

Induction of Labor

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Induction of Labor

- Statistics
- Cervical Ripening
- Induction of Labor
- Specific Situations

Induction of Labor

- Definition: “Iatrogenic stimulation of uterine contractions to accomplish delivery prior to the onset of spontaneous labor”
- One of the most common obstetrical procedures in the United States

Statistics

- Rate of induction:
 - 90/1000 in 1989
 - 184/1000 in 1997
 - 205/1000 in 2001
- From 1990 to 2006 the frequency went from 9.5 to 22.5% of pregnancies
- Now more than 1 out of every 5 births

Reasons

- Better induction agents
- Patient and clinician desire to control timing of delivery
- Relaxed attitude about marginal indications
- Patient and clinician fear of fetal demise
- Increase in high risk pregnancies

Reasons

- The increase is mostly elective

Indications

- Post dates
- Abruption
- Chorioamnionitis
- Preeclampsia
- Premature rupture of membranes
- Maternal disease
- Fetal growth restriction
- Nonreassuring antenatal testing
- Fetal demise

Contraindications

- Malpresentation
- Placenta previa or vasa previa
- Prior transfundal uterine incision
- Need for emergent delivery
 - Cord prolapse
 - Nonreassuring fetal status
 - Maternal hemorrhage
- Active genital herpes infection

Cervical Ripening

- Definition: “Complex process that results in physical softening and distensibility of the cervix, ultimately leading to partial cervical effacement and dilatation”
- Remodeling of the cervix involves enzymatic dissolution of collagen fibrils, increase in water content, and chemical changes

The Cervix

- Initially 20% smooth muscle, 50% collagen, and 30% ground substance including elastin, chondroitin, dermatan sulfates, and hyaluronidase
- The vascularity and water content increase throughout gestation

- Hyaluronidase which weakly binds to collagen increases from 6 to 33%
- Dermatan and chondroitin sulfates which tightly bind to collagen decrease
- Collagenase and elastase enzymes increase to break down the structure of the collagen

The Bishop Score

Score	Dilation	Efface	Station	Consist	Position
0	Closed	0-30	-3	Firm	Posterior
1	1-2	40-50	-2	Medium	Mid
2	3-4	60-70	-1 or 0	Soft	Anterior
3	5-6	80	$\geq +1$		

- Friedman in 1966 compared the Bishop score and success of labor induction
- 19.5% of patient with a Bishop score of < 5 failed
- 4% with a score of 5 to 8 failed
- No one failed with a score of 9 or more
- If the score is >8 , the chance of a vaginal delivery with induction is similar to that of spontaneous labor
- If the score is <6 , cervix ripening is indicated

Techniques

- **Mechanical**
 - Low cost
 - Low risk of tachysystole
 - Few side effects
 - No refrigeration or expiration dates
 - Increased risk of infection
- **Hormonal**
 - Risk of uterine rupture
 - Risk of tachysystole
 - More side effects
 - May be more effective

Techniques

- Prostaglandins
 - Prepidil, Cervadil, Cytotec
- Mifepristone
- Mechanical Dilators
 - Laminaria, EASI
- Membrane Stripping

Prostaglandins

- 20 carbon compound
- Dinoprostone, E2 analog
- PREPIDIL (Pharmacia, Upjohn, Kalamazoo, MI)
- FDA approved in 1992
- 2.5 ml gel containing 0.5mg of dinoprostone

- Instilled in the external cervical os
- Can be repeated every 6 hours up to a total of 3 doses
- \$75 per dose
- Needs refrigeration
- 1% rate of hyperstimulation
- Fetal monitoring for 30 minutes to 2 hours after administration

- CERVIDIL (Forest Laboratories, St. Louis, MO)
- FDA approved in 1995
- 10 mg vaginal insert that releases prostaglandin E2 at 0.3mg/hr for 12 hours
- May need to be removed earlier if active labor is initiated
- 5% rate of hyperstimulation
- \$150 per dose

- Needs refrigeration
- Fetal monitoring for entire duration and at least 15 minutes after removal
- Both are reported to increase the probability of a successful induction, shorten the interval to delivery, and decreased the amount of oxytocin required

- MISOPROSTOL (Cytotec; Searle, Chicago, IL)
- Prostaglandin E1 analog
- FDA approved for peptic ulcer disease
- \$0.52 per 100ug tablet
- Hyperstimulation is dose dependent and occurs in 3 to 5% of cases
- Does not need refrigeration

