UPDATE ON SUCCESSFUL INDUCTION OF LABOR

Frank Witter, MD,* and Lawrence Devoe, MD†

ABSTRACT

Induction of labor is indicated when the benefits to the mother or the fetus outweigh the benefits of continuing the pregnancy. Induction of labor involves a complex set of interventions that defies routine and presents numerous choices and challenges for clinicians and mothers. It is deemed successful when it initiates uterine contractions, progressively dilates and effaces the cervix, and leads to the normal vaginal birth of the baby with no maternal complications. Induction is deemed a failure when active labor is not achieved or cesarean delivery is required. From 1989 to 2002, the rate of labor induction in American women has more than doubled. The increasing use of labor induction has been supported by the expansion of medical indications for delivery before the onset of spontaneous labor, thanks to advances in obstetrical science. Elective induction has become more popular, as timed delivery can provide more patient and physician convenience. Other contributing factors include the ready availability of effective cervical ripeners, medicolegal issues, patient demand, and financial gain. This trend over time has important implications for clinical practice because, as several investigators have reported, elective induction consistently results in a 2- or 3-fold increase in the risk of cesarean delivery. The most important variable influencing successful labor induction is appropriate patient selection.

Recent studies provide new evidence to weigh when selecting patients for induction, making optimal clinical decisions as the trial of labor progresses, and, in the long term, affecting an appropriate rate of cesarean delivery. This article is intended to assist clinicians in building the best case for success before deciding to induce labor, in addition to review the evidence that supports the decision to induce labor and the decision not to induce labor. (Adv Stud Med. 2005;5(9D):S888-S898)

Induction of labor is the process of inducing uterine contractions to produce delivery before the onset of spontaneous labor, and it is indicated when the benefits to the mother or the fetus outweigh those of allowing the pregnancy to continue. It has been used commonly since synthetic oxytocin became available to obstetricians in the 1950s as a means to reduce the risks of post-term pregnancy. Over the past 2 decades, a better understanding of the mechanisms of labor, an enhanced ability to detect and manage antepartum fetal and maternal complications, and the development of new cervical ripening agents have improved the obstetrician’s ability to manage parturition. As a result, induction has become an option that physicians are exercising successfully and more frequently for the benefit of the mother and the fetus.

Indications for induction of labor are not absolute, and obstetricians should consider maternal and fetal conditions, gestational age, cervical status, and other factors. Table 1 lists the most common indications for induction of labor. Labor may also be induced for logistical reasons, such as risk of rapid labor, distance from hospital, or psy-
chosocial reasons. However, given statistical trends, there appears to be an overuse of elective indications.

Generally, the contraindications to the induction of labor are the same as those for spontaneous labor and vaginal delivery listed in Table 2. These contraindications should be considered within the context of the clinical situation of the individual patient. Several other conditions serve as relative contraindications to induction of labor and are listed in Table 3. These conditions deserve special attention, and may require consultation. Generally speaking, these relative contraindications may be mitigated by a favorable cervix and vertex presentation.

**PATIENT SELECTION**

The primary key to a successful induction of labor is proper patient selection. When selecting patients, consideration must be given to several interdependent factors: parity, gestational age, estimated fetal weight, prior uterine surgery, and cervical status.

**PARITY**

For nulliparous patients, induction is the most significant risk factor for cesarean delivery. A 7.5-year retrospective review of more than 21,000 pregnancies by Yeast et al. found that the nulliparas undergoing induction of labor had twice the cesarean delivery rate of those who entered labor spontaneously. Other studies have demonstrated that the risk of cesarean delivery among nulliparas was increased for medically indicated and elective inductions. An additional study linked induction of labor with increases in hospital pre-delivery time and greater costs. The risk for failed induction and cesarean delivery of nulliparas increase significantly when the cervical Bishop scores are unfavorable (see “Cervical Status” section later in this article). Among parous patients, the only predictor of induction failure is previous cesarean delivery (see “Prior Uterine Surgery” section later in this article).

