OXYTOCIN:
WHEN TO START & WHEN TO STOP

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DISCLOSURES

- I have received honorarium from Smith + Nephew for educational lectures on wound care and negative pressure wound therapy
- I trained and practiced primarily with oxytocin use for labour induction and augmentation but have recently become a big fan of misoprostol

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COMING SOON!

THE SOCIETY OF OBSTETRICIANS AND GYNAECOLOGISTS OF CANADA

Watch this space for the new SOGC Clinical Practice Guidelines:
Cervical Ripening and Induction of Labour

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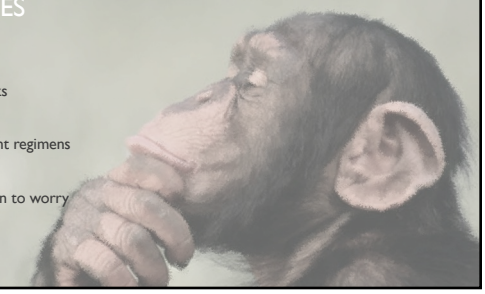
OBJECTIVES

- Review the risks
- Discuss different regimens
- Red flags / when to worry



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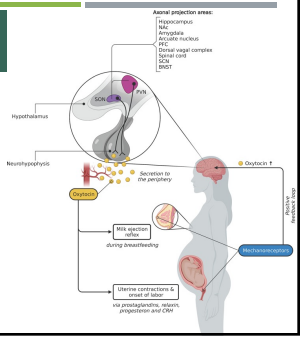
WHAT IS OXYTOCIN?

- Oxytocin is a peptide
- Three primary oxytocin signaling genes:
  - OXT (20p13, structural gene for oxytocin), OXTR (3p25.3, oxytocin receptor), and CD38 (4p15.32, oxytocin secretion)
- Primarily synthesized by the hypothalamus in the supraoptic nucleus and the paraventricular nucleus for both systemic and central release
- From a physical perspective:
  - Rhythmic uterine contractions
  - Let down reflex (breastmilk expression)
- From a psychosocial perspective:
  - Interactions with dopaminergic and muscarinic acetylcholine signaling to modulate cognitive state processes involved in complex human behaviors
    - Recognition
    - Trust
    - Parent-infant bonding
    - Romantic attachment
    - Sexual arousal and orgasm



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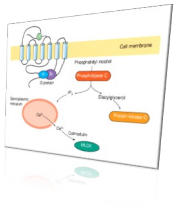
MYOMETRIAL OXYTOCIN RECEPTORS

- Oxytocin receptor activation triggers the release of intracellular calcium and local prostaglandin production
- Receptors are produced by the myometrium from 13 weeks' onwards, reach a clinically significant concentration at ~20 weeks', and peak at term
- Oxytocin action is limited by the concentration of receptors in the smooth muscle of the uterus. Repeated doses may cause desensitization of the receptors and decreased response (Vallera 2017).



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EXOGENOUS INTRAVENOUS PHARMACOKINETICS

- Onset of action (Uterine contractions): 1 minute
- Steady state achieved (max response): 40 minutes
- Duration of action: 1 hour
- Half-life: 1 to 6 minutes; decreased in late pregnancy
- Excretion: Urine (small amount unchanged)

- Cost: 10 units/mL (per mL): $2.31 - $4.61 CAD

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ISMP Institute for Safe Medication Practices An ECRI Affiliate

- Since 2007, the *Institute for Safe Medication Practices (ISMP)* has included IV oxytocin among its list of medications that have a heightened risk of causing significant patient harm when used in error

- **Maternal deaths:** Caused by hypertensive episodes, subarachnoid hemorrhage, or rupture of the uterus
- **Fetal deaths:** When used for induction of labour or for augmentation in the first and second stages of labour

- ISMP suggest there may be benefit from mitigation strategies, including standardized use (e.g., order, storage, preparation, and overall administration), proper labeling, applying clinical decision supports, and/or applying independent double checks

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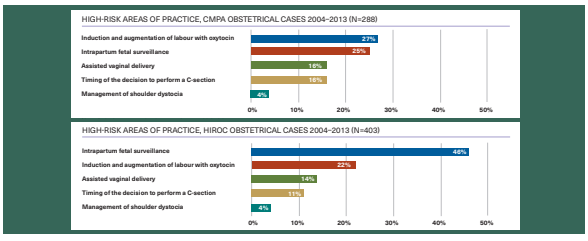
HIROC — DELIVERY IN FOCUS: Strengthening obstetrical care in Canada — CMPA



