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## Induction of Labor

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

*More than 22% of all gravid women undergo induction of labor in the United States, and the overall rate of induction of labor in the United States has more than doubled since 1990 to 225 per 1,000 live births in 2006 (1). The goal of induction of labor is to achieve vaginal delivery by stimulating uterine contractions before the spontaneous onset of labor. Generally, induction of labor has merit as a therapeutic option when the benefits of expeditious delivery outweigh the risks of continuing the pregnancy. The benefits of labor induction must be weighed against the potential maternal and fetal risks associated with this procedure (2). The purpose of this document is to review current methods for cervical ripening and induction of labor and to summarize the effectiveness of these approaches based on appropriately conducted outcomes-based research. These practice guidelines classify the indications for and contraindications to induction of labor, describe the various agents used for cervical ripening, cite methods used to induce labor, and outline the requirements for the safe clinical use of the various methods of inducing labor.*

### Background

In 1948, Theobald and associates described their use of the posterior pituitary extract, oxytocin, by intravenous drip for labor induction (3). Five years later, oxytocin was the first polypeptide hormone synthesized by du Vigneaud and associates (4). This synthetic polypeptide hormone has since been used to stimulate uterine contractions. Other methods used for induction of labor include membrane stripping, amniotomy, nipple stimulation, and administration of prostaglandin E analogues.

### Cervical Ripening

The goal of cervical ripening is to facilitate the process of cervical softening, thinning, and dilating with resultant reduction in the rate of failed induction and

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induction to delivery time. Cervical remodeling is a critical component of normal parturition. Observed changes not only include collagen breakdown and rearrangement but also changes in the glycosaminoglycans, increased production of cytokines, and white blood cell infiltration (5). If induction is indicated and the status of the cervix is unfavorable, agents for cervical ripening may be used. The status of the cervix can be determined by the Bishop pelvic scoring system (Table 1) (6). An unfavorable cervix generally has been defined as a Bishop score of 6 or less in most randomized trials. If the total score is more than 8, the probability of vaginal delivery after labor induction is similar to that after spontaneous labor.

Effective methods for cervical ripening include the use of mechanical cervical dilators and administration of synthetic prostaglandin E<sub>1</sub> (PGE<sub>1</sub>) and prostaglandin E<sub>2</sub> (PGE<sub>2</sub>) (7–10). Mechanical dilation methods are effective in ripening the cervix and include hygroscopic dilators, osmotic dilators (*Laminaria japonicum*), Foley catheters (14–26 F) with inflation volume of 30–80 mL, double balloon devices (Atad Ripener Device), and extraamniotic saline infusion using infusion rates of 30–40 mL/h (11–19). *Laminaria japonicum* ripens the cervix but may be associated with increased peripartum infections (7, 20). In women undergoing induction with an unfavorable cervix, mechanical methods, except extraamniotic saline infusion, are associated with a decreased cesarean delivery rate when compared with oxytocin alone (18). Multiple studies have demonstrated the efficacy of mechanical cervical dilators. There is insufficient evidence to assess how effective (vaginal delivery within 24 hours) mechanical methods are compared with prostaglandins (18). Advantages of the Foley catheter include low cost when compared with prostaglandins, stability at room temperature, and reduced risk of uterine tachysystole with or without fetal heart rate (FHR) changes (18, 21).

Misoprostol, a synthetic PGE<sub>1</sub> analogue, can be administered intravaginally, orally, or sublingually and is used for both cervical ripening and induction of labor. It

currently is available in a 100-mcg (unscored) or a 200-mcg tablet, and can be broken to provide 25-mcg or 50-mcg doses. There is extensive clinical experience with this agent and a large body of published reports supporting its safety and efficacy when used appropriately. No studies indicate that intrapartum exposure to misoprostol (or other prostaglandin cervical ripening agents) has any long-term adverse health consequences to the fetus in the absence of fetal distress, nor is there a plausible biologic basis for such a concern. Although misoprostol currently is approved by the U.S. Food and Drug Administration (FDA) for the prevention of peptic ulcers, the FDA in 2002 approved a new label on the use of misoprostol during pregnancy for cervical ripening and for the induction of labor. This labeling does not contain claims regarding the efficacy or safety of misoprostol, nor does it stipulate doses or dose intervals. The majority of adverse maternal and fetal outcomes associated with misoprostol therapy resulted from the use of doses greater than 25 mcg.

Two PGE<sub>2</sub> preparations are commercially available: a gel available in a 2.5-mL syringe containing 0.5 mg of dinoprostone and a vaginal insert containing 10 mg of dinoprostone. Both are approved by the FDA for cervical ripening in women at or near term. The vaginal insert releases prostaglandins at a slower rate (0.3 mg/h) than the gel. Compared with placebo or oxytocin alone, vaginal prostaglandins used for cervical ripening increase the likelihood of delivery within 24 hours, do not reduce the rate of cesarean delivery, and increase the risk of uterine tachysystole with associated FHR changes (22).

## Methods of Labor Induction

### Oxytocin

Oxytocin is one of the most commonly used drugs in the United States. The physiology of oxytocin-stimulated labor is similar to that of spontaneous labor, although individual patients vary in sensitivity and response to oxytocin. Based on pharmacokinetic studies of synthetic

**Table 1. Bishop Scoring System**

Score	Factor				
	Dilation (cm)	Position of Cervix	Effacement (%)	Station*	Cervical Consistency
0	Closed	Posterior	0–30	–3	Firm
1	1–2	Midposition	40–50	–2	Medium
2	3–4	Anterior	60–70	–1, 0	Soft
3	5–6	—	80	+1, +2	—

\*Station reflects a –3 to +3 scale.

Modified from Bishop EH. Pelvic scoring for elective induction. *Obstet Gynecol* 1964;24:267.

oxytocin, uterine response ensues after 3–5 minutes of infusion, and a steady level of oxytocin in plasma is achieved by 40 minutes (23). The uterine response to oxytocin depends on the duration of the pregnancy; there is a gradual increase in response from 20 to 30 weeks of gestation, followed by a plateau from 34 weeks of gestation until term, when sensitivity increases (24). Lower body mass index and greater cervical dilation, parity, or gestational age are predictors of successful response to oxytocin for induction (25).