**GESTATIONAL AGE**

A precise estimation of delivery date is subject to error. Pregnancy is considered to reach term at 37 weeks. After 42 weeks’ gestation, pregnancy is considered post-term, according to a definition supported by the American College of Obstetricians and Gynecologists (ACOG). An estimated 7% of the 4 million infants born in the United States during 2001 were delivered at 42 weeks.

---

**Table 1. Obstetric and Medical Indications for the Induction of Labor**

- Abruptio placentae
- Fetal demise
- Postdate pregnancy
- Premature rupture of the membranes
- Pregnancy-induced hypertension or pre-eclampsia
- Chorioamnionitis
- Maternal medical conditions, such as diabetes mellitus, renal disease, chronic pulmonary disease, or chronic hypertension
- Fetal compromise

**Table 2. Contraindications to the Induction of Labor**

- Placenta or vasa previa
- Transverse fetal lie
- Prolapsed umbilical cord
- Prior classic uterine incision or transfundal uterine surgery
- Pelvic structural abnormality
- Invasive cervical cancer

**Table 3. Relative Contraindications to the Induction of Labor**

- Abnormal fetal heart rate patterns
- Breech presentation
- Maternal heart disease
- Multifetal pregnancy
- Polyhydramnios
- Presenting part above the pelvic inlet
- Severe maternal hypertension
Induction for a post-term indication has been shown to reduce the likelihood of perinatal death. Many current practitioners consider postdatism to commence at 41 weeks, a threshold supported in a study by Divon et al that demonstrated a significant increase in the odds ratio for fetal death from 41 weeks’ gestation onward. However, adopting a national policy of inducing labor at 41 weeks would mean that approximately 500,000 additional women would be subjected to an intervention that has not yet been conclusively proved as necessary.

**Estimated Fetal Weight**

The term macrosomia is used to describe a large fetus, and although a precise definition has not been established, it is generally regarded to refer to a fetus weighing 4000 to 4500 grams. Fetal macrosomia increases the risk of cesarean delivery and birth injury or permanent brachial plexus palsy due to shoulder dystocia. Several risk factors contributing to macrosomia have been identified. These risk factors include maternal diabetes and/or obesity, multiparity, prolonged gestation, increased maternal age, male fetus, and a previous birth weighing more than 4000 grams. Accurate diagnosis of macrosomia can only be established after delivery of the infant. Ultrasonographic measurements, although accurate for estimating the weight of small preterm fetuses, have not proved sufficiently reliable in the diagnosis of macrosomia.

Because of this uncertainty in accurate estimation of fetal weight, the decision to induce labor when macrosomia is suspected has been controversial, especially because it is preferable to avoid shoulder dystocia, a potentially devastating complication. Several studies have reported that induction did not reduce the rate of cesarean delivery or shoulder dystocia when macrosomia was suspected. Rouse et al analyzed the effects of a policy of inducing labor in cases of suspected macrosomia as compared with standard obstetrical management. They concluded that for nondiabetic women, a policy of elective cesarean delivery is medically and economically unsound. However, current practice supports the induction of labor for the nondiabetic woman with a fetus estimated to weigh more than 5000 grams, and for the woman with diabetes with a fetus estimated to weigh more than 4500 grams.

**Prior Uterine Surgery**

Management of the gravida with a prior cesarean delivery has been one of the most consistently debated topics in modern obstetrics. For most of the 20th century, after Cragin's remark “once a cesarean, always a cesarean,” a scarred uterus was thought to contraindicate labor because of the risk of uterine rupture. Catastrophic uterine rupture may result in hysterectomy, massive transfusion, neonatal asphyxia, or death of the mother or fetus. Cragin's dictum is a historical relic as it dated from an era when the classical uterine incision was the norm. The low transverse cesarean incision has now become the norm, and researchers in the 1970s showed that vaginal birth after cesarean delivery (VBAC) could safely and routinely be attempted. By 1990, in an effort to stem the rising tide of cesarean birth in the United States, the US Public Health Service recommended increasing the rate of VBAC to 35% within a decade, and in 2000 increased the target rate to 37% by 2010. The rate reached 31% in 1998, but by 2002 it had declined to 12.7% as reports of adverse experiences, and particularly of uterine rupture, raised serious concern and heightened controversy. As rates of cesarean delivery continue to rise in the United States, the pool of patients with the potential to attempt VBAC is also growing.

