Induction of Labor
Provocation de travail

DR. DEAN LEDUC
MONTFORT HOSPITAL
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VANCOUVER, BC
Induction of Labor

I HAVE NO FINANCIAL RELATIONSHIPS TO DISCLOSE

I WILL DISCUSS OFF-LABEL USE OF MISOPROSTOL

I WILL NOT DISCUSS INVESTIGATIONAL PRODUCTS
Induction of Labor

Objectives

- Review SOGC IOL guideline
  - Importance cervical status
  - Selection method to optimize VD
  - Prevention of induction
  - Choices of induction agent
- Literature since publication
Induction rates, 1995-2005
Induction rates, 2007-2012

BORN Ontario
Induction rate by region in Ontario

Southwest: 30.4%
West: 26.5%
Toronto: 22.3%
South-East: 23.9%
North: 25.1%
Ontario: 24.3%

BORN, 2011-12
Induction of labor represent *25-33%* of our intrapartum workload
Indications – High Priority

- Pre-eclampsia > 37 weeks*
- Term PROM / GBS positive
- Chorioamnionitis
- Suspected fetal compromise
- Stable antepartum hemorrhage
- Significant maternal disease

*change in the 2013 SOGC guidelines
Indications – Other

- Post dates (>41 weeks)
- Post-term (> 42 weeks)
- Oligohydramnios
- IUGR
- **Gestational HTN > 38 weeks***
- Term PROM / GBS negative
- Twin >= 38 weeks
- Intrauterine fetal demise (IUFD)/prior IUFD
- **Diabetes (not controlled)***
- Logistical (precipitous labor, distance)
Indications - unacceptable

- Suspected fetal macrosomia in non-diabetic women*
- Patient / care provider convenience
Complications of IOL

- Failure to achieve labor / delivery
- CS
- Operative vaginal delivery
- Tachysystole ± fetal changes
- Chorioamnionitis
- Cord prolapse with ARM
- Uterine rupture
Contra-indications to vaginal delivery
Induction of Labor

HOW DOES CERVICAL STATUS HELP ME?
Cervical factors and successful induction

Bishop > 6
CS rate same as spontaneous labor

Resources

Neilsen 2005, Durodola 2005, Osmundson 2010
Cervical factors and prediction of success

Cervical dilation
  >
Effacement, station, position
  >
Consistency

Crane, 2006
Failed induction defined as inability to achieve active phase of labor > 4cm despite adequate exposure to cervical priming and oxytocin stimulation (high dose protocol)

Xenakis, 1997
Failed induction / CS rate

Xenakis, 1997
WHAT ABOUT OTHER CLINICAL FACTORS FOR SUCCESS?
## Risk factors associated with IOL success

<table>
<thead>
<tr>
<th>Factor</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiparity</td>
<td>4.63</td>
</tr>
<tr>
<td>Bishop score &gt; 4</td>
<td>2.2</td>
</tr>
<tr>
<td>BMI &gt; 30</td>
<td>0.6</td>
</tr>
<tr>
<td>Age &gt; 35</td>
<td>0.79</td>
</tr>
</tbody>
</table>
## Risk factors associated with IOL failure

<table>
<thead>
<tr>
<th></th>
<th>Vrounraets, 2005</th>
<th>Ennen, 2005</th>
<th>Erhnedal, 2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR</td>
<td>OR</td>
<td>OR</td>
<td></td>
</tr>
<tr>
<td>Nulliparity</td>
<td>3.85</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bishop score</td>
<td>2.3 (BS&lt;5)</td>
<td>2.4 (BS &lt;1)</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>2.87 (&gt;30)</td>
<td>1.9 (&gt;40)</td>
<td>4.3 (&gt;30) / 6.3 (&gt;40)</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
<td>1.9</td>
<td>1.8</td>
</tr>
<tr>
<td>Age</td>
<td>1.6 (&gt;30)</td>
<td>2.4 (&gt;35)</td>
<td>2.0 (&gt;25)</td>
</tr>
</tbody>
</table>
Pre-induction factors – Risk for failure

- Unfavorable cervix (Bishop ≤ 6)
  - Ennen, Pevnver, Ehrendal
- Obesity (BMI > 40)
  - Ennen, Coonrod
- Estimated fetal weight > 4000gm
  - Ennen, Coonrod
- Diabetes mellitus, pre-existing
  - Ennen, Coonrod
- Maternal age > 35
  - Pevnver, Ehrendal, Coonrod
What about other methods cervical assessment?

