Perinatal Substance Use: Screening, Treatment, & Impact on Pregnancy Outcome

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September 16, 2021

Dignity Health.

Disclosures

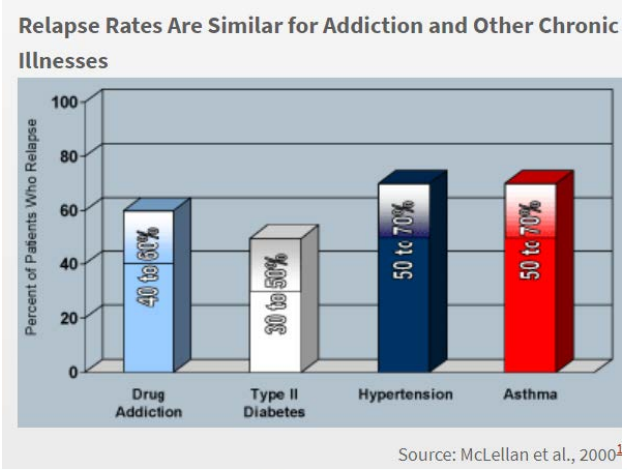
- I am the executive director of Options for Recovery on the campus of Harbor-UCLA Medical Center. It was established in 1990 as one of the first perinatal treatment centers in LA County.

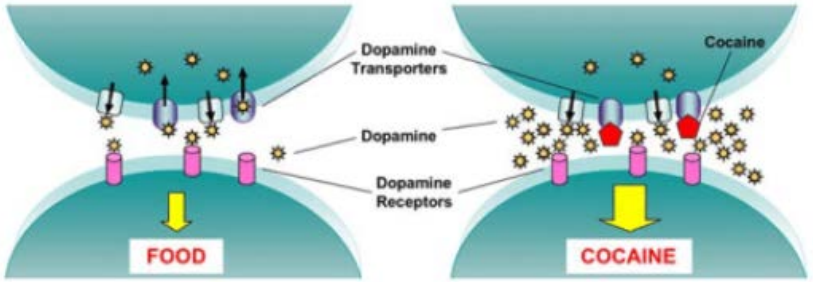
Learning Objectives

- Use non-stigmatizing language that reflects an accurate, science-based understanding of substance use disorder (SUD) and is consistent with your professional role
- Screen and identify pregnant women with SUD
- Deliver appropriate services to pregnant and postpartum women with SUD
- Describe the impact of alcohol, tobacco, and common drugs of abuse on pregnant women and their fetuses

Addiction

- Defined as a **chronic, relapsing** brain disease that is characterized by compulsive drug seeking and use, despite harmful consequences and long-lasting changes in the brain
- Nearly all addictive drugs directly or indirectly target the brain's reward system by flooding the circuit with dopamine
- Dopamine is a neurotransmitter present in regions of the brain that regulate movement, emotion, cognition, motivation, and reinforcement of rewarding behaviors





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Substance Use Disorder

Loss of control
- more than intended
  - amount used
  - time spent
- unable to cut down
- giving up activities
- craving

Physiology
- tolerance
- withdrawal

formerly "dependence"

Consequences
- unfulfilled obligations
  - work
  - school
  - home
- interpersonal problems
- dangerous situations
- medical problems

formerly "abuse"

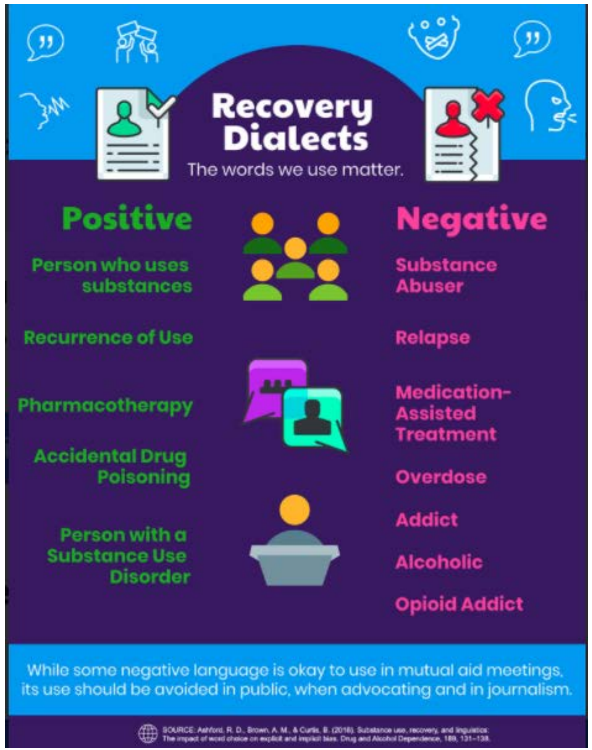
- A ***substance use disorder*** is defined by having 2 or more • in the past year resulting in distress or impairment.
- **Tolerance** and **withdrawal** alone don't necessarily imply a disorder.
- Severity is rated by the number of symptoms present:
  - 2-3 = mild
  - 4-5 = moderate
  - 6+ = severe

Diagnostic and Statistical Manual V

Words Matter

- Stigma is discrimination against an identifiable group of people
- Stigma about people with SUD might include inaccurate or unfounded thoughts or beliefs
- FACT: Addiction is a chronic, treatable brain disease from which patients can recover and continue to lead healthy lives.
- Impact of stigma on person with SUD: decreased willingness to seek treatment or trust provider

Terms to Use, Terms to Avoid, and Why



- Use person-first language
- The change shows that a person “has” a problem, rather than “is” a problem.
- The terms avoid eliciting negative associations, punitive attitudes, and individual blame
- It’s a misconception that pharmacotherapy merely “substitutes” one drug or “one addiction” for another.

Screening for Perinatal Substance Use

- **Why?:** Identification of substance use during pregnancy allows for interventions aimed at improving maternal and fetal health, by linking to appropriate **services and supports**
  - Golden opportunity to change the lifecourse of 2 generations
- **When?:** First prenatal visit and each trimester, including PP
- **Who?:** All patients
- **How?:** Using a validated screening tool

5 P's

- **Parents:** Did any of your parents have a problem with alcohol or other drug use?
- **Partner:** Does your partner have a problem with alcohol or drug use?
- **Peers:** Do any of your peers have a problem with alcohol or drug use?
- **Past:** In the past, have you had difficulties in your life because of alcohol or drug use, including prescription medications?
- **Pregnancy:** Since becoming pregnant, have you used alcohol or other drugs?
- Scoring: Any "yes" should trigger further questions

NIDA Quick Screen

Since becoming pregnant, how often have you used the following*:	Never	Once or Twice	Monthly	Weekly	Daily or Almost daily
1. Alcohol (≥ 3 drinks/day)					
2. Tobacco products					
3. Prescription drugs for nonmedical reasons					
4. Illegal drugs including marijuana					

If the patient says “NO” for all drugs in the Quick Screen, reinforce abstinence. Screening is complete.

If the patients says “Yes” to one or more days of heavy drinking, she is an *at risk drinker.*

If the patient says “Yes” to any tobacco use, advise to quit.