The ACOG has estimated the risk of uterine rupture for women undergoing trial of labor with different kinds of prior uterine incisions. Classical and T-shaped incisions carry a 4% to 9% risk of uterine rupture, low vertical incisions carry a risk of 1% to 7%, and low transverse incisions a 0.2% to 1.5% risk. Many reports in the literature indicate that 60% to 80% of trials of labor after a previous cesarean delivery result in a successful vaginal birth, but as Wing and Paul point out, these reports likely suffer from selection bias. More realistic estimates of overall success for VBAC range from 65% to 70%. The ACOG list of selection criteria for attempting VBAC is listed in Table 4. It is also recommended that VBAC should only be attempted if a physician and facilities for performing an emergency cesarean section are readily available. Contraindications to VBAC are listed in Table 5, and include a classical or T-shaped uterine incision or the inability to perform an emergency cesarean section.

Although the risk of uterine rupture in women with previous cesarean sections increases with a trial of labor, the absolute risk remains low. Landon et al recently conducted a multicenter, prospective observational study among more than 33,000 patients. They
reported a risk of 0.7% (ie, 7 in 1000) for uterine rupture among women with a prior low transverse incision who underwent a trial of labor. After correcting for selection bias, the investigators concluded that the risk of an adverse perinatal outcome in this group of patients was approximately 1 in 2000. Other studies with similar findings suggest that in attempting VBAC, absolute risk of uterine rupture resulting in fetal mortality or morbidity is 1 in 1000.

Landon et al also reported a finding of importance to the consideration of labor induction in the presence of a scarred uterus. The use of uterotonic agents for inducing labor significantly increases the risk of uterine rupture among women attempting VBAC. The odds ratio for uterine rupture was almost 3 times greater for VBAC patients undergoing labor induction than for VBAC patients who entered labor spontaneously, and it was almost 2.5 times greater in patients whose labor was augmented. This study allowed investigators to point to oxytocin and prostaglandins as factors for the increased risk of uterine rupture. An earlier study by Lyndon-Rochelle et al found an increased risk of uterine rupture associated with the use of prostaglandins, as compared with oxytocin alone. In view of these findings, the VBAC patient who is being considered for induction of labor should receive a clear explanation of the distinction between relative and absolute risk of uterine rupture, and a discussion of the induction agents and their associated risks. Among the available prostaglandin agents, there is limited clinical evidence that suggests misoprostol, in particular, should be avoided in women with prior cesarean birth.

**Cervical Status**

Bishop established the relationship between cervical ripeness and the likelihood of entering spontaneous labor more than 40 years ago. The Bishop scoring system has also been used as a gauge for successful induction of labor (Table 6). A favorable cervix from the standpoint of induction of labor is considered to be a score of 9 or higher.

Since the introduction of prostaglandin agents for the express purpose of ripening the unfavorable cervix, cervical condition has diminished in status as a factor in the decision-making process regarding labor induction. A recent prospective study by Vrouenraets et al of 1300 nulliparous women has shed new light on the

---

**Table 4. ACOG Selection Criteria for Attempting VBAC**

<table>
<thead>
<tr>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>One or 2 previous low transverse cesarean deliveries</td>
</tr>
<tr>
<td>Clinically adequate pelvis</td>
</tr>
<tr>
<td>No other uterine scar or previous rupture</td>
</tr>
<tr>
<td>Physician readily available throughout labor, capable of monitoring labor</td>
</tr>
<tr>
<td>and performing emergency cesarean delivery</td>
</tr>
<tr>
<td>Availability of anesthesia and personnel for emergency cesarean delivery</td>
</tr>
</tbody>
</table>

ACOG = American College of Obstetricians and Gynecologists; VBAC = vaginal birth after cesarean delivery.