- Fetal fibronectin + TVUS
- Shown to predict successful induction
- Neither superior to Bishop score

Crane, 2006
Reasons for Induction

- Post-dates: 37%
- PROM: 13%
- Other - DM, oligo, HTN: 50%

BORN, 2011-12
Induction of Labor

POST- DATES
Routine vs Indicated Induction of Labour at 41 or > 41 weeks GA

Gulmezoglu AM et al, Cochrane Library
Issue 6, 2012

Outcome | RR | 95% CI
--- | --- | ---
Perinatal death (>41) | 0.31 | (0.12, 0.88)
MAS (41) | 0.27 | (0.11, 0.68)
MAS (>41) | 0.61 | (0.40, 0.92)
C/S (41) | 0.74 | (0.58, 0.96)
C/S (>41) | 0.91 | (0.82, 1.00)
Assisted Vag Del (41) | 1.09 | (0.40, 2.98)
Assisted Vag Del (>41) | 1.05 | (0.65, 1.16)
Apgar<7 at 5 min (41) | 0.55 | (0.12, 2.55)
Apgar<7 at 5 min (>41) | 0.75 | (0.44, 1.26)

NNT = 410

Relative Risk (95% Confidence Interval)
Induction of Labor

HOW DID THIS ALL START?
Hannah Trial

- IOL vs serial monitoring in post term pregnancy
- 3407 women
- > 41 weeks, uncomplicated, singleton, vertex pregnancy, cx < 3cm
- RCT at >= 41 weeks
  - Induction within 2-3 days (study group) vs monitored (control group)
  - Serial monitoring – Kick count and AFV + NST 2-3 per week
    - Induced if NST abnormal, low AFV (< 3cm), OBS complication, 44 weeks
- Outcomes
  - Rate of CS
  - Perinatal mortality and neonatal morbidity

NEJM, 1992
# Hannah Trial

<table>
<thead>
<tr>
<th></th>
<th>Induction group</th>
<th>Serial monitor group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numbers</td>
<td>1701</td>
<td>1706</td>
<td></td>
</tr>
<tr>
<td>Method induction</td>
<td>PG x 3,</td>
<td>Oxytocin/ ARM /</td>
<td></td>
</tr>
<tr>
<td></td>
<td>oxytocin/ARM</td>
<td>CS</td>
<td></td>
</tr>
<tr>
<td>CS</td>
<td>360 (21.1%)</td>
<td>418 (24.5%)</td>
<td>0.03</td>
</tr>
<tr>
<td>CS fetal distress</td>
<td>5.7%</td>
<td>8.3%</td>
<td>0.003</td>
</tr>
<tr>
<td>Perinatal deaths</td>
<td>2</td>
<td>0*</td>
<td>NS</td>
</tr>
</tbody>
</table>

- 2 infants with lethal congenital abnormalities excluded
- 1 death – IUFD, presence of meconium, , HIE
- 1 death – labor, acute fetal distress, NRP, meconium aspiration
Hannah Trial (NEJM, 1992)

- **Conclusion**
  - Lower rate of CS in induction group
  - Similar perinatal mortality and neonatal morbidity

- Resulted in the routine offer of induction > 41 weeks
SOGC Guidelines

- **Management of Post Term Pregnancy, 1994**
  - Patient should be offered elective delivery.
  - Labor should be induced or CS in the case that a VD is contraindicated.

- **Post-term Pregnancy, 1997**
  - A policy of induction for women who reach 41 weeks is preferred due to higher risk of adverse maternal, fetal and neonatal outcomes.

- **Induction of Labor at Term, 2001**
  - Indication should be discussed.
  - Ripening of the cervix should be considered before induction.

