Perinatal Management of Emerging Substance Use Threats

Implications for Perinatal Care

ASAM 56th Annual Conference – Saturday –April 26th – 1:15 – 2:30 pm

- Niraj R. Chavan, MD, MPH, FACOG, FASAM
- Maria Manriquez, MD, FACOG, FASAM
- Cresta Jones, MD, FACOG, FASAM

Disclosure Information

- Niraj Chavan
  - No Disclosures
- Maria Manriquez
  - No Disclosures
- Cresta Jones
  - No Disclosures

Learning Objectives

- Address the perinatal impact of emerging topics related to substance use/misuse
- Introduce key management considerations for perinatal exposure to or use of emerging substances
- Introduce newer applications for established care such as harm reduction and for the changing landscape of cannabis use in the United States

Perinatal “MED” talks

- Perinatal considerations with xylazine exposure
- Perinatal considerations with nitazenes and tianeptine
- Kratom use and pregnancy
- Perinatal harm reduction
- Prenatal implications of CBD and cannabis
- Impactful legislative advocacy in the context of prenatal cannabis use

Xylazine and Pregnancy

Niraj R. Chavan, MD, MPH, FACOG, FASAM
Saint Louis University / SSM Health

Flesh-eating ‘zombie drug’ saturating Los Angeles streets, officials say

BY VIVIAN CHOW AND KAREEN WYNTER - 05/12/23 9:41 AM ET

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HEALTH

16 Comments

$2 tests to detect ‘tranq’ are first strike at US ‘zombie drug’ epidemic

By Andrew Court

Published March 27, 2023 | Updated March 27, 2023, 5:21 p.m. ET

‘Good luck’: A warning from Philadelphia as xylazine spreads to Minnesota’s drug supply

Ryan Raiche KSTP
Updated: May 2, 2023 - 7:08 PM
Published: May 1, 2023 - 9:44 AM

https://kstp.com/5-investigates/good-luck-a-warning-from-philadelphia-as-xylazine-spreads-to-minnesotas-drug-supply/
https://nypost.com/2023/03/27/tests-to-detect-flesh-rotting-tranq-move-to-market-amid-fear-of-new-nationwide-drug-epidemic/
https://thehill.com/homenews/4001566-flesh-eating-zombie-drug-saturating-los-angeles-streets-officials-say/

APRIL 12, 2023

Biden-Harris Administration Designates Fentanyl Combined with Xylazine as an Emerging Threat to the United States