### Membrane Stripping

Stripping or sweeping the amniotic membranes is commonly practiced to induce labor. Significant increases in phospholipase A<sub>2</sub> activity and prostaglandin F<sub>2α</sub> (PGF<sub>2α</sub>) levels occur from membrane stripping (26). Stripping membranes increases the likelihood of spontaneous labor within 48 hours and reduces the incidence of induction with other methods (27). Although membrane sweeping has been associated with increased risk of prelabor rupture of membranes (28), other published systematic reviews, including one with 1,525 women, have not corroborated this finding (27). Women who undergo membrane stripping may experience discomfort from the procedure as well as vaginal bleeding and irregular uterine contractions within the ensuing 24 hours (27). There are insufficient data to guide clinical practice for membrane stripping in women whose group B streptococcus culture is positive.

### Amniotomy

Artificial rupture of the membranes may be used as a method of labor induction, especially if the condition of the cervix is favorable. Used alone for inducing labor, amniotomy can be associated with unpredictable and sometimes long intervals before the onset of contractions. There is insufficient evidence on the efficacy and safety of amniotomy alone for labor induction (29). In a trial of amniotomy combined with early oxytocin infusion compared with amniotomy alone, the induction-to-delivery interval was shorter with the amniotomy-plus-oxytocin method (30). There are insufficient data to guide the timing of amniotomy in patients who are receiving intrapartum prophylaxis for group B streptococcal infection.

### Nipple Stimulation

Nipple stimulation or unilateral breast stimulation has been used as a natural and inexpensive nonmedical method for inducing labor. In a systematic review of 6 trials including 719 women that compared breast stimulation with no intervention, a significant decrease in the number of women not in labor at 72 hours was noted, but

only in women with favorable cervixes (31). None of the women had uterine tachysystole with or without FHR changes, and there were no differences in meconium-stained amniotic fluid or cesarean delivery rates (31). Breast stimulation was associated with a decrease in postpartum hemorrhage (31). This method has only been studied in low-risk pregnancies.

### Labor Induction Terminology

At a 2008 workshop sponsored by the American College of Obstetricians and Gynecologists, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, and the Society for Maternal–Fetal Medicine on intrapartum electronic FHR monitoring, the definitions for FHR pattern categorization were reviewed and updated. The existing classification systems for FHR patterns were assessed and new recommendations for use in the United States were made (32). In particular, it was determined that the terms hyperstimulation and hypercontractility should be abandoned. It was recommended that the term tachysystole, with or without corresponding FHR decelerations, be used instead.

### Uterine Contractions

Uterine contractions are quantified as the number of contractions present in a 10-minute window, averaged over 30 minutes. Contraction frequency alone is a partial assessment of uterine activity. Other factors such as duration, intensity, and relaxation time between contractions are equally important in clinical practice. The following represents terminology to describe uterine activity:

- *Normal*: Five contractions or less in 10 minutes, averaged over a 30-minute window
- *Tachysystole*: More than five contractions in 10 minutes, averaged over a 30-minute window

Listed are characteristics of uterine contractions:

- Tachysystole should always be qualified as to the presence or absence of associated FHR decelerations.
- The term tachysystole applies to both spontaneous and stimulated labor. The clinical response to tachysystole may differ depending on whether contractions are spontaneous or stimulated.

The majority of literature cited in this Practice Bulletin was published prior to the 2008 NICHD definitions and interpretations of FHR tracings. Consequently, it is difficult to generalize the results of the cited literature, which used nonstandardized and ambiguous definitions for FHR patterns.

## Clinical Considerations and Recommendations

### ► *What are the indications and contraindications to induction of labor?*

Indications for induction of labor are not absolute but should take into account maternal and fetal conditions, gestational age, cervical status, and other factors. Following are examples of maternal or fetal conditions that may be indications for induction of labor:

- Abruptio placentae
- Chorioamnionitis
- Fetal demise
- Gestational hypertension
- Preeclampsia, eclampsia
- Premature rupture of membranes
- Postterm pregnancy
- Maternal medical conditions (eg, diabetes mellitus, renal disease, chronic pulmonary disease, chronic hypertension, antiphospholipid syndrome)
- Fetal compromise (eg, severe fetal growth restriction, isoimmunization, oligohydramnios)

Labor also may be induced for logistic reasons, for example, risk of rapid labor, distance from hospital, or psychosocial indications. In such circumstances, at least one of the gestational age criteria in the box should be met, or fetal lung maturity should be established. A mature fetal lung test result before 39 weeks of gestation, in the absence of appropriate clinical circumstances, is not an indication for delivery.

The individual patient and clinical situation should be considered in determining when induction of labor is contraindicated. Generally, the contraindications to labor induction are the same as those for spontaneous labor and vaginal delivery. They include, but are not limited to, the following situations:

- Vasa previa or complete placenta previa
- Transverse fetal lie
- Umbilical cord prolapse
- Previous classical cesarean delivery
- Active genital herpes infection
- Previous myomectomy entering the endometrial cavity

### ► *What criteria should be met before the cervix is ripened or labor is induced?*

Assessment of gestational age and consideration of any potential risks to the mother or fetus are of paramount

#### Confirmation of Term Gestation

- Ultrasound measurement at less than 20 weeks of gestation supports gestational age of 39 weeks or greater.
- Fetal heart tones have been documented as present for 30 weeks by Doppler ultrasonography.
- It has been 36 weeks since a positive serum or urine human chorionic gonadotropin pregnancy test result.

importance for appropriate evaluation and counseling before initiating cervical ripening or labor induction. The patient should be counseled regarding the indications for induction, the agents and methods of labor stimulation, and the possible need for repeat induction or cesarean delivery. Although prospective studies are limited in evaluating the benefits of elective induction of labor, nulliparous women undergoing induction of labor with unfavorable cervixes should be counseled about a two-fold increased risk of cesarean delivery (33, 34, 35). In addition, labor progression differs significantly for women with an elective induction of labor compared with women who have spontaneous onset of labor (36). Allowing at least 12–18 hours of latent labor before diagnosing a failed induction may reduce the risk of cesarean delivery (37, 38).

Additional requirements for cervical ripening and induction of labor include assessment of the cervix, pelvis, fetal size, and presentation. Monitoring FHR and uterine contractions is recommended as for any high-risk patient in active labor. Although trained nursing personnel can monitor labor induction, a physician capable of performing a cesarean delivery should be readily available.

### ► *What is the relative effectiveness of available methods for cervical ripening in reducing the duration of labor?*

A systematic review found that in patients with an unfavorable cervix, Foley catheter placement before oxytocin induction significantly reduced the duration of labor (21). This review also concluded that catheter placement resulted in a reduced risk of cesarean delivery. When the Foley catheter was compared with PGE<sub>2</sub> gel, the majority of the studies have found no difference in duration of induction to delivery or cesarean delivery rate. The use of prostaglandins is associated with an increased risk of tachysystole with or without FHR changes when compared with the Foley catheter (21). The use of different size Foley catheters, insufflation volumes, as well as dif-

ferent misoprostol protocols, yields inconsistent results to determine induction to delivery times, cesarean delivery rate, and risk of meconium passage (18, 21). The addition of oxytocin along with the use of the Foley catheter does not appear to shorten the time of delivery in a randomized controlled trial (39).

