

# Methods for Cervical Ripening and Induction of Labor

JOSIE L. TENORE, M.D., S.M., Northwestern University Medical School, Chicago, Illinois

Induction of labor is common in obstetric practice. According to the most current studies, the rate varies from 9.5 to 33.7 percent of all pregnancies annually. In the absence of a ripe or favorable cervix, a successful vaginal birth is less likely. Therefore, cervical ripening or preparedness for induction should be assessed before a regimen is selected. Assessment is accomplished by calculating a Bishop score. When the Bishop score is less than 6, it is recommended that a cervical ripening agent be used before labor induction. Nonpharmacologic approaches to cervical ripening and labor induction have included herbal compounds, castor oil, hot baths, enemas, sexual intercourse, breast stimulation, acupuncture, acupressure, transcutaneous nerve stimulation, and mechanical and surgical modalities. Of these nonpharmacologic methods, only the mechanical and surgical methods have proven efficacy for cervical ripening or induction of labor. Pharmacologic agents available for cervical ripening and labor induction include prostaglandins, misoprostol, mifepristone, and relaxin. When the Bishop score is favorable, the preferred pharmacologic agent is oxytocin. (Am Fam Physician 2003;67:2123-8. Copyright© 2003 American Academy of Family Physicians.)

See page 2050 for definitions of strength-of-evidence levels.



Labor is a process through which the fetus moves from the intrauterine to the extrauterine environment. It is a clinical diagnosis defined as the initiation and perpetuation of uterine contractions with the goal of producing progressive cervical effacement and dilation. The exact mechanisms responsible for this process are currently not well understood.<sup>1</sup> Induction of labor refers to the process whereby uterine contractions are initiated by medical or surgical means before the onset of spontaneous labor.

Over the past few years, there has been an increasing awareness that if the cervix is unfavorable, a successful vaginal birth is less likely. Various scoring systems for cervical assessment have been introduced. In 1964, Bishop systematically evaluated a group of multiparous women for elective induction and developed a standardized cervical scoring system. The Bishop score (Table 1)<sup>1</sup> helps delineate patients who would be most likely to achieve a successful induction. The duration of labor is inversely correlated with the Bishop score; a score that exceeds 8 describes the patient most likely to achieve a successful vaginal birth. Bishop scores of less than 6 usually require that a cervical ripening method be used before other methods.<sup>2-4</sup>

TABLE 1  
Bishop Score

*The rightsholder did not grant rights to reproduce this item in electronic media. For the missing item, see the original print version of this publication.*

## Nonpharmacologic Cervical Ripening

### HERBAL SUPPLEMENTS

Given rapid growth in the herbal-supplement industry, it is not surprising that patients request information about alternative agents for labor induction. Com-

See editorial on page 2076.

*Infection, bleeding, membrane rupture, and placental disruption are potential risks of using mechanical methods for cervical ripening.*

monly prescribed agents include evening primrose oil, black haw, black and blue cohosh, and red raspberry leaves. Although evening primrose oil is the remedy most commonly used by midwives,<sup>5</sup> it is unclear whether this substance can ripen the cervix or induce labor. Black haw, which has been described as having a uterine tonic effect,<sup>6</sup> has been used to prepare women for labor. Black cohosh has a similar mechanism of action, while blue cohosh may stimulate uterine contractions. Red raspberry leaves are used to enhance uterine contractions once labor is initiated. The risks and benefits of these agents are still unknown because the quality of evidence is based on a long tradition of use by a certain population<sup>6</sup> and anecdotal case reports. The only conclusion that can be made at this time is that the role of herbal remedies in cervical ripening or labor induction is still uncertain.<sup>7</sup>

#### **CASTOR OIL, HOT BATHS, AND ENEMAS**

Castor oil, hot baths, and enemas also have been recommended for cervical ripening or labor induction. The mechanisms of action for these methods are unknown. Review of the literature indicates that one poorly designed study involving 100 participants studied castor oil versus no treatment. While there did not appear to be any difference in obstetric or neonatal outcomes, all women ingesting the castor oil reported being nauseated. At this time, no evidence supports the use of these three modalities as viable methods for cervical ripening or labor induction.<sup>7,8</sup>

---

#### **The Author**

JOSIE L. TENORE, M.D., S.M., is a full-time faculty member and assistant professor in the Department of Family Medicine at Northwestern University Medical School, Chicago, and Evanston Northwestern Healthcare. She received her medical training at the University of Toronto Faculty of Medicine, Ontario, and earned a master of science degree in maternal and child health at Harvard School of Public Health, Boston.