- **Induction of Labor, 2013**
Induction of Labor

PREVENTION OF POST-DATES
Prevention of post dates (>41 weeks)

- **Accurate dating**
  - LMP
  - 1\textsuperscript{st} trimester US +/- 5 days
  - 2\textsuperscript{nd} trimester US +/- 10 days

- **Sweeping membranes** – 3 circumferential rotations within the cervix or massage for 15-30 sec
  - Weekly after 38 weeks (Yildirm, 2009)
    - NNT (to prevent one induction) = 8
  - Twice weekly after 41 weeks (de Miranda, 2006)
    - NNT (to prevent one induction) = 6

- **Intercourse**
  - No difference (Tan, 2007)
Women < 41 weeks induced for post dates

Southwest: 26.1%
West: 25.9%
Toronto: 21.0%
South-East: 18.6%
North: 26.5%
Ontario: 22.6%

BORN, 2011-12
Prevention of post dates (>41 weeks)

- Quality improvement program
  - Induction committee used to review each request for induction request and enforce the use of proper indication
    - Fisch, 2009 – reduction elective inductions < 39 weeks
    - Oshiro, 2009 - reduction elective inductions < 39 weeks
    - Reisner, 2008 - reduction elective inductions < 39 weeks and unfavorable cervix
  - Decrease CS rate for all institutions

- Institutional philosophy
  - Low induction centers had a lower overall CS rate compared to higher induction centers
Methods of induction

- Mechanical - Foley
- Prostaglandins
  - PGE2 – dinoprostone
  - PGE1 - misoprostol
- ARM
- Oxytocin
- Breast stimulation
Mechanical

- Catheter
- Contra-indications
  - Absolute – low lying placenta
  - Relative – APH, ruptured membranes, infection
- Advantages
  - Less tachysystole
  - Can be used as an outpatient
  - VBAC
  - No increase rates maternal / neonatal infection
  - No increase risk CS compared to PG
- Disadvantages
  - Increase need for oxytocin
PROBAAT studies
(Prostaglandin versus balloon for IOL)

- Foley (30ml) vs:
  - Prostaglandin E2 gel (PROBAAT), 2011
  - Prostaglandin 10mcg vaginal insert (PROBAAT-P), 2013
  - Misoprostol 25mcg vaginal tablet (PROBAAT-M), 2013
- Prospective, RCT, not blinded
- Single, term, cephalic, intact membranes, unfavorable cervix (Bishop <6), no prior CS
- ARM when favorable, oxytocin augmentation prn
- Outcomes
  - Primary – CS
  - Secondary – maternal and neonatal morbidity
- Included meta-analyses in their results

Eikhelder, 2013
PROBAAT (Foley vs PGE2 gel)

- 824 women, 412 Foley, 412 vaginal PGE2 gel

Results:
- Similar rate of CS (23% vs 20%)
- Similar rate of fetal distress (7% vs 9%)
- More oxytocin augmentation with Foley group (86% vs 59%, p<0.001)
- Similar hyperstimulation rates (2% vs 3%)
- All cases of hyperstimulation with Foley had oxytocin
- Longer intervention-delivery time similar with Foley (29h vs 17h, p<0.001)

Jozwiak, 2011
PROBAAT-P (Foley vs PGE2 pessary)

- 226 women, 107 Foley, 119 vaginal inserts
- Results:
  - Similar rate of CS (20% vs 22%)
  - Similar rate of fetal distress
  - Less hyperstimulation with Foley alone but similar when oxytocin used
  - Intervention-delivery time similar (28h vs 27h)

Jozwiak, 2013
PROBAAT-M (Foley vs PGE1)

- 120 women, 56 Foley, 64 misoprostol
- Results:
  - Non-significant difference in rate of CS (25% Foley vs 17% miso, RR 1.46 95% CI 0.72-2.94)
  - More CS due to dystocia in Foley group (14% vs 3%)
  - No difference in hyperstimulation
  - Intervention-delivery time longer in Foley group (36h vs 25h, p<0.001)

Jozwiak, 2013
RCT outpatient (61 women) vs inpatient (50 women) Foley for IOL unfavourable cervix

Results:
- Similar change in Bishop score
- No difference in oxytocin, epidural rate, induction time, Apgar and cord pH
- Less hospitalization time for outpatient group

Sciscione, Obstet Gynecol, 2001
Outpatient Foley vs Inpatient PGE2

- RCT outpatient Foley (50 women) vs inpatient vaginal PGE2 (51 women) for IOL unfavourable cervix