If the patient says “Yes” to use of illegal drugs or prescription drugs for non-medical reasons, proceed to **Question 1 of the NIDA-Modified ASSIST**

Discussion with Your Patient

- In the SBIRT model, patients who **screen positive** are provided with nonjudgmental information about risks of continued use for both the mother and fetus and then referred for appropriate treatment.
- Additional discussion points that can be helpful to determine degree of use and guide treatment selection include:
  - Pattern of use: frequency, length of most recent pattern of use, time of last use; where, when and with whom?
  - Route of administration: oral, intranasal, “skin popping” (SQ), IV
  - Quantity used: amount spent on daily, weekly or monthly basis
  - Additional symptoms: tolerance or withdrawal symptoms for each substance used
  - Prior substance use treatment: longest period of abstinence; use of 12-step groups

SBIRT=screening, brief intervention & referral to treatment

Laboratory Testing

- Universal laboratory testing for evidence of drug use is NOT recommended because of its limitations
- Patients should be informed of potential ramifications of a positive test result and should give **informed consent prior to testing**
- Medically indicated drug testing without written informed consent is acceptable if patient is unconscious or showing obvious signs of intoxication and needs to be tested in order to render appropriate medical care.

Possible Clinical Indications for Lab Testing in Pregnancy

- Previous positive drug test
- Monitoring compliance with methadone or buprenorphine
- Abruptio placentae
- Idiopathic preterm labor
- Idiopathic fetal growth restriction
- Frequent requests for prescription drugs that are commonly misused
- Noncompliance with prenatal care
- Unexplained fetal demise

Identify Comorbid Conditions

- **Psychiatric illness** including PMADs
  - Co-occurring mental health conditions are common (50-65%) especially depression, anxiety, and PTSD
- **Adverse Childhood Experiences (ACEs)**
  - In one large study, people with a history of ≥ 5 adverse childhood events were 7-10 x more likely to report illicit drug use and addiction
- **Intimate partner violence**
  - IPV is common in this patient population (60%)

LOS ANGELES COUNTY
SUBSTANCE USE TREATMENT SERVICES

Free for Medi-Cal, My Health LA, and Other County-Funded Eligible Youth and Adults

HOW DO INDIVIDUALS FIND SERVICES?

There are several ways to get started with substance use treatment:

- ✓ Call the toll-free Substance Abuse Service Helpline (SASH) at **1-844-804-7500**. A call agent who can conduct a brief screening and referral can be reached 24-hours per day and 7 days per week. Translation services are available.
- ✓ Visit the online directory to find providers near a preferred location such as work, home or, school. This tool is available at **http://sapccis.ph.lacounty.gov/sbat/**.

With either option, a provider can be selected that meets language, cultural, service, or location needs. An intake appointment should be scheduled no later than 10 calendar days from the screening or referral.

WHO IS ELIGIBLE?

Youth and adults can access no-cost substance use treatment services at any network provider if these criteria are met:

Fees cannot be charged for services if medical necessity is met (assessed to need treatment)
No one can be turned away or asked to pay if eligible for Medi-Cal or My Health LA even if the application is incomplete or in-process

- ✓ **Medi-Cal Eligible** *(active benefits are not required at time of screening, referral, or intake)* OR
- ✓ **My Health LA Eligible** *(active participation is not required at time of screening, referral, or intake)* OR
- ✓ **Other County Funded Program Participant** *(such as AB 109)* AND
- ✓ **Los Angeles County Resident**

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WHAT SERVICES ARE AVAILABLE?

- ✓ **Brief Outpatient for At-Risk Youth and Young Adults**
- ✓ **Outpatient Treatment**
- ✓ **Intensive Outpatient Treatment**
- ✓ **Short-Term Residential Treatment**
- ✓ **Withdrawal Management (formerly Detox)**
- ✓ **Medication-Assisted Treatment/Opioid Treatment Program**
- ✓ **Recovery Support Services**
- ✓ **Recovery Bridge Housing – Time Limited**

WHAT IS MEDICAL NECESSITY?

To receive these services, individuals need to be assessed with a substance use disorder (SUD) diagnosis by a qualified clinician or counselor, and need to receive services that meet, but do not exceed, their level of need. Youth and young adults (age 12-20) can be served if at-risk for developing a SUD.

County of Los Angeles Public Health
Substance Abuse Prevention and Control

Substance Abuse Service Helpline	1-844-804-7500
Provider Map	http://sapccis.ph.lacounty.gov/sbat/
Patient Information	http://publichealth.lacounty.gov/sapc/PatientPublic.htm

Pregnancy and Substance Use

- **Vast majority (83%)** of pregnant women will achieve abstinence from at least one substance by the end of second trimester
- Mostly no medical intervention
- More likely to achieve abstinence from alcohol, marijuana, and cocaine, than cigarettes
- Only 32% of smokers achieved abstinence
- Women with OCD and GAD were more likely to achieve abstinence whereas those with PTSD less likely to abstain

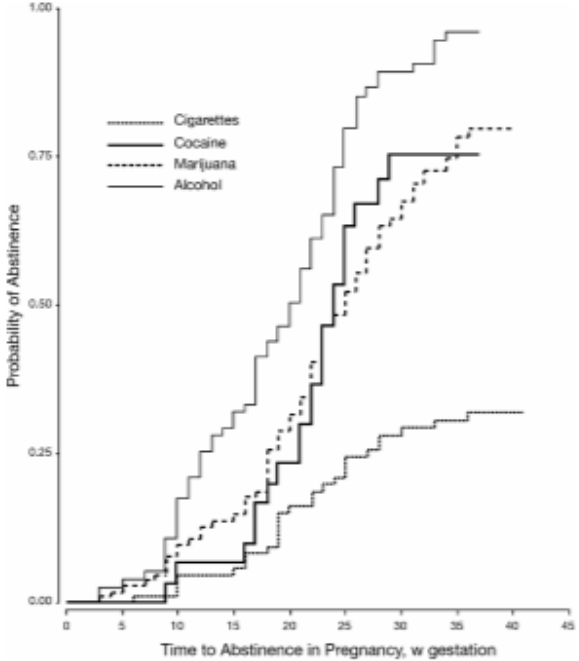

Figure 2. Time to Abstinence in Pregnancy by Drug
Kaplan-Meier estimates of the time interval in pregnancy (weeks in pregnancy) to abstinence from cigarettes, alcohol, marijuana or cocaine.