Data from American College of Obstetricians and Gynecologists.

**Table 5. ACOG Contraindications for Attempting VBAC**

<table>
<thead>
<tr>
<th>Contraindication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous classical or T-shaped incision or transfundal uterine surgery</td>
</tr>
<tr>
<td>Contracted pelvis</td>
</tr>
<tr>
<td>Medical or obstetric complication that precludes vaginal delivery</td>
</tr>
<tr>
<td>Inability to perform immediate emergency cesarean delivery because of unavailable surgeon, anesthesia, or sufficient staff or facility</td>
</tr>
</tbody>
</table>

ACOG = American College of Obstetricians and Gynecologists; VBAC = vaginal birth after cesarean delivery.

Data from American College of Obstetricians and Gynecologists.

**Table 6. Bishop Cervical Scoring System**

<table>
<thead>
<tr>
<th>Bishop Cervical Scoring System</th>
<th>0</th>
<th>1–2</th>
<th>3–4</th>
<th>5–6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dilatation</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>%</td>
<td>0–30</td>
<td>40–50</td>
<td>60–70</td>
<td>80</td>
</tr>
<tr>
<td>Effacement</td>
<td>0–3</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Station</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Consistency</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>NA</td>
</tr>
<tr>
<td>Position</td>
<td>Post</td>
<td>Mid</td>
<td>Ant</td>
<td>NA</td>
</tr>
</tbody>
</table>

NA = not applicable.

Data from Bishop.
limits of this practice. In this study, cesarean delivery rates were 12.0% in women entering labor spontaneously (n = 765), 23.4% in women induced for medical reasons (n = 435), and 23.8% in women electively induced (n = 189). After adjusting for the Bishop score at admission, no significant differences in the rate of cesarean birth were found among the 3 groups of patients. Using a multivariable logistic regression analysis, the authors demonstrated that a Bishop score of 5 or lower is associated with more than double the risk of cesarean delivery, regardless of the indication for induction. They concluded that induction for elective reasons among nulliparous patients should be discouraged in the case of an unripe Bishop score, and especially in the presence of additional risk factors.

Vahratian et al found that cervical ripening before elective induction in nulliparous women increases risk of cesarean delivery by 3.5 times during the first stage of labor, as compared with elective induction that does not require cervical ripening. Elective induction without cervical ripening was associated with a faster labor progression and did not increase the risk of cesarean delivery. As a Foley catheter was used to ripen the cervix in this study, it is possible that direct hormonal methods of cervical ripening may produce a different labor curve. Nonetheless, the evidence in this study, combined with that reported by Vrouenraets et al, point to an increased risk of cesarean delivery among nulliparous women undergoing induction of labor with a low Bishop score, regardless of the cervical ripening method used.

**Prediction of Success**

Although it is not possible to predict precisely the likelihood that an induction will succeed or fail, several factors favor successful vaginal delivery. These factors include: a favorable Bishop score, vertex presentation of the fetus, and multiparous patients without prior uterine incision. Researchers have investigated whether biochemical markers, such as fetal fibronectin (fFN), may be useful in predicting outcome of labor induction. fFN is a glycoprotein present in high concentrations in maternal blood and amniotic fluid, and it is thought to reflect the progress of cervical remodeling prior to labor. A level of 50 ng/mL in cervical-vaginal secretions taken from the posterior vaginal fornix is considered to be a positive predictor of preterm birth.

Garite et al reported that fFN appears to predict which patients will have shorter and easier inductions of labor and lower cesarean section rates, including nulliparous patients with low Bishop scores. Ahner et al reported that patients undergoing induction and who test positive for fFN may have a significantly shorter labor and require fewer prostaglandin tablets. Both of these studies are limited in size, thus they lack sufficient power to establish the reliability of fFN to predict induction and labor outcome. However, if reliability of this marker could be demonstrated, it may aid clinicians in selecting patients for labor induction. A positive fFN assay would predict the onset of spontaneous labor within days, and patients could be counseled to wait. A negative fFN assay, when combined with a low Bishop score, may defer an induction in the absence of a medical indication.

