Opioid Use in Pregnant Women and Prenatal Care

Murray F Dweck MD, FACOG
Medical Director/OBGYN
Florida Department of Health - Brevard
Objectives

* Summarize contextual and co-morbid factors observed among many women with substance use disorders, specifically opioids

* Discuss the basics of opioid use in pregnancy and how this is managed at the Department of Health

* Compare and contrast the benefits and risks of providing methadone or buprenorphine for the mother and fetus

* Identify characteristics of a competent medication-assisted treatment program for women
**Opioid Use in Women**

- 28% of privately insured women and 39% of Medicaid-enrolled women filled prescriptions for opioids like Percocet, Vicodin, OxyContin, every year
- More than 16K deaths/yr attributed to use of opioid prescriptions
- A study from 2015 suggested that “opioid use among women of reproductive age is a concern because they have been linked to birth defects and adverse pregnancy outcomes”, suggesting that this was a fetus problem... when actually the complex health effects on women themselves is also a very important health and social effect that needs to be addressed as well.

**CDC (MMWR)** Opioid prescription claims Among Women of reproductive age –US 2008-2012
Opioid Use in Pregnancy

A pregnant woman never takes pills alone
Public health approach is needed to provide prevention of opioid use disorder across the lifespan for:

- Neonates and infants
- Pregnant mothers
- Women and men of reproductive age prior to conception
- Youths
- Older adults
Opioid Use in Pregnant Women

Opioid prescription abuse is the fastest rising addiction and public health problem in the US.
Opioid Use in Pregnancy

Increase in Affected Infants:
- 2,920 in the year 2000
- 21,732 in the year 2012
Opioid Use in Pregnancy

21,000 babies born in the U.S. in 2012 with neonatal abstinence syndrome.
Pregnant women with opioid use disorders can be effectively treated with methadone or buprenorphine. Both these medications should not be considered “off-label” use in the treatment of pregnant patients with an opioid use disorder

(Jones et al., Am J Obstet Gynecol. 2014)
Why are more individuals, including pregnant women, using opioids?

There has been an increase in the access to these medications

Pain became the 5th vital sign in the early 21st century
Among pregnant women in the United States, approximately 18% smoked cigarettes, 9.4% drank alcohol, and 5% used illicit drugs in the past month. The two most common drugs used by non-pregnant women have been alcohol and tobacco. Among pregnant women, approximately .2% used heroin, and 1% used pain relievers non-medically in the past month.
Individual states have implemented strategies to address the opioid epidemic and NAS by prescription drug monitoring to reduce inappropriate prescribing and overdose deaths.

Interestingly only 4 states-Florida, Georgia, Tennessee, and Kentucky have made NAS a reportable condition to the state health departments to improve public health surveillance.

Implementation of this passive surveillance can help states successfully target prevention and treatment measures including access to medication-assisted treatment that has been recommended by ACOG.
Implications for Public Health Practice

- Prevention efforts such as promotion of effective use of Rx drug monitoring programs to reduce inappropriate prescribing
- Clinicians should follow appropriate prescribing guidelines for opioid medications and provide screening and treatment for opioid use disorders among pregnant and non-pregnant women of reproductive age
- Make sure adequate treatment resources exist to address the effects of maternal opioid use and NAS
* Patients relate to injuries from auto accidents from years ago when they were given Percocet or Lortabs
* Admit to taking more pills than their prescription allows, sometimes up to 20+ pills per day
* Drug screen is usually positive for opiates in addition to Benzodiazepines, THC and even cocaine
Opioid Use in Pregnancy

* Signs and Symptoms that suggest Substance Abuse
  * Seek PNC late in pregnancy
  * Non-compliance with appointments
  * Poor weight gain
  * Sedation, intoxication, withdrawal, or erratic behavior
  * Track marks from IV injections, abscesses, cellulitis
  * Co-existent HIV, Hep B or Hep C
Other Red Flags for Abuse