ONDCP ▸ BRIEFING ROOM ▸ PRESS RELEASES

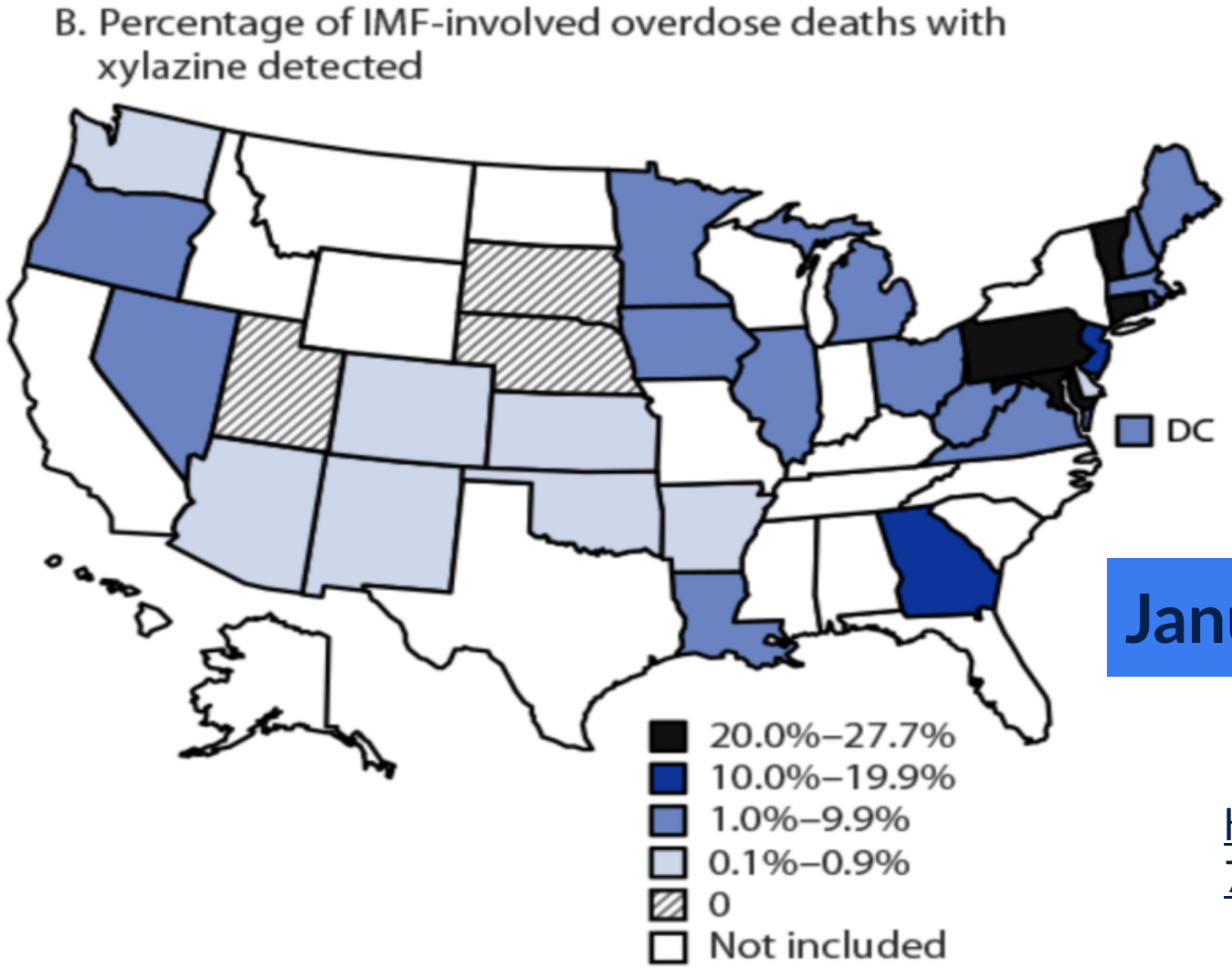
https://www.whitehouse.gov/ondcp/briefing-room/2023/04/12/biden-harris-administration-designates-fentanyl-combined-with-xylazine-as-an-emerging-threat-to-the-united-states/

Xylazine

- Developed in 1962 by Bayer pharmaceuticals as an antihypertensive
- Trials in humans stopped due to hypotension and CNS depression
- FDA approved for veterinary use as a sedative, analgesic, and muscle relaxant
- Used alone or in combination (e.g. with ketamine, barbiturates)

Greene SA; J Vet Pharmacol Ther. 1988

Percentage of drug overdose deaths involving illicitly manufactured fentanyl (IMF), by xylazine detection -31 states and DC



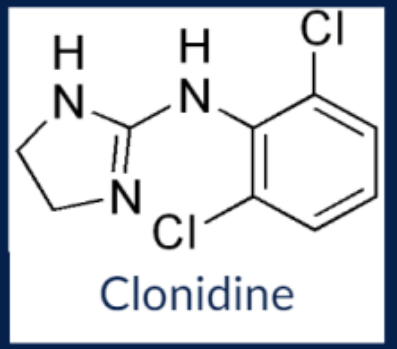
January 2021 – June 2022

https://www.cdc.gov/mmwr/volumes/72/wr/mm7226a4.htm#F2_down

Xylazine – Pharmacology/Toxicology

- Alpha-2 adrenergic agonist that stimulates central alpha-2 receptors:
  - Decreases sympathetic outflow → sedation
  - Naloxone does not reverse the effects of xylazine
- Similar to imidazoline compounds
  - Clonidine, dexmedetomidine, oxymetazoline, tetrahydrozoline, tizanidine, lofexidine
- Pharmacokinetics
  - Time to effect is 1-2 minutes with IV administration (Other routes described include IM, SC, PO, IN, IH)
  - Duration of effect up to 4 hours