- Results:
  - OPC had shorter antenatal hospital stay (21.3h vs 32.4h)
  - Similar VDs (66% vs 71%), induction-delivery time (33.5h vs 31.3h), total hospital inpatient time (96h vs 105h)
  - OPC had less pain (26% vs 58%), more sleep (5.8h vs 3.4h) and more need for oxytocin (88% vs 59%)
  - IP more likely to deliver within 12h (53% vs 28%)

Henry, BMC Preganancy and Childbirth, 2013
Mechanical – Single vs double lumen

- RCT, 330 women, > 36 weeks, nulliparous, BS<5

<table>
<thead>
<tr>
<th></th>
<th>Single lumen</th>
<th>Double lumen</th>
<th>PGE2</th>
<th>P score</th>
</tr>
</thead>
<tbody>
<tr>
<td>CS</td>
<td>36%</td>
<td>43%</td>
<td>37%</td>
<td>NS</td>
</tr>
<tr>
<td>Induction to delivery time</td>
<td>25.8h</td>
<td>30.6h</td>
<td>25.8h</td>
<td>P=0.043</td>
</tr>
<tr>
<td>Tachysystole</td>
<td>None</td>
<td>None</td>
<td>14%</td>
<td>P=0.050</td>
</tr>
<tr>
<td>Pain score &gt;3</td>
<td>36%</td>
<td>55%</td>
<td>63%</td>
<td>P&lt; 0.001</td>
</tr>
</tbody>
</table>

Foley had lower CS rate, lower induction-delivery time and less pain

Pennell, BJOG 2009
## Maternal / neonatal infection – Foley vs PG

- **Systematic review, 30 RCTs**

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Foley</th>
<th>Pharmacological</th>
<th>Pooled OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal infection</td>
<td>7.6%</td>
<td>5.0%</td>
<td>1.5 (1.07-2.09)</td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>7.6%</td>
<td>3.7%</td>
<td>2.05 (1.22-3.44)</td>
</tr>
<tr>
<td>Endometritis</td>
<td>5.1%</td>
<td>3.2%</td>
<td>1.47 (0.74-1.94)</td>
</tr>
<tr>
<td>Neonatal infection</td>
<td>3.2%</td>
<td>2.5%</td>
<td>1.2 (0.48 – 2.97)</td>
</tr>
</tbody>
</table>

Higher rate for all mechanical but rates similar for studies limited to Foley catheters.

Heinemann, AJOG, 2008
Mechanical - summary

- Safe
- Outpatient
- Unfavourable cervix
- VBAC
- More need for oxytocin
Prostaglandins

- **Prostaglandin E₂ – dinoprostone**
  - Intracervical gel - Cervidil®
  - Intravaginal gel - Prostin®
  - Intravaginal pessary - Prepidil®

- **Prostaglandin E₁ – misoprostol**
  - Oral
  - Vaginal
Prostaglandin E2 – Intact Membranes

- Kelly, Cochrane, 2009
- 63 studies, 10 441 women, intact membranes
- No difference CS

<table>
<thead>
<tr>
<th></th>
<th>PG</th>
<th>placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>No SVD 24h</td>
<td>18%</td>
<td>99%</td>
</tr>
<tr>
<td>Oxytocin stimulation</td>
<td>21.6%</td>
<td>40.3%</td>
</tr>
<tr>
<td>Tachysystole</td>
<td>4.6%</td>
<td>0.51%</td>
</tr>
</tbody>
</table>

Prostaglandins work with intact membranes
Prostaglandin E2 - PROM

- Dare, Cochrane, 2006
- 12 trials, 6814 women, PROM > 37 weeks

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Relative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>CS</td>
<td>0.94 (0.82-1.08)</td>
</tr>
<tr>
<td>Operative VD</td>
<td>0.98 (0.84-1.16)</td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>0.74 (0.56-0.97)</td>
</tr>
<tr>
<td>Endometritis</td>
<td>0.3 (0.12-0.74)</td>
</tr>
<tr>
<td>Neonatal infection</td>
<td>0.83 (0.61-1.12)</td>
</tr>
<tr>
<td>NICU</td>
<td>0.72 (0.57-0.92)</td>
</tr>
<tr>
<td>Negative experience</td>
<td>0.45 (0.37-0.54)</td>
</tr>
</tbody>
</table>

