Substance Use in Pregnancy: What Providers Need to Know

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- I have no relevant financial relationships with any commercial interests
Objectives

- Discuss what is addiction—and what is not
- Review epidemiology of substance use in pregnancy
- Discuss social impacts of punitive response to maternal substance use
- Compare treatment approaches, including MAT, for pregnant and breastfeeding women with opiate use disorder
- Discuss marijuana use in pregnancy

What is Addiction?

- Addiction is defined as a primary, chronic disease of brain reward, motivation, memory, and related circuitry.
- Perinatal Addiction is an emerging field that recognizes the biopsychosocial complexity of substance use disorder care in the setting of pregnancy
- Seeks to provide comprehensive services to the patient and family in the pre-conception, pregnancy, delivery, and post-partum periods

Neurobiology: A refresher

- We cannot talk about addiction without starting the understanding the concept of “reward”
Dopamine: The Currency

Natural Rewards

Stimuli. Dopamine. Repeat.
Not the entire story

- Reward teaches us via “positive reinforcement”
  - Behavior produces positive reward
    - Dopamine
    - The positive reward makes the behavior more likely to occur
    - “Fires together, wires together”

And...

Negative Reinforcement

- Different than punishment
  - Negative reinforcement encourages the behavior
  - Punishment discourages the behavior
- Very powerful learning mechanism
  - We can fatigue (become tolerant) to receiving the same positive reinforcement, or the same punishment
  - However, use of a behavior to escape negative:
    - Physical symptoms (withdrawal)
    - Emotions (guilt, shame, depression, anxiety)
    - Trauma (either ongoing or PTSD)

  Is EXTREMELY powerful

Tolerance and Dependence

Expected, physiological adaptations to presence of enough substance over enough time

- Tolerance: Needing and increasing amount of a substance to achieve the desired effect
- Dependence: physiological adaptation to presence of substance such that substance is now required to maintain homeostasis
- Withdrawal: substance specific set of symptoms related to absence of substance of dependence

These findings alone, especially if prescribed medication, are not enough to diagnoses addiction
Natural History of Dependence

- Normal
- Positive Reinforcement
- Tolerance & Physical Dependence
- Negative Reinforcement
- Acute use
- Chronic use

Substance Use Disorder
- The five Cs:
  - Craving
  - Compulsive use
  - Continued use despite harm (consequences)
  - Impaired control over drug use
  - Chronicity
- Inability to fulfill work and social obligations
- Use in dangerous situations
- Legal problems
- Interpersonal problems
- Mild (1-3), Moderate (4-5), Severe (6+)

A Different Perspective
- “Ritualized, compulsive comfort seeking” Dr. Sumrok
- Addiction as an adaptive response to environment
  - Trauma/Loss
  - Systematic/Generational oppression, racism
  - Mental Anguish (depression, Anxiety, PTSD, mania)
  - Social insecurity, phobia
  - Isolation
  - Boredom
A Different Perspective

- Johann Hari “Chasing the Scream”, TedTalk
  - “The opposite of addiction is not sobriety. The opposite of addiction is connection.”

- Maia Szalavitz “Unbroken Brain”
  - Learning and Developmental approach

- Gabor Mate “In the Realm of Hungry Ghosts”
  - Need for community, social and criminal justice policy reform

Epidemiology

- A difficult number to nail down!
  - Depends on patient self-report
  - Toxicology screenings
  - Only known data of women who present for care.
    - Movement towards out-of-hospital birthing to avoid toxicology testing, particularly for THC
  - Depends on what is “socially acceptable”
    - Alcohol, tobacco, marijuana?

Epidemiology

- Estimates vary between 2-24%, depending on screening tool used:
  - Illicit Substances 5.9%
  - Alcohol 8.5%
  - Nicotine 15.9%

- Highest rate of substance use in women is in years of childbearing (ages 15-35yrs)

- Many of these urine toxicology reports do not account for prescription substances

- Biased information: minority women (particularly black women) over-represented in toxicology testing and reporting, even though there is equal incidence across all SES
Starting the Conversation

- 4 “P”s
  - Parents?
  - Partner/Peers?
  - Past?
  - Present?