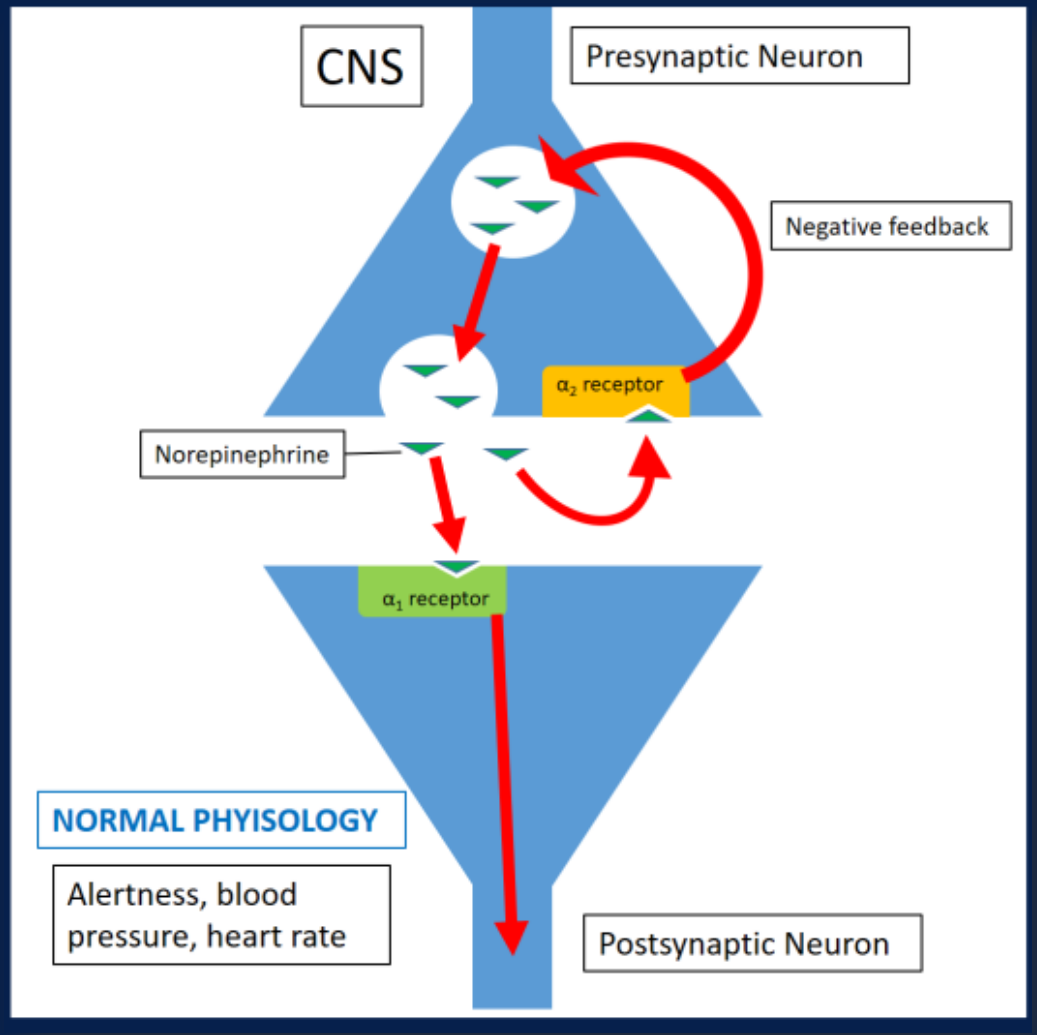
Xylazine

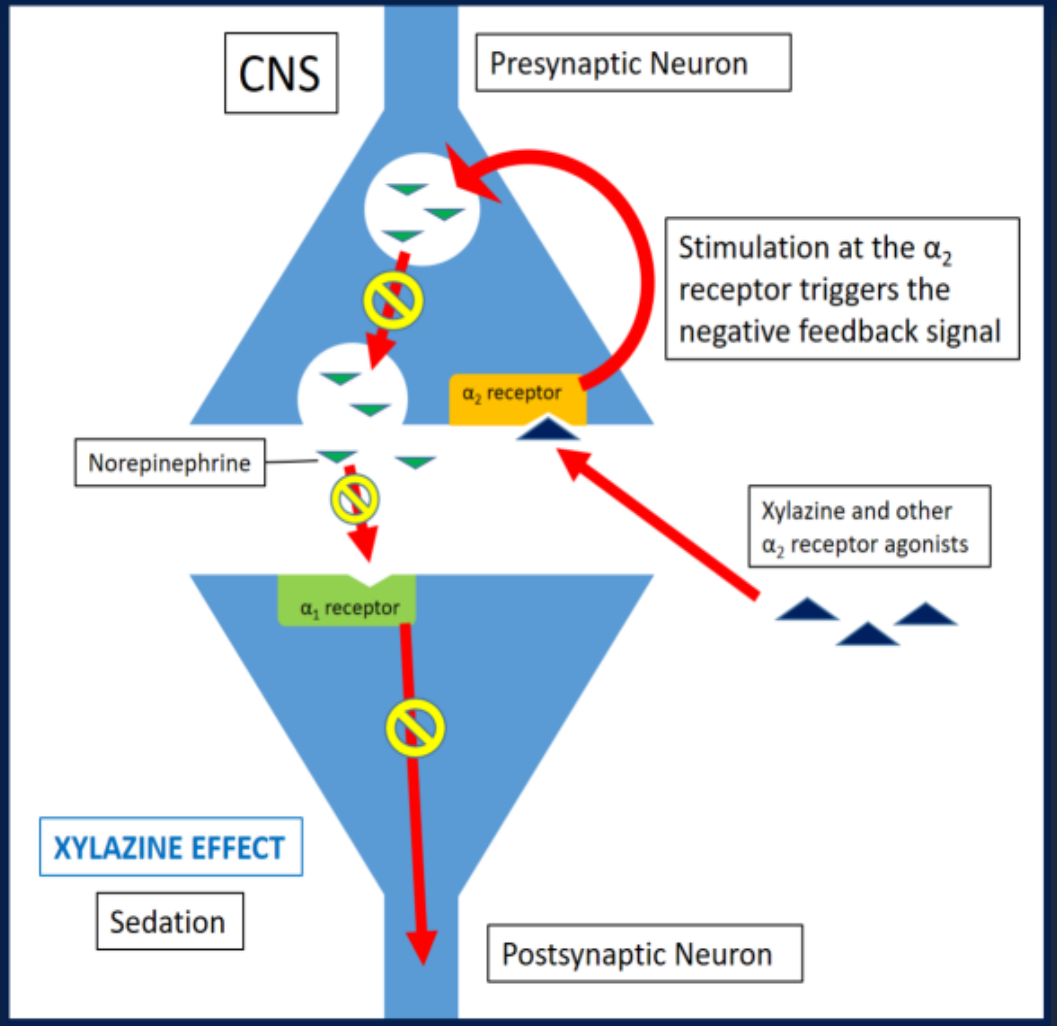


Clonidine

Xylazine and clonidine are structurally similar and have *some* similar effects

Pharmacology / Toxicology of Xylazine





Managing Suspected Xylazine Overdose

- Treat with naloxone - typically opioid co-use
- Continue to monitor closely
- Implement additional supportive care
- Bradycardia and hypotension - atropine, IVF, vasopressors
- Ongoing research
  - Intranasal atipamezole as reversal agent in dogs
  - Yohimbe, Tolazoline used in equine settings

Vohra 2023, Mumba 2023, Focken 2023, Sue 2023

Xylazine and pregnancy –what do we know?

- Very limited human data
- Inpatient labor & delivery cross sectional data - Prevalence is more common than previously thought
- Human umbilical cord studies - crosses the placenta
- Animal studies - decreased uterine blood flow, increased uterine vascular resistance, and decreased fetal growth

Trammel 2024, Mumba 2023, Noonan 2023, Jansen 1984

Summary of Pregnancy Data

Review

Xylazine Use in Pregnancy: The Effects of the Fentanyl Adulterant Xylazine on Pregnant Patients and the Developing Fetus

Grace Noonan, B.A.[1], Roopa Sethi, M.D.[1,2]

[1]University of Kansas School of Medicine, Kansas City, KS

[2]Department of Psychiatry and Behavioral Sciences

Received June 2, 2023; Accepted for publication Oct. 2, 2023; Published online Oct. 30, 2023
https://doi.org/10.17161/kjm.vol16.20624

KANSAS JOURNAL *of* MEDICINE

Summary of Pregnancy Data

Table 1. Animal studies included in final analysis.