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Drug Alcohol Depend. 2015; 150:147-155

Postpartum and Substance Use

- **80% of women** who were abstinent in the last month of pregnancy returned to using at least one substance within 2 years of delivery
- More likely to relapse to cigarettes, alcohol, and marijuana than cocaine
- Relapse to cocaine was only 34% that of cigarettes
- Women with MDD were more likely to relapse than women without a diagnosis of depression

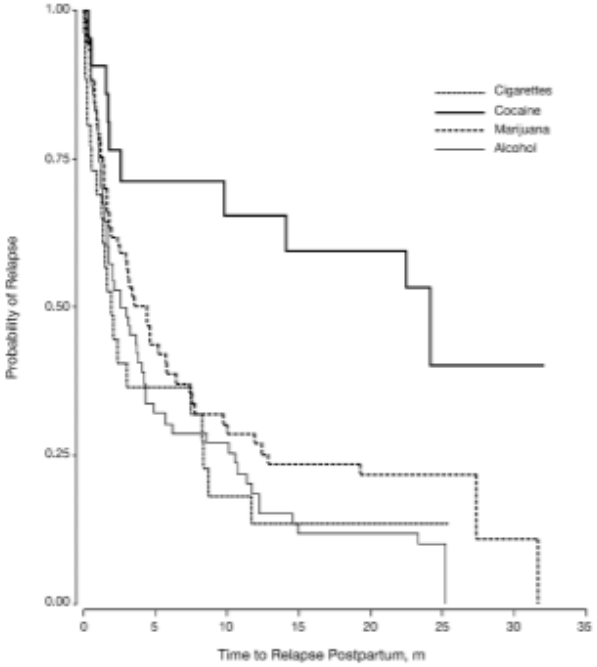


Figure 3. Time to Relapse After Delivery by Drug
Kaplan-Meier estimates of the time from delivery until relapse to cigarettes, alcohol, marijuana or cocaine in the 24 months postpartum.

Dignity Health.

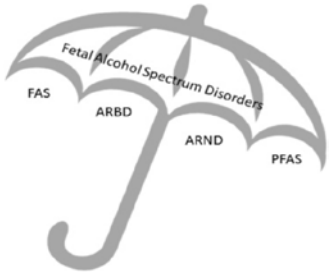
Drug Alcohol Depend. 2015; 150:147-155

Terminology of Alcohol Use by Women

- **Risky use** refers to consumption of alcohol that puts an individual at risk for health consequences, but not as severe as to meet diagnostic criteria for alcohol use disorder:
  - > 7 **standard drinks**/week on average
  - > 3 drinks on any day
- **Binge drinking** defined by the NIAAA as “drinking so much within ~2 hr. that blood alcohol concentration levels reach 0.08g/dL”, typically 4 standard drinks for women
- **Heavy alcohol use** is binge drinking on ≥ 5 occasions in the past month
- **Alcohol use disorder** (AUD) is characterized by a problematic pattern of alcohol use leading to clinically significant impairment or distress, as manifested by 11 specific psychosocial, behavioral, or physiologic criteria (DSM-5)

Alcohol Use During Pregnancy

- Despite public education, alcohol use during pregnancy has steadily increased from 2006 to the present
  - In the 2015-2017 survey by CDC, nearly 4% of pregnant women reported binge drinking in the past 30 days and nearly 12% reported any alcohol consumption
- A safe level of alcohol consumption during pregnancy has not been determined
  - Assessing the impact of alcohol on fetal development is challenging because of: variation in maternal alcohol clearance rates, fetal developmental sensitivity, genetic (maternal & fetal) susceptibility, drinking pattern, maternal age, maternal nutrition, and confounders, i.e., polysubstance use
- **Alcohol is a teratogen** with irreversible CNS effects that impacts fetal growth and development at all stages of pregnancy



Alcohol use during pregnancy can lead to lifelong effects.

Up to 1 in 20 US school children may have FASDs.

JAMA 2018; 319:474

People with FASDs can experience a mix of the following problems:

Physical issues

- low birth weight and growth
- problems with heart, kidneys, and other organs
- damage to parts of the brain

Which leads to...

Behavioral and intellectual disabilities

- learning disabilities and low IQ
- hyperactivity
- difficulty with attention
- poor ability to communicate in social situations
- poor reasoning and judgment skills

These can lead to...

Lifelong issues with

- school and social skills
- living independently
- mental health
- substance use
- keeping a job
- trouble with the law

Drinking while pregnant costs the US $5.5 billion (2010).

SOURCES: CDC Vital Signs, February 2016. American Journal of Preventive Medicine, November 2015.

Effects of Alcohol on Breastfeeding Infants

- Alcohol consumption by lactating women is common in U.S.; women tend to return to their regular drinking pattern 1-3 mo. PP, although less likely to binge
- Less than 2% of the alcohol dose consumed by the mother is transferred to her milk and blood. Alcohol is not stored in breast milk but its level parallels that found in maternal blood
  - Peak alcohol levels -0.5-1 hr. after drinking, declining thereafter
  - Therefore, lactating women should not nurse for several hours after drinking
- Alcohol use inhibits lactation (20% less milk produced) and results in modified feeding patterns by the infant and shorter sleep periods
- Adverse effects on gross motor development and early learning
- No safe levels of alcohol consumption while breast feeding

https://pubs.niaaa.nih.gov/publications/arh25-3/230-234.htm#

Tobacco Use During Pregnancy

- About one in 14 pregnant women who gave birth in the United States in 2016 smoked cigarettes during pregnancy; varied widely by state (from 25.1% in West VA to **1.6% in CA**), maternal age, race and Hispanic origin, and education
- Screen all pregnant patients for use of any tobacco products
- Educate patients and partners about consequences of tobacco use for both mother and fetus
  - Maternal: subfertility; ↑ risk of ectopic pregnancy; ↓ risk for preeclampsia; ↑ risk of gestational diabetes; lung cancer (the 2nd leading cause of death in women aged 25-39 yr.)

Impact of Tobacco Use During Pregnancy

Fetus

- 50% ↑ risk of SB
- 2-5 x ↑ risk of PPROM
- 1.5-3.5 x↑ risk of LBW
- 3.5 x ↑ risk of placental abruption; also ↑ risk for placental previa
- 2x ↑ risk of PTB, esp. < 32 wk GA
- Small ↑ risk of miscarriage
- Congenital anomalies: cleft lip ± cleft palate, gastroschisis, anal atresia, transverse limb reduction defects, cardiac defects, digital anomalies, bilateral renal agenesis or hypoplasia

Neonate

- Increased signs of stress, hypertonicity, irritability, and excitability with an apparent dose-dependent relationship
- 20% ↑ risk of NND

Cigarette smoking is associated with decreased milk volume production, lower milk fat concentration, and consequently, shorter duration of lactation.