*Address correspondence to Josie L. Tenore, M.D., S.M., Northwestern University Medical School, Department of Family Medicine, 303 E. Chicago Ave., Chicago, IL 60611 (e-mail: josietenore@hotmail.com). Reprints are not available from the author.*

#### **SEXUAL INTERCOURSE**

Sexual intercourse is commonly recommended for promoting labor initiation. Sexual relations usually involve stimulation of the breasts and nipples, which can promote the release of oxytocin. With penetration, the lower uterine segment is stimulated. This stimulation results in a local release of prostaglandins. Female orgasms have been shown to include uterine contractions, and human semen contains prostaglandins, which are responsible for cervical ripening. Only one study of 28 women resulted in minimally useful data, so the role of sexual intercourse as a method of promoting labor initiation remains uncertain.<sup>7,9</sup> [Reference 9—Evidence level B, systematic review of nonrandomized controlled trials]

#### **BREAST STIMULATION**

Breast massage and nipple stimulation have been shown to facilitate the release of oxytocin from the posterior pituitary gland. The most commonly prescribed technique involves gently massaging the breasts or applying warm compresses to the breasts for one hour, three times a day. Oxytocin is released, and studies have demonstrated an abnormal fetal heart rate (FHR) tracing similar to that occurring in oxytocin challenge testing in higher-risk pregnancies. This abnormal rate may be caused by a reduction in placental perfusion and fetal hypoxia.<sup>7</sup> Two poorly designed studies conducted in the 1970s and 1980s demonstrated a difference in the intervention groups, but the poor study design suggests that evidence is lacking to support breast stimulation as a viable method of inducing labor.<sup>7</sup>

#### **ACUPUNCTURE/TRANSCUTANEOUS NERVE STIMULATION**

Acupuncture involves the insertion of very fine needles into designated locations with the purpose of preventing or curing disease. In the Chinese system of medicine, it is thought that acupuncture stimulates channels of qi (pronounced “chee”), or energy. This energy flows along 12 meridians, with designated points along these meridians. Each point is given a name and a number and is associated with a specific organ system or function.<sup>10</sup>

In Western medicine, it is thought that acupuncture and transcutaneous nerve stimulation (TENS) may stimulate the release of prostaglandins and oxytocin. Most of the studies involving acupuncture were poorly designed and do not meet the rigorous criteria for analysis set forth by the

**TABLE 2**  
**Technique for Insertion of Hygroscopic Dilators**

The perineum and vagina are prepped with antiseptic. Using a sterile speculum examination to visualize the cervix, the dilator is introduced into the endocervix, allowing the "tails" to fall into the vagina. Dilators are progressively placed until the endocervix is "full." The number of dilators used is noted in the medical record. A sterile gauze pad is placed in the vagina to maintain the position of the dilators.

*Information from Adair CD. Nonpharmacologic approaches to cervical priming and labor induction. Clin Obstet Gynecol 2000;43:447-54.*

Cochrane reviewers. A well-designed randomized controlled trial (RCT) is needed to evaluate the role of acupuncture and TENS in labor induction.<sup>11</sup> [Evidence level B, systematic review of non-RCTs]

#### MECHANICAL MODALITIES

All mechanical modalities share a similar mechanism of action—namely, some form of local pressure that stimulates the release of prostaglandins.<sup>1</sup> The risks associated with these methods include infection (endometritis and neonatal sepsis have been associated with natural osmotic dilators), bleeding, membrane rupture, and placental disruption.

Hygroscopic dilators absorb endocervical and local tissue fluids, causing the device to expand within the endocervix and providing controlled mechanical pressure. The products available include natural osmotic dilators (e.g., Laminaria japonicum) and synthetic osmotic dilators (e.g., Lamichel). The main advantages of using hygroscopic dilators include outpatient placement and no FHR-monitoring requirements. The technique for placing hygroscopic dilators is described in *Table 2*.<sup>7</sup>

Balloon devices provide mechanical pressure directly on the cervix as the balloon is filled. A Foley catheter (26 Fr) or specifically designed balloon devices can be used. The technique is described in *Table 3*.<sup>7,12-15</sup>

Currently, several RCTs are comparing use of a balloon device with administration of an extra-amniotic saline infusion, laminaria, or prostaglandin E<sub>2</sub> (PGE<sub>2</sub>). Results from these trials indicate that each of these methods is

effective for cervical ripening and each has comparable cesarean-section delivery rates in women with an unfavorable cervix.<sup>12-14,16-18</sup> [References 12 through 14, 16, and 17—Evidence level A, RCT]