Prostaglandins work with ruptured membranes
Sweeping + PGE2

- Foong, 2000, RCT, 130 nullip + 118 multip, term
  - Benefits limited to nullips with unfavourable cervix
    - Shorter induction labor time (13.6h vs 17.3h)
    - Increase vaginal delivery (83.3% vs 58.2%)
- Tan, 2006, RCT, 264 women, term
  - Benefits to nullip and multips
    - Higher SVD (69% vs 56%)
    - Shorter induction-labor time (14h vs 19h)
    - Less oxytocin (46% vs 59%)
    - More post-sweeping pain

Prostaglandins work better when sweeping is performed at the time of insertion.
Time of day

- Dodd, 2006, Obstet Gynecol
- RCT, 620 women, > 37 weeks, PG induction

<table>
<thead>
<tr>
<th>Time of admission</th>
<th>0800h</th>
<th>2000h</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxytocin infusion</td>
<td>45%</td>
<td>54%</td>
<td>0.83 (0.7-0.97)</td>
</tr>
<tr>
<td></td>
<td>(126/280)</td>
<td>(184/340)</td>
<td></td>
</tr>
<tr>
<td>Operative vaginal delivery (nullip only)</td>
<td>16.1%</td>
<td>34.2%</td>
<td>0.47 (0.25-0.90)</td>
</tr>
<tr>
<td></td>
<td>(10/62)</td>
<td>(28/82)</td>
<td></td>
</tr>
</tbody>
</table>

No difference primary outcomes – vaginal delivery < 24h, CS, tachysystole with FH changes
Less intervention when started in morning
### Outpatient Induction with vaginal PGE2

- **Biem, JOGC, 2003**
- **300 women, > 37 weeks, reactive NST, Bishop <7**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Outpatient (n=150)</th>
<th>Inpatient (n=150)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Satisfaction</td>
<td>56%</td>
<td>39%</td>
<td>&lt; 0.008</td>
</tr>
<tr>
<td>Delivery &lt; 24h</td>
<td>115</td>
<td>107</td>
<td>NS</td>
</tr>
<tr>
<td>Time to labor</td>
<td>9.8h</td>
<td>11.4h</td>
<td>NS</td>
</tr>
<tr>
<td>Time to delivery</td>
<td>21.4h</td>
<td>20.7h</td>
<td>NS</td>
</tr>
<tr>
<td>Oxytocin</td>
<td>22</td>
<td>29</td>
<td>NS</td>
</tr>
<tr>
<td>CS</td>
<td>35</td>
<td>37</td>
<td>NS</td>
</tr>
<tr>
<td>Epidural</td>
<td>117</td>
<td>115</td>
<td>NS</td>
</tr>
<tr>
<td>Tachysystole</td>
<td>15</td>
<td>15</td>
<td>NS</td>
</tr>
<tr>
<td>Non-reassuring FH</td>
<td>4</td>
<td>1</td>
<td>NS</td>
</tr>
</tbody>
</table>
Induction of Labor

How many doses of PGE2 can I give?
Methods for repetitive doses PGE2

- Retrospective cohort 3514 nulliparous induced for post-dates
- Bishop < 6
- Compared <2 and > 2 (max 5) doses PGE2 tabs/gel
  - PGE2 licensed for 2 doses only
- Maternal and neonatal outcomes
  - Mode of delivery – CS, SVD, AVD
  - Indication for CS – failed IOL, dystocia
  - Oxytocin stimulation
  - Epidural
  - PPH
  - Terbutaline use for “hyperstimulation”
  - NICU admission
  - Apgar < 7 at 5 minutes

Ayaz, Eur J Obstet Gynecol, 2013
Results for repetitive doses PGE2

Maternal outcomes

Ayaz, Eur J Obstet Gynecol, 2013
Results for repetitive doses PGE2

Neonatal outcomes

Ayaz, Eur J Obstet Gynecol, 2013
Results for repetitive doses PGE2

Ayaz, Eur J Obstet Gynecol, 2013
Results for repetitive doses PGE2

Conclusion by authors:
- No increased maternal or neonatal morbidity

Increased number of doses of PGE2:
- Increase CS
- Increased failed IOL (cervix not favorable to perform ARM)
- Increase dystocia
- Decrease SVD
Induction of Labor