- Asking about peer/partner substance use is more highly associated with individual’s risk the younger the age of the woman

Screening Tools

- SBIRT
- AUDIT-C/AUDIT
- T-ACE
- DAST
- Adolescents:
  - Ages 12-17: S2BI
  - Ages 14-21: CRAFFT

Maternal Risks

- Lack of prenatal care can lead to missed diagnoses, which can be life threatening
  - Pre-eclampsia/Eclampsia
  - Miscarriage, premature ROM, premature labor
  - Placenta previa, accreta
  - Bacteremia, endocarditis
  - Infectious disease, STIs (HIV, Hep C, Hep B)

The most common reason for women not presenting for prenatal care is not lack of care for themselves or their unborn, it is fear: being “found out”, being reported to social services, and losing custody of infant (or other children)
Fetal Risks

- Pre-term delivery
- Intra-uterine growth restriction
- Low birth weight (SGA)
- Placental insufficiency/abruption
- Amnionitis
- Birth defects
- Fetal Alcohol Effects/Spectrum Disorders
- Neurocognitive impairment
- Neonatal Abstinence Syndrome


*Note: Number of pregnancy-related deaths per 100,000 live births per year.

Maternal deaths in Colorado 1999-2015

Deaths per 100,000 live births
Maternal Deaths in CO

Post-Partum Deaths in CO

The War on Drugs
In most cases when a woman is imprisoned, a child is displaced. 28% of women (18yo+) provide support and care to chronically ill, disabled, or aged family members or friends.

**Case #1: Opiates**

- “Anna” is 23 yo G2P1001 at approx 27 weeks gestation by unsure LMP.
- Pt presents to ED with opiate withdrawal: vomiting, cramping, sweats, chills, tremor, anxiety
- Pt reports she has been taking oxycodone daily for past 3 years. Has been receiving prescription from PCP since car accident 3 years ago.
- Doctor “cut me off” 3 months ago when discovered pregnancy
Case #1: Opiates

- Pt reports that since stopped receiving prescription, has been getting pills from family/friends. Started buying on street, also some heroin (smoked), no injection use, no other substance use
- Pt estimates taking between 50-80mg oxycodone per day plus intermittent smoked heroin when can’t get pills
- “I want to stop, but the withdrawals are so bad, and I don’t want to lose my baby”
- No OB care yet this pregnancy
- Lost job, family is “going to kick me out”

Options for opioid dependence during pregnancy

- Detoxification
- Methadone
- Buprenorphine
- Naltrexone/Vivitrol

Why has detoxification from opioids during pregnancy been long avoided?

Narcotic withdrawal in pregnancy: Stillbirth incidence with a case report

José Luis Rementeria, M.D.
Semio N. Sunag, M.D.

A stillborn infant was born to a drug-addicted mother who had withdrawal symptoms shortly before delivery. Mechanisms are proposed to help explain the possible relationship between the maternal withdrawal and the still birth. Statistic were also presented to show an increased stillborn and maternal mortality rate in the overall pregnant drug-addicted population.
Detoxification: Just because something can be done...

- 93 patients
- All offered detoxification
- Gestational age about 20 weeks at entry
- Duration of detoxification: 25 days
- There was no f/u of how the women fared after delivery

Detox can be done, but are we treating women only for the benefit of the fetus?

Detox doable. Is it effective?

- Relapse:
  - 48% by time of delivery (range 17-96%)
  - Includes additional risks of HIV, Hep B, Hep C, bacterial infections, incarceration, overdose, death
- NAS:
  - 20-80% (compared to 50% with MAT)
  - Includes additional risk of social service involvement, loss of custody

Treating a chronic condition with an acute treatment without clear fetal benefit =

Clinical Mismatch

Benefits of Opioid Agonist Therapy (Methadone/Buprenorphine)

### Maternal Benefits
- 70% reduction in overdose related deaths
- Decrease in risk of HIV, HBV, HCV
- Increased engagement in prenatal care and recovery treatment