**When Has Induction Failed?**

The typical labor course in inductions is different from that of spontaneous labor. Investigators have reported a foreshortening of all phases of labor, in addition to lengthening of the active phase of labor among nulliparous women requiring cervical ripening before induction. There is currently no consensus as to what constitutes a “failed induction,” which is partly because of the fact that an induced labor may be non-progressive at different cervical dilatation and station. Furthermore, the decision to consider an induction as failed may be influenced by patient parity. One protocol suggested that nulliparous women could safely remain in the latent phase for up to 12 hours. Simon and Grobman conducted a study to determine the most clinically relevant definition of a failed induction of labor among nulliparous women. They studied a cohort of 397 nulliparous women, 32% of whom underwent cervical ripening. They defined the latent phase of labor as starting at the time after oxytocin had been initiated and amniotomy had been performed, and concluding when the patient achieved 4-cm dilatation and 80% effacement or 5-cm dilatation with any degree of effacement. Patients with a latent phase of labor lasting 12 hours had a 59% chance of vaginal delivery, whereas those patients with 18 hours of latent labor still had a 32% chance of vaginal delivery without unacceptable rates of maternal or neonatal complications. Although this study is limited in size and comes from a single institution, it does sug-
gest that a firm line on limiting latency may not be appropriate for all healthy nulliparas.

CERVICAL RIPENING AND INDUCTION AGENTS

Cervical ripening is a complex biochemical process that leads to the alteration of intracervical collagen matrices. An increase in the enzyme cyclooxygenase-2 provokes a local increase of prostaglandin E2 (PGE2) in the cervix, which leads to the cascade of changes collectively referred to as cervical ripening. The cervix thins, softens, relaxes, and opens in response; thus, the uterine contractions can enable the cervix to retract over the presenting fetus, resulting in its vaginal delivery. As noted earlier in this article, the Bishop score may be used to determine the need for cervical ripening agents to facilitate labor induction. Ripening methods fall into 2 broad categories: mechanical methods, which include membrane stripping, osmotic dilators, and balloon catheters, and pharmacologic methods, which include the use of oxytocin, dinoprostone, and misoprostol. There are few comparative trials of cervical ripening methods of sufficient size and reliability that would allow the obstetrician to distinguish a clearly superior method.

MECHANICAL AGENTS

MEMBRANE STRIPPING

Membrane stripping, a practice described in ancient Greek medical writings, is the oldest known method for cervical ripening.30 The technique is accomplished by inserting the examining finger through the internal cervical opening and sweeping 360° to separate the membranes from the lower uterine segment. Membrane stripping is commonly practiced and is begun at 38 completed weeks of gestation and continued weekly thereafter. It is thought to produce cervical ripening by provoking the local release of prostaglandins, and is associated with a greater frequency of spontaneous labor and fewer inductions for postdatism. Efficacy of this approach is controversial. Nulliparous women and women with unfavorable cervixes show the greatest decrease in postdate pregnancies, but other studies have yielded conflicting results.31,32 Complications arising from this technique include infection, inadvertent rupture of the membranes, and bleeding from low-lying or placenta previa. Placenta previa can be avoided with the use of ultrasound imaging for placental localization. The procedure cannot be used if the cervix will not allow passage of at least 1 finger. Published studies are limited and somewhat contradictory, making it difficult to assess the true value of this intervention.

OSMOTIC DILATORS

Laminaria, made from the desiccated stems of cold water seaweed, have been used for cervical ripening for more than 100 years. More recently, synthetic hygroscopic dilators have also become available. They are placed in the endocervix for 4 to 12 hours, increase in diameter 3- to 4-fold primarily by extracting water from cervical tissues, and produce gradual cervical dilatation with minimal discomfort. Their mechanism of action appears to be completely mechanical; typically, they do not stimulate regular uterine contractions. Osmotic dilators are effective in decreasing time to vaginal delivery, but they have several limitations.33 They have been associated with increased maternal postpartum and neonatal infections, thus they should not be used with ruptured membranes.34 It is also essential to carefully document the number of dilators inserted and count them upon removal. Osmotic dilators are advantageous in the outpatient setting, as they can be used without fetal monitoring, and because they have not been implicated in uterine rupture, they can be used safely for cervical ripening in patients who are VBAC candidates.