Studies examining extraamniotic saline infused through the Foley catheter compared with use of the Foley catheter with concurrent oxytocin administration report conflicting results on the time from induction to delivery (19, 40, 41). Differences in methodology could explain the opposing findings. The Foley catheter is a reasonable and effective alternative for cervical ripening and inducing labor.

Intracervical or intravaginal PGE<sub>2</sub> (dinoprostone) commonly is used and is superior to placebo or no therapy in promoting cervical ripening (42). Several prospective randomized clinical trials and two meta-analyses have demonstrated that PGE<sub>1</sub> (misoprostol) is an effective method for cervical ripening (43–48). Misoprostol administered intravaginally has been reported to be either superior to or as efficacious as dinoprostone gel (48–51). Vaginal misoprostol has been associated with less use of epidural analgesia, more vaginal deliveries within 24 hours, and more uterine tachysystole with or without FHR changes compared with dinoprostone and oxytocin (48). In contrast, misoprostol compared with oxytocin for cervical ripening resulted in longer intervals to active labor and delivery in a randomized controlled trial (52). It is difficult, however, to compare the results of studies on misoprostol because of differences in endpoints, including Bishop score, duration of labor, total oxytocin use, successful induction, and cesarean delivery rate. Pharmacologic methods for cervical ripening do not decrease the likelihood of cesarean delivery.

#### ► *How should prostaglandins be administered?*

One quarter of an unscored 100-mcg tablet (ie, approximately 25 mcg) of misoprostol should be considered as the initial dose for cervical ripening and labor induction. The frequency of administration should not be more than every 3–6 hours. In addition, oxytocin should not be administered less than 4 hours after the last misoprostol dose. Misoprostol in higher doses (50 mcg every 6 hours) may be appropriate in some situations, although higher doses are associated with an increased risk of complications, including uterine tachysystole with FHR decelerations.

If there is inadequate cervical change with minimal uterine activity after one dose of intracervical dinoprostone, a second dose may be given 6–12 hours later. The manufacturers recommend a maximum cumulative dose

of 1.5 mg of dinoprostone (three doses or 7.5 mL of gel) within a 24-hour period. A minimum safe time interval between prostaglandin administration and initiation of oxytocin has not been determined. According to the manufacturers' guidelines, after use of 1.5 mg of dinoprostone in the cervix or 2.5 mg in the vagina, oxytocin induction should be delayed for 6–12 hours because the effect of prostaglandins may be heightened with oxytocin. After use of dinoprostone in sustained-release form, delaying oxytocin induction for 30–60 minutes after removal is sufficient. Limited data are available on the use of buccal or sublingual misoprostol for cervical ripening or induction of labor, and these methods are not recommended for clinical use until further studies support their safety (53).

#### ► *What are the potential complications with each method of cervical ripening, and how are they managed?*

Tachysystole with or without FHR changes is more common with vaginal misoprostol compared with vaginal prostaglandin E<sub>2</sub>, intracervical prostaglandin E<sub>2</sub>, and oxytocin (48). Tachysystole (defined in some studies as greater than 5 uterine contractions in 10 minutes in consecutive 10-minute intervals) and tachysystole with associated FHR decelerations are increased with a 50-mcg or greater dose of misoprostol (43, 47, 48, 54). There seems to be a trend toward lower rates of uterine tachysystole with FHR changes with lower dosages of misoprostol (25 mcg every 6 hours versus every 3 hours) (48).

The use of misoprostol in women with prior cesarean delivery or major uterine surgery has been associated with an increase in uterine rupture and, therefore, should be avoided in the third trimester (55, 56). An increase in meconium-stained amniotic fluid also has been reported with misoprostol use (47, 48). Although misoprostol appears to be safe and effective in inducing labor in women with unfavorable cervixes, further studies are needed to determine the optimal route, dosage, timing interval, and pharmacokinetics of misoprostol. Moreover, data are needed on the management of complications related to misoprostol use and when it should be discontinued. If uterine tachysystole and a Category III FHR tracing (defined as either a sinusoidal pattern or an absent baseline FHR variability and any of the following: recurrent late decelerations, recurrent variable decelerations, or bradycardia) occurs with misoprostol use and there is no response to routine corrective measures (maternal repositioning and supplemental oxygen administration), cesarean delivery should be considered (32). Subcutaneous terbutaline also can be used in an attempt to correct the Category III FHR tracing or uterine tachysystole.

The intracervical PGE<sub>2</sub> gel (0.5 mg) has a 1% rate of uterine tachysystole with associated FHR changes while the intravaginal PGE<sub>2</sub> gel (2–5 mg) or vaginal insert is associated with a 5% rate (42, 57, 58). Uterine tachysystole typically begins within 1 hour after the gel or insert is placed but may occur up to 9 1/2 hours after the vaginal insert has been placed (57–59).

Removing the PGE<sub>2</sub> vaginal insert usually will help reverse the effect of uterine tachysystole. Irrigation of the cervix and vagina is not beneficial. Maternal side effects from the use of low-dose PGE<sub>2</sub> (fever, vomiting, and diarrhea) are quite uncommon (60). Prophylactic antiemetics, antipyretics, and antidiarrheal agents usually are not needed. The manufacturers recommend that caution be exercised when using PGE<sub>2</sub> in patients with glaucoma, severe hepatic or renal dysfunction, or asthma. However, PGE<sub>2</sub> is a bronchodilator, and there are no reports of bronchoconstriction or significant blood pressure changes after the administration of the low-dose gel.

Increased maternal and neonatal infections have been reported in connection with the use of *Laminaria japonicum* and hygroscopic dilators when compared with the PGE<sub>2</sub> analogues (7, 13, 20). The Foley catheter can cause significant vaginal bleeding in women with a low-lying placenta (21). Other reported complications include rupture of membranes, febrile morbidity, and displacement of the presenting part (61).

► ***What are the recommended guidelines for fetal surveillance after prostaglandin use?***

The prostaglandin preparations should be administered where uterine activity and the FHR can be monitored continuously for an initial observation period. Further monitoring can be governed by individual indications for induction and fetal status.

The patient should remain recumbent for at least 30 minutes. The FHR and uterine activity should be monitored continuously for a period of 30 minutes to 2 hours after administration of the PGE<sub>2</sub> gel (62). Uterine contractions usually are evident in the first hour and exhibit peak activity in the first 4 hours (62, 63). The FHR monitoring should be continued if regular uterine contractions persist; maternal vital signs also should be recorded.

