivered at 24 hours with mechanical techniques. In another metaanalysis comparing Foley catheter placement with intravaginal dinoprostone inserts, rates of cesarean delivery were similar, but uterine tachysystole was less frequent with catheter use (Jozwiak, 2013).

Transcervical Catheter

Generally, these techniques are only used when the cervix is unfavorable because the catheter tends to come out as the cervix opens. It is suitable for women with intact or ruptured membranes. In most cases, a Foley catheter is placed through the internal cervical os, and downward tension is created by taping the catheter to the thigh (Mei-Dan, 2014). A modification of this—*extraamnionic saline infusion (EASI)*—adds a constant saline infusion through the catheter into the space between the internal os and placental membranes (Fig. 26-2). Karjane and coworkers (2006) reported that chorioamnionitis was significantly less frequent when infusion was done compared with no infusion—6 versus 16 percent. Similarly, in a large metaanalysis, transcervical catheters were not associated with higher rates of maternal or fetal infection (McMaster, 2015).

FIGURE 26-2

Extraamnionic saline infusion (EASI) through a 26F Foley catheter that is placed through the cervix. The 30-mL balloon is inflated with saline and pulled snugly against the internal os, and the catheter is taped to the thigh. Room-temperature normal saline is infused through the catheter port of the Foley at 30 or 40 mL/hour by intravenous infusion pump.



Source: F. Gary Cunningham, Kenneth J. Leveno, Steven L. Bloom, Catherine Y. Spong, Jodi S. Dashe, Barbara L. Hoffman, Brian M. Casey, Jeanne S. Sheffield: *Williams Obstetrics*, 25th Edition

As discussed above, transcervical catheters do not reduce the cesarean delivery rate compared with prostaglandins. The PROBAAT trials (-I, -P, -M, and II), in which cervical ripening with a Foley catheter was compared with vaginal dinoprostone gel, dinoprostone vaginal inserts, and vaginal or oral misoprostol, reported similar outcomes between the mechanical technique and the prostaglandin agents. Also, fewer overall cases of cardiotocographic changes were seen in the mechanical technique group (Jozwiak, 2011, 2013, 2014; Ten Eikelder, 2016).

Similar cesarean delivery rate results are found in other comparison studies. Schoen and coworkers (2017) observed that concurrent oxytocin with a transcervical Foley catheter shortened the median time-to-delivery compared with a Foley catheter followed by oxytocin. However, rates of cesarean delivery were unchanged. Connolly and associates (2016) reported similar findings for women within intact membranes undergoing labor induction. Amorosa and colleagues (2017) found no benefit for transcervical catheter coupled with oxytocin compared against oxytocin alone for women with ruptured membranes. Other studies of concurrent misoprostol reported reduced time-to-delivery without affecting cesarean delivery rates (Carbone, 2013; Levine, 2016). Finally, the concurrent addition of tension does not appear to enhance catheter efficacy. Fruhman and coworkers (2017) randomized 140 women to transcervical Foley catheter with and without tension, and reported similar vaginal delivery rates within 24 hours or overall.

Hygroscopic Cervical Dilators

Cervical dilation can be accomplished using hygroscopic osmotic cervical dilators, as described for early pregnancy termination (Chap. 18, First-Trimester Abortion Methods). Intuitive concerns of ascending infection have not been verified, and their use appears to be safe. Placement generally requires a speculum and positioning of the woman on an examination table. Several studies performed in the 1990s compared hygroscopic cervical dilators and prostaglandins and found few benefits of this mechanical technique. And, more recent studies verified these conclusions (Maier, 2017).

METHODS OF INDUCTION AND AUGMENTATION

Labor induction has primarily been effected with the use of amniotomy, prostaglandins, and oxytocin, alone or in combination. Because preinduction cervical ripening frequently eventuates in labor, studies to determine induction efficacy for some of these agents have produced sometimes confusing results. The use of prostaglandins for labor augmentation has generally been considered experimental due to their high rates of uterine tachysystole.