BALLOON CATHETERS

The most common balloon catheter now in use for cervical ripening is a number 14 Foley with a 30-mL balloon. It is used effectively in a simple protocol developed by Sciscione et al.35 The catheter is passed through the cervix until the balloon is above the internal opening, and then the balloon is inflated with 30 mL of saline. Placed on gentle traction and taped to the patient’s leg, the catheter advances into the endocervical canal as tension is periodically adjusted to maintain a gentle pressure. It is allowed to be expelled spontaneously, after which oxytocin is begun immediately.

Balloon catheters used for cervical ripening can shorten time to vaginal delivery, although in some instances, ripening effects may be limited. The catheter produces a mechanical distension of the lower uterine segment leading to release of prostaglandins, thus making this method mechanical and biologic.36 Intermittent fetal monitoring is required with balloon
ripening, as uterine activity may be stimulated. Limitations of this method include increased infection and bleeding from the cervix. Balloon catheters should not be used with ruptured membranes because of the risk of infection and dislodgement of the presenting part. If membranes are ruptured, the catheter should be removed after slow deflation of the balloon. This method of ripening is appropriate for patients who are candidates for VBAC.

**PHARMACOLOGIC AGENTS**

**OXYTOCIN**

Oxytocin has been traditionally considered an agent for induction of labor rather than cervical ripening. Numerous regimens for intravenous infusion of oxytocin now exist. Sensitivity to oxytocin is influenced by gestational age and maternal parity. However, individual patient response to oxytocin may vary considerably, making “a one size fits all” approach to oxytocin infusion rates impractical and potentially risky. Protocols using low-dose infusions of oxytocin have also been used for cervical ripening. In general practice, oxytocin alone appears to be a poor cervical ripener.37

**PROSTAGLANDINS**

In 1968, successful labor induction using an intravenous prostaglandin analogue infusion was reported for the first time. In subsequent years, investigators documented the efficacy of PGE2 in cervical ripening, and showed that even small doses applied locally result in improved Bishop scores independent of uterine activity and with few systemic side effects.30 Today, 2 prostaglandin analogues are available commercially and in common use for achieving cervical ripening: dinoprostone (PGE2, in 2 formulations) and misoprostol (PGE1), a gastrointestinal medication for treatment of ulcers that is used off-label. Studies attempting to compare the efficacy of both agents are somewhat confusing because of differences in endpoints, which variously include Bishop score, duration of labor, total oxytocin use, successful induction, and cesarean delivery rate. Furthermore, available studies are not adequately powered, enrolling at best 100 or 200 patients.

With close to 1 million inductions of labor performed annually in the United States, the affected population is several orders of magnitude greater than the samples in these studies. Taken as a whole, the published data seem to indicate that both prostaglandin analogues have a comparable efficacy; however, it remains unclear whether use of these agents improve obstetric outcomes.38-40 Administration of prostaglandin analogues usually shorten the process of cervical ripening and induction of labor; clinicians must balance these advantages with complications that accompany their use. It can be stated with some certainty that none of the prostaglandins decrease the rate of cesarean delivery.41 The attributes of commercially available prostaglandin analogues used for cervical ripening are summarized in Table 7.