#### SURGICAL METHODS

*Stripping of the Membranes.* Stripping of the membranes causes an increase in the activity of phospholipase A<sub>2</sub> and prostaglandin F<sub>2α</sub> (PGF<sub>2α</sub>) as well as causing mechanical dilation of the cervix, which releases prostaglandins. The membranes are stripped by inserting the examining finger through the internal cervical os and moving it in a circular direction to detach the inferior pole of the membranes from the lower uterine segment.<sup>7,19</sup> [Reference 19—Evidence level C, consensus opinion] Risks of this technique include infection, bleeding, accidental rupture of the membranes, and patient discomfort. The Cochrane reviewers concluded that stripping of the membranes alone does not seem to produce clinically important benefits, but when used as an adjunct does seem to be associ-

**TABLE 3**  
**Technique for Placement of Balloon Dilators**

The catheter is introduced into the endocervix by direct visualization or blindly by locating the cervix with the examining fingers and guiding the catheter over the hand and fingers through the endocervix and into the potential space between the amniotic membrane and the lower uterine segment.

The balloon reservoir is inflated with 30 to 50 mL of normal saline.

The balloon is retracted so that it rests on the internal os.

Additional steps that may be taken:

- Apply pressure by adding weights to the catheter end.
  - Constant pressure: attach 1 L of intravenous fluids to the catheter end and suspend it from the end of the bed.
  - Intermittent pressure: gently tug on the catheter end two to four times per hour.
- Saline infusion<sup>12</sup>:
  - Inflate catheter with 40 mL of sterile water or saline.
  - Infuse sterile saline at a rate of 40 mL per hour using an infusion pump.
  - Remove six hours later or at the time of spontaneous expulsion or rupture of membranes (whichever occurs first).
- Prostaglandin E<sub>2</sub> infusion<sup>14</sup>

*Information from references 7, and 12 through 15.*

TABLE 4

**Technique for Performing Amniotomy**

A pelvic examination is performed to evaluate the cervix and station of the presenting part.  
 The fetal heart rate is recorded before and after the procedure.  
 The presenting part should be well applied to the cervix.  
 The membranes over the fetal head are removed by the examining finger.  
 A cervical hook is inserted through the cervical os by sliding it along the hand and fingers (hook side toward the hand).  
 The membranes are scratched or hooked to effect rupture.  
 The nature of the amniotic fluid is recorded (clear, bloody, thick or thin, meconium).

*Information from references 7 and 19.*

ated with a lower mean dose of oxytocin needed and an increased rate of normal vaginal deliveries.<sup>20</sup> [Evidence level A, RCT]

**Amniotomy.** It is hypothesized that amniotomy increases the production of, or causes a release of, prostaglandins locally. Risks associated with this procedure include umbilical cord prolapse or compression, maternal or neonatal infection, FHR deceleration, bleeding from placenta previa or low-lying placenta, and possible fetal injury. The technique for performing amniotomy is described in *Table 4*.<sup>7,19</sup>

Only two well-controlled trials studied the use of amniotomy alone, and the evidence did not support its use for induction of labor.<sup>21</sup> [Evidence level A, systematic review of RCTs]

**Pharmacologic Cervical Ripening or Labor Induction****PROSTAGLANDINS**

Prostaglandins act on the cervix to enable ripening by a number of different mechanisms. They alter the extracellular ground substance of the cervix, and PGE<sub>2</sub> increases the activity of collagenase in the cervix. They cause an increase in elastase, glycosaminoglycan, dermatan sulfate, and hyaluronic acid levels in the cervix. A relaxation of cervical smooth muscle facilitates dilation. Finally, prostaglandins allow for an increase in intracellular calcium levels, causing contraction of myometrial muscle.<sup>22,23</sup> Risks associated with the use of prostaglandins include uterine hyperstimulation and maternal side effects such as nausea, vomiting, diarrhea, and fever. Currently, two prostaglandin analogs are available for the purpose of cervical ripening, dinoprostone gel (Prepidil) and dinoprostone inserts (Cervidil). Prepidil contains 0.5 mg of dinoprostone gel, while Cervidil contains 10 mg of dinoprostone in pessary form. The techniques for gel and pessary placement are described in *Tables 5 and 6*, respectively.<sup>19</sup>