SB=stillbirth; PPROM=preterm, premature rupture of membranes; LBW=low birth weight; PTB= preterm birth; NND=neonatal death

Long-term effects on offspring of women who used tobacco products during pregnancy

- 2x ↑ risk of SIDS
- Respiratory infections: bronchitis, pneumonia
- Short stature
- Childhood obesity
- Lower reading and spelling scores; decreased school performance
- Lower late adolescent executive function
- Conduct disorders in boys; adolescent-onset drug dependency in girls
- 60% ↑ risk of ADHD (dose response relationship)
- ↑ risk of asthma
- ↑ risk of type 2 diabetes mellitus
- ↑ risk of Tourette Syndrome & chronic tic disorders

Marijuana Use During Pregnancy

- CDC analyzed data from 8 states participating in 2017 PRAMS Marijuana Supplement
  - 9.8% of women self-reported marijuana use prior to pregnancy
  - 4.2% continued to use marijuana during pregnancy
  - 5.5% used marijuana after pregnancy
- Most common reasons for use during pregnancy: to relieve stress or anxiety, nausea and vomiting, and pain
- Most common modes of use:
  - Smoking 91.0%
  - Eating 7.1%
  - Dabbing 4.5%
  - Drinking 0.5%
  - Other 0.5%

32% of pregnant women who use marijuana during pregnancy are using daily or almost daily

MMWR 2020; 69:1058-1063

Cannabis Use Disorder: Clinical Manifestations

- Acute intoxication:
  - Physiologic signs: ↑HR, ↑BP, ↑RR, “red eye”, nystagmus, dry mouth, slowed/slurred speech, and ataxia; sedation, ↑appetite
  - Psychological manifestations: euphoria (“high”) & relaxation; ↑ sociability
  - Impaired attention, concentration, short term memory, & risk assessment
  - Undesired effects: depression, anxiety (eg, panic attacks), perceptual disturbances, transient paranoia or frank psychosis, new-onset mania
  - Common ED presentations: psychiatric (acute anxiety, agitation, or psychosis), cardiovascular (chest pain, palpitations), cannabinoid hyperemesis syndrome

Cannabis Use Disorder: Clinical Manifestations (cont'd)

- Persistent symptoms
  - Neurocognitive impairment: resolves with abstinence after 3 days-one month
  - Chronic mood changes: persistent depressive disorder or MDD
  - Impairment in school or work function; recurrent interpersonal problems
  - Chronic cannabis use, especially in early adolescence, associated with increased risk of psychosis and development of schizophrenia

Impact of Marijuana Use During Pregnancy

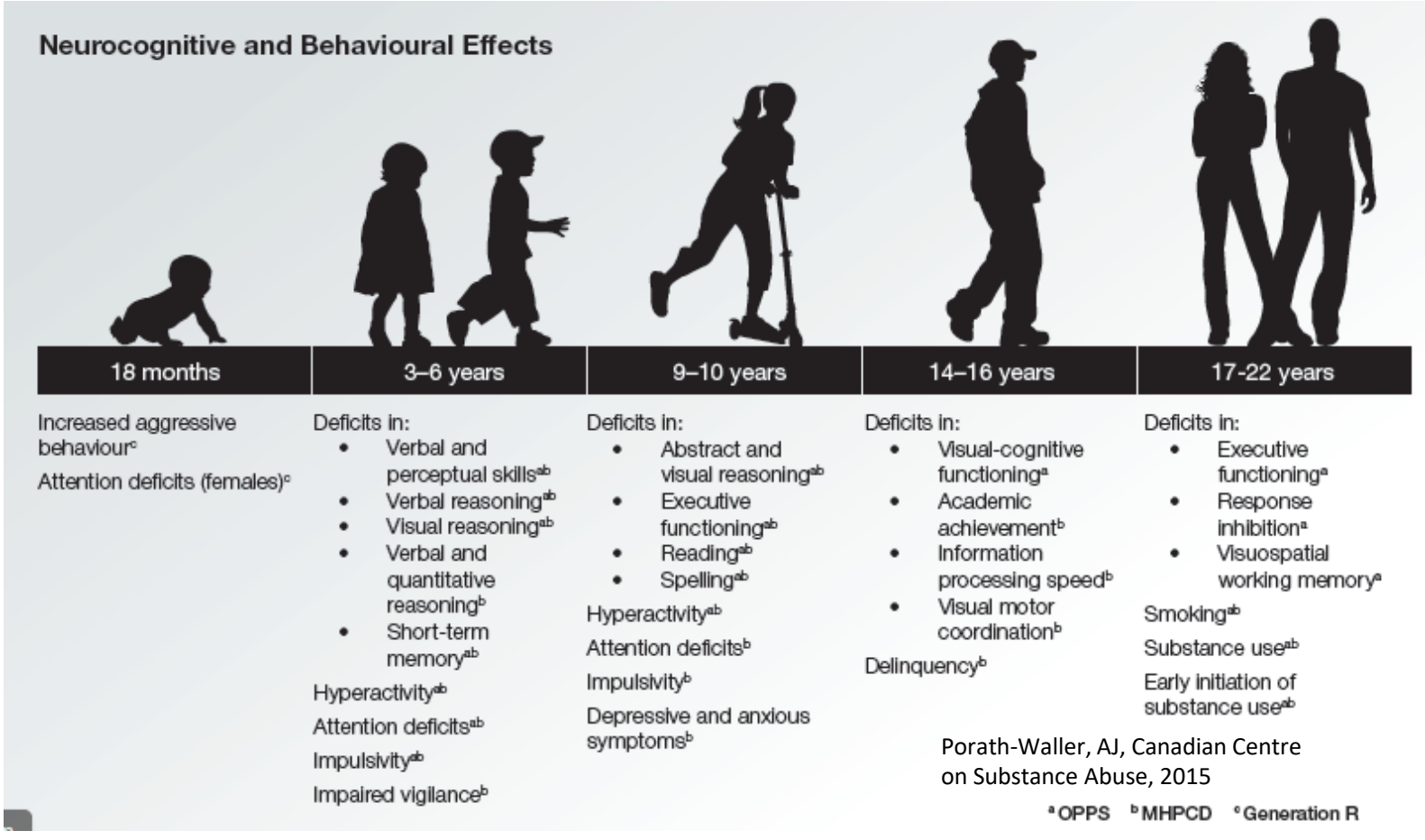
- Increased miscarriages (SAb)
- Increased stillbirths (SB)
- Increased neural tube defects –THC interferes with fetal folic acid uptake
- Increased PTB - controversial
- Increased LBW
- Impact of developing fetal brain
  - THC crosses placenta, enters fetal circulation, passes through blood-brain barrier and is concentrated in fetal brain (60% fat)
  - Brain densely populated with CB1 receptors that mediate THC's properties
  - THC interferes with early neural stem cell survival & proliferation, migration & differentiation of both glial and neuronal lineages, as well as neuronal connectivity & synaptic function

Impact of Marijuana Exposure In Utero on Newborn

- Exaggerated startle response
- Increased tremors
- Altered sleep patterns
- Increased irritability
- Increased muscle tone
- Uncoordinated suck-swallow reflex
- Tachycardia
- Increased blood pressure
- Thermoregulation instability

J Perinatology 2020; 40:1470-1476

Effects on Neurocognitive & Behavioral Functioning



Chemicals Listed Effective January 3, 2020 As Known to The State of California To Cause Reproductive Toxicity (Developmental Endpoint): Cannabis (Marijuana) Smoke and Δ9-Tetrahydrocannabinol (Δ9-THC)

Jan 23, 2020

Effective January 3, 2020, the Office of Environmental Health Hazard Assessment is adding cannabis (marijuana) smoke and Δ^9-tetrahydrocannabinol (Δ^9-THC) to the list of chemicals known to the state to cause reproductive toxicity (developmental endpoint) for purposes of the Safe Drinking Water and Toxic Enforcement Act of 1986 (Proposition 65)[1]. At a public meeting on December 11, 2019, the Developmental and Reproductive Toxicant Identification Committee (DARTIC) in its official capacity as the "state's qualified experts" determined t cannabis (marijuana) smoke and Δ^9-tetrahydrocannabinol (Δ^9-THC) were shown to cause reproductive toxicity based on the developmental endpoint. Regulations for the listing of chemicals by the DARTIC are set out in Title 27, California Code of Regulations, section 25305(b)(1).