**DINOPROSTONE/PROSTAGLANDIN E2**

Prostaglandin E2 is currently dosed by intracervical or intravaginal routes. It is available as a gel or as a removable vaginal pessary, and has been shown to decrease time to vaginal delivery when used as a cervical ripener.32 PGE2 has a 3-fold mechanism of action: it softens the cervix by altering the extracellular collagen matrix, it enhances dilatation by relaxing cervical smooth muscle, and it causes uterine contractions. If uterine contractions are inhibited, the effectiveness of PGE2 as a cervical ripener is significantly diminished.43 PGE2 also has 2 other advantageous properties. First, it is rapidly eliminated once it is absorbed. Second, it induces gap junctions in the myometrium, which helps to coordinate uterine contractions. This makes the uterus more responsive to subsequent oxytocin administration. An important limitation to the use of PGE2 as a cervical ripener is the occasional phenomenon of uterine hyperstimulation, which may lead to fetal compromise. Vaginal administration is associated with higher rates of uterine activity when compared with intracervical application, but this limitation is mitigated by the ability to remove the formulation supplied as a controlled-release vaginal pessary.44 Intracervical PGE2 gel is dosed every 6 hours, and generally more than 1 dose is required. At least 50% of patients treated in one study needed 3 doses to achieve cervical ripening, rendering this method an expensive option. Intracervical PGE2 cannot be used with ruptured membranes because it can easily spread into the uterine cavity and cause hyperstimulation. Because of its volume, it cannot be used with cervical effacement of more than 50%, as it will not fit into a cervix of this length. Fetal monitoring is required for at least 2 hours, and must be continued in the presence of contractions. The gel cannot be removed if hyperstimulation occurs.
Intravaginal PGE\textsubscript{2} is dosed in 2 forms: as a locally prepared gel of 2.5 mg in 5 mL of gel, or as a vaginal controlled-release insert available commercially. Locally produced gel is economical, but prone to variation from batch to batch, and in the event of uterine hyperstimulation, cannot be removed. Doses should not be repeated more often than every 4 hours. Fetal monitoring is required for at least 2 hours, and must be continued in the presence of contractions. The controlled-release vaginal insert releases PGE\textsubscript{2} continuously at the rate of 0.3/mg/hr and requires only a single dose, making its additional cost fixed and pre-

<table>
<thead>
<tr>
<th>Table 7. Attributes of Commercially Available Prostaglandin Analogues</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dinoprost (PGE\textsubscript{2} Cervical Gel)</strong></td>
</tr>
<tr>
<td><strong>Description</strong></td>
</tr>
<tr>
<td><strong>FDA status</strong></td>
</tr>
<tr>
<td><strong>Pharmacokinetics</strong></td>
</tr>
<tr>
<td><strong>Initial dose</strong></td>
</tr>
<tr>
<td><strong>Route</strong></td>
</tr>
<tr>
<td><strong>Maximum number of doses</strong></td>
</tr>
<tr>
<td><strong>Mechanisms of action</strong></td>
</tr>
<tr>
<td><strong>Use in VBAC</strong></td>
</tr>
<tr>
<td><strong>Price per dose</strong></td>
</tr>
<tr>
<td><strong>Refrigeration</strong></td>
</tr>
<tr>
<td><strong>Uterine hyperstimulation</strong></td>
</tr>
<tr>
<td><strong>Oxytocin administration</strong></td>
</tr>
<tr>
<td><strong>Efficacy as cervical ripener</strong></td>
</tr>
<tr>
<td><strong>Medicolegal</strong></td>
</tr>
<tr>
<td><strong>Cesarean delivery rate</strong></td>
</tr>
</tbody>
</table>

ACOG = American College of Obstetricians and Gynecologists; FDA = US Food and Drug Administration; PGE\textsubscript{1} = prostaglandin E\textsubscript{1}, PGE\textsubscript{2} = prostaglandin E\textsubscript{2}, VBAC = vaginal birth after cesarean delivery.
dictable. Because of its release profile, continuous fetal monitoring is required because of the risk of hyperstimulation, which is easily reversed by removing the insert and often without the need for tocolytic agents. Comparative trials indicate that intravaginal administration of PGE2 is superior to intracervical application because time to delivery is shorter. Limited data also indicate that the controlled-release vaginal insert is superior to intravaginal gel because more patients using the insert go into labor without oxytocin.45