- Lost/Stolen Rx
- Call for Early Refills, “Vacation refills”
- Calling unfamiliar physicians
- Physician shopping
Opioid Use in Pregnancy

* Includes the use of heroin and misuse of prescription opioid analgesic medications
* May develop with repeated use of these drugs
* Opioids include: codeine, fentanyl, morphine, opium, methadone, oxycodone, Demerol, hydrocodone, propoxyphene, and buprenorphine
* They can be swallowed, injected, inhaled, smoked, chewed, or used as suppositories
* Increase the risk of other disorders-HIV, Hepatitis B, C
Most Common Opiates Used by Pregnant Women

* Hydrocodone: Vicodin; Lortab
* Oxycodone: OxyContin; Percocet
* Methadone
* Heroin
* Studies have shown an increased risk of congenital heart defects with codeine in the 1st trimester, but most others have not shown an increase in rate of birth defects after perinatal exposure to oxycodone and others, but methadone and buprenorphine were not studied specifically and the small concern for increased risk of birth defects with opioid-assisted therapy in pregnancy must be weighted against the risk of continuing illicit drug use in pregnancy.
Pregnancy makes a difference in long term recovery

- In a study out of the Journal of Addictive Diseases in 2006, 66% of women who entered treatment while pregnant used no drugs while only 27% of non-pregnant women remained drug free. (p<.0005)
Opiate Withdrawal in Pregnancy

* It is important to avoid withdrawal during pregnancy
* The risk of adverse events from withdrawal is far greater than from the treatment of Neonatal Abstinence
Withdrawal Symptoms

* **Clinical Picture**

* Patients may present with abdominal pain, cramps, nausea, vomiting, diarrhea, contractions

* Yawning, lacrimation, restlessness, increase heart rate, diaphoresis, chills, hot flashes

* Tremors, seizures, increased respiratory rate
Opioid Use in Pregnancy

- Withdrawal symptoms usually occur up to 72 hours and subside within a week for short acting opioids (oxycodone) and long acting opioids (methadone) 24-36 hours and can last for weeks.
- Cravings can last for years resulting in relapse.
- Treatment in pregnancy is crucial as offspring may suffer acute neonatal abstinence syndrome that can lead to death.
During pregnancy repeated use of opioids causes risks for mother and fetus:

- Increased risk fetal growth restriction (IUGR)
- Placental abruption
- Fetal death
- Preterm labor
- Meconium stained amniotic fluid
- Prostitution, theft, increased risk STDs, violence to support the addiction, legal consequences, loss of child custody, and incarceration, and death
*All pregnant women should be routinely asked about their use of alcohol and drugs*

*Rx opioids and meds used for non-medical reasons*

*Inform that these questions are asked to all pregnant patients to ensure they get the care they need for them and the fetus and that all is confidential*

*This non-judgmental approach will lead to the most inclusive disclosure*
Here at the Health Department we take care of everyone that is pregnant and no one is denied care for any reason.

- We provide a non-judgmental approach.
- We do not drug screen our patients, what happens at the hospitals is not in our control.
- We want complete Access to prenatal care.
- We want patients to feel comfortable and look forward to their maternity visits to be able to achieve the best outcome for the mother and child.
- We regularly communicate, with signed record releases, with the Methadone clinics and managing physicians to see how our patients are doing and any recommendations that we or they may have to help improve the care of our maternity patients.
**Prenatal History**

**Date:** 1/8/16

<table>
<thead>
<tr>
<th>Birth Date</th>
<th>Age</th>
<th>Race</th>
<th>Marital Status</th>
<th>Address</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Occupation:** Unemployed  
**Preferred Language:** English  
**Husband's Name:**  
**Father of Baby:**

**Menstrual History**

- LMP: 10-19-15  
- Menstrual Frequency: Q 5 Days  
- Menarche (Age Onset): 12  
- On Birth Control at Conception: Yes  