Study	Objective	N	Results
Hodgson DS, et. al[11]	To determine effects of sedation achieved by xylazine on cardiopulmonary function and uterine blood flow in cows in late gestation	8	Xylazine reduces uterine blood flow and accessibility of oxygenated blood to the uterus.
Waldvogel D, et. al[12]	To determine changes in Doppler sonographic measures of uterine and placental blood vessels in cows during the last four weeks of pregnancy after receiving Xylazine	9	Xylazine decreased maternal and fetal pulse rate and decreased uterine blood flow while increasing the uterine artery resistance index.
Thaete LG, et. al[13]	To identify effects of a Ketamine/Xylazine combination on fetal growth rate at different points in gestation in mice	203	Ketamine/Xylazine cohort showed significantly decreased fetal growth at various times throughout gestation

Table 2. Human studies included in final analysis.

Study	Objective	N	Results
Spoerke DG, et. al[10]	Case series of Xylazine overdose	3	All patients developed bradycardia and respiratory depression in response to Xylazine
Midthun KM, et. al[14]	To use umbilical cord tissue from drug-exposed mothers to identify common drugs of abuse and adulterants as a marker of in utero exposure	300	Xylazine in 3% of the study participants' umbilical cord tissue of all who were positive for opioid use.

Noonan 2023

Prenatal Xylazine Use – Reality Check

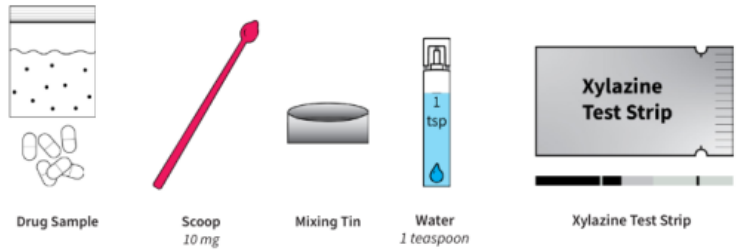
- No currently approved medication to treat xylazine overdose
- No currently approved medication to treat xylazine withdrawal
- Non-healing skin lesions, forearms and lower legs => Necrosis/eschar 1-3 days from initial wound
- Very limited data available on human pregnancy and embryo development

Harm Reduction: Xylazine Test Strips

Xylazine Test Strip Instructions

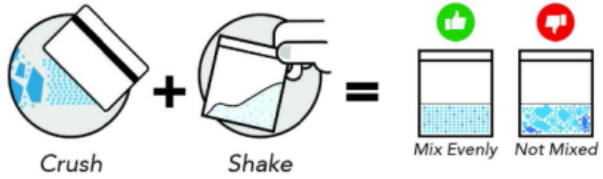
Instructions for testing pill and powdered substances. Always test before using! Xylazine test strips should only be used on opiates.

1 What you'll need



This fact sheet serves as a guide to testing a portion of the substance. This method should be used if you cannot dilute and test all of it.

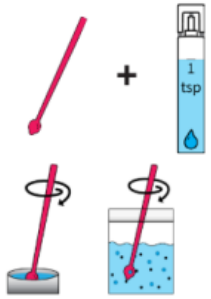
2 Prepare mixture



Before testing, make sure the drugs are well mixed. Xylazine can clump in one part of the sample, which can give inaccurate test results if not thoroughly mixed.

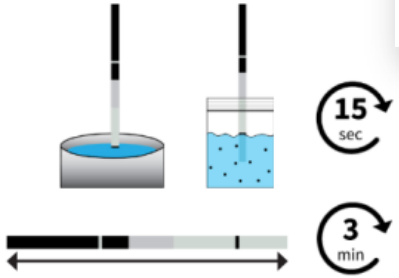
3 Measure & dilute

1. **Scoop and dilute.**
   1 scoop + 1 teaspoon water
2. **Stir it up.**
   Make sure drug sample and water are well mixed.