A complete, updated Proposition 65 chemical list is available on the OEHHA website at https://oehha.ca.gov/proposition-65/proposition-65-list.

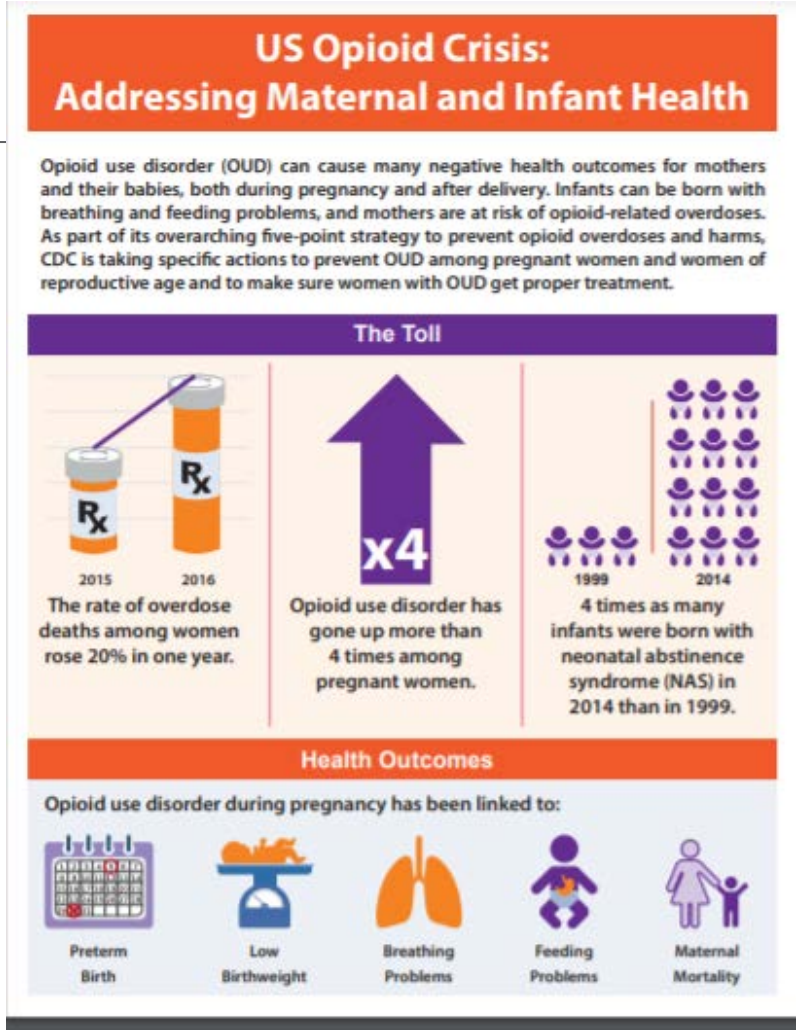
Breastfeeding and Cannabis

- Cannabinoids are secreted in breastmilk
  - THC is in higher concentrations in breastmilk than in mother's plasma
  - **Average Milk: Plasma ratio = 6:1**
- Estimated half-life of THC in breastmilk = 17 (3.3) days with a projected time to elimination greater than 6 wk.
- **THC accumulates in breast milk**
  - Concern for accumulation of cannabinoids in nursing infant because of slow elimination from body fat stores & continuous daily exposure
- Concentrations of metabolites 11-OH-THC, 9-carboxy-THC in fetal fecal sample were higher than in mother's milk
    - This indicates that THC is absorbed and metabolized by infant

N Engl J Med 1982; 307:819-820; Pediatrics 2018; 104:1076

Opioid Use During Pregnancy

- Opioid use in pregnancy has escalated dramatically in recent years, paralleling the epidemic seen in the general population
- In 2019 about 7% of women reported using prescription opioid pain relievers during pregnancy; of those, 1 in 5 reported misuse of prescription opioids
- There's also been a sharp rise in rates of heroin use & a 300%↑ in OD deaths involving heroin, often adulterated by fentanyl (50-100 x stronger than morphine)



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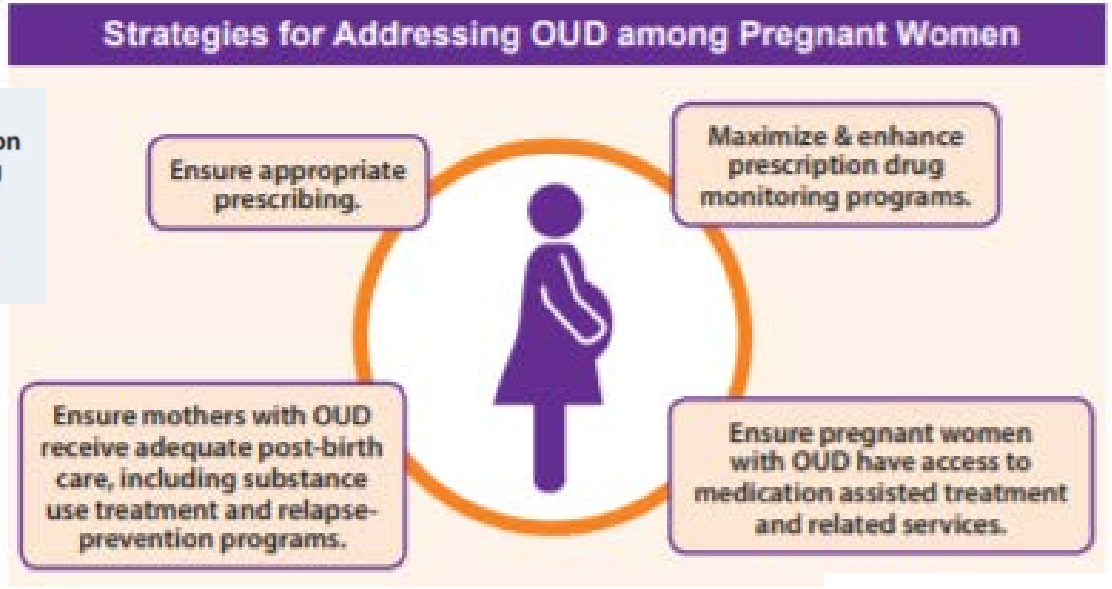
Opioid Use Disorder