**Past Pregnancies (Last Six)**

<table>
<thead>
<tr>
<th>Date / Month / Year</th>
<th>Gestation Weeks</th>
<th>Length of Labor</th>
<th>Birth Weight</th>
<th>Sex</th>
<th>Type of Delivery</th>
<th>Anesthesia</th>
<th>Place of Delivery</th>
<th>Preterm Labor</th>
<th>Comments / Complications or Additional Pregnancies</th>
</tr>
</thead>
<tbody>
<tr>
<td>4/2010</td>
<td>39</td>
<td>16 hrs</td>
<td>7.3</td>
<td>M</td>
<td>SVD</td>
<td>Ep: PMC</td>
<td>NO</td>
<td></td>
<td>N/A</td>
</tr>
</tbody>
</table>

**Medical History**

- O Neg + Pos: PT Fam  
- Detail Positive Remarks: Date & Treatment

1. Diabetes  
2. Hypertension / Stroke  
3. Heart Disease / MVP  
4. Autoimmune Disorder  
5. Kidney Disease / UTI  
6. Neurologic / Epilepsy  
7. Psychiatric  
8. Depression  
9. Postpartum Depressive  
10. Hepatitis / Liver Disease  
11. Varicose Veins / Phlebitis  
12. Thyroid Dysfunction  
13. Asthma / TB  
14. Cancer

- Tobacco: Amt/Day Pre Pregnancy, Amt/Day Pregnant, # Years Used, Alcohol: Amt/Day Pre Pregnancy, Amt/Day Pregnant, # Years Used

**History of IV Drug Use, Diamide**

- Xanax: Diamide, Morphine, Current
- Taking 1-2 mg of Xanax daily and is seen at clinic

**Healthy Start**

094-041816.28
<table>
<thead>
<tr>
<th>Condition</th>
<th>+</th>
<th>+</th>
<th>Mother, Patient no meds BP today: 125/81</th>
</tr>
</thead>
<tbody>
<tr>
<td>2. HYPERTENSION / STROKE</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. HEART DISEASE / MVP</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>4. AUTOIMMUNE DISORDER</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>5. KIDNEY DISEASE / UTI</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>6. NEUROLOGIC / EPILEPSY</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>7. PSYCHIATRIC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. DEPRESSION</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. POSTPARTUM DEPRESSION</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. HEPATITIS / LIVER DISEASE</td>
<td></td>
<td></td>
<td>Hep C</td>
</tr>
<tr>
<td>11. VARICOSITIES / PHLEBITIS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12. THYROID DYSFUNCTION</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13. ASTHMA / TB</td>
<td>+</td>
<td>0</td>
<td>Patient Diagnosed 2013 no current meds</td>
</tr>
<tr>
<td>14. CANCER</td>
<td></td>
<td>+</td>
<td>mgF</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drug Use / Abuse</th>
<th>AMT/DAY PRE PREGNANCY</th>
<th>AMT/DAY PREGNANT</th>
<th># YEARS USED</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOBACCO</td>
<td>1/2 FL 1 DAY</td>
<td>1/2 FL 1 DAY</td>
<td>15</td>
</tr>
<tr>
<td>DRUG USE / ABUSE</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

History of IV Drug use: dilaudid, xanax, oxycodone, morphine. Currently taking 140 mg of methadone daily and is seen at Orlando Methadone Treatment Center. Has had...
Methadone-maintenance therapy since the 1970’s and was mainly for heroin treatment but used now for other opioids

- Rationale for use is to prevent complications of narcotic withdrawal
- Encourage Pre-natal care and drug treatment
- Reduce criminal activity
- Reduces risk of complications
- Neonatal Abstinence syndrome which is a treatable condition
Increased Opioid Metabolism

* Increases with each trimester in about 35% of patients
* Doses may increase by 50%
* May require more drug to treat pain
* Avoid chronic withdrawal in 3\textsuperscript{rd} trimester
* Slightly higher doses of Methadone may have better outcomes
* Need the appropriate dose to prevent withdrawal - not lowest possible dose
* Efforts to wean off or “detox” opiates during pregnancy carry increased risk to harm the fetus
Treatment

