# OPIOIDS AND PREGNANCY

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# DISCLOSURES

I have no financial disclosures or conflicts of interest.

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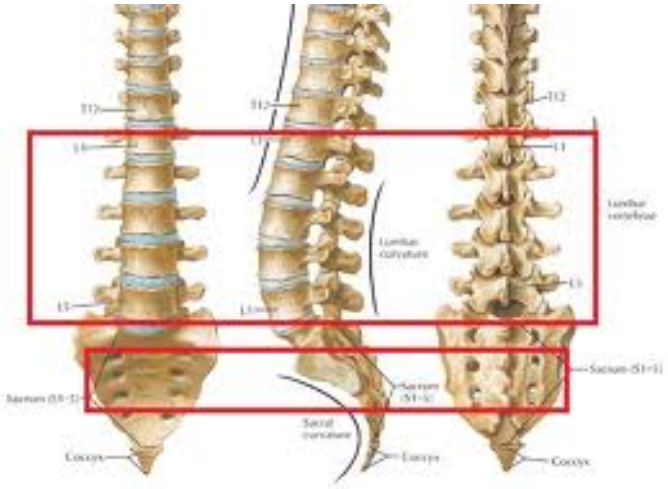
# OBJECTIVES FOR THE TALK

- Avoiding opioids:
  - Review efficacy of non-pharmacologic therapies
  - Review safety of non-opioid medications
- Describe risks of opioids during pregnancy
  - ***Fetal***
  - ***Obstetrical***
  - ***Neonatal***
- Discuss role of taper/detoxification of opiates during pregnancy

# PAIN IN PREGNANCY

*Musculoskeletal*

- *Acute: sciatica, pubic symphysitis*
- *Chronic: back pain, exacerbation of prior injuries*



- 2/3 of women complain of low back pain
- 1/5 of women complain of pelvic pain

# NON-PHARMACOLOGIC THERAPIES

2013 Cochrane Review

- 26 trials (n=4093 pregnant women)
- Low to moderate quality evidence
- Treatment of lumbar, lumbopelvic and pelvic pain
    - *Acupuncture*
    - *Physical therapy*
    - *Exercise (strength, stability or water)*
    - *Osteopathic manipulation*
    - *Support belt*

Pennick, et al. 2013 Cochrane Library.

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# NON-PHARMACOLOGIC THERAPIES

Address psychosocial contributors to pain:

- *Psychiatric conditions*
- *Social stressors*
- *Intimate partner violence*

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# NON-OPIOID PHARMACOTHERAPY

*NSAIDs: Category C or D*

- First trimester use: not strongly associated with anomalies
- Long-term use contraindicated: **oligohydramnios,** childhood asthma?
- Use > 30 weeks: **premature closure of fetal ductus arteriosus**
- Short course (<48 hr) NSAIDs may be used for uterine tocolysis, surgical or musculoskeletal pain

*Tylenol:  Category B*

- Fetal toxicity in maternal overdose
- Recent studies show association with childhood asthma, ADHD and potentially autism

# GENERAL PRINCIPLES

- High rates of opioid prescriptions in reproductive age women ***preconception and during pregnancy***
- Reproductive age women (age 15-44)

  39% of women with Medicaid versus 28% with private insurance filled an opioid prescription every year
- Pregnant women

  21% of pregnant women with Medicaid versus 14% with private insurance filled an opioid prescription
- Nearly 4-fold increase in rates of opioid prescriptions to pregnant women during 2000-2009

Ailes et al. MMWR 2015.
Bateman et al. Anesthesiology 2014
Patrick et al. JAMA 2012.