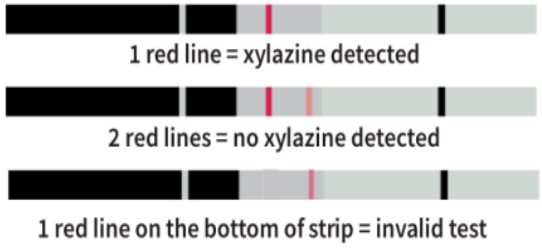
4 Use test strip

1. Hold strip in mixture for *15 seconds*.
2. Place strip on flat surface for *3 minutes*.



5 Interpret the results

Read results:



1 red line = xylazine detected

2 red lines = no xylazine detected

1 red line on the bottom of strip = invalid test

Takeaways

- Xylazine is a potent central nervous system (CNS) depressant => found as an adulterant in the illicit drug supply => increases the risk of respiratory depression and fatal overdose.
- Linked to overdose deaths => In combination with other substances
- Naloxone has no impact on xylazine alone – but should still be considered first line therapy for xylazine-involved overdoses due to nearly ubiquitous fentanyl co-use
- Xylazine can cause severe skin wounds regardless of route of use.
- Xylazine urine drug testing is currently only available from reference laboratories (send-out) => Check with your local laboratory
- Prenatal Xylazine use is a reality – urgent need to address gaps in care

Perinatal Nitazenes and Tianeptine Exposure

Cresta W Jones MD, FASAM, FACOG
University of Minnesota

You are contacted by the emergency department to assess a patient .....

- 30 weeks pregnant by current ultrasound
- Administered naloxone for respiratory arrest in the community
- Urine toxicology without evidence of opioids/opiates
- Patient reports taking only prenatal vitamins and a cognitive supplement that she gets at the local convenience store

Perinatal Nitazenes and Tianeptine

- Nitazenes
  - 1950s
- Tianeptine
  - 1989

Nitazenes

- Developed in the 1950s
- Analgesics
- Never approved for medical use
- Synthesis using historical pharmacology research

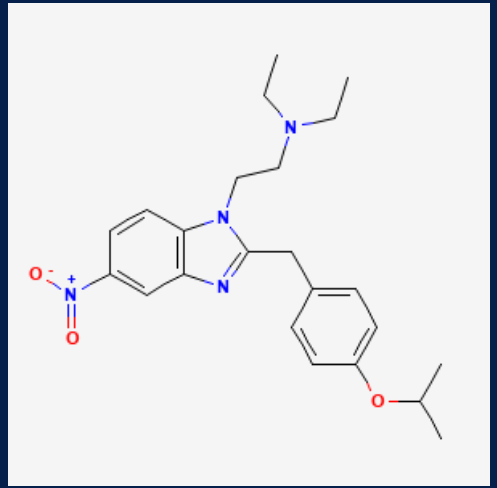
Novel potent opioids (NPO)