### Fetal Benefits
- Reduces fluctuations in maternal opioid levels; reducing fetal stress
- Decrease in intrauterine fetal demise
- Decrease in intrauterine growth restriction
- Decrease in preterm delivery
Opioid Maintenance Therapy

- Methadone:
  - Maintenance Therapy Remains the Standard of Care
  - Methadone and buprenorphine are safe and effective treatment options in pregnancy
  - The decision of which therapy to start is complex and should be individualized for each woman
  - Based on available options, patient preference, patients’ previous treatment experiences, disease severity, social supports, and intensity of treatment needed

Fischer et al. 1998, 1999
Jones et al. 2010

Pharmacotherapy: Priority

Support Pharmacotherapy in Pregnancy | Don’t Support Pharmacotherapy
- ASAM
- ACOG
- AAFP
- AAP
- SAMHSA
- CDC
- WHO
- AWHONN
- JOGNN
(partial list)
Neonatal Abstinence Syndrome

- NAS is not unique to opiates
  - Several medications can place infant at risk for withdrawal symptoms after birth
  - Like many treatments in medicine, there is a balance of risk and benefit
- NAS risk not related to maternal methadone or buprenorphine dose
- Impossible to predict before birth which infants will have NAS that requires pharmacotherapy
- Babies are not born “addicted”

MOTHER Study
Randomized trial of methadone versus buprenorphine

Primary outcome: NAS
- Similar prevalence of treatment for NAS
- Less neonatal abstinence severity and treatment (bup)
- Shorter neonatal LOS (bup)
- Bigger HC

Jones, NEJM, 2010

Doctor, is there ANY way to reduce the chance my baby will have withdrawal?
Breastfeeding

- Both methadone and buprenorphine are considered safe, and without presence of any other contraindication, women receiving MAT are encouraged to breastfeed their infant, regardless of dose of medication.

- Breastfeeding decreases rates of NAS
  - It’s not the medicine in the milk, it’s the presence and bonding with the mother
  - Significant reduction is days in the hospital, medication required, and medical cost when moms and babies are able to stay together (rooming in)

Case #1: Opiates

- “Anna”: admitted to antepartum unit, started suboxone as well as fluids, adjuvant withdrawal meds, fetal monitoring reassuring.
  - IV fluids
  - Clonidine 0.1mg q 4 hr prn
  - Zofran, phenergan
  - Gabapentin, trazodone, hydroxyzine
- Pt discharged 24 hrs later after stabilizing on suboxone.
- Followed pt in clinic for remainder of pregnancy, delivered at 39w6d via uncomplicated NSVD. Retained custody of infant.

Case #1: Opiates

- Medication Assisted Treatment (MAT)
  - Not just about meds, but are critical component of treatment for opiate use disorder
- Interdisciplinary care crucial: substance use, OB, family med/pediatrician, etc.
- Complete spectrum of care should be considered:
  - Residential
  - Intensive Outpatient (IOP)
  - Outpatient
  - Relapse Prevention
  - Psychiatric Care
Case #3: Marijuana

- “Cassie” is 21 yo G1P0 at 12 weeks by LMP
- Reports daily use of marijuana
- Works in dispensary
- Boyfriend uses daily marijuana as well
- Smokes cigarettes (half pack/day)

BRINGS YOU A BUNDLE OF JOY.

BRINGS ON A BUNDLE OF QUESTIONS.

Case #3: Marijuana

- Reports history of bipolar disorder diagnosed at age 15. States “was on every medication but I stopped them all when I moved out” (age 18)
- Since then, pt. reports has been using daily marijuana to manage mood symptoms, stress
- Has increased marijuana use since became pregnant to help with morning sickness
- Smokes flower only
- No dabs, shatter, or wax (up to 90% THC)

Case #3: Marijuana

- Patient unsure if would be willing to reduce marijuana use. Reports “its been the only thing that helps me and I don’t want to be back on all those psych meds”
- Pt. states “I’ve done my research and in Jamaica the babies are actually smarter because all the moms use marijuana in pregnancy” and “my friend had a baby and smoked throughout her pregnancy, and her baby is fine”
- Reports would be willing to cut down on tobacco
Marijuana

- Legal in Colorado
- Increasingly socially accepted
- Women of reproductive age are one of the fastest growing consumers of both medical and retail marijuana

**Shift in Social Acceptability**

**Pregnancy and pot use**

- 21% of Americans think it's OK for a pregnant woman to use pot for nausea or pain

Among Americans who use marijuana regularly, 40% think it's OK for a pregnant woman to use pot for nausea or pain

Why are pregnant women using marijuana in the first place?