# GENERAL PRINCIPLES

- Physiologic changes during pregnancy:
  - Increased volume of distribution
  - Change in protein binding
  - Increased hepatic metabolism
  - Increased renal clearance
- For chronic opioid users (including long acting and methadone), may require INCREASE in dose and/or frequency (daily → BID)
- Anesthesia may be more complicated in labor or postpartum (especially after cesarean section)

# TERATOGENICITY

- Opioids are known to cross the placenta
- Several recent epidemiologic studies demonstrate increase risk of neural tube, abdominal wall and cardiac defects
- Baseline risk of congenital anomalies is 2-3%

*"No clear pattern of teratogenicity with opioids during the first trimester"*

Yazdy, et al. Obstet Gynecol 2013
Broussard, et al. Am J Obstet Gynecol 2011
ACOG Committee Opinion #524, May 2012

# OPIOIDS AND ADVERSE OUTCOMES

*Association with adverse pregnancy outcomes:*

- Preterm delivery, poor fetal growth, stillbirth
- Higher rates of depression, anxiety, and chronic medical conditions
- Increased health care costs

*Data may be confounded by:*

- Comorbid medical complications, obesity, nutritional and socioeconomic status, alcohol, tobacco and illegal drugs

Whiteman, et al. J Pregnancy 2014

# OPIOIDS AND NEUROBEHAVIOR

## Fetal effect (at peak methadone level):

*Decreased fetal heart rate variability, lower baseline, fewer accelerations, less motor activity and breathing*

*High incidence of non-reactive NSTs*

## Feeding difficulty in opiate exposed infants

*Altered sucking patterns*

*May affect development of brainstem respiratory and swallow centers*

Jansson et al, *Am J Obstet Gynecol* 2005.

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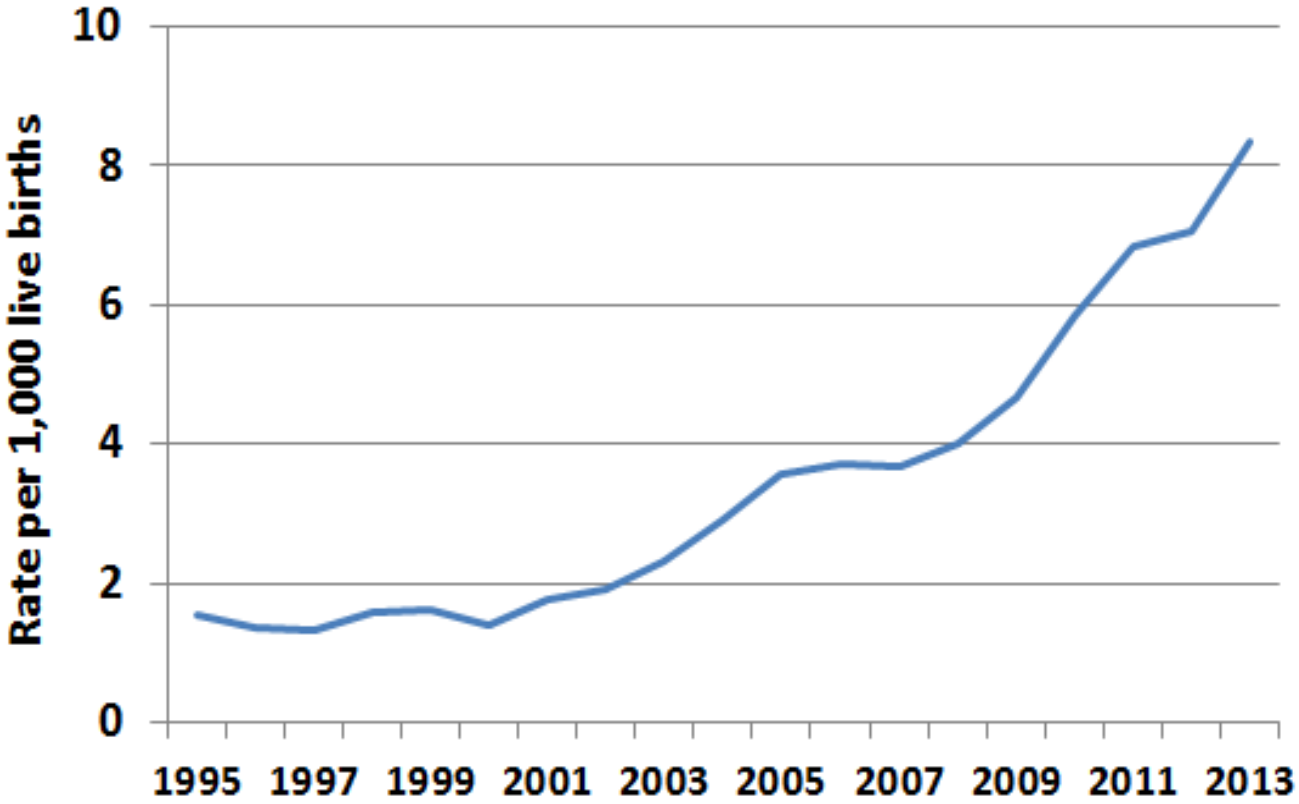
# NEONATAL ABSTINENCE SYNDROME