Is PGE2 safe in grand-multiparous women?
PGE2 safety in grand-multiparous women

- Retrospective study of 1376 women, parity > 5
- VD 96.6% of women
- No difference in:
  - CS
  - Operative vaginal delivery
  - PPH (all received 20U oxytocin im/iv + 0.2mg ergot)
  - One case of uterine rupture (one day after perforated appendix)

Haas, Journal Maternal-Fetal and Neonatal Medicine, 2013; 26
PGE2 – Summary

- Bishop < 7 (unfavorable cervix)
- PGE2 are effective agents of cervical ripening
- Safe with ruptured membranes at term
- Safe in asthma
- Outpatient for low risk women
- Cannot be used in VBAC (contrary to NICE 2008 guidelines)
- Sweep + insertion
- Less intervention when applied in the morning
WHAT ABOUT MISOPROSTOL?
Prostaglandin E1 - misoprostol

- Cervical ripening agent + uterotonic
- Approved for prevention and treatment of gastric ulcers
- First study published 1987 to describe successful induction of labor of stillbirth
- > 100 RCTs for obstetrical care
- Inexpensive, stability at room temperature, rapid onset
Misoprostol vs placebo / PGE2

- Hofmeyr, 2010
- Cochrane review, 121 trials
  - Compared to placebo
    - Less failure to achieve vaginal delivery < 24h (RR 0.51)
    - More tachysystole
  - Compared to PGE2 / oxytocin
    - Less epidural use
    - Less failure to achieve vaginal delivery < 24h
    - Less oxytocin augmentation
    - More meconium stained liquor
    - More tachysystole
Misoprostol vs Dinoprostone

- Multiple reviews (Cochrane, 2006; Crane, 2006; Kundodyiwa, 2009; Cochrane 2010)
  - Lower CS
  - More tachysystole
  - Similar or less need for oxytocin
  - Trend more meconium
  - Less failure to achieve vaginal delivery < 24 hours
  - No increase maternal / fetal adverse events
Misoprostol – Oral vs Vaginal

- Cochrane review (Alfiveric, 2006) found that oral had:
  - Less tachysystole without FH changes (RR 0.37)
  - More need for oxytocin (RR 1.28)
  - More meconium (RR 1.27)

- RCT 204 women (Colon, 2005) – 25mcg PO vs 50mcg PV
  - Less tachysystole with FH changes (2.2% vs 5.4%)
  - Lower CS rate (19.4% vs 32.4%)
  - No difference induction-delivery time or side effects (fever, shivering, nausea)

- RCT 120 women (Cecatti, 2006) – 12.5mcg PO vs 25mcg PV
  - No difference mode of delivery, induction-delivery time, oxytocin use
Misoprostol – Dosing

• **Vaginal – 25mcg vs 50 mcg**
  - More need for oxytocin
  - Less tachysystole ± fetal heart rate changes
  - Longer induction – delivery time
  - More use oxytocin
  - Less vaginal deliveries < 24h

• **Oral – 25mcg/50mcg vs placebo**
  - Less prolonged labor
  - Less need oxytocin
  - Lower CS rate
Misoprostol – Dosing

- Vaginal – 25mcg every 4 hours
- Oral – 50mcg every 4 hours / 25mcg every 2 hours
- Oxytocin – can be used 4 hours after the last dose
Misoprostol vs Foley

- **Adenji (2005)**
  - RCT, 96 women, 50mcg vaginal vs Foley
    - Reached favorable cervix (Bishop ≥ 6) faster
    - Lower use oxytocin
    - Same induction-delivery time

- **Afolabi (2005)**
  - RCT, 100 women, 100mcg vaginal vs Foley
    - Shorter induction-delivery time
Misoprostol / Term PROM

- Krupa (2005) – open RCT, 150 women
- 25mcg vaginal vs expectant ± oxytocin management
  - Shorter latency period
  - Shorter recruitment time to delivery
  - Trends
    - Lower oxytocin use
    - Lower CS