Prostaglandin E_1

Both vaginal and oral misoprostol are used for either cervical ripening or labor induction. For labor induction in women at or near term with either prematurely ruptured membranes or a favorable cervix, 100 µg of oral or 25 µg of vaginal misoprostol has similar efficacy compared with intravenous oxytocin. From these studies, evidence supports that oral misoprostol may be superior (Alfirevic, 2014; Hofmeyr, 2010; Lo, 2003). Misoprostol may be associated with a greater rate of uterine tachysystole, particularly at higher doses. Also, induction with PGE_1 may prove ineffective and require subsequent induction or augmentation with oxytocin. Thus, although there are trade-offs regarding the risks, costs, and ease of administration of each drug, either is suitable for labor induction. At Parkland Hospital, we administer an initial oral 100-µg dose, which may be repeated after 6 hours for inadequate labor. Six hours after the second dose or in those with tachysystole, an oxytocin infusion is begun, if needed, for hypotonic labor. Döbert and colleagues (2017) have described preliminary use of a misoprostol vaginal insert.

For *labor augmentation*, results of a randomized controlled trial showed oral misoprostol, 75 µg given at 4-hour intervals for a maximum of two doses, to be safe and effective (Bleich, 2011). The 75-µg dose was based on a previous dose-finding study (Villano, 2011). Although there was more uterine tachysystole among women with labor augmented with misoprostol, the frequency of nonreassuring fetal status or cesarean delivery did not differ between oxytocin and misoprostol.

Oxytocin

In many instances, preinduction cervical ripening and labor induction are simply a continuum. Thus, “ripening” can also stimulate labor. If not, induction or augmentation may be continued with solutions of oxytocin given by infusion pump. Its use in augmentation is a key component in the *active management of labor,* described in Chapter 22 (Labor Management Protocols). With oxytocin use, the American College of Obstetricians and Gynecologists (2016) recommends fetal heart rate and uterine contraction monitoring. Contractions can be monitored either by palpation or by electronic means.

Intravenous Oxytocin Administration

The goal of induction or augmentation is to effect uterine activity sufficient to produce cervical change and fetal descent, while avoiding development of a nonreassuring fetal status. In general, oxytocin is discontinued if the number of contractions persists with a frequency of more than five in a 10-minute period or more than seven in a 15-minute period or with a persistent nonreassuring fetal heart rate pattern. Oxytocin discontinuation nearly always rapidly lowers contraction frequency. When oxytocin is stopped, its concentration in plasma rapidly falls because the half-life is approximately 3 to 5 minutes. Seitchik and associates (1984) found that the uterus contracts within 3 to 5 minutes of beginning an oxytocin infusion and that a plasma steady state is reached in 40 minutes. Response is highly variable and depends on preexisting uterine activity, cervical status, pregnancy duration, and individual biological differences. Caldeyro-Barcia and Poseiro (1960) reported that the uterine response to oxytocin increases from 20 to 30 weeks' gestation and rises rapidly at term (Chap. 24, Intrapartum Surveillance of Uterine Activity).

Oxytocin Dosage

A 1-mL ampule containing 10 units of oxytocin usually is diluted into 1000 mL of a crystalloid solution and administered by infusion pump. A typical infusate consists of 10 or 20 units, which is 10,000 or 20,000 mU or one or two 1-mL vials, respectively, mixed into 1000 mL of lactated Ringer solution. This mixture results in an oxytocin concentration of 10 or 20 mU/mL, respectively. To avoid bolus administration, the infusion should be inserted into the main intravenous line close to the venipuncture site.

Oxytocin is generally very successful when used to stimulate labor. In one large Cochrane metaanalysis, oxytocin was compared with expectant management, and fewer women—8 versus 54 percent—failed to deliver vaginally within 24 hours with oxytocin (Alfirevic, 2009). This analysis studied different oxytocin dosing regimens.

Oxytocin Regimens

Several evidence-based regimens for labor stimulation are now recommended by the American College of Obstetricians and Gynecologists (2016). These and others are shown in Table 26-3. Initially, only variations of low-dose protocols were used in the United States. Subsequently, O'Driscoll and colleagues (1984) described their Dublin protocol for the active management of labor that called for oxytocin at a starting dosage of 6 mU/min and advanced in 6-mU/min increments. Subsequent comparative trials during the 1990s studied high-dose (4 to 6 mU/min) versus conventional low-dose (0.5 to 1.5 mU/min) regimens, both for labor induction and for augmentation.

TABLE 26-3

Various Low- and High-Dose Oxytocin Regimens Used for Labor Induction

Regimen	Starting Dose (mU/min)	Interval (min)	Incremental Increase (mU/min)
Low-dose	0.5–1.5	15–40	1
	2	15	4, 8, 12, 16, 20, 25, 30
High-dose	4	15	4
	4.5	15–30	4.5
	6	20–40[a]	6[b]

[a]Uterine tachysystole is more common with shorter intervals.