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ADVERSE REACTIONS

- Cardiovascular: Cardiac arrhythmia, hypertensive crisis, hypotension, subarachnoid hemorrhage, tachycardia, ventricular premature contractions
- Endocrine & metabolic: Water intoxication with hyponatremia (severe water intoxication with seizure and coma is associated with a slow oxytocin infusion over 24 hours and in cases using >40 mu/min)
- Gastrointestinal: Nausea, vomiting
- Genitourinary: Postpartum hemorrhage, uterine rupture
- Hematologic & oncologic: Pelvic hematoma
- Hypersensitivity: Anaphylaxis

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CONTRAINDICATIONS (PRODUCT LABEL)

- Hypersensitivity
- Significant cephalopelvic disproportion
- Unfavorable fetal positions or presentations
- Fetal distress when delivery not imminent
- Hypertonic or hyperactive uterus
- Contraindicated vaginal delivery (invasive cervical Ca, active genital HSV, cord prolapse, funic presentation, complete placenta previa, vasa previa)
- OB emergencies where surgical intervention is favored
- If adequate uterine activity doesn't achieve satisfactory progress

***Canadian labeling*:**

- Severe toxemia (preeclampsia)
- Prematurity or unripe cervix
- Predisposition to uterine rupture (eg, grand multiparity, overdistention of the uterus, previous caesarian delivery, other surgery involving the uterus)
- Prolonged use in uterine inertia
- Factors predisposing to thromboplastin or AFE (eg, prolonged retention of dead fetus, placental abruption)
- Serious medical or obstetric conditions and any condition in which fetal distress already occurs
- Inability of physician to be in attendance

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INDICATIONS FOR INDUCTION

When used for elective (non-medically indicated) IOL, oxytocin is being used off-label
The ARRIVE trial

HIGH PRIORITY

- Chorioamnionitis
- PET without severe features ≥37 weeks gestation
- PET with severe features at any gestational age
- PROM, at or near term, with GBS+
- Post-term pregnancy (>42+0 weeks)
- Significant maternal disease not responding to treatment
- Significant yet stable antepartum hemorrhage
- Suspected fetal compromise

OTHER INDICATIONS

- AMA ≥40 years at 39 weeks gestation
- Diabetes mellitus (glucose control may guide timing)
- Fetal growth restriction
- Intrahepatic cholestasis of pregnancy
- Intrauterine fetal death (IUFD)
- IUFD in a prior pregnancy to alleviate anxiety or risk
- Logistical issues (i.e. prior precipitous labour, distance)
- Oligohydramnios
- Post dates pregnancy >41+0 weeks gestation
- PROM, at or near term, with GBS-
- Uncomplicated DC twins by 38 weeks or MC by 37 weeks
- Uncomplicated gestational hypertension >38 weeks

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IS THE CERVIX FAVOURABLE?

	0	1	2	3
Position	Posterior	Mid	Anterior	
Consistency	Firm	Medium	Soft	
Cervical Length (prev effacement)	≥ 4 cm (prev 0-30%)	2-3 cm (prev 31-50%)	1-2 cm (prev 51-80%)	<1 cm (prev >80%)
Dilatation	0 cm	1-2 cm	3-4 cm	≥ 5 cm
Fetal Station	-3	-2	-1/0	+1/+2

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INDICATIONS FOR AUGMENTATION

- Latent phase labour: > 20 hours if nulliparous, > 14 hours if parous
- Slow progress of active labour: cervical dilatation rate of < 0.5-1 cm per hour
- Active phase labour with arrest of dilatation > 2 hours with inadequate uterine activity
- Second-stage arrest of descent with inadequate contractions, defined as:
  - A contraction pattern > 2-3 minutes apart, lasting < 80-90 seconds, and not palpating strong
  - A contraction pattern demonstrating < 220 MVU with IUPC
- If oxytocin is utilized for 1st stage augmentation, the time to delivery is shortened by ~2 hours (Alhafez 2020)

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PROVINCIAL RECOMMENDATIONS

- *"Obstetrical care providers are reminded to decrease or stop oxytocin when the fetal heart rate tracing is abnormal."*
- *Safe Administration of Oxytocin Guideline Report (Original 2019, revised 2022)*
- Endorsed by: SOGC, Ontario College of Family Physicians, Association of Ontario Midwives, Canadian Association of Perinatal and Women's Health Nurses, HIROC