► ***Are cervical ripening methods appropriate in an outpatient setting?***

Limited information is available on the safety of outpatient management of induction of labor. In a randomized, double-blind, controlled trial comparing 2 mg of intravaginal PGE<sub>2</sub> gel with placebo for 5 consecutive days as

an outpatient procedure, it was noted that PGE<sub>2</sub> gel was effective and safe for initiation of labor in women at term with a Bishop score of 6 or less (64). No significant differences in adverse outcomes were noted in another randomized trial of 300 women at term comparing the use of controlled-release PGE<sub>2</sub> in an outpatient versus inpatient setting (65). Larger controlled studies are needed to establish an effective and safe dose and vehicle for PGE<sub>2</sub> before use on an outpatient basis can be recommended. However, outpatient use may be appropriate in carefully selected patients. Mechanical methods may be particularly appropriate in the outpatient setting. A randomized trial comparing the Foley catheter in an outpatient versus inpatient setting for preinduction cervical ripening demonstrated similar efficacy and safety with a reduction of hospital stay of 9.6 hours (66).

► ***What are the potential complications of various methods of induction?***

The side effects of oxytocin use are principally dose related; uterine tachysystole and Category II or III FHR tracings are the most common side effects. Uterine tachysystole may result in abruptio placentae or uterine rupture. Uterine rupture secondary to oxytocin use is rare even in parous women (67). Water intoxication can occur with high concentrations of oxytocin infused with large quantities of hypotonic solutions, but is rare in doses used for labor induction.

Misoprostol appears to be safe and beneficial for inducing labor in a woman with an unfavorable cervix. Although the exact incidence of uterine tachysystole with or without FHR changes is unknown and the criteria used to define this complication are not always clear in the various reports, there are reports of uterine tachysystole with or without FHR changes occurring more frequently in women given misoprostol compared with women given PGE<sub>2</sub> (43, 45, 48, 68). There does not appear to be a significant increase in adverse fetal outcomes from tachysystole without associated FHR decelerations (68, 69). The occurrence of complications does appear to be dose-dependent (10, 48). Clinical trials have shown that at an equivalent dosage, the vaginal route produces greater clinical efficacy than the oral route (53). Oral misoprostol administration is associated with fewer abnormal FHR patterns and episodes of uterine tachysystole with associated FHR changes when compared with vaginal administration (70, 71).

The potential risks associated with amniotomy include prolapse of the umbilical cord, chorioamnionitis, significant umbilical cord compression, and rupture of vasa previa. The physician should palpate for an umbilical cord and avoid dislodging the fetal head. The FHR

should be assessed before and immediately after amniotomy. Amniotomy for induction of labor may be contraindicated in women known to have HIV infection because duration of ruptured membranes has been identified as an independent risk factor for vertical transmission of HIV infection (29).

Stripping the amniotic membranes is associated with bleeding from undiagnosed placenta previa or low-lying placenta, and accidental amniotomy. Bilateral breast stimulation has been associated with uterine tachysystole with associated FHR decelerations. In a systematic review, breast stimulation was associated with an increased trend in perinatal death (31). Until safety issues are studied further, this practice is not recommended in an unmonitored setting.

► ***When oxytocin is used for induction of labor, what dosage should be used and what precautions should be taken?***

Any of the low- or high-dose oxytocin regimens outlined in Table 2 are appropriate for labor induction (72–78). Low-dose regimens and less frequent increases in dose are associated with decreased uterine tachysystole with associated FHR changes (70). High-dose regimens and more frequent dose increases are associated with shorter labor and less frequent cases of chorioamnionitis and cesarean delivery for dystocia, but increased rates of uterine tachysystole with associated FHR changes (74, 79).

Each hospital's obstetrics and gynecology department should develop guidelines for the preparation and administration of oxytocin. Synthetic oxytocin generally

**Table 2. Labor Stimulation with Oxytocin: Examples of Low- and High-Dose Oxytocin**

Regimen	Starting Dose	Incremental Increase (mU/min)	Dosage Interval (min)
Low-Dose	0.5–2	1–2	15–40
High-Dose	6	3–6*	15–40

\*The incremental increase is reduced to 3 mU/min in presence of hyperstimulation and reduced to 1 mU/min with recurrent hyperstimulation.

Data from Hauth JC, Hankins GD, Gilstrap LC 3rd, Strickland DM, Vance P. Uterine contraction pressures with oxytocin induction/augmentation. *Obstet Gynecol* 1986;68:305–9; Satin AJ, Leveno KJ, Sherman ML, Brewster DS, Cunningham FG. High- versus low-dose oxytocin for labor stimulation. *Obstet Gynecol* 1992;80:111–6; Crane JM, Young DC. Meta-analysis of low-dose versus high-dose oxytocin for labour induction. *J SOGC* 1998;20:1215–23; Cummiskey KC, Dawood MY. Induction of labor with pulsatile oxytocin. *Am J Obstet Gynecol* 1990;163:1868–74; Blakemore KJ, Qin NG, Petrie RH, Paine LL. A prospective comparison of hourly and quarter-hourly oxytocin dose increase intervals for the induction of labor at term. *Obstet Gynecol* 1990;75:757–61; Mercer B, Pilgrim P, Sibai B. Labor induction with continuous low-dose oxytocin infusion: a randomized trial. *Obstet Gynecol* 1991;77:659–63; and Muller PR, Stubbs TM, Laurent SL. A prospective randomized clinical trial comparing two oxytocin induction protocols. *Am J Obstet Gynecol* 1992;167:373–80; discussion 380–1.

is diluted 10 units in 1,000 mL of an isotonic solution for an oxytocin concentration of 10 mU/mL. Oxytocin should be administered by infusion using a pump that allows precise control of the flow rate and permits accurate minute-to-minute control. Bolus administration of oxytocin can be avoided by piggybacking the infusion into the main intravenous line near the venipuncture site.

A numeric value for the maximum dose of oxytocin has not been established. The FHR and uterine contractions should be monitored closely. Oxytocin should be administered by trained personnel who are familiar with its effects.

► ***How should complications associated with oxytocin use be managed?***

If uterine tachysystole with Category III FHR tracings occur, prompt evaluation is required and intravenous infusion of oxytocin should be decreased or discontinued to correct the pattern (32). Additional measures may include turning the woman on her side and administering oxygen or more intravenous fluid. If uterine tachysystole persists, use of terbutaline or other tocolytics may be considered. Hypotension may occur following a rapid intravenous injection of oxytocin; therefore, it is imperative that a dilute oxytocin infusion be used even in the immediate puerperium.