The Cochrane reviewers examined 52 well-designed studies using prostaglandins for cervical ripening or labor induction. Compared with placebo (or no treatment), use of vaginal prostaglandins increased the likelihood that a vaginal delivery would occur within 24 hours. In addition, the cesarean section rate was comparable in all studies. The only drawback appears to be an increased rate of uterine hyperstimulation and accompanying FHR changes.<sup>16,18,24</sup>

**MISOPROSTOL**

Misoprostol (Cytotec) is a synthetic PGE<sub>1</sub> analog that has been found to be a safe and inexpensive agent for cer-

TABLE 5

**Technique for Placement of Dinoprostone Gel (Prepidil)**

Patient selection:

- Patient is afebrile.
- No active vaginal bleeding is present.
- Fetal heart rate tracing is reassuring.
- Patient gives informed consent.
- Bishop score is < 4.

Bring gel to room temperature before application, per manufacturer's instructions.

Monitor fetal heart rate and uterine activity continuously starting 15 to 30 minutes before gel introduction and continuing for 30 to 120 minutes after gel insertion.

Introduce the gel into the cervix as follows:

- If the cervix is uneffaced, use the 20-mm endocervical catheter to introduce the gel into the endocervix just below the level of the internal os.
- If the cervix is 50 percent effaced, use the 10-mm endocervical catheter.

After application of the gel, the patient should remain recumbent for 30 minutes before being allowed to ambulate.

May repeat every six hours, up to three doses in 24 hours.

End points for ripening include strong uterine contractions, a Bishop score of ≥ 8, or a change in maternal or fetal status.

Maximum recommended dosage is 1.5 mg of dinoprostone (3 doses) in 24 hours.

Do not start oxytocin for six to 12 hours after placement of the last dose, to allow for spontaneous onset of labor and protect the uterus from overstimulation.

*Information from Hadi H. Cervical ripening and labor induction: clinical guidelines. Clin Obstet Gynecol 2000;43:524-36.*

**TABLE 6**  
**Technique for Placement of Dinoprostone Vaginal Inserts (Cervidil)**

Patient selection (see Table 5)

Using a small amount of water-miscible lubricant, place the tab into the posterior fornix of the cervix. As the device absorbs moisture and swells, it releases dinoprostone at a rate of 0.3 mg per hour for 12 hours.

Monitor fetal heart rate and uterine activity continuously, starting 15 to 30 minutes before introduction of the insert. Because hyperstimulation may occur up to nine and one-half hours after placement of the insert, fetal heart rate and uterine activity should be monitored from placement of the insert until 15 minutes after it is removed.

After insertion, the patient should remain recumbent for two hours. Remove the insert by pulling the cord after 12 hours, when active labor begins, or if uterine hyperstimulation occurs.

*Information from Hadi H. Cervical ripening and labor induction: clinical guidelines. Clin Obstet Gynecol 2000;43:524-36.*

vical ripening, although it is not labeled by the U.S. Food and Drug Administration for that purpose.

Clinical trials indicate that the optimal dose and dosing interval is 25 mcg intravaginally every four to six hours.<sup>1,25</sup> Higher doses or shorter dosing intervals are associated with a higher incidence of side effects, especially hyperstimulation syndrome, defined as contractions lasting longer than 90 seconds or more than five contractions in 10 minutes. Risks also include tachysystole, defined as six or more uterine contractions in 10 minutes for two consecutive 10-minute periods, and hypersystole, a single contraction of at least two minutes' duration.

Finally, uterine rupture in women with previous cesarean section is also a possible complication, limiting its use to women who do not have a uterine scar.<sup>25-28</sup> [Reference 27—Evidence level B, cohort study] The technique for use of vaginal misoprostol is described in *Table 7*.<sup>29</sup> [Evidence level A, RCT]

The Cochrane reviewers concluded that use of misoprostol resulted in an overall lower incidence of cesarean section. In addition, there appears to be a higher incidence of vaginal delivery within 24 hours of application and a reduced need for oxytocin (Pitocin) augmentation.<sup>30</sup> [Evidence level A, systematic review of RCTs] Additional review of the literature indicates that misoprostol is an effective agent for cervical ripening.<sup>15,31</sup> [Reference 15—Evidence level A, RCT; Reference 31—Evidence level A, systematic review of RCTs]

#### MIFEPRISTONE

Mifepristone (Mifeprex) is an antiprogesterone agent. Progesterone inhibits contractions of the uterus, while