* Methadone Maintenance
* Managed by addiction treatment specialists within registered/licensed out-patient methadone treatment programs
* Prescribed on a daily basis by substance abuse treatment program (comprehensive package)
  * Prenatal care
  * Chemical dependency counseling
  * Family therapy, nutritional education, and other psychosocial services
Treatment

* It’s important for the obstetrician to communicate with treatment programs about patients care and dosage concerns
* Doses should be adjusted throughout pregnancy to avoid withdrawal symptoms (craving, abdominal cramps, nausea, insomnia, irritability and anxiety).
* Not all women require increases in dosages, but this is decided on by addiction specialist
* Starting dosages vary but can start at 10-30mg/day
* Data on dosage and Neonatal abstinence syndrome have been conflicting and confusing
Meta-analysis concluded that the severity of Neonatal Abstinence Syndrome does not appear to differ based on the maternal dosage of Methadone treatment.

These findings all underscore the need to provide pregnant women with an adequate dose of methadone to avoid signs and symptoms of opioid withdrawal and the euphoric effects of misused opioids.

*Cleary, BJ, et al. Methadone dose and Neonatal Abstinence Syndrome-systematic review and meta-analysis; Addiction, 2010*
Interestingly:

* With the exception of buprenorphine, it is illegal for a physician to prescribe opioids for the treatment of opioid dependence, including methadone, outside of a licensed treatment program.

* Buprenorphine, prescribed by physicians that have undergone a specific credentialing, is the only opioid approved for treatment of opioid dependence in the office setting.

  * Drug addiction and treatment act of 2000

* All physicians should be aware of the state and federal regulations regarding prescribing medications for the treatment of opioid dependence.
Emerging evidence supports the use of Buprenorphine for opioid-assisted treatment during pregnancy and patients may be offered this therapy.

Buprenorphine has been found safe and effective in worldwide studies and recent studies indicate it is also safe for use in neonatal withdrawal.

Acts on the same receptors as heroin and morphine.

Has become standard of care in opiate dependency management in Europe and the United Kingdom.

* Johnson RE: Use of Buprenorphine in pregnancy; pt. management and effects on neonate; Drug and ETOH Dependence, 2003;
Single agent or in combination with Naloxone

Naloxone is an opioid antagonist used to reduce diversion and can cause severe withdrawal when injected but when used in combination sublingually has rare adverse effects.

In pregnancy we use buprenorphine, minus Naloxone, to avoid any potential prenatal exposure especially to prevent naloxone injection or “intrauterine withdrawal”.

Majority of patients conceived under Suboxone treatment.
BUPRENORPHINE vs METHADONE

* Advantages over Methadone
  * Lower risk of overdose, may have oral rx for maintenance
  * Less drug interactions
  * Outpatient treatment by trained and approved physicians - without the need for daily visits to licensed treatment center
  * May increase availability of treatment and decrease stigma
  * Less Neonatal Abstinence Syndrome & increased efficacy
  * Decreased hospital stay

* Disadvantages
  * Reports of hepatic dysfunction
  * Lack of long term infant data and child effects
  * More difficult induction and risk of precipitated withdrawal
  * Increased risk of diversion
  * Increased Cost

* Johnson RE: Use of Buprenorphine in pregnancy; pt. management and effects on neonate; Drug and ETOH Dependence, 2003;
Until recently data on use in pregnancy has been limited but now shows promise as a potential 1st line treatment.

A multicenter randomized clinical trial that compared the neonatal effects of buprenorphine and methadone in 175 patients showed that the buprenorphine exposed neonates required:

- 89% less morphine to treat NAS
- 43% shorter hospital stay
- 58% less duration of treatment for NAS

Patients to be considered for this type of treatment:

* Must be able to self-administer the drug

* Maintain compliance with treatment regimen and patients that require more intensive structure and supervision may not be candidates
Prior recommendations limited use buprenorphine to:

- Patients that refused or unable to take methadone, or for women when methadone was not available
- If patients were already on Methadone therapy it is not advisable to switch due to risk of precipitated withdrawal
- If patients refuse maintenance therapy, medically supervised withdrawal should be undertaken in the 2nd trimester under the supervision of a physician experienced in perinatal addiction treatment, especially if the choice is continued illicit drug use
Women in labor should be treated as if they were not taking opioids as their maintenance dosage will not cover adequate pain control and they may require higher doses.