[b]With uterine tachysystole and after oxytocin infusion is discontinued, it is restarted at one half the previous dose and then increased at 3 mU/min incremental doses.

Data from Merrill, 1999; Satin, 1992, 1994; Xenakis, 1995.

From Parkland Hospital, Satin and associates (1992) evaluated an oxytocin regimen using an initial and incremental dosage of 6 mU/min compared with one using 1 mU/min. Increases at 20-minute intervals were provided as needed. Among 1112 women undergoing induction, the 6-mU/min regimen resulted in a shorter mean admission-to-delivery time, fewer failed inductions, and no cases of neonatal sepsis. Among 1676 women who had labor augmentation, those who received the 6-mU/min regimen had a shorter duration-to-delivery time, fewer forceps deliveries, fewer cesarean deliveries for dystocia, and lower rates of intrapartum chorioamnionitis or neonatal sepsis. With this protocol, uterine tachysystole was managed by oxytocin discontinuation followed by resumption when indicated and at half the stopping dosage. Thereafter, the dosage was increased at 3 mU/min when appropriate, instead of the usual 6-mU/min increase used for women without tachysystole. No adverse neonatal effects were observed.

Xenakis and coworkers (1995) reported benefits using an incremental oxytocin regimen starting at 4 mU/min. In another study, 816 women were randomly assigned for labor induction and 816 for augmentation with incremental oxytocin given at either 1.5 or 4.5 mU/min (Merrill, 1999). Women randomized to the 4.5 mU/min dosage had significantly shorter mean durations of induction-to-second-stage labor and induction-to-delivery times. Nulliparas randomized to the 4.5 mU/min dosage had a significantly lower cesarean delivery rate for dystocia compared with those given 1.5 mU/min dosage—6 versus 12 percent. Thus, benefits favor higher-dose regimens of 4.5 to 6 mU/min compared with lower dosages of 0.5 to 1.5 mU/min.

In 1990 at Parkland Hospital, routine use of the 6-mU/min oxytocin beginning and incremental dosage was incorporated and continues through today. In other labor units, a 2-mU/min beginning and incremental oxytocin regimen is preferred and administered. With either regimen, dosages are employed for either labor induction or augmentation. Although a Cochrane metaanalysis of randomized and quasi-randomized trials comparing high-dose versus low-dose regimens for labor induction at term reported no benefit of higher dosing, the metaanalysis included studies judged to have high potential bias. The authors concluded that the results might be confounded by these poor-quality studies (Budden, 2014).

Interval between Incremental Dosing

Intervals to increase oxytocin doses vary from 15 to 40 minutes (see Table 26-3). Satin and associates (1994) addressed this aspect with a 6-mU/min regimen providing increases at either 20- or 40-minute intervals. Women assigned to the 20-minute interval regimen for labor augmentation had a significantly reduced cesarean delivery rate for dystocia compared with that for the 40-minute interval regimen—8 versus 12 percent. As perhaps expected, uterine tachysystole was significantly more frequent with the 20-minute escalation regimen.

Other investigators reported even more frequent incremental increases. Frigoletto (1995) and Xenakis (1995) and their coworkers gave oxytocin at 4 mU/min with increases as needed every 15 minutes. Merrill and Zlatnik (1999) started with 4.5 mU/min doses and increased this every 30 minutes. López-Zeno and associates (1992) used 6 mU/min doses and 15-minute intervals. Thus, there are several acceptable oxytocin protocols that at least appear dissimilar. But, a comparison of protocols from two institutions indicates that this is not so:

1. The Parkland Hospital protocol uses a starting dose of oxytocin at 6 mU/min, which is increased by 6-mU/min every 40 minutes, and employs flexible dosing based on uterine tachysystole.

2. The University of Alabama at Birmingham Hospital protocol begins oxytocin at 2 mU/min and increases it as needed every 15 minutes to 4, 8, 12, 16, 20, 25, and 30 mU/min.

Thus, although the regimens at first appear disparate, if there is no uterine activity, either regimen is delivering 12 mU/min by 45 minutes into the infusion.

Maximal Oxytocin Dosage

The *maximal* effective dose of oxytocin to achieve adequate contractions in all women is different. Wen and colleagues (2001) studied 1151 consecutive nulliparas and found that the likelihood of progression to vaginal delivery decreased at and beyond an oxytocin dosage of 36 mU/min. Still, at a dosage of 72 mU/min, half of the nulliparas were delivered vaginally. Thus, if contractions are not adequate—less than 200 Montevideo units—and if the fetal status is reassuring and labor has arrested, an oxytocin infusion dose greater than 48 mU/min has no apparent risks.