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HOW TO PREPARE OXYTOCIN

Provincial Council for Maternal and Child Health
building a brighter future

- All hospitals should use a standardized low-dose oxytocin protocol and order set
- Minimizes medication errors and ensure precise and transparent drug administration
- Verbal or remote orders for oxytocin should not be given to RN staff
- Continuous fetal heart rate monitoring should be instituted and assessed prior to oxytocin
- Independent double check should be performed
  - Preparing the medication
  - Setting the initial pump infusion rate via an IV Smart Pump
- 10 units in 500mL RL or NS (final concentration 20 mU/mL)

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HOW TO ADMINISTER OXYTOCIN

Provincial Council for Maternal and Child Health
building a brighter future

- Only low-dose protocols should be used
- To reduce errors, must be administered/documented in mU/min rather than mL/hr
- Patients should receive continuous one-to-one care by a registered healthcare professional for support, advocacy, comfort measures, and monitoring
- The oxytocin protocol and order set must provide clear start, stop and restart guidelines:
  - An in-person assessment and written order by the prescriber is required before the nurse or midwife can start or restart the infusion
  - The need to reduce or stop the infusion when there is:
    - Atypical or abnormal fetal heart rate (FHR) findings
    - Uterine tachysystole with or without FHR changes
- The oxytocin rate should not be increased if there is adequate uterine activity
- In the event that a healthcare practitioner provides care that deviates from the protocol, the indication must be justified and documented in the patient's chart
- Oxytocin must not be administered for the convenience of the staff or in the presence of concerning fetal health surveillance (FHS) as defined by the SOGC

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COMMONLY USED PROTOCOLS

	Low-Rate Protocol	Expedited-Rate Protocol
Initial rate of oxytocin	1-2 mU/minute	4-6 mU/minute
Increase interval	30 minutes	30 minutes
Rate increment	1-2 mU	4-6 mU
Maximum rate	20-30 mU/minute	20-30 mU/minute
Benefits	Less tachysystole Lower total dose	Shorter time to delivery
Risks	Longer time to delivery	More tachysystole with or without FHR changes
Relative contraindications		TOLAC, parity ≥5, second stage, augmentation of labour

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WHEN TO STOP

- Ensure one-to-one care frequently monitoring:
  - Frequency of uterine activity
  - Contraction duration, strength, and resting tone (cannot do this out of the room)
- If unable to monitor FHR during epidural insertion
- Once optimal contraction pattern achieved, if no progression (station/effacement/dilatation) over ~2-4 hours = operative delivery
- Oxytocin should be reduced (by 50%) or stopped in the presence of:
  - Atypical FHR, and/or
  - Uterine tachysystole without FHR changes
- Oxytocin should be stopped in the presence of:
  - Abnormal FHR, or
  - Tachysystole with atypical/abnormal FHR changes
- The physician should be immediately notified and review the patient
- Intrauterine resuscitation interventions may include:
  - Stop or decrease oxytocin
  - Change maternal position to left or right lateral
  - Check vital signs, including differentiation of maternal and FHR
  - Ask patient to modify or pause pushing efforts in the active 2nd stage
  - Improve hydration with IV fluid bolus, if indicated
  - Perform VE to rule out cord prolapse, assess progress, scalp stimulation
  - Consider tocolysis when tachysystole with atypical/abnormal tracing
  - Consider amnioinfusion in complicated variable decelerations
  - Provide supportive care to reduce maternal anxiety
  - Consider oxygen by mask only when maternal hypoxia and/or hypovolemia

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Table 7. Classification of normal uterine activity and tachysystole

Characteristic	Normal	Tachysystole (term for all forms of excessive UA; includes any of the following)
Frequency	≤5 contractions in 10 minutes, averaged over 30 minutes[47]	>5 (≥6) contractions in 10 minutes, averaged over 30 minutes
Duration	<90 seconds	>90 seconds
Intensity	Palpation: Mild, moderate, or strong IUPC: >25 mm Hg and <75 mm Hg above the baseline except in second stage	
Resting tone	Uterus soft on palpation for a minimum of 30 seconds IUPC: <25 mm Hg[47]	Resting period between contractions of <30 seconds OR the uterus remains firm or >25 mm Hg between contractions

IUPC: intrauterine pressure catheter; UA: uterine activity.