*Using vaginal prostaglandins increases the likelihood that vaginal delivery will occur within 24 hours.*

mifepristone counteracts this action. Currently, seven trials are underway involving 594 women using mifepristone for cervical ripening. Results have shown that women treated with mifepristone are more likely to have a favorable cervix within 48 to 96 hours when compared with placebo. In addition, these women were more likely to deliver within 48 to 96 hours and less likely to undergo cesarean section. However, little information is available about fetal outcomes and maternal side effects; thus, there is insufficient information to support the use of mifepristone for cervical ripening.<sup>32</sup>

#### RELAXIN

The hormone relaxin is thought to promote cervical ripening. Cochrane reviewers evaluated results of four studies involving 267 women and concluded that there is insufficient support for the use of relaxin at this time. As with many of the other methods described in this review, further trials are needed.<sup>33</sup>

**TABLE 7**  
**Technique for Intravaginal Application of Misoprostol (Cytotec) Tablets**

Place one fourth of a tablet of misoprostol intravaginally, without the use of any gel (gel may prevent the tablet from dissolving).

The patient should remain recumbent for 30 minutes.

Monitor fetal heart rate and uterine activity continuously for at least three hours after misoprostol application before the patient is allowed to ambulate.

When oxytocin (Pitocin) augmentation is required, a minimum interval of three hours is recommended after the last misoprostol dose.

Not recommended for cervical ripening in patients who have a uterine scar.

*Information from Vengalil SR, Guinn DA, Olabi NF, Burd LI, Owen J. A randomized trial of misoprostol and extra-amniotic saline infusion for cervical ripening and labor induction. Obstet Gynecol 1998;91 (5 pt 1):774-9.*

### OXYTOCIN

As pregnancy progresses, the number of oxytocin receptors in the uterus increases (by 100-fold at 32 weeks and by 300-fold at the onset of labor). Oxytocin activates the phospholipase C-inositol pathway and increases intracellular calcium levels, stimulating contractions in myometrial smooth muscle.<sup>23</sup> Oxytocin is the preferred pharmacologic agent for inducing labor when the cervix is favorable or ripe. Numerous randomized, placebo-controlled studies have focused on the use of oxytocin in labor induction. It has been found that low-dose (physiologic) and high-dose (pharmacologic) oxytocin regimens are equally effective in establishing adequate labor patterns.<sup>34,35</sup>

*The author indicates that she does not have any conflicts of interest. Sources of funding: none reported.*