- Cochrane Review-62 trials
- Compared to placebo, significant cervical ripening ($p=0.09$, CI 0.03 to 0.24)
- Compared to Cervidil, Prepidil, and oxytocin, there is less epidural use, fewer failures to achieve vaginal delivery, and more hyperstimulation (dose dependent)
- Misoprostol is the most effective ripening agent

- Doses not exceeding 25ug every 3 to 6 hours appears to have a similar effectiveness and risk of uterine hyperstimulation to other methods of labor induction
- ACOG Committee Opinion: Misoprostol is a safe and effective agent for cervical ripening and labor induction when used appropriately
- Contraindicated with a prior uterine scar

Other Routes

- Oral—
 - Faster peak but then more rapid decline in concentration
 - More GI complaints, in particular vomiting, and fever
 - May be appropriate for SROM
- Buccal and sublingual—
 - High bioavailability
 - Possibly less side effects and less tachysystole, but still experimental

Mifepristone

- RU 486 in Europe
- Mifeprex (Danco Laboratories, LLC) in USA
- 200 mg oral tablets
- Antiprogestosterone action from competitive inhibition at the progesterone receptor site
- www.fda.gov/cder/drug/infopage/mifepristone/default.htm
- Cochrane Review-7 trials

- Compared to placebo, women who received mifepristone were more likely to have a favorable cervix by 48 hours, have delivered by 48 hours, and were less likely to undergo a Cesarean delivery (RR 0.71, 95% CI 0.53-0.95)
- Two new studies from February 2005 in women >36 weeks' gestation: both showed no benefit and one had a trend towards higher Cesarean section rates and more fetal distress compared to oxytocin

Mechanical Dilators

- LAMINARIA
- made from the seaweed of *Laminaria japonicum*
- Expand by osmosis to 3 fold the original size
- Up to 10 dilators for at least 4 hours
- Synthetic hygroscopic dilators are now available (Lamicel)

- Only 2 to 4 are required in the cervix
- Usually used with oxytocin
- Compared to oxytocin use alone, dilators reduced the risk of cesarean from 32 to 17% (CI 0.33-0.91)
- May be associated with an increased risk of peripartum infections
- Safe for women with a uterine scar

- FOLEY CATHETER
- First described by Embrey and Mollison in 1967
- Works by direct stretching pressure of the balloon on the cervix and lower uterine segment and by the secretion of prostaglandins by membrane separation
- Multiple techniques: different size catheters, placement trans or supracervically, with or without oxytocin, and with or without weights
- All seem to be comparable to other methods
- Labor induction using a transcervical Foley catheter has not been associated with uterine rupture

- Cysto Bladder Irrigator Set
- 24 FR 30cc Foley
- 4 way Stopcock
- 5-In-1 Connector
- 30cc Syringe
- Run saline at 30cc/hour
- Leave in for 4 hours or until it falls out
- May also start oxytocin infusion

- Prostaglandin may be slightly more effective (Misoprostol)
- No risk for tachysystole
- Safe in women with a uterine scar
- May have a slightly higher risk of infection

Membrane Stripping

- Separating the amniotic membrane from the lower uterine segment causes a significant release of prostaglandins
- One randomized trial showed 2/3 of women who underwent membrane stripping labored spontaneously in 72 hours compared to only 1/3 without stripping
- Eight women need to have membrane stripping to avoid one formal labor induction

Induction of Labor

- Amniotomy
- Oxytocin

Amniotomy

- Artificial rupture of the membranes when the cervix is favorable
- A trial of amniotomy alone compared to with oxytocin showed shorter induction to delivery times with the added oxytocin

Oxytocin

- Oxytocin is a 9 amino acid peptide that is normally produced in the hypothalamus and secreted by the posterior pituitary gland in a pulsatile fashion
- When given intravenously, uterine response occurs after 3 to 5 minutes of infusion

- Steady state occurs in plasma by 40 minutes
- The uterine response to oxytocin increases from 20 to 34 weeks of gestation then plateaus
- It increases again in labor
- Oxytocin has only about 1% the antidiuretic affect of vasopressin and water intoxication is usually only seen at high concentrations (40 to 50U over 3L of fluid)
- Boluses can cause hypotension and tachycardia
- Should always be on an infusion pump

- Dosing regimens
 - Low dose: 0.5 to 1mU/min increasing by 1 to 2mU every 30 to 40min
 - High dose: 6mU/min increasing by 1 to 6mU every 15 to 30min
- ACOG has no specific recommendations
- Patka et al. showed that higher doses resulted in a shorter induction, but did not decrease the incidence of Cesarean deliveries
- Xenakis et al. used 4mU/min increased by 4mU every 15min compared to low dose and showed a reduction in cesarean delivery from 25.7 to 10.4% with no increase in hyperstimulation