► ***Are there special considerations that apply for induction in a woman with ruptured membranes?***

The largest randomized study to date found that oxytocin induction reduced the time interval between premature rupture of membranes and delivery as well as the frequencies of chorioamnionitis, postpartum febrile morbidity, and neonatal antibiotic treatments, without increasing cesarean deliveries or neonatal infections (80). These data suggest that for women with premature rupture of membranes at term, labor should be induced at the time of presentation, generally with oxytocin infusion, to reduce the risk of chorioamnionitis. An adequate time for the latent phase of labor to progress should be allowed.

The same precautions should be exercised when prostaglandins are used for induction of labor with ruptured membranes as for intact membranes. Intravaginal PGE<sub>2</sub> for induction of labor in women with premature rupture of membranes appears to be safe and effective (81). In a randomized study of labor induction in women with premature rupture of membranes at term, only one dose of intravaginal misoprostol was necessary for successful labor induction in 86% of the patients (67). There is no evidence that use of either of these prostag-

landins increases the risk of infection in women with ruptured membranes (67, 81). There is insufficient evidence to guide the physician on use of mechanical dilators in women with ruptured membranes.

A meta-analysis that included 6,814 women with premature rupture of membranes at term compared induction of labor with prostaglandins or oxytocin to expectant management (82). A significant reduction in the risk of women developing chorioamnionitis or endometritis and a reduced number of neonates requiring admission to the neonatal intensive care unit was noted in the women who underwent induction of labor compared with expectant management (82).

► ***What methods can be used for induction of labor with intrauterine fetal demise in the late second or third trimester?***

The method and timing of delivery after a fetal death depends on the gestational age at which the death occurred, on the maternal history of a previous uterine scar, and maternal preference. Although most patients will desire prompt delivery, the timing of delivery is not critical; coagulopathies are associated with prolonged fetal retention and are uncommon. In the second trimester, dilation and evacuation can be offered if an experienced health care provider is available, although patients should be counseled that dilation and evacuation may limit efficacy of autopsy for the detection of macroscopic fetal abnormalities.

Labor induction is appropriate at later gestational ages, if second-trimester dilation and evacuation is unavailable, or based on patient preference. Much of the data for management of fetal demise has been extrapolated from randomized trials of management of second trimester pregnancy termination. Available evidence from randomized trials supports the use of vaginal misoprostol as a medical treatment to terminate nonviable pregnancies before 24 weeks of gestation (83). Based on limited data, the use of misoprostol between 24 to 28 weeks of gestation also appears to be safe and effective (84, 85). Before 28 weeks of gestation, vaginal misoprostol appears to be the most efficient method of labor induction, regardless of cervical Bishop score (84, 86), although high-dose oxytocin infusion also is an acceptable choice (87, 88). Typical dosages for misoprostol use are 200–400 mcg vaginally every 4–12 hours. After 28 weeks of gestation, induction of labor should be managed according to usual obstetric protocols. Cesarean delivery for fetal demise should be reserved for unusual circumstances because it is associated with potential maternal morbidity without any fetal benefit.

Several studies have evaluated the use of misoprostol at a dosage of 400 mcg every 6 hours in women with a stillbirth up to 28 weeks of gestation and a prior uterine scar (85, 89). There does not appear to be an increase in complications in those women. Further research is required to assess effectiveness and safety, optimal route of administration, and dose.

In patients after 28 weeks of gestation, cervical ripening with a transcervical Foley catheter has been associated with uterine rupture rates comparable to spontaneous labor (90) and this may be a helpful adjunct in patients with an unfavorable cervical assessment. Therefore, in patients with a prior low transverse cesarean delivery, trial of labor remains a favorable option. There are limited data to guide clinical practice in a patient with a prior classical cesarean delivery, and the delivery plan should be individualized.

## **Summary of Recommendations and Conclusions**

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

- Prostaglandin E analogues are effective for cervical ripening and inducing labor.
- Low- or high-dose oxytocin regimens are appropriate for women in whom induction of labor is indicated (Table 2).
- Before 28 weeks of gestation, vaginal misoprostol appears to be the most efficient method of labor induction regardless of Bishop score, although high-dose oxytocin infusion also is an acceptable choice.
- Approximately 25 mcg of misoprostol should be considered as the initial dose for cervical ripening and labor induction. The frequency of administration should not be more than every 3–6 hours.
- Intravaginal PGE<sub>2</sub> for induction of labor in women with premature rupture of membranes appears to be safe and effective.
- The use of misoprostol in women with prior cesarean delivery or major uterine surgery has been associated with an increase in uterine rupture and, therefore, should be avoided in the third trimester.
- The Foley catheter is a reasonable and effective alternative for cervical ripening and inducing labor.

***The following recommendation is based on evidence that may be limited or inconsistent (Level B)***

- ▶ Misoprostol (50 mcg every 6 hours) to induce labor may be appropriate in some situations, although higher doses are associated with an increased risk of complications, including uterine tachysystole with FHR decelerations.

## Proposed Performance Measure

Percentage of patients in whom gestational age is established by clinical criteria when labor is being induced for logistic or psychosocial indications