### REFERENCES

1. Norwitz E, Robinson J, Repke J. Labor and delivery. In: Gabbe SG, Niebyl JR, Simpson JL, eds. *Obstetrics: normal and problem pregnancies*. 4th ed. New York: Churchill Livingstone, 2002:353-94.
2. American College of Obstetricians and Gynecologists. *Induction of labor*. Practice bulletin no. 10. Washington, D.C.: ACOG, 1999.
3. Ludmir J, Sehdev HM. Anatomy and physiology of the uterine cervix. *Clin Obstet Gynecol* 2000; 43:433-9.
4. Edwards RK, Richards DS. Preinduction cervical assessment. *Clin Obstet Gynecol* 2000;43:440-6.
5. McFarlin BL, Gibson MH, O'Rear J, Harman P. A national survey of herbal preparation use by nurse-midwives for labor stimulation. *J Nurse Midwifery* 1999;44:205-16.
6. Belew C. Herbs and the childbearing woman. Guidelines for midwives. *J Nurse Midwifery* 1999; 44:231-52.
7. Adair CD. Nonpharmacologic approaches to cervical priming and labor induction. *Clin Obstet Gynecol* 2000;43:447-54.
8. Kelly AJ, Kavanagh J, Thomas J. Castor oil, bath and/or enema for cervical priming and induction of labour. *Cochrane Database Syst Rev* 2002;2: CD003099.
9. Kavanagh J, Kelly AJ, Thomas J. Sexual intercourse for cervical ripening and induction of labour. *Cochrane Database Syst Rev* 2002;2:CD003093.
10. Beal MW. Acupuncture and acupressure. Applications to women's reproductive health care. *J Nurse Midwifery* 1999;44:217-30.
11. Smith CA, Crowther CA. Acupuncture for induction of labour. *Cochrane Database Syst Rev* 2002;2:CD002962.
12. Lin A, Kupferminc M, Dooley SL. A randomized trial of extra-amniotic saline infusion versus laminaria for cervical ripening. *Obstet Gynecol* 1995; 86(4 part 1):545-9.
13. Rouben D, Arias F. A randomized trial of extra-amniotic saline infusion plus intracervical Foley catheter balloon versus prostaglandin E2 vaginal gel for ripening the cervix and inducing labor in patients with unfavorable cervixes. *Obstet Gynecol* 1993;82:290-4.
14. Sherman DJ, Frenkel E, Pansky M, Caspi E, Bukovsky I, Langer R. Balloon cervical ripening with extra-amniotic infusion of saline or prostaglandin E2: a double-blind, randomized controlled study. *Obstet Gynecol* 2001;97:375-80.
15. Buccellato CA, Stika CS, Frederiksen MC. A randomized trial of misoprostol versus extra-amniotic sodium chloride infusion with oxytocin for induction of labor. *Am J Obstet Gynecol* 2000;182: 1039-44.
16. Goldman JB, Wigton TR. A randomized comparison of extra-amniotic saline infusion and intracervical dinoprostone gel for cervical ripening. *Obstet Gynecol* 1999;93:271-4.
17. Guinn DA, Goepfert AR, Christine M, Owen J, Hauth JC. Extra-amniotic saline, laminaria, or prostaglandin E(2) gel for labor induction with unfavorable cervix: a randomized controlled trial. *Obstet Gynecol* 2000;96:106-12.
18. Schreyer P, Sherman DJ, Ariely S, Herman A, Caspi E. Ripening the highly unfavorable cervix with extra-amniotic saline instillation or vaginal prostaglandin E2 application. *Obstet Gynecol* 1989;73: 938-42.
19. Hadi H. Cervical ripening and labor induction: clinical guidelines. *Clin Obstet Gynecol* 2000;43:524-36.
20. Foong LC, Vanaja K, Tan G, Chua S. Membrane sweeping in conjunction with labor induction. *Obstet Gynecol* 2000;96:539-42.
21. Bricker L, Luckas M. Amniotomy alone for induction of labour. *Cochrane Database Syst Rev* 2002;2:CD002862.
22. Witter FR. Prostaglandin E2 preparations for preinduction cervical ripening. *Clin Obstet Gynecol* 2000;43:469-74.
23. Arias F. Pharmacology of oxytocin and prostaglandins. *Clin Obstet Gynecol* 2000;43:455-68.
24. Kelly AJ, Kavanagh J, Thomas J. Vaginal prostaglandin (PGE2 and PGF2a) for induction of labour at term. *Cochrane Database Syst Rev* 2002;2:CD003101.
25. Goldberg AB, Greenberg MB, Darney PD. Misoprostol and pregnancy. *N Engl J Med* 2001;344:38-47.
26. American College of Obstetricians and Gynecologists. *Induction of labor with misoprostol*. ACOG committee opinion 228. Washington, D.C.: ACOG, 1999:2.
27. Lydon-Rochelle M, Holt VL, Easterling TR, Martin DP. Risk of uterine rupture during labor among women with a prior cesarean delivery. *N Engl J Med* 2001;345:3-8.
28. Sanchez-Ramos L, Gaudier FL, Kaunitz AM. Cervical ripening and labor induction after previous cesarean delivery. *Clin Obstet Gynecol* 2000;43: 513-23.
29. Vengalil SR, Guinn DA, Olabi NF, Burd LI, Owen J. A randomized trial of misoprostol and extra-amniotic saline infusion for cervical ripening and labor induction. *Obstet Gynecol* 1998;91(5 part 1):774-9.
30. Hofmeyr GJ, Gulmezoglu AM. Vaginal misoprostol for cervical ripening and induction of labour. *Cochrane Database Syst Rev* 2002;2:CD000941.
31. Sanchez-Ramos L, Kaunitz AM. Misoprostol for cervical ripening and labor induction: a systematic review of the literature. *Clin Obstet Gynecol* 2000;43:475-88.
32. Neilson JP. Mifepristone for induction of labour. *Cochrane Database Syst Rev* 2002;2:CD002865.
33. Kelly AJ, Kavanagh J, Thomas J. Relaxin for cervical ripening and induction of labour. *Cochrane Database Syst Rev* 2002;2: CD003103.
34. Zeeman GG, Khan-Dawood FS, Dawood MY. Oxytocin and its receptor in pregnancy and parturition: current concepts and clinical implications. *Obstet Gynecol* 1997;89(5 pt 2):873-83.
35. Stubbs TM. Oxytocin for labor induction. *Clin Obstet Gynecol* 2000;43:489-94.