Special Cases

- Prior cesarean delivery
- Post dates
- Macrosomia
- Elective induction

Prior Uterine Scar

- Lyndon-Rochelle et al. reported a retrospective cohort analysis of 20,095 women from 1987 to 1996 who delivered a child after a primary cesarean delivery
- Uterine rupture rates:
 - 1.6/1000 with repeat cesarean, no labor
 - 5.2/1000 with spontaneous labor
 - 7.7/1000 induced without prostaglandin
 - 24.5/1000 induced with prostaglandin

Relative risk of a uterine rupture was increased by all prostaglandins:

- 15.6 (8.1 to 30.0) for all
- 14.1 (6.1 to 33.0) even prior to misoprostol
- The study is limited by coding issues
- In a review by Sanchez-Ramos et al, they concluded that PGE2 and oxytocin were safe and that only misoprostol should be avoided
- ACOG Committee Opinion: Induction with **prostaglandins** is discouraged, the use of oxytocin is not precluded by the data

- A recent study by Bujold et al. evaluate the Bishop score for predicting the success of an induction in patients with a previous Cesarean delivery
- A score of ≥ 6 was associated with a successful VBAC ($p < 0.001$)
- Number of future pregnancies should be part of counseling

- Recent decision model analysis:
- For women who desire only one child, an elective repeat Cesarean is safest
- For women who desire more than one child, a TOLAC is safest especially when considering future risk of hysterectomy

- For women who are undecided
- Spontaneous labor: TOLAC
- Delivery required:
 - Bishop score ≥ 6 : induction of labor
 - Bishop score < 6 : repeat Cesarean section

Post Term

- Definition: “a pregnancy that has extended to or beyond 42 weeks of gestation or 294 days from the first day of the last menstrual period”
- Approximately 6% of pregnancies
- Risks: primigravidity, prior post term, male fetal gender, obesity, placental sulfatase deficiency, and fetal anencephaly

- Perinatal mortality at 42 weeks is twice that at term (4 to 7 vs 2 to 3 per 1000 deliveries)
- Recent meta-analysis of induction vs. expectant management at 41 weeks by Sanchez-Ramos et al.
- 16 studies included
- Women who were induced had lower cesarean delivery rates at 20.1 vs. 22% (OR 0.88, CI 0.78 to 0.99)

- There were no differences in perinatal mortality, NICU admission, meconium aspiration, or abnormal Apgar scores
- Overall, labor induction decreased the risk of a cesarean delivery by 12% regardless of the Bishop score
- Conclusion: Women should be induced at ≥ 41 weeks of gestation

Macrosomia

- Estimated fetal weight of ≥ 4500 grams

Gestational age	10%	50%	90%
37	2541	3117	3755
38	2714	3263	3867
39	2852	3400	3980
40	2929	3495	4060
41	2948	3527	4094
42	2935	3522	4098

Macrosomia

- The outcomes for both retrospective and prospective studies do not support a policy of labor induction for macrosomia
- Frieson et al. found a higher cesarean delivery rate when labor was induced (24% vs. 10%) when controlling for gestational age and parity

- Leaphart et al. looked at nondiabetic women who were induced for suspected macrosomia compared to spontaneous labor in women who were matched for birth weight. Despite a lower mean weight in the induced group, the cesarean rate was higher (36% vs. 17%)
- Although intended to reduce Cesarean delivery rates, induction for macrosomia actually increases them
- Conclusion: Do not induce for macrosomia

Elective

- ACOG: Labor may be induced for risk of rapid labor, distance from the hospital, or psychosocial indications
- A decision analysis of elective induction at 39 weeks vs awaiting spontaneous labor showed 12,000 excess cesarean deliveries at a cost of \$100 million per year

- Must first confirm term gestation by:
 - Fetal heart tones have been documented for 30 weeks by Doppler
 - It has been 36 weeks since a positive pregnancy test from a reliable laboratory
 - An ultrasound measurement of a CRL at 6 to 12 weeks supports a gestational age of at least 39 weeks
 - An ultrasound at 13 to 20 weeks confirms a gestational age of at least 39 weeks determined by clinical history and physical exam

- Largest retrospective study by Yeast et al. of 7001 consecutive inductions showed an increased rate of cesarean delivery for nulliparous women who were induced compared to spontaneous labor (16.2% vs. 7.9%, $p < 0.01$)
- Increased RR of 2.8 when the cervix was unfavorable
- Conclusion: Do not induce nulliparous women electively

References

Ventura SJ, Martin JA, Curtin SC, Mathews TJ. Births: Final data for 1997. National Center for Health Statistics, National Vital Statistics Reports, 1997;47:1-96.