Study stopped due to lack of funding
More studies required
Misoprostol - summary

- Safe and effective agent for induction
- Reduce CS rate in unfavourable cervix
- Intact membranes only (further studies needed)
- Not for out-patient use or VBAC
- Dose
  - 50mcg oral every 4 hours
  - 25mcg vaginally every 4 hours
- EFM same as PGE2
  - 30 minutes after administration
  - 60 minutes after any tachysystole
- Oxytocin 4 hours after the last dose
- All doses/routes cause more tachysystole
- Oral route needs more oxytocin but has less tachysystole than vaginal route
Amniotomy

- No studies comparing amniotomy to placebo
- Used when the cervix is favourable
- Cochrane 2007 (Howarth)
  - ARM + oxytocin had more vaginal deliveries < 24h than ARM alone
  - ARM + oxytocin had less operative vaginal deliveries than placebo
  - ARM + oxytocin had more PPH and maternal dissatisfaction than vaginal PGs
Oxytocin

- Cochrane 2009 (Alfiveric)
- Oxytocin vs PG for cervical ripening
  - Increase un-successful vaginal delivery < 24h (70% vs 21%)
  - Fewer vaginal deliveries (51% vs 35%)
  - Increase CS (19.1% vs 13.7%), regardless of membrane status
Low dose vs high dose?
How high?
How fast?
Oxytocin – High vs Low

Studies showing benefit of oxytocin have used one or the other.

No studies of comparing one dosing regimens.

Regional variation / local expertise.

How much can the fetus tolerate?
Oxytocin – High vs Low

<table>
<thead>
<tr>
<th></th>
<th>Low dose</th>
<th>High dose</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial dose</strong></td>
<td>1-2 mU/min</td>
<td>4-6 mU/min</td>
</tr>
<tr>
<td><strong>Increase interval</strong></td>
<td>30 minutes</td>
<td>30 minutes</td>
</tr>
<tr>
<td><strong>Dose increment</strong></td>
<td>1-2 mU</td>
<td>4-6 mU</td>
</tr>
<tr>
<td><strong>Usual dose for good labor</strong></td>
<td>8-12 mU/min</td>
<td>8-12 mU/min</td>
</tr>
<tr>
<td><strong>Max dose for reassessment</strong></td>
<td>20, 30, 40 mU/min</td>
<td>20, 30, 40 mU/min</td>
</tr>
</tbody>
</table>

Use of oxytocin is not a cookbook recipe but rather a dynamic process that requires constant evaluation and of the maternal (pain, uterine contraction frequency and strength, cervical changes) and fetal (fetal heart, presentation, station) factors.
Induction of Labor – other agents

Other agents without proven benefit:
- Castor oil (Kelly, Cochrane 2009– nausea, no benefit
- Breast stimulation (Kavanagh, Cochrane 2009 – more women in labor at 72 hours compared to no treatment
- Acupuncture (Smith, Cochrane 2009)– no data
- Homeopathic medications (Cochrane 2010)– not enough evidence
WHAT ABOUT TERM PROM?
Women preference – induction vs expectant/ oxytocin and PG

<table>
<thead>
<tr>
<th></th>
<th>Oxytocin</th>
<th></th>
<th>PG</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Induction</td>
<td>Expectant</td>
<td>P value</td>
<td>Induction</td>
<td>Expectant</td>
</tr>
<tr>
<td>Nothing they disliked</td>
<td>74 (5.9%)</td>
<td>17 (13.7%)</td>
<td>&lt;0.001</td>
<td>64 (5.1%)</td>
<td>124 (11.7%)</td>
</tr>
<tr>
<td>Would repeat in the study</td>
<td>847 (67.3%)</td>
<td>756 (59.9%)</td>
<td>&lt;0.001</td>
<td>837 (66.5%)</td>
<td>746 (59.2%)</td>
</tr>
</tbody>
</table>

Conclusion – women preferred induction with oxytocin or PG vs expectant

Hannah, NEJM, 1996
WHAT ABOUT TERM PROM +GBS?
TERM PROM Study

- 5041 women
- GBS culture at time of PROM (no universal screening)
- IV oxytocin vs PGE2 gel q 6h
- Less GBS disease in oxytocin induction group than PGE2 induction + either expectant group
- Inadequate prophylaxis for both groups
  - 23% induction group and 28% in expectant (4 days later) group