## References

1. Martin JA, Hamilton BE, Sutton PD, Ventura SJ, Menacker F, Kirmeyer S, et al. Births: final data for 2006. *Natl Vital Stat Rep* 2009;57:1–102. (Level II-3)
2. Agency for Healthcare Research and Quality. Maternal and neonatal outcomes of elective induction of labor. AHRQ Evidence Report/Technology Assessment No. 176. Rockville (MD): AHRQ; 2009. (Systematic review)
3. Theobald GW, Graham A, Campbell J, Gange PD, Driscoll WJ. Use of post-pituitary extract in obstetrics. *Br Med J* 1948;2:123–7. (Level III)
4. du Vigneaud V, Ressler C, Swan JM, Roberts CW, Katsoyannis PG, Gordon S. The synthesis of an octapeptide amide with the hormonal activity of oxytocin. *J Am Chem Soc* 1953;75:4879–80. (Level III)
5. Smith R. Parturition. *N Engl J Med* 2007;356:271–83. (Level III)
6. Bishop EH. Pelvic scoring for elective induction. *Obstet Gynecol* 1964;24:266–8. (Level III)
7. Krammer J, Williams MC, Sawai SK, O'Brien WF. Preinduction cervical ripening: a randomized comparison of two methods. *Obstet Gynecol* 1995;85:614–8. (Level I)
8. Fletcher HM, Mitchell S, Simeon D, Frederick J, Brown D. Intravaginal misoprostol as a cervical ripening agent. *Br J Obstet Gynaecol* 1993;100:641–4. (Level I)
9. Porto M. The unfavorable cervix: methods of cervical priming. *Clin Obstet Gynecol* 1989;32:262–8. (Level III)
10. Wing DA, Jones MM, Rahall A, Goodwin TM, Paul RH. A comparison of misoprostol and prostaglandin E2 gel for preinduction cervical ripening and labor induction. *Am J Obstet Gynecol* 1995;172:1804–10. (Level I)
11. Atad J, Hallak M, Ben-David Y, Auslender R, Abramovici H. Ripening and dilatation of the unfavourable cervix for induction of labour by a double balloon device: experience with 250 cases. *Br J Obstet Gynaecol* 1997;104:29–32. (Level III)
12. Blumenthal PD, Ramanauskas R. Randomized trial of Dilapan and Laminaria as cervical ripening agents before induction of labor. *Obstet Gynecol* 1990;75:365–8. (Level I)
13. Chua S, Arulkumaran S, Vanaja K, Ratnam SS. Preinduction cervical ripening: prostaglandin E2 gel vs hygroscopic mechanical dilator. *J Obstet Gynaecol Res* 1997;23:171–7. (Level I)
14. Gilson GJ, Russell DJ, Izquierdo LA, Qualls CR, Curet LB. A prospective randomized evaluation of a hygroscopic cervical dilator, Dilapan, in the preinduction ripening of patients undergoing induction of labor. *Am J Obstet Gynecol* 1996;175:145–9. (Level I)
15. Lin A, Kupferminc M, Dooley SL. A randomized trial of extra-amniotic saline infusion versus laminaria for cervical ripening. *Obstet Gynecol* 1995;86:545–9. (Level I)
16. Lyndrup J, Nickelsen C, Weber T, Molnitz E, Guldbaek E. Induction of labour by balloon catheter with extra-amniotic saline infusion (BCEAS): a randomised comparison with PGE2 vaginal pessaries. *Eur J Obstet Gynecol Reprod Biol* 1994;53:189–97. (Level I)
17. Mullin PM, House M, Paul RH, Wing DA. A comparison of vaginally administered misoprostol with extra-amniotic saline solution infusion for cervical ripening and labor induction. *Am J Obstet Gynecol* 2002;187:847–52. (Level I)
18. Boulvain M, Kelly A, Lohse C, Stan C, Irion O. Mechanical methods for induction of labour. *Cochrane Database of Systematic Reviews* 2001, Issue 4. Art. No.: CD001233. DOI: 10.1002/14651858.CD001233. (Level III)
19. Guinn DA, Davies JK, Jones RO, Sullivan L, Wolf D. Labor induction in women with an unfavorable Bishop score: randomize controlled trial of intrauterine Foley catheter with concurrent oxytocin infusion versus Foley catheter with extra-amniotic saline infusion with concurrent oxytocin infusion. *Am J Obstet Gynecol* 2004;191:225–9. (Level I)
20. Kazzi GM, Bottoms SF, Rosen MG. Efficacy and safety of Laminaria digitata for preinduction ripening of the cervix. *Obstet Gynecol* 1982;60:440–3. (Level II-2)
21. Gelber S, Sciscione A. Mechanical methods of cervical ripening and labor induction. *Clin Obstet Gynecol* 2006;49:642–57. (Level III)
22. Kelly AJ, Kavanagh J, Thomas J. Vaginal prostaglandin (PGE2 and PGF2a) for induction of labour at term. *Cochrane Database of Systematic Reviews* 2003, Issue 4. Art. No.: CD003101. DOI: 10.1002/14651858.CD003101. (Level III)
23. Seitchik J, Amico J, Robinson AG, Castillo M. Oxytocin augmentation of dysfunctional labor. IV. Oxytocin pharmacokinetics. *Am J Obstet Gynecol* 1984;150:225–8. (Level III)
24. Caldeyro-Barcia R, Poseiro JJ. Physiology of the uterine contraction. *Clin Obstet Gynecol* 1960;3:386–408. (Level III)
25. Satin AJ, Leveno KJ, Sherman ML, McIntire DD. Factors affecting the dose response to oxytocin for labor stimulation. *Am J Obstet Gynecol* 1992;166:1260–1. (Level II-3)