- Clinical presentations
  - **Acute intoxication**: slurred speech, sedated (“nodding”), pinpoint pupils, ± fresh injection sites; duration depends on half-life of opioid taken and patient’s tolerance to opioids
  - **No acute effects**: patients who have developed a tolerance may show no acute effects after use of the drug at a typical dose
    - Patients with mild disorder may maintain jobs and relationships
    - Patients with severe disorder may be impoverished and engaged in illegal behavior (shoplifting, burglary, prostitution) to support habit
  - **Opioid withdrawal**: anxiety, restlessness, goosebumps, insomnia, yawning, watery eyes, runny nose, dilated pupils, body aches, sweating, vomiting, abdominal cramps, diarrhea, fever, shaking, ↑HR, ↑RR, ↑BP, hallucinations, seizures

Management of OUD during Pregnancy

Issuing guidance on opioid prescribing for chronic pain, including for pregnant women



ACOG Committee Opinion #711, Aug. 2017

For pregnant women with an opioid use disorder, opioid agonist pharmacotherapy is the recommended therapy and is preferable to medically supervised withdrawal because withdrawal is associated with high relapse rates, which lead to worse outcomes. More research is needed to assess the safety (particularly regarding maternal relapse), efficacy, and long-term outcomes of medically supervised withdrawal.

Pharmacotherapy for OUD during Pregnancy

- ACOG and other major medical organizations have concluded that the available evidence support the use of either methadone or buprenorphine as a potential first-line medication for pregnant women who are new to treatment
- Considerations include:
  - **Program availability**: OTPs not available in every community; CA Hub and Spoke Project implemented in some rural communities in CA
  - **Availability of comprehensive treatment**: pharmacotherapy, psychiatric and social work services; individual & group counseling; case management; prenatal care; parenting counseling
  - **Patient preference**
  - **Maternal & perinatal outcome:** higher attrition rate from BUP vs methadone (33% vs 18%)
  - **Neonatal opioid withdrawal syndrome** (NOWS) formerly known as neonatal abstinence syndrome (NAS): favors BUP with lower risk of NOWS requiring treatment, shorter neonatal length of hospital stay, & less morphine needed to treat NOWS

MEDICATIONS FOR OPIOID OVERDOSE, WITHDRAWAL & ADDICTION

Medications for opioid overdose, withdrawal, and addiction are safe, effective and save lives.

The National Institute on Drug Abuse supports research to develop new medicines and delivery systems to treat opioid use disorder and other substance use disorders, as well as other complications of substance use (including withdrawal and overdose), to help people choose treatments that are right for them.

FDA-approved medications for opioid addiction, overdose, and withdrawal work in various ways.

Opioid Receptor Agonist
Medications attach to opioid receptors in the brain to block withdrawal symptoms and cravings.

Opioid Receptor Partial Agonist
Medications attach to and partially activate opioid receptors in the brain to ease withdrawal symptoms and cravings.

Opioid Receptor Antagonist
Medications block activity of opioid receptors in the brain to prevent euphoric effects (the high) of opioids and alcohol and help reduce cravings.

Adrenergic Receptor Agonist
A medication that attaches to and activates adrenergic receptors in the brain and helps alleviate withdrawal symptoms.

REDUCES OPIOID USE AND CRAVINGS

Methadone
Daily liquid or tablet
Dolophine®, Methadose®
Generics available

Naltrexone
Monthly injection
Vivitrol®

Buprenorphine
Daily tablet
Monthly injection
Sublocade®
Generic tablets available

Buprenorphine/ Naloxone
Daily film under the tongue or tablet
Zubsolv®, Suboxone®
Generics available

TREATS WITHDRAWAL SYMPTOMS

Lofexidine
As-needed tablet
Lucemyra®

REVERSES OVERDOSE

Naloxone
Emergency nasal spray or injection
Narcan®
Generics available

Heroin

Fatal Doses

- 2/3 of people who primarily use heroin additionally use prescription opioids
- **Unlike the 1960-1980s, the first opioid abused is now most frequently a prescription opioid, rather than heroin**
- Illicit use of fentanyl, a highly potent synthetic opioid used to “cut” heroin, has grown in the U.S., contributing to the rise in ODs
- Pharmacology
  - Heroin has a half-life of 30 minutes, but a duration of action of 4-5 hr. due to active metabolites including morphine
  - More lipid soluble than other opioids, allowing it to cross the blood-brain barrier within 15-20 sec. and reach high brain levels

Psychosocial Interventions for OUD

- **Contingency management therapy** uses therapeutically applied incentives and other reinforcements to increase one or more target behaviors (eg, reductions in drug use, medication compliance, treatment attendance)
- **Motivational interviewing** is a psychotherapeutic approach designed to explore and resolve ambivalence to behavior change
- **Cognitive-behavioral therapy** based on perspective that thoughts, emotions, and physical sensations can affect behaviors such as opioid use and vice versa; helps people develop awareness of their cognitive distortions that negatively impact their mood and likelihood of relapse; components include:
  - Psychoeducation
  - Identifying triggers to drug use & coping skills to manage emotions without drugs
  - Enhancing interpersonal functioning
  - Enhancing drug refusal and problem solving skills
  - Increasing recovery focused activities

Other Interventions for OUD

- **Addiction counseling** is abstinence-oriented individual and group therapies provided by credentialed addiction counselors in a formal treatment setting
  - Efficacy is weak as an adjunct to pharmacotherapy for OUD
  - Typically the only “talk therapy” provided by OTPs
- **Mutual help groups** may involve peer groups or meetings, as well as opportunities to engage in one-on-one support, recovery activities, and service work
  - Narcotics Anonymous
  - Methadone Anonymous
  - Medication-Assisted Recovery Services

Safety: *Consensus Statement*

COUNCIL ON PATIENT SAFETY IN WOMEN'S HEALTH CARE
safe health care for every woman

National Partnership for Maternal Safety

Consensus Bundle on Obstetric Care for Women With Opioid Use Disorder

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Obstet Gynecol 2019; 134:365-375

Stimulant Use Disorders (SUD)

- SUDs involve any of the class of drugs that include cocaine, methamphetamine, prescription stimulants (eg, Adderal, Ritalin, Dexadrine, Concerta), and MDMA, commonly known as ecstasy or Molly, which has stimulant and hallucinogenic properties
- Stimulants have similar mechanisms of action and addiction to them leads to similar clinical manifestations
  - Cocaine and methylphenidate (Concerta) reinforcing properties mediated by its ability to block the dopamine transporter and increase dopaminergic activity in critical brain regions
  - Amphetamines and other diverted pharmaceutical stimulants both block the dopamine transporter as well as stimulate release of dopamine
  - Synthetic cathinones, beta-ketone amphetamine analogs known as “bath salts”, block reuptake of dopamine, norepinephrine, & serotonin, as well as stimulate release of dopamine

J Med Toxicol 2012; 8:33

Impact of Cocaine Use Disorder on Pregnancy

- Cocaine crosses the placenta and fetal blood-brain barrier; vasoconstriction is the major purported mechanism for fetal and placental damage
- Cocaine significantly increases the risks of:
  - Preterm birth (OR 3.38, 95% CI 2.72-4.21)
  - LBW (OR 3.66, 95% CI 2.90-4.63)
  - SGA infant (OR 3.23, 95% CI 2.43-4.30)
  - Reduced BW (-492 gm, 95% CI -562 to -421 gm)
- Other reported increased risks: miscarriage, *abruptio placentae,* decreased length (-0.71 cm) & HC (-0.43 cm) at birth