- Maintain doses of methadone and buprenorphine as this will also reduce anxiety.
- Consider the use of anti-inflammatories, Ketorolac.
- Epidural or spinal anesthesia may be used.
- Pediatrics-Neonatology notified of all deliveries.
Minimal amounts of methadone and buprenorphine are found in breast milk despite the dose and breastfeeding should be encouraged.

May or may not need dosage reduction after delivery.

Must monitor patients receiving opioids after delivery for over sedation.

Continue treatment with addiction support after delivery—psychosocial support services, dependency treatment and relapse prevention programs.
Breastfeeding will help with bonding of mother and infant by providing adequate immunity together to aid in reducing the severity of NAS and enhancing recovery.
* Data is somewhat limited and most studies have not found significant differences in cognitive development between children up to 5 years old vs matched controlled groups
* Enriching childhood experiences and improving the quality of the home environment are likely to be beneficial

Neonatal Abstinence Syndrome (NAS)

- **Neonatal Abstinence Syndrome** often results when a pregnant woman uses opioids (e.g., heroin, oxycodone) during pregnancy.
- Defined by alterations in the:
  - **Central nervous system**
    - high-pitched crying, irritability
    - exaggerated reflexes, tremors and tight muscles
    - sleep disturbances, seizures
  - **Autonomic nervous system**
    - sweating, fever, yawning, and sneezing
  - **Gastrointestinal distress**
    - poor feeding (uncoordinated sucking reflexes), vomiting and loose stools
  - **Signs of respiratory distress**
    - nasal stuffiness and rapid breathing
Neonatal Abstinence Syndrome (NAS)

- Exposure to illicit or prescription drug
- Passes via placenta to baby
- Dependency to drug (mom and baby)
- Withdrawal symptoms occur shortly after birth
Neonatal Abstinence Syndrome (NAS)
Neonatal Abstinence Syndrome (NAS)

SYMPTOMS OF NAS

- High Pitched Crying
- Sleeping Problems
- Hyperactive Reflex (startle response)
- Tremors
- Muscle Tightness
- Seizures
Neonatal Abstinence Syndrome (NAS)

- We know that treatment with Methadone and or Buprenorphine improves pregnancy outcomes and risky behavior but may put the neonate at risk for NAS
- Characterized by hyperactivity of the central and autonomic nervous system, excessive crying, seizures
- Infants exposed to Methadone, withdrawal may start anytime within the first 2 weeks of life, usually within the first 72 hours and can last several days to weeks
- Infants exposed to buprenorphine, withdrawal may start within the first 12-48 hrs, peak at 72-96 hrs and, resolve by 7 days, may not even require treatment
- Treatment is adequate when infant has rhythmic feeding, weight gain and sleep cycles

- Substance Abuse and Mental Health Services Administration; 2008
- Johnson RE. Use of Buprenorphine in pregnancy, pt management and effects on Neonate, Drug and ETOH Dependency, 2003
Neonatal Abstinence Syndrome

* **Treatment**

  * Combination therapy-clonidine, phenobarbital, dilute morphine drops
  * Increase morphine dose until signs of withdrawal are controlled
  * Maintain controlling dose for a few days
  * Then start weaning morphine dose
Opioid Use in Pregnancy
Early identification of opioid-dependent pregnant women improves maternal and fetal outcomes

Pregnancy should be co-managed by the OB/GYN and addiction specialist

Medically supervised withdrawal should be discouraged during pregnancy, especially when maintenance is available

All infants born to women who used opioids in pregnancy should be monitored for NAS and treated if indicated