26. McColgin SW, Bennett WA, Roach H, Cowan BD, Martin JN Jr, Morrison JC. Parturitional factors associated with membrane stripping. *Am J Obstet Gynecol* 1993;169:71–7. (Level I)
27. Boulvain M, Stan C, Irion O. Membrane sweeping for induction of labour. *Cochrane Database of Systematic Reviews* 2005, Issue 1. Art. No.: CD000451. DOI: 10.1002/14651858.CD000451.pub2. (Level III)
28. Hill MJ, McWilliams GD, Garcia-Sur D, Chen B, Munroe M, Hoeldtke NJ. The effect of membrane sweeping on prelabor rupture of membranes: a randomized controlled trial. *Obstet Gynecol* 2008;111:1313–9. (Level I)
29. Bricker L, Luckas M. Amniotomy alone for induction of labour. *Cochrane Database of Systematic Reviews* 2000, Issue 4. Art. No.: CD002862. DOI: 10.1002/14651858.CD002862. (Level III)
30. Moldin PG, Sundell G. Induction of labour: a randomised clinical trial of amniotomy versus amniotomy with oxytocin infusion. *Br J Obstet Gynaecol* 1996;103:306–12. (Level I)
31. Kavanagh J, Kelly AJ, Thomas J. Breast stimulation for cervical ripening and induction of labour. *Cochrane Database of Systematic Reviews* 2005, Issue 3. Art. No.: CD003392. DOI: 10.1002/14651858.CD003392.pub2. (Level III)
32. Macones GA, Hankins GDV, Spong CY, Hauth J, Moore T. The 2008 National Institute of Child Health and Human Development Workshop Report on Electronic Fetal Monitoring. *Obstet Gynecol* 2008;11:661–6. (Level III)
33. Moore LE, Rayburn WF. Elective induction of labor. *Clin Obstet Gynecol* 2006;49:698–704. (Level III)
34. Luthy DA, Malmgren JA, Zingheim RW. Cesarean delivery after elective induction in nulliparous women: the physician effect. *Am J Obstet Gynecol* 2004;191:1511–5. (Level II-2)
35. Vrouwenraets FP, Roumen FJ, Dehing CJ, van den Akker ES, Aarts MJ, Scheve EJ. Bishop score and risk of cesarean delivery after induction of labor in nulliparous women. *Obstet Gynecol* 2005;105:690–7. (Level II-2)
36. Vahratian A, Zhang J, Troendle JF, Sciscione AC, Hoffman MK. Labor progression and risk of cesarean delivery in electively induced nulliparas. *Obstet Gynecol* 2005;105:698–704. (Level II-2)
37. Rouse DJ, Owen J, Hauth JC. Criteria for failed labor induction: prospective evaluation of a standardized protocol. *Obstet Gynecol* 2000;96:671–7. (Level II-3)
38. Simon CE, Grobman WA. When has an induction failed? *Obstet Gynecol* 2005;105:705–9. (Level II-2)
39. Pettker CM, Pocock SB, Smok DP, Lee SM, Devine PC. Transcervical Foley catheter with and without oxytocin for cervical ripening: a randomized controlled trial. *Obstet Gynecol* 2008;111:1320–6. (Level I)
40. Karjane NW, Brock EL, Walsh SW. Induction of labor using a Foley balloon, with and without extra-amniotic saline infusion. *Obstet Gynecol* 2006;107:234–9. (Level II-1)
41. Lin MG, Reid KJ, Treaster MR, Nuthalapaty FS, Ramsey PS, Lu GC. Transcervical Foley catheter with and without extraamniotic saline infusion for labor induction: a randomized controlled trial. *Obstet Gynecol* 2007;110:558–65. (Level I)
42. Rayburn WF. Prostaglandin E2 gel for cervical ripening and induction of labor: a critical analysis. *Am J Obstet Gynecol* 1989;160:529–34. (Level III)
43. Buser D, Mora G, Arias F. A randomized comparison between misoprostol and dinoprostone for cervical ripening and labor induction in patients with unfavorable cervixes. *Obstet Gynecol* 1997;89:581–5. (Level I)
44. Sanchez-Ramos L, Kaunitz AM, Wears RL, Delke I, Gaudier FL. Misoprostol for cervical ripening and labor induction: a meta-analysis. *Obstet Gynecol* 1997;89:633–42. (Level III)
45. Sanchez-Ramos L, Peterson DE, Delke I, Gaudier FL, Kaunitz AM. Labor induction with prostaglandin E1 misoprostol compared with dinoprostone vaginal insert: a randomized trial. *Obstet Gynecol* 1998;91:401–5. (Level I)
46. Srisomboon J, Piyamongkol W, Aiewsakul P. Comparison of intracervical and intravaginal misoprostol for cervical ripening and labour induction in patients with an unfavourable cervix. *J Med Assoc Thai* 1997;80:189–94. (Level I)
47. Wing DA, Rahall A, Jones MM, Goodwin TM, Paul RH. Misoprostol: an effective agent for cervical ripening and labor induction. *Am J Obstet Gynecol* 1995;172:1811–6. (Level I)
48. Hofmeyr GJ, Gulmezoglu AM. Vaginal misoprostol for cervical ripening and induction of labour. *Cochrane Database of Systematic Reviews* 2003, Issue 1. Art. No.: CD000941. DOI: 10.1002/14651858.CD000941. (Level III)
49. Gregson S, Waterstone M, Norman I, Murrells T. A randomised controlled trial comparing low dose vaginal misoprostol and dinoprostone vaginal gel for inducing labour at term. *BJOG* 2005;112:438–44. (Level I)
50. Garry D, Figueroa R, Kalish RB, Catalano CJ, Maulik D. Randomized controlled trial of vaginal misoprostol versus dinoprostone vaginal insert for labor induction. *J Matern Fetal Neonatal Med* 2003;13:254–9. (Level I)
51. Pandis GK, Papageorghiou AT, Ramanathan VG, Thompson MO, Nicolaides KH. Preinduction sonographic measurement of cervical length in the prediction of successful induction of labor. *Ultrasound Obstet Gynecol* 2001;18:623–8. (Level II-3)
52. Fonseca L, Wood HC, Lucas MJ, Ramin SM, Phatak D, Gilstrap LC 3rd, et al. Randomized trial of preinduction cervical ripening: misoprostol vs oxytocin. *Am J Obstet Gynecol* 2008;199(3):305.e1–5. (Level I)
53. Muzonzini G, Hofmeyr GJ. Buccal or sublingual misoprostol for cervical ripening and induction of labour. *Cochrane Database of Systematic Reviews* 2004, Issue 4. Art. No.: CD004221. DOI: 10.1002/14651858.CD004221.pub2. (Level III)
54. Magtibay PM, Ramin KD, Harris DY, Ramsey PS, Ogburn PL Jr. Misoprostol as a labor induction agent. *J Matern Fetal Med* 1998;7:15–8. (Level I)
55. Wing DA, Lovett K, Paul RH. Disruption of prior uterine incision following misoprostol for labor induction in