Am J Obstet Gynecol 2011; 204:340.e1

Methamphetamine Use Disorder

- The fastest rising drug of abuse worldwide
- 2.1% of Americans have tried it at some time in their lives
  - Similar rates of use among men and women (0.32 vs. 0.23%)
- MA use in U.S. increased in 1990s reaching epidemic proportions in early 2000s in Western and Midwestern regions
  - Reduced access to precursors (eg, pseudoephedrine)→falling prevalence by mid-2000s
  - On the rise again associated with 40% increase in mortality from 2015-2016
- Manufacturing: primarily made in super labs in Mexico now

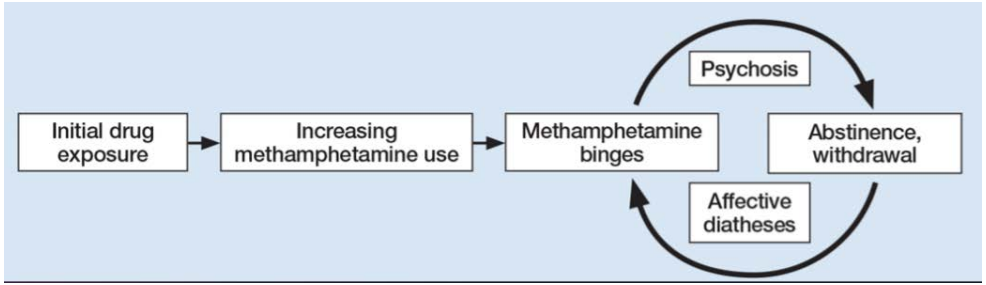
Methamphetamine Use Disorder (MUD)

- Comorbidity – Chronic MA users have high rates of comorbid psychiatric disorders
  - Primary psychotic disorder: 28.6%, including schizophrenia, schizoaffective disorder, or a manic episode
  - Primary mood disorder: 32.3%, including bipolar disorder and major depression
  - Primary anxiety disorder: 26.5% , including generalized anxiety disorder, social phobia, and PTSD
  - ADHD: 33-40%

Psychiatry Res 2011; 186:356

Methamphetamine Use Disorder: Clinical Manifestations

- Cognitive effects: episodic memory, executive functions, information processing speed, motor skills, language, visuoconstructional abilities
- Course: **MA users more likely to develop addiction soon after onset of use** compared to users of other stimulants
  - Characterized by repeated periods of intense use with intermittent sobriety and relapse; use averaged 12 d/mo. in chronic users
  - 5 trajectories of MA use
    - Increasing 15%
    - Decreasing 21%
    - High use 22%
    - Moderate use 35%
    - Low use 7%



Methamphetamine & Obstetric Outcomes

- More antepartum admissions
- Preterm delivery 17%
- Pre-eclampsia 9%
- Placental abruption 4.3%
- Severe maternal morbidity and mortality 3.8%
- More expensive

TABLE 2—Adjusted Health Outcomes, Health Care Utilization, and Expenditures Among Hospital Deliveries Complicated by Amphetamine and Opioid Use: National Inpatient Sample, United States, 2014–2015

Variables	Amphetamine Use (n = 18 050)	Opioid Use (n = 50 011)	Other Hospital Deliveries (n = 7 545 380)
Antenatal diagnoses, weighted % (95% CI)			
Preeclampsia	9.3 (8.2, 10.4)	4.4 (4.0, 4.9)	4.8 (4.7, 4.8)
Placental abruption	4.3 (3.6, 5.0)	3.1 (2.8, 3.5)	1.0 (1.0, 1.1)
Clinical outcomes, weighted % (95% CI)			
Preterm delivery (< 37 wk)	16.7 (15.3, 18.0)	12.6 (11.9, 13.4)	5.8 (5.7, 5.9)
Cesarean delivery	37.4 (35.6, 39.3)	34.5 (33.5, 35.6)	32.6 (32.3, 32.8)
Severe maternal morbidity or mortality	3.8 (3.1, 4.4)	2.4 (2.1, 2.7)	1.6 (1.6, 1.7)
Health care utilization: hospital transfer, weighted % (95% CI)	1.1 (0.7, 1.4)	0.63 (0.47, 0.81)	0.14 (0.12, 0.16)
Length of stay, days, mean (95% CI)			
All deliveries	2.9 (2.9, 3.0)	3.0 (2.9, 3.1)	2.6 (2.6, 2.7)
Vaginal deliveries	2.4 (2.3, 2.5)	2.5 (2.5, 2.6)	2.2 (2.2, 2.2)
Cesarean deliveries	4.0 (3.8, 4.1)	4.3 (4.1, 4.4)	3.6 (3.5, 3.6)
Cost per delivery hospitalization, US $, mean (95% CI)[a]			
All deliveries	5700 (5500, 5900)	5400 (5200, 5500)	4600 (4600, 4700)
Vaginal deliveries	4100 (4000, 4200)	4300 (4100, 4500)	3500 (3500, 3600)
Cesarean deliveries	7300 (7100, 7600)	7500 (7200, 7800)	6100 (6000, 6200)

Note. CI = confidence interval. The sample size was n = 7 611 192. All proportions are survey-weighted and represented as rate per 100 delivery hospitalizations (95% CI) unless otherwise noted. Adjusted for age, payer, income, rural compared with urban residence, and hospital region.

[a]Costs are inflation-adjusted to 2015 US dollars.

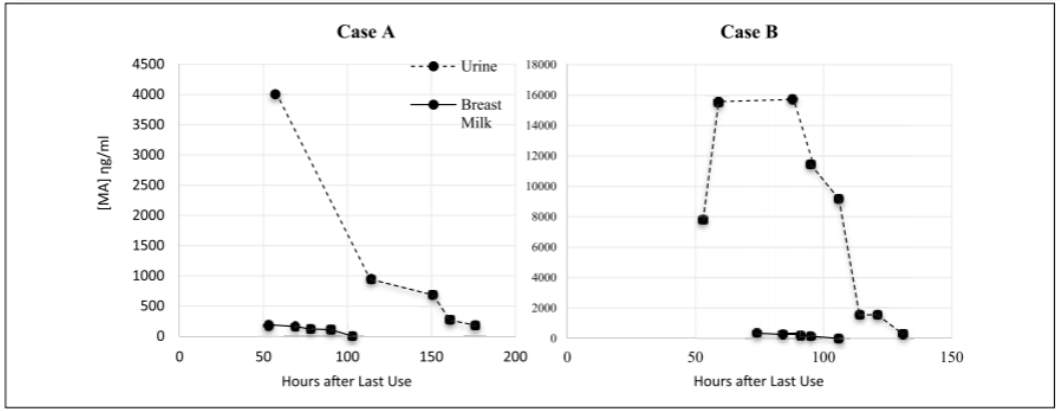
Am J Public Health 2019; 109: 148-154

Impact of MA Use During Pregnancy

- The most common effects noted in newborns:
  - Growth restriction
  - Decreased weight, length, and head circumference (HC)
- Echoencephalography revealed congenital anomalies in MA exposed infants including:
  - Cardiac anomalies
  - Cranial abnormalities
  - Abnormal brain development closely resembling those of ill, asphyxiated infants

Obstet Gynecol 1988; 72:541-544; J Dev Behav Pediatri 2003; 24:17-23; J Pediatr 1989; 115:770-778

Transfer of MA into Breast Milk and Urine of PP Women Who Smoked MA during Pregnancy



MA is hydrophilic
Very low concentrations of MA are in breast milk.