Martin JA, Hamilton BE, Ventura SJ, Menacker F, Park MM, Sutton PD. Births: Final data for 2001. National Center for Health Statistics, National Vital Statistics Reports, 2001;51:1-103.

American College of Obstetricians and Gynecologists. Induction of Labor. ACOG Practice Bulletin 10. Washington DC: ACOG, 1999.

Danforth DN, Veis A, Breen M, et al. The effect of pregnancy and labor on the human cervix: changes in collagen, glycoproteins, and glycosaminoglycans. *Am J Obstet Gynecol* 1974;120:641-45.

Bishop EM. Pelvic scoring for elective induction. *Obstet Gynecol* 1964;24:266-68.

Friedman EA, Niswander KR, Bayonet-Rivera NP, Sachtleben MR. Relation of prelabor evaluation to inducibility and the course of labor. *Obstet Gynecol* 1966;28:495-501.

Rayburn, WF. Preinduction cervical ripening: basis and methods of current practice. *Obstet Gynecol Survey* 2002;57(10):683-92.

Wing, DA. Labor induction with misoprostol. *Am J Obstet Gynecol* 1999;181(2):339-45.

Hofmeyer GJ, Gulmezoglu AM. Vaginal misoprostol for cervical ripening and induction of labour (Cochrane Review). In: The Cochrane Library, Issue 3, 2001. Oxford: Update Software.

American College of Obstetrics and Gynecology. Induction of labor with misoprostol. ACOG Committee Opinion 228. Washington, DC: ACOG 1999.

French L. Oral prostaglandin E2 for induction of labor (Cochrane Review). In: The Cochrane Library, Issue 1, 2005. Oxford: Update Software.

Muzonzini G, Hofmeyr GJ. Buccal or sublingual misoprostol for cervical ripening and induction of labor (Cochrane Review). In: The Cochrane Library, Issue 4, 2004. Oxford: Update Software.

Wolf SB, Sanchez-Ramos L, Kaunitz AM. Sublingual misoprostol for labor induction: a randomized clinical trial. *Obstet Gynecol* 2005;105:365-71.

Neilson JP. Mifepristone for induction of labor (Cochrane Review). In: *The Cochrane Library, Issue 1, 2005*. Oxford: Update Software.

Berkane N, Verstraete L, Uzan S, Boog G, Maria B. Use of mifepristone to ripen the cervix and induce labor in term pregnancies. *Am J Obstet Gynecol* 2005;192:114-20.

Wing DA, Guberman C, Fassett M. A randomized comparison of oral mifepristone to intravenous oxytocin for labor induction in women with prelabor rupture of membranes beyond 36 weeks' gestation. *Am J Obstet Gynecol* 2005;192:445-51.

Boulvain M, Kelly A, Lohse C, et al. Mechanical methods for induction of labor (Cochrane Review). In: The Cochrane Library, Issue 4, 2001. Oxford: Update Software.

Kazzi GM, Bottoms SF, Rosen MG. Efficacy and safety of laminaria digitata for preinduction ripening of the cervix. *Obstet Gynecol* 1982;60:440-443.

Embrey MP, Mollison. The unfavorable cervix and induction of labor using a cervical balloon. *J Obstet Gynaecol Br Common* 1967;74:44-5.

Lyndrup J, Nickelsen C, Weber T, Molnitz E, Guldbaek E. Induction of labor by balloon catheter: a randomized comparison with PGE2 vaginal peccaries. *Eur J Obstet Gynecol Reprod Biol* 1994;47:189-92.

Manabe Y, Manabe A, Takahashi A. Prostaglandin levels in amniotic fluid during balloon-induced cervical softening and labor at term. *Prostaglandins* 1982;23:247-8.

Sciscione AC, Nguyen L, Manley J, Pollock M, Maas B, Colmorgen G. A randomized comparison of transcervical Foley catheter to intravaginal misoprostol for preinduction cervical ripening. *Obstet Gynecol* 2001;97:603-7.

Barrilleaux PS, Bofill JA, Terrone DA, Magann EF, May WL, Morrison JC. Cervical ripening and induction of labor with misoprostol, dinoprostone gel, and a Foley catheter: a randomized trial of 3 techniques. *Am J Obstet Gynecol* 2002;186:1124-29.

Bujold E, Blackwell SC, Gauthier RJ. Cervical ripening with a transcervical Foley catheter and the risk of uterine rupture. *Obstet Gynecol* 2004;103:18-23.