- women with previous cesarean delivery. *Obstet Gynecol* 1998;91:828–30. (Level III)
56. Induction of labor for VBAC. ACOG Committee Opinion No. 342. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2006;108:465–7. (Level III)
  57. Rayburn WF, Wapner RJ, Barss VA, Spitzberg E, Molina RD, Mandsager N, et al. An intravaginal controlled-release prostaglandin E2 pessary for cervical ripening and initiation of labor at term. *Obstet Gynecol* 1992;79:374–9. (Level I)
  58. Witter FR, Rocco LE, Johnson TR. A randomized trial of prostaglandin E2 in a controlled-release vaginal pessary for cervical ripening at term. *Am J Obstet Gynecol* 1992;166:830–4. (Level I)
  59. Witter FR, Mercer BM. Improved intravaginal controlled-release prostaglandin E2 insert for cervical ripening at term. The Prostaglandin E2 insert Study Group. *J Matern Fetal Med* 1996;5:64–9. (Level I)
  60. Brindley BA, Sokol RJ. Induction and augmentation of labor: basis and methods for current practice. *Obstet Gynecol Surv* 1988;43:730–43. (Level III)
  61. Sherman DJ, Frenkel E, Tovbin J, Arieli S, Caspi E, Bukovsky I. Ripening of the unfavorable cervix with extraamniotic catheter balloon: clinical experience and review. *Obstet Gynecol Surv* 1996;51:621–7. (Level III)
  62. Bernstein P. Prostaglandin E2 gel for cervical ripening and labour induction: a multicentre placebo-controlled trial. *CMAJ* 1991;145:1249–54. (Level I)
  63. Miller AM, Rayburn WF, Smith CV. Patterns of uterine activity after intravaginal prostaglandin E2 during preinduction cervical ripening. *Am J Obstet Gynecol* 1991;165:1006–9. (Level II-1)
  64. O'Brien JM, Mercer BM, Cleary NT, Sibai BM. Efficacy of outpatient induction with low-dose intravaginal prostaglandin E2: a randomized, double-blind, placebo-controlled trial. *Am J Obstet Gynecol* 1995;173:1855–9. (Level I)
  65. Biem SR, Turnell RW, Olatunbosun O, Tauh M, Biem HJ. A randomized controlled trial of outpatient versus inpatient labour induction with vaginal controlled-release prostaglandin-E2: effectiveness and satisfaction. *J Obstet Gynaecol Can* 2003;25:23–31. (Level I)
  66. Sciscione AC, Muench M, Pollock M, Jenkins TM, Tildon-Burton J, Colmorgen GH. Transcervical Foley catheter for preinduction cervical ripening in an outpatient versus inpatient setting. *Obstet Gynecol* 2001;98:751–6. (Level I)
  67. Flannely GM, Turner MJ, Rassmussen MJ, Stronge JM. Rupture of the uterus in Dublin; an update. *J Obstet Gynaecol* 1993;13:440–3. (Level II-3)
  68. Sanchez-Ramos L, Chen AH, Kaunitz AM, Gaudier FL, Delke I. Labor induction with intravaginal misoprostol in term premature rupture of membranes: a randomized study. *Obstet Gynecol* 1997;89:909–12. (Level I)
  69. Wing DA, Ortiz-Omphroy G, Paul RH. A comparison of intermittent vaginal administration of misoprostol with continuous dinoprostone for cervical ripening and labor induction. *Am J Obstet Gynecol* 1997;177:612–8. (Level I)
  70. Topozada MK, Anwar MY, Hassan HA, el-Gazaerly WS. Oral or vaginal misoprostol for induction of labor. *Int J Gynaecol Obstet* 1997;56:135–9. (Level I)
  71. Weeks A, Alfievic Z. Oral misoprostol administration for labor induction. *Clin Obstet Gynecol* 2006;49:658–71. (Level III)
  72. Hauth JC, Hankins GD, Gilstrap LC 3rd, Strickland DM, Vance P. Uterine contraction pressures with oxytocin induction/augmentation. *Obstet Gynecol* 1986;68:305–9. (Level II-2)
  73. Satin AJ, Leveno KJ, Sherman ML, Brewster DS, Cunningham FG. High- versus low-dose oxytocin for labor stimulation. *Obstet Gynecol* 1992;80:111–6. (Level II-1)
  74. Crane JM, Young DC. Meta-analysis of low-dose versus high-dose oxytocin for labour induction. *J SOGC* 1998;20:1215–23. (Level III)
  75. Cummiskey KC, Dawood MY. Induction of labor with pulsatile oxytocin. *Am J Obstet Gynecol* 1990;163:1868–74. (Level I)
  76. Blakemore KJ, Qin NG, Petrie RH, Paine LL. A prospective comparison of hourly and quarter-hourly oxytocin dose increase intervals for the induction of labor at term. *Obstet Gynecol* 1990;75:757–61. (Level I)
  77. Mercer B, Pilgrim P, Sibai B. Labor induction with continuous low-dose oxytocin infusion: a randomized trial. *Obstet Gynecol* 1991;77:659–63. (Level I)
  78. Muller PR, Stubbs TM, Laurent SL. A prospective randomized clinical trial comparing two oxytocin induction protocols. *Am J Obstet Gynecol* 1992;167:373–80; discussion 380–1. (Level I)
  79. Hannah ME, Ohlsson A, Farine D, Hewson SA, Hodnett ED, Myhr TL, et al. Induction of labor compared with expectant management for prelabor rupture of the membranes at term. TERMPROM Study Group. *N Engl J Med* 1996;334:1005–10. (Level I)
  80. Merrill DC, Zlatnik FJ. Randomized, double-masked comparison of oxytocin dosage in induction and augmentation of labor. *Obstet Gynecol* 1999;94:455–63. (Level I)
  81. Ray DA, Garite TJ. Prostaglandin E2 for induction of labor in patients with premature rupture of membranes at term. *Am J Obstet Gynecol* 1992;166:836–43. (Level I)
  82. Dare MR, Middleton P, Crowther CA, Flenady VJ, Varatharaju B. Planned early birth versus expectant management (waiting) for prelabour rupture of membranes at term (37 weeks or more). *Cochrane Database of Systematic Reviews* 2006, Issue 1. Art. No.: CD005302. DOI: 10.1002/14651858.CD005302.pub2. (Level III)
  83. Neilson JP, Hickey M, Vazquez J. Medical treatment for early fetal death (less than 24 weeks). *Cochrane Database of Systematic Reviews* 2006, Issue 3. Art. No.: CD002253. DOI: 10.1002/14651858.CD002253.pub3. (Level I)
  84. Dickinson JE, Evans SF. The optimization of intravaginal misoprostol dosing schedules in second-trimester pregnancy termination [published erratum appears in *Am J Obstet Gynecol* 2005;193:597]. *Am J Obstet Gynecol* 2002;186:470–4. (Level I)

85. Dickinson JE. Misoprostol for second-trimester pregnancy termination in women with a prior cesarean delivery. *Obstet Gynecol* 2005;105:352–6. (Level II-2)
86. Tang OS, Lau WN, Chan CC, Ho PC. A prospective randomised comparison of sublingual and vaginal misoprostol in second trimester termination of pregnancy. *BJOG* 2004;111:1001–5. (Level I)
87. Toaff R, Ayalon D, Gogol G. Clinical use of high concentration oxytocin drip. *Obstet Gynecol* 1971;37:112–20. (Level II-3)
88. Winkler CL, Gray SE, Hauth JC, Owen J, Tucker JM. Mid-second-trimester labor induction: concentrated oxytocin compared with prostaglandin E2 vaginal suppositories. *Obstet Gynecol* 1991;77:297–300. (Level II-3)
89. Daskalakis GJ, Mesogitis SA, Papantoniou NE, Mouloupoulos GG, Papapanagiotou AA, Antsaklis AJ. Misoprostol for second trimester pregnancy termination in women with prior caesarean section. *BJOG* 2005;112:97–9. (Level II-2)
90. Bujold E, Blackwell SC, Gauthier RJ. Cervical ripening with transcervical Foley catheter and the risk of uterine rupture. *Obstet Gynecol* 2004;103:18–23. (Level II-2)

The MEDLINE database, the Cochrane Library, and ACOG’s own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 1985 and January 2009. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles. When reliable research was not available, expert opinions from obstetrician–gynecologists were used.

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

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

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

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

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

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

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