- Depression
- Anxiety
- Stress
- Pain
- Nausea and vomiting
- Fun/recreation
- Other (sleep, seizures, migraine, cancer, to increase appetite)
Maternal Outcomes
- Concurrent substance use/misuse (tobacco>alcohol>prescriptions>illicits)
- Decreased prenatal care, out of hospital birth (fear)
- Intoxication: accidents, paranoia, psychosis, physical illness/toxicity
- Withdrawal
- Asthma/pulm dx (96% of marijuana use reported in pregnancy is used via smoking)
- Increase risk of dysfunctional labor, precipitous labor, and meconium-stained amniotic fluid

Fetal Outcomes
- THC freely crosses placenta and BBB
  - Fetal plasma concentrations equal to (or higher?) than maternal levels
- Increased rates of preterm delivery
  - Hard to separate from tobacco effects in many studies
- Low birth weight> head circ > length
- Growing evidence that THC may alter certain receptors in the brain during fetal development, particularly in limbic system and prefrontal cortex

Neonatal→Childhood Outcomes
- Acute:
  - Poor feeding
  - Excessive weight loss
  - Hypotonia
- Long-term:
  - Increasing data demonstrating impairment in learning, memory, attention, school performance, growth
  - Some effects not appreciated fully until late childhood or adolescence
Case #3: Marijuana

ACOG Committee Opinion 637:
“Pregnant women or women contemplating pregnancy should be encouraged to discontinue their use of marijuana….There are insufficient data to evaluate the effects of marijuana use on infants during lactation and breastfeeding, and in the absence of such data, marijuana use is discouraged”

Case #3: Marijuana

- Counseling is key:
  - Recommendation is cessation of use (and 2nd hand smoke)
  - Not enough information about marijuana in pregnancy and breastfeeding
  - Information that we do have does not reveal any benefit, and some concern for harms (preterm delivery, meconium)
  - Significant evidence for harm in later period of brain development (adolescence)
  - Many hospitals are testing for THC at birth

Case #3: Marijuana

- No matter our personal beliefs or feelings about marijuana, we owe it to our patients to explain the current medico-legal climate:
  - Marijuana is legal in CO (18+ medical, 21+recreation)
  - THC is a Federal Schedule I substance
  - In CO, any infant who tests positive at birth for a Federal Schedule I or Schedule II or III (without a prescription) is a reportable event under Child Abuse and Neglect law
  - Harm Reduction and Safe Storage
A Needed Balance

- How can we help health care providers engage women with marijuana use in pregnancy and breastfeeding?
- How can we ensure that any legislation regarding mothers or infants testing positive for THC does not impair mother-infant bonding or increase punitive action towards mothers with substance use?
- How can we work to support much-needed research without threatening mother with reporting to social services?

If all else fails...

- “I will still take care of you”
- “You are not alone”

Contact Info

- Denver Health OB Addiction Medicine clinic in Pav C WCC
  - Mandy Langer, Care Coordinator: amanda.langer@dhha.org or pager: 303-234-2643 or office: 303-602-4865

- University of Colorado:
  - Anschutz: OB Addiction Medicine
    - Contact OB Clinic 720-848-1060 or Jennifer.Wolff@uchealth.org
    - 720-848-1717
  - Boulder: Outpatient Addiction Medicine (no prenatal care yet)
    - 303-544-3630

- Kaylin.Klie@dhha.org
- Kaylin.Klie@ucdenver.edu
References and Resources

- Meier, MH et al. Persistent cannabis users show neuropsychological decline from childhood to midlife. PNAS August 2012. E2657-E2664.