Chung JH, Huang WH, Rumney PJ, Garite TJ, Nageotte MP. A prospective randomized controlled trial that compared misoprostol, Foley catheter, and combination misoprostol-Foley catheter for labor induction. *Am J Obstet Gynecol* 2003;189:1031-33.

Lin A, Kupferminc M, Dooley SL. A randomized trial of extra-amniotic saline infusion versus laminaria for cervical ripening. *Obstet Gynecol* 1995;86:545-49.

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;91:774-79.

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.

Guinn DA, Davies JK, Jones RO, Sullivan L, Wolf D.
Labor induction in women with an unfavorable Bishop score: randomized 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.

Levey KA, MacKenzie AP, Stephenson C, Bercik R, Kuczynski E, Funai EF. Increased rates of chorioamnionitis with extra-amniotic saline infusion method of labor induction. *Obstet Gynecol* 2004;103:724-8.

Allot HA, Palmer CR. Sweeping the membranes: a valid procedure in stimulating the onset of labour? *Br J Obstet Gynaecol* 1993;100:898-903.

Moldin PG, Sundell G. Induction of labour: a randomized clinical trial of amniotomy versus amniotomy with oxytocin infusion. Br J Obstet Gynaecol 1996;103:306-12.

Seitchik J, Amico J, Robinson AG, Castillo M. Oxytocin augmentation of dysfunctional labor. IV. Oxytocin pharmacokinetics. Am J Obstet Gynecol 1984;150:225-28.

Caldeyro-Barcia R, Poserio JJ. Physiology of the uterine contraction. Clin Obstet Gynecol 1960;3:386-408.

Dudley, D. Oxytocin: use and abuse, science and art. Clin Obstet Gynecol 1997;40:516-24.

Patka JH, Lodolce AE, Johnston AK. High- versus low-dose oxytocin for augmentation or induction of labor. *An of Pharmaco* 2005;39:95-101.

Xenakis EMJ, Langer O, Piper JM. Et al. Low-dose versus high-dose oxytocin augmentation of labor-a randomized trial. *Am J Obstet Gynecol* 1995;173:1874-78.

Lydon-Rochelle M, Holt VL, Easterling TR, Martin DP. Risk of Uterine rupture during labor among women with a prior cesarean delivery. *NEJM* 2001;345:3-8.

Sanchez-Ramos L, Gaudier FL, Kaunitz AM. Cervical ripening and labor induction after previous cesarean delivery. *Clinical Obstet Gynecol* 2000;43:513-23.

American College of Obstetrics and Gynecology.
Induction of labor for vaginal birth after cesarean
delivery. ACOG Committee Opinion 271. Washington,
DC: ACOG 2002.

Bujold E, Blackwell SC, Hendler I, Berman S, Sorokin Y,
Gauthier RJ. Modified Bishop's score and induction of
labor in patients with a previous cesarean delivery. Am
J Obstet Gynecol 2004;191:1644-8.

American College of Obstetricians and Gynecologists.
Vaginal Birth after Previous Cesarean Delivery. ACOG
Practice Bulletin 54. Washington DC: ACOG, 2004.

Sanchez-Ramos L, Olivier F, Delke I, Kaunitz AM. Labor
induction versus expectant management for postdates
pregnancies: a systematic review with meta-analysis.
Obstet Gynecol 2003;101:1312-18.

Berkus MD, Conway D, Langer O. The large fetus.
Clin Obstet Gynecol 1999;42:766-89.

Friesen CD, Miller AM, Rayburn WF. Influence of
spontaneous or induced labor on delivery the
macrosomic fetus. Am J Perinatol 1995;12:63-66.

Leaphart WL, Meyer MC, Capeless EL. Labor induction
with a prenatal diagnosis of fetal macrosomia.
J Matern Fetal Med 1997;6:99-102.

Yeast JD, Jones A, Poskin M. Induction of labor and
the relationship to cesarean delivery: a review of 7001
consecutive inductions. Am J Obstet Gynecol
1999;180:628-33.

Wing, DA. Elective induction of labor in the USA.
Current Opinion in Obstet Gynecol 2000;12:457-62.

Up to Date:

Induction of Labor, Wing, Deborah, MD. May 2010

Techniques for Cervical Ripening prior to Labor Induction, Wing,
Deborah, MD. May 2010

Induction of Labor in Women with a prior Cesarean Delivery, Wing,
Deborah, MD. May 2010

Post Term Pregnancy, Norwitz, Errol, MD, PhD. May 2010.