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Table 15. Classification of intrapartum EFM tracings

	Normal	Atypical	Abnormal
Uterine activity	• Normal contraction pattern	• Tachysystole may be present with normal, atypical, or abnormal tracings; monitor closely for concerning FHR characteristics	
Baseline	• 110–160 bpm	• 100–110 bpm • >160 bpm for 30–80 minutes • Rising baseline • Arrhythmia (irregular rhythm)	• <100 bpm • >160 bpm for >80 minutes • Erratic baseline
Variability	• 6–25 bpm • ≤5 bpm for <40 minutes	• ≤5 bpm for 40–80 minutes	• ≤5 bpm for >80 minutes • ≥25 bpm for >10 minutes • Sinusoidal
Acceleration	• Spontaneous accelerations but not required • Acceleration with scalp stimulation	• Absence of acceleration with scalp stimulation	• Usually absent (accelerations, if present, do not change classification of tracing)
Deceleration	• None • Non-repetitive uncomplicated variable decelerations • Early decelerations	• Repetitive uncomplicated variables • Non-repetitive complicated variables • Intermittent late decelerations • Single prolonged deceleration ≥2 minutes but <3 minutes	• Repetitive complicated variables • Recurrent late decelerations • Single prolonged deceleration ≥3 minutes but <10 minutes
Interpret clinically (in light of total situation)	• No evidence of fetal compromise	• Physiologic response	• Possible fetal compromise
Terminology	**Recurrent**: Decelerations occur with ≥50% of uterine contractions in any 20-minute window. **Intermittent**: Decelerations occur with <50% of uterine contractions in any 20-minute segment. **Repetitive**: ≥3 in a row **Non-repetitive**: 1 or maximally 2 in a row		

EFM: electronic fetal monitoring; FHR: fetal heart rate.

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STOPPING ONCE IN ACTIVE LABOUR?

Cochrane Library
Cochrane Database of Systematic Reviews

Discontinuation of intravenous oxytocin in the active phase of induced labour (Review)

Boie S, Glavind J, Velu AV, Mol BWJ, Uldbjerg N, de Graaf I, Thornton JG, Bor P, Bakker JJH

- Can outcomes be improved by discontinuation of IV oxytocin (for IOL) once active labour established?
- 10 completed RCTs involving 1888 subjects (1998 – 2016), analyzed by intention to treat
- Many trials had design limitations and were judged to be at either **high or unclear risk of bias**
- Compared with continuation of IV oxytocin, discontinuation of IV oxytocin may:
  - Reduce the CS rate, risk ratio (RR) 0.69, 95% CI 0.56 to 0.86 (low certainty)
  - (Analysis of those who reached the active phase of labour showed no difference, RR 0.92, 95% CI 0.65 to 1.2)
  - Reduces the risk of uterine tachysystole with abnormal FHR, RR 0.15, 95% CI 0.05 to 0.46 (moderate certainty)
  - Reduces atypical/abnormal FHR patterns, RR 0.65, 95% CI 0.51 to 0.83 (moderate certainty)
  - However, no effect on chorioamnionitis, use of analgesia/epidural, low Apgar scores or abnormal cord gases

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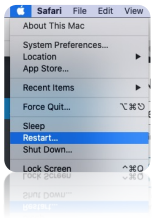
RESTARTING

- FHR tracing should be normal
- If <30 mins have elapsed since stopping:
  - Re-start at 50%-100% of the previous rate
- If >30 mins have elapsed since stopping:
  - Re-start from initial protocol rate (1-2 mU/min)



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IF GOING ABOVE HOSPITAL PROTOCOL

- Obstetrician consultation, guidance and oversight
- Consider placement of intrauterine pressure catheter to make things objective
  - Titrate oxytocin up to optimal contraction pattern
  - Aim for 200-250 Montevideo units (MVU) per 10 minutes
- If >30 mU/min with administration >24 hours consider laboratory surveillance for hyponatremia every 4-6 hours

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SPECIAL POPULATIONS

- Intrauterine fetal death
- Significant maternal arrhythmias or risk

- Previous cesarean section
- Breech presentation

- Second twin at vaginal delivery

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FINAL THOUGHTS & TAKE HOME

- Use a hospital-based protocol and order set
- Educate all staff and promote in-room one-to-one care
- Use a low-rate/low-dose protocol
- Once in active labour, continue with oxytocin (perhaps reduce, but don't stop)
- Follow SOGC guidelines for labour care, fetal monitoring and induction/augmentation of labour
- If you are deviating from the standard of care: see the patient and document your rationale/discussion
- Remember the pharmacokinetics
- Tocolysis probably doesn't fix things, time does
- Please try not to become complacent with oxytocin

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THANKS FOR HAVING ME ☺
ANY QUESTIONS?

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