## *Neonatal Abstinence Syndrome (NAS)*

- 30-80% of infants exposed to opioids in utero require treatment for NAS (60-90% exposed to methadone)
- Symptoms include: irritability, tremulousness, sweating, nasal stuffiness, poor suckling, diarrhea, vomiting and seizure
- Postnatal Finnegan score grades the degree of psychomotor irritability, vasomotor and gastrointestinal disturbances

# NEONATAL ABSTINENCE SYNDROME

Infant Hospitalizations for Neonatal Abstinence Syndrome
in Washington State 1990-2013




Source: Inpatient Hospital Discharge & Birth Certificate Data,
NAS= ICD diagnosis code of 779.5

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# NEONATAL ABSTINENCE SYNDROME

## *Timing of NAS*

- Short acting opiates have earlier onset of NAS symptoms than methadone or long-acting opiates
- Can occur from the first 24 hours to day 14 of life
- Usually within first 72 hours

## *Maternal dose and NAS*

- Neither the incidence or severity of NAS directly correlate with maternal methadone dose
- Buprenorphine is associated with a lower incidence and shorter duration of NAS

Seligman, et al. J Pediatrics 2010.
Brogly, et al. Am J of Epidemiology 2014.

# OPIOIDS AND LACTATION

*American Academy of Pediatrics supports breastfeeding in patients on methadone (no dose limitation)*

- Infants receive 2-3% of weight adjusted maternal dose via breast milk
- Breastfeeding may reduce the severity of NAS and shorten length of hospital stay
- Short acting opiates commonly prescribed after cesarean section without concern for lactation

American Academy of Pediatrics Committee on Drugs: The transfer of drugs and other chemicals into human milk. 2001 *Pediatrics*

# AN ARGUMENT FOR DETOXIFICATION?

*Rationale:*

- Minimize maternal/fetal opiate exposure
- Lower risk of overdose and diversion
- Decrease risk of teratogenicity/in utero effect
- Decrease risk of neonatal abstinence syndrome

# OPIATE WITHDRAWAL IN PREGNANCY

*Opiate withdrawal/detoxification in pregnancy*

- Associated with preterm labor and/or fetal distress, meconium, stillbirth, elevated amniotic fluid epinephrine and norepinephrine
- Reports of miscarriage during first trimester
- Concern for recividism (illegal opioids)
- Use of nalaxone, an opioid antagonist, contraindicated in pregnancy unless maternal overdose (includes buprenorphine-naloxone)

UpToDate: Methadone maintenance therapy during pregnancy
ACOG Committee Opinion #524, May 2012

# EVIDENCE IN SUPPORT OF DETOXIFICATION

*Inpatient detoxification experience:*

Taper by <20% of stable dose every 3 days

- Dashe 1998: 59% successful detox, no increase in complications
- Luty 2003: 21 day program, no second trimester loss or increase in PTB
- Stewart, 2013: 56% successful detox, no increase in complications

Dashe et al. *Obstet Gynecol* 1998.
Luty et al. *J Subst Abuse Treat* 2003.
Stewart et al. *Am J Obstet Gynecol 2013.*

# CONCLUSIONS

- Ideal to avoid opioid use ***pre-conception***
- ***Avoid initiation*** of opioids during pregnancy to minimize fetal risks and neonatal complications
- Initiation of opioids during pregnancy requires ***counseling*** and documentation
- ***Anesthesia*** and ***Inpatient Pediatric*** consult should be considered for women on chronic opioids prior to delivery
- Controversy exists regarding ***safety of outpatient opiate detoxification***

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# QUESTIONS?

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