Risks versus Benefits

Unless the uterus is scarred, uterine rupture associated with oxytocin infusion is rare, even in parous women. Flannelly and associates (1993) reported no cases of uterine ruptures, with or without oxytocin, in 27,829 nulliparas. There were eight instances of overt uterine rupture during labor in 48,718

parous women. Only one of these was associated with oxytocin use. A population-based retrospective review from Denmark reported a rupture rate of 3.3 per 100,000 women without prior cesarean, with the highest risk among multiparas (Thisted, 2015). Our experiences from Parkland Hospital are that oxytocin induction and augmentation are associated with uterine rupture (Happe, 2017). During an 8-year period in which there were about 95,000 births, 15 women suffered a primary uterine rupture, and 14 of these cases were associated with oxytocin use. In half of these women, prostaglandins were also given before augmentation with oxytocin.

Oxytocin has amino-acid homology similar to arginine vasopressin and has significant antidiuretic action. When infused at doses of 20 mU/min or more, renal free water clearance drops markedly. If aqueous fluids are infused in appreciable amounts along with oxytocin, *water intoxication* can lead to convulsions, coma, and even death. In general, if oxytocin is to be administered in high doses for a considerable period of time, its concentration should be increased rather than raising the flow rate of a more dilute solution. Consideration also should be given to use of crystalloids—either normal saline or lactated Ringer solution.

Uterine Contraction Pressures

Contraction forces in spontaneously laboring women range from 90 to 390 Montevideo units (Chap. 24, Intrapartum Surveillance of Uterine Activity). Caldeyro-Barcia (1950) and Seitchik (1984) with their coworkers found that the mean or median spontaneous uterine contraction pattern between 140 and 150 Montevideo units resulted in progression to vaginal delivery.

In the management of active-phase arrest, and with no contraindication to intravenous oxytocin, decisions must be made with knowledge of the safe upper range of uterine activity. Hauth and colleagues (1986) described an effective and safe protocol for oxytocin augmentation for active-phase arrest. With it, more than 90 percent of women achieved an average of at least 200 to 225 Montevideo units. They later reported that nearly all women in whom active-phase arrest persisted despite oxytocin generated more than 200 Montevideo units (Hauth, 1991). Importantly, despite no labor progression, no adverse maternal or perinatal effects were noted in those ultimately requiring cesarean delivery. There are no data regarding safety and efficacy of contraction patterns in women with a prior cesarean delivery, with twins, or with an overdistended uterus.

Active-Phase Arrest

First-stage arrest of labor is defined as a completed latent phase and contractions exceeding 200 Montevideo units for more than 2 hours without cervical change. Some have attempted to define a more accurate duration for active-phase arrest (Spong, 2012). Arulkumaran and coworkers (1987) extended the 2-hour limit to 4 hours and reported a 1.3-percent cesarean delivery rate in women who continued to have adequate contractions and progressive cervical dilation of at least 1 cm/hr. In women without progressive cervical dilation who were allowed another 4 hours of labor, half required cesarean delivery.

Rouse and colleagues (1999) prospectively managed 542 women at term with active-phase arrest and no other complications. Their protocol was to achieve a sustained pattern of at least 200 Montevideo units for a *minimum* of 4 hours. This time frame was extended to 6 hours if activity of 200 Montevideo units or greater could not be sustained. Almost 92 percent of these women were delivered vaginally. As discussed in Chapter 23 (Active-Phase Protraction), these and other studies support the practice of allowing an active-phase arrest of 4 hours (Rouse, 2001).

Zhang and coworkers (2002) analyzed labor duration from 4 cm to complete dilatation in 1329 nulliparas at term. They found that before dilation of 7 cm was reached, lack of progress for more than 2 hours was not uncommon in those who delivered vaginally. Alexander and associates (2002) reported that epidural analgesia prolonged active labor by 1 hour compared with duration of the active phase as defined by Friedman (1955). Consideration of these changes in the management of labor, especially in nulliparas, may safely reduce the cesarean delivery rate.