MISOPROSTOL/PROSTAGLANDIN E1

Misoprostol is a PGE1 analogue approved by the US Food and Drug Administration for use as an ulcer medication. When used off-label for cervical ripening, it can decrease the time to vaginal delivery. Its primary advantages are that it needs no refrigeration and is inexpensive. It acts primarily by producing uterine contractions, and can be administered orally and intravaginally. Studies by Wing et al have determined that the safest regimen involves intravaginal administration of 25 µg of misoprostol.46 Misoprostol should not be used in the presence of any of the following conditions: a Bishop score of 8 or higher, 3 or more contractions in 10 minutes, cervical dilatation of 3 cm or greater, ruptured membranes, or prior uterine scar. Dosing can be repeated every 4 hours, provided none of these conditions develop and no hyperstimulation occurs. The maximum time that cervical ripening with misoprostol should be permitted is 24 hours or 6 total doses. Misoprostol has a higher likelihood of producing excessive uterine activity, especially if used at higher doses than recommended or for longer durations. Continuous fetal monitoring is required with its use.

Misoprostol has several significant disadvantages. It is not formulated for vaginal use, and the oral tablets (100 µg) must be quartered to produce the correct dose. The dose may vary as a result of errors in manually quartering a small pill, and in this final form, it is poorly absorbed. Misoprostol also frequently produces hyperstimulation, which cannot be reversed without resorting to a tocolytic agent. Because of the reported risk of uterine rupture, misoprostol should not be used in patients attempting VBAC. Its use also carries medicolegal considerations for the obstetrician as it carries a black box warning contraindicating use among pregnant women and is being used in an off-label manner.

Pharmacologic approaches to cervical ripening carry the risk of uterine hyperstimulation. Therefore, clinicians who use these approaches should understand the treatment of this complication. The stages of hyperstimulation are defined as: tachysystole (>5 contractions within 10 minutes that are >45 seconds in duration), hyperstimulation (a single contraction lasting 2–3 minutes), and hyperstimulation syndrome (definition of tachysystole and/or hyperstimulation plus nonreassuring fetal heart rate patterns). Depending on the specific method used, treatment may be initiated by device removal if a controlled-release PGE2 vaginal insert is used, or discontinuation of an oxytocin infusion. With all other pharmacologic agents, the use of pharmacologic therapy, such as a β agonist (terbutaline) may be required. Additional measures in any instance may include oxygen administration, intravenous fluid-loading, and left lateral positioning.

CONCLUSIONS

Induction of labor involves not just a single intervention, but a complex set of interventions that present many choices and challenges for clinicians and mothers. Induction of labor is indicated when the benefits to the mother or the fetus outweigh the benefits of continuing the pregnancy. Induction of labor is being used more frequently in the United States for a variety of indications, including logistic factors. It has contributed to the rising rate of cesarean delivery, and as a result, it is increasingly important for practitioners to increase the chances of success when deciding to induce labor.

The factors that predict success include a favorable Bishop score (>8), vertex presentation of the fetus, and multiparous patients without a prior uterine scar. Recent investigations have shown that allowing a longer latent phase (up to 18 hours) can lead to a greater number of vaginal deliveries. Among patients with a prior cesarean delivery attempting vaginal delivery, it is best to avoid uterotonic pharmacologic agents for cervical ripening and rely instead on mechanical methods. Nulliparas who are undergoing induction of labor will experience an increased rate of cesarean delivery.

Recent reports have demonstrated that nulliparas with an unfavorable Bishop score are at especially heightened risk for cesarean delivery, and if induction in these cases is elective, it is best to await the spontaneous onset of labor. In general, elective inductions should be undertaken only when the risk of a failed vaginal delivery is not increased above the level of what would normally be
expected from onset of spontaneous labor. The choice of agents for cervical ripening and induction depends upon clinician preference and the presence or absence of specific contraindications. These considerations, the exercise of particular caution in cases involving nulliparas and parous patients with previous cesarean delivery, and a carefully considered choice of cervical ripening alternatives all contribute to the successful induction of labor.

REFERENCES