- Half-life of MA in breast milk was 11.3 and 40.3 hr.
- Absolute infant doses were 21.3 and 51.7 µg/kg/d
- MA disappears from breast milk ~1 day before maternal urine MA becomes negative
- Assuming the mother is abstaining from MA use, breastfeeding can be safely initiated in mothers whose urine MA has turned negative for ≥ 24 hr.

Dignity Health.

J Human Lactation 2016; 32:333-339

Infant Development, Environment, and Lifestyle Study (IDEAL): Prospective, Longitudinal Study of MA-Exposure

- 412 maternal-child pairs (204 MA exposed & 208 unexposed pairs) from United States and New Zealand
- Neonatal outcomes
  - ↑ admission to NICU 17%
  - ↓ arousal and ↑ physiological stress
  - Improved at one month of age
  - Poor suck
- Neonatal withdrawal syndrome
  - More jitteriness
  - Rarely requiring medication
- ↓HC and length
- Less breastfeeding
- > 50% referred to CPS

J Dev Behav Pediatr 2003;24:17-23

- Poor fine motor performance at age 1 yr.; no difference by age 3
- Modest ↓height during first 3 yr
- Ages 3 & 5
  - MA exposure was associated with increased emotional reactivity and anxious/depressed problems at both ages
  - Externalizing and attention-deficit/hyperactivity disorder problems by age 5 years

Neurotoxicol Terat 2011; 33:176-184

Pediatrics 2012; 129:681-688

IDEAL Study: School-Aged Outcomes following Prenatal Methamphetamine Exposure: 7.5 Year Follow-Up

Child Behavior Checklist (CBCL) Scores

Mean (SD)	PME	Comparison	Overall
Externalizing*	56.8 (10.9)	54.2 (9.4)	55.5 (10.3)
Rule-Breaking Behavior*	2.9 (2.6)	2.2 (2.0)	2.6 (2.3)
Aggressive Behavior*	8.4 (6.8)	6.6 (5.2)	7.5 (6.1)
Internalizing	51.6 (9.6)	50.1 (9.5)	50.9 (9.6)
Anxious/Depressed	3.3 (2.7)	3.0 (2.8)	3.1 (2.8)
Withdrawn	1.5 (1.8)	1.2 (1.6)	1.4 (1.7)
Somatic Complaints	1.3 (1.7)	1.2 (1.6)	1.3 (1.6)
Total Problems	54.8 (10.6)	53.3 (9.3)	54.1 (10.0)

*Difference between PME and comparisons, $p < 0.05$

- CBCL is widely used to identify problem behavior in children; higher scores indicate more problems
- MA exposed children were exposed to significantly more early adversity than controls
  - Higher rates of extreme poverty
  - Higher rates of changes in primary caregiver
- Increased externalizing, rule-breaking and aggressive behavior

J Pediatr 2016; 70:34-38

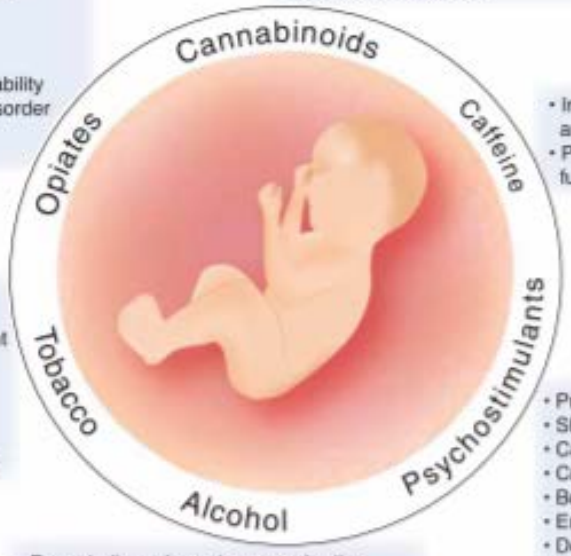
Dignity Health.

Impact of Prenatal MA Exposure on Developing Brain

- Significant advances have been made in understanding the neurotoxic effects of MA on brain structure in adults
  - Abuse of MA over time causes damage to dopaminergic and serotonergic brain regions, most prominent in the basal ganglia, also called the striata, which includes the putamen and globus pallidus dorsally, and the nucleus accumbens ventrally
  - Because striatal structures have the highest densities of dopaminergic synapses, neurotoxic effects of MA may be expected to be most pronounced in these regions
  - Limbic volume reductions have been observed in the cingulate and medial temporal lobes in MA abusers
- Striatal and limbic structures, known to be sites of neurotoxicity in adult MA abusers, may be more vulnerable to prenatal MA exposure than alcohol exposure and that more severe striatal damage is associated with more severe cognitive deficit

Addiction 2007; 102 [Suppl 1]:16 –32; J Neurosci 2010; 30:3876-3885

Prenatal Effects of Drugs of Abuse



- Decreased growth
- Deficits in attention
- Increased impulsivity
- Long-term deficits in executive function
- Depression diagnosis
- Future substance use

- Neonatal abstinence syndrome
- Preterm birth and obstetric complications
- Attenuated myelination in infants
- Respiratory insufficiency
- Heart defects
- Reduced growth
- Deficits in cognitive and motor ability
- Attention deficit hyperactivity disorder
- Lower IQ
- Behavioral problems

- Increased risk of growth restriction and prematurity (at high levels)
- Possible decrease in executive function at school age

- Decreased birthweight
- Altered response to stimuli
- Poorer academic achievement
- Poorer cognition
- Attention deficits and hyperactivity
- Adolescent aggression
- Oppositional defiance issues

- Preterm labor
- Short- and long-term growth defecits
- Cardiac and cardiovascular anomalies
- Cranial and brain abnormalities
- Behavior problems
- Emotional and social effects
- Deficits in attention, memory and motivation
- Anxious/depressed behaviors and symptoms
- Aggression and delinquent behavior

- Prematurity and spontaneous abortion
- Limb and facial development
- Reduced growth
- Cognitive delays and impairments
- Reduced brain volumes
- Abnormalities in the corpus callosum
- Deficits in attention, memory, verbal fluency, executive functioning, reaction times, and motor learning

Neuropharmacology 2015; 40:61-87

Questions?