Hannah, AJOG, 1997
WHAT ABOUT PPROM?
Misoprostol / PROM > 34 weeks

- Bricker (2007)
- RCT 758 women
- 2 groups compared to vaginal dinoprostone ± oxytocin
  - Bishop > 6 -> 25 mcg oral vs oxytocin
  - Bishop ≤ 6 -> 50 mcg vaginal vs dinoprostone ± oxytocin
- Terminated early due to lack of funding (needed 1890 women)
- No difference CS or vaginal delivery rates
- Trends in misoprostol group
  - Less use of oxytocin
  - Less epidural use
  - Less CS for dystocia
  - More effective than dinoprostone in the setting of an unfavourable cervix
  - Less effective than oxytocin in the setting of favourable cervix

More studies required
### Induction of Labor- Promexil 1

- **RCT PPROM 34-37 weeks**
- **IOL (n=266) vs expectant management (n=266)**
  - IOL within 24 hours (oxytocin or PGE2)
  - EM group induced at 37 weeks

<table>
<thead>
<tr>
<th>Condition</th>
<th>IOL (n=266)</th>
<th>EM (n=266)</th>
<th>RR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonatal sepsis</td>
<td>7 (2.6%)</td>
<td>11 (4.1%)</td>
<td>0.64 (0.25-1.6)</td>
</tr>
<tr>
<td>RDS</td>
<td>21 (7.8%)</td>
<td>17 (6.3%)</td>
<td>1.3 (0.67-2.3)</td>
</tr>
<tr>
<td>CS</td>
<td>36 (13%)</td>
<td>37 (14%)</td>
<td>0.98 (0.64-1.65)</td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>6 (2.3%)</td>
<td>15 (5.6%)</td>
<td>0.4 (0.16-1.02)</td>
</tr>
<tr>
<td>Histological chorio</td>
<td>43 (22%)</td>
<td>62 (32%)</td>
<td>0.69 (0.49-0.96)</td>
</tr>
</tbody>
</table>

VanDerHam, Promexil 1, Plos Med, 2012
Induction of Labor - Promexil 2

- RCT PPROM 34-37 weeks
- IOL (n=100) vs expectant management (n=95)
  - IOL within 24 hours (oxytocin or PGE2)
  - EM group induced at 37 weeks

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<tr>
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<th>EM (n=95)</th>
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<tbody>
<tr>
<td>Neonatal sepsis</td>
<td>3 (3%)</td>
<td>4 (4.1%)</td>
<td>0.07 (0.17-3.2)</td>
</tr>
<tr>
<td>RDS</td>
<td>6 (6%)</td>
<td>5 (5.1%)</td>
<td>1.2 (0.37-3.7)</td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>0</td>
<td>4 (4.3%)</td>
<td></td>
</tr>
<tr>
<td>Histological chorioamnionitis</td>
<td>12 (18%)</td>
<td>18 (31%)</td>
<td>0.64 (0.33-1.2)</td>
</tr>
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VanDerHam, Promexil 2, AJOG, 2012
Summary

- Prevention – dating, sweeping, enforcement, philosophy
- Indication / likelihood of success / failure
- Delay induction unfavorable cervix (> 41+2 weeks)
- Misoprostol safe for term + intact membranes
- Avoid oxytocin for an unfavourable cervix
- PGE2 safe for ruptured membranes at term
- Outpatient induction with PGE2 and Foley
- Add oxytocin sooner rather than later after ARM
- VBAC – Foley ± oxytocin
## Term – unfavourable cervix

### Intact membranes

<table>
<thead>
<tr>
<th>Preferred</th>
<th>Acceptable</th>
<th>Contra-indicated</th>
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<tbody>
<tr>
<td>Mechanical</td>
<td>Amniotomy</td>
<td>PGE2 and PGE1 VBAC</td>
</tr>
<tr>
<td>PGE2</td>
<td>Oxytocin (high presentation with risk of prolapse)</td>
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<td>PGE1 (oral=vaginal)</td>
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### Ruptured membranes

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<td>PGE2 (GBS -)</td>
<td>Oxytocin</td>
<td>PGE1</td>
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<tr>
<td>Oxytocin (GBS+)</td>
<td>PGE2 (GBS+)</td>
<td>?</td>
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### Term – Favourable cervix

#### Intact membranes

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All other references can be found in the 2013 SOGC Induction of labor Guidelines