As data have accrued, investigators have increasingly questioned the thresholds for labor arrest disorders established by Friedman and others in the 1960s. In particular, investigators with the *Consortium on Safe Labor* reported that half of cases of dystocia after labor induction occurred before 6 cm of cervical dilation (Boyle, 2013; Zhang, 2010c). Even for women with spontaneous labor, these researchers found that active-phase labor was more likely to occur at 6 cm, and after slow progress between 4 and 6 cm (Zhang, 2010a). Additionally, they reported that a 2-hour threshold for diagnosing arrest disorders may be too brief when cervical dilation is <6 cm (Zhang, 2010b). This is discussed in detail in Chapter 23 (Obstetric Care Consensus Committee). Importantly, however, these studies of data from the Collaborative Perinatal Project included only singleton term gestation with spontaneous onset of labor, vaginal delivery, and a normal perinatal outcome. By excluding abnormal outcomes, cesarean deliveries, and those who were more than 6 cm dilated upon arrival, the above studies that sought to redefine the labor curve have been faulted for introducing biases that limit general use of these findings (Cohen, 2015a,b).

Amniotomy for Induction and Augmentation

Elective amniotomy with the intention of accelerating labor is often performed. Shown in Table 26-4, amniotomy at approximately 5-cm dilation accelerated spontaneous labor by 1 to 1½ hours. Importantly, neither the need for oxytocin stimulation nor the overall cesarean delivery rate was increased. Although the incidences of mild and moderate cord compression patterns were raised following amniotomy, cesarean delivery rates for fetal distress were not higher. Most importantly, there were no adverse perinatal effects.

TABLE 26-4

Randomized Clinical Trials of Elective Amniotomy in Early Spontaneous Labor at Term

		Effects of Amniotomy					
Study	**Number**	**Mean Dilation at Amniotomy**	**Mean Shortening of Labor**	**Need for Oxytocin**	**Cesarean Delivery Rate**	**Abnormal Tracing**	**Neonatal Effects**
Fraser (1993)	925	<5 cm	125 min	None	None[a]	None	None
Garite (1993)	459	5.5 cm	81 min	Decreased	None	Increased[b]	None
UK Amniotomy Group (1994)	1463	5.1 cm	60 min	None	None	NA	None

[a]No effect on overall rate; cesarean delivery for fetal distress significantly increased.

[b]Increased mild and moderate umbilical cord compression patterns.

NA = not assessed.

For labor induction, artificial rupture of the membranes—sometimes called *surgical induction*—can be used and always implies a commitment to delivery. The main disadvantage of amniotomy used alone for labor induction is the unpredictable and occasionally long interval until labor onset. That said, in a randomized trial, Bakos and Bäckström (1987) found that amniotomy alone or combined with oxytocin was superior to oxytocin alone. Mercer and colleagues (1995) randomly assigned 209 women undergoing oxytocin induction to either early amniotomy at 1 to 2 cm or late amniotomy at 5 cm. Early amniotomy was associated with a 4-hour reduction in labor duration. With early amniotomy, however, the incidence of chorioamnionitis was elevated.

For labor augmentation, amniotomy is commonly performed when labor is abnormally slow. Rouse and associates (1994) found that amniotomy with oxytocin augmentation for arrested active-phase labor shortened the time to delivery by 44 minutes compared with that of oxytocin alone. Although amniotomy did not alter the delivery route, one drawback was that it significantly increased the incidence of chorioamnionitis.

Regardless of the indication, amniotomy is associated with a risk of cord prolapse. To minimize this risk, disengagement of the fetal head during amniotomy is avoided. Toward this goal, fundal or suprapubic pressure or both may be helpful. Some clinicians prefer to rupture membranes during a contraction. If the vertex is not well applied to the lower uterine segment, a gradual egress of amnionic fluid can sometimes be accomplished by several membrane punctures with a 26-gauge needle held with a ring forceps and with direct visualization using a vaginal speculum. In many of these, however, membranes tear and fluid is lost rapidly. Because of the risk of cord prolapse or rarely abruption, the fetal heart rate is assessed before and immediately after amniotomy.

Membrane Stripping for Labor Induction

Labor induction by membrane “stripping” is a frequent practice. Several studies have suggested that membrane stripping is safe and lowers the

incidence of postterm pregnancy without consistently raising the incidence of ruptured membranes, infection, or bleeding. Authors of one large metaanalysis found that membrane stripping reduced the number of women remaining undelivered after 41 weeks without elevating the infection risk. They concluded that eight women would need to undergo membrane stripping to avoid one labor induction. Downsides are discomfort and associated bleeding (Boulvain, 2005).

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