Not currently regulated by law

Pergolizzi 2023

Nitazenes

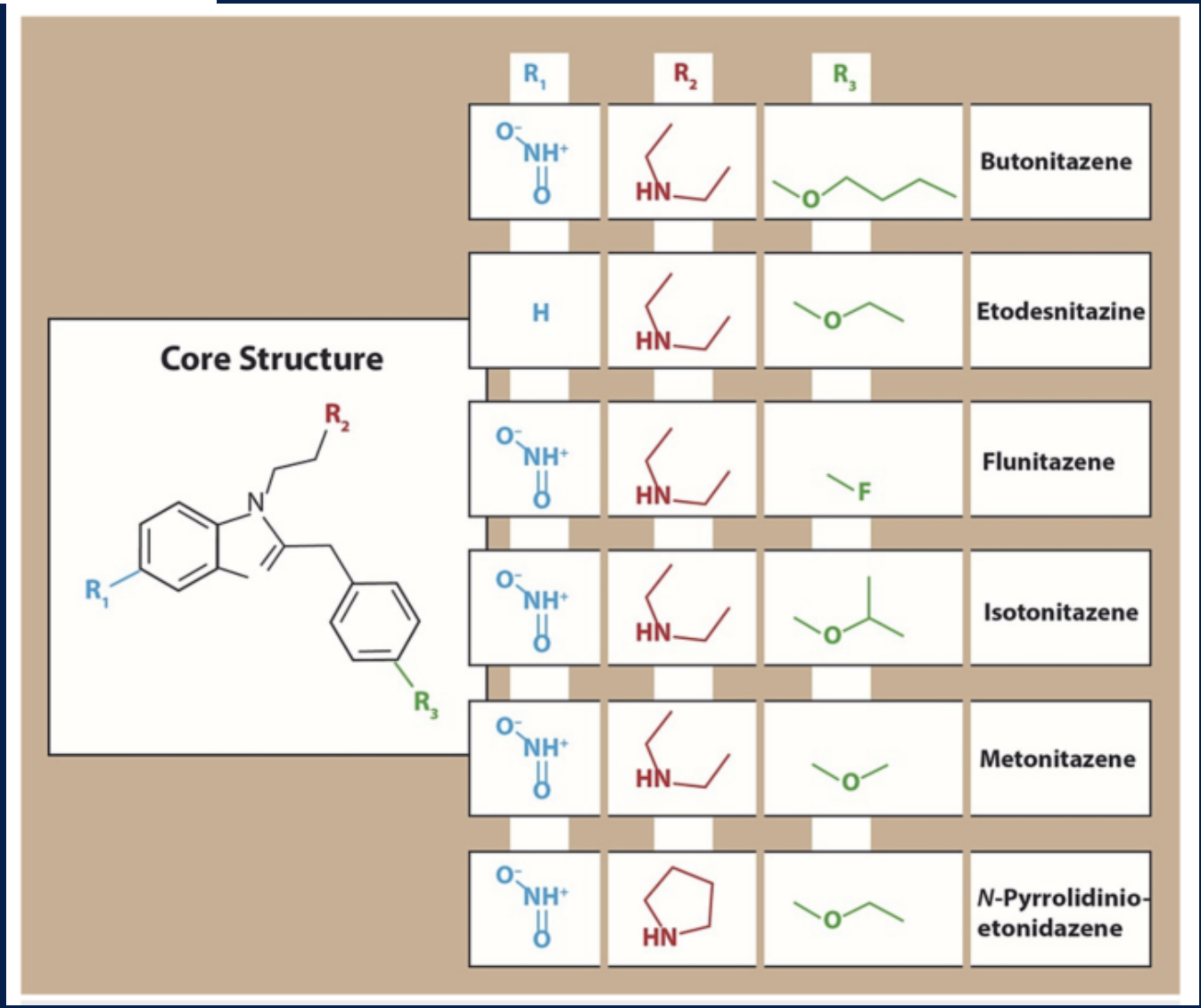
- Isotonitazene (Iso, Tony)
- First detected drug supply 2019
- Temporary schedule 1 (2021)



Pergolizzi 2023

Old Drugs and New Challenges: A Narrative Review of Nitazenes

Joseph Pergolizzi Jr [1], Robert Raffa [2], Jo Ann K. LeQuang [3], Frank Breve [4], Giustino Varrassi [5]



Pergolizzi 2023

Journal of Medical Toxicology
https://doi.org/10.1007/s13181-025-01059-8

REVIEW

Naloxone Dosing and Hospitalization for Nitazene Overdose: A Scoping Review

Jonathan C. Berger[1] · Alec D. Severe[1] · Mohamed S. Jalloh[1] · Alex F. Manini[1,2]

	Relative potency to heroin
Heroin	1
Fentanyl	50
Metonitazene	50
Protonitazene	100
Isotonitazene	250
Etonitazene	500

Table: **The relative potency of fentanyl and selected nitazenes in comparison to heroin[2,3]**

Holland et al., 2024

Nitazenes

- Patient Education
  - Discuss potency and risk of overdose
  - Limited research of pregnancy-specific effects
- Screening and Testing - nitazene test strips
- Naloxone
- Consider evidence-informed treatment with MOUD

Tianeptine

- Antidepressant vs. nootropic supplement
- Opioid μ receptor agonist, anxiolytic
- Zaza, Tianaa Red, gas station heroin
- Prescribed dose 50 mg/day; non-prescribed 2500+ mg

Bence 2016; Ikeri 2024, Romero 1992; Orescanin-Dusic 2012, Wagner 2023

Tianeptine

- Varied indications for use
- Opioid withdrawal
- Reversal with naloxone
- MOUD to treat?

Bence 2016; Ikeri 2024, Romero 1992; Orescanin-Dusic 2012, Wagner 2023

Tianeptine

- Patient education
  - Discuss potency and risk of overdose
  - Limited research of pregnancy-specific effects
- Evaluation of psychiatric disorder (depression or anxiety)
- Overdose management

Tianeptine, an Antidepressant with Opioid Agonist Effects: Pharmacology and Abuse Potential, a Narrative Review. Edinoff, A et al. Pain Ther. 2023 Jul 15;12(5):1121-1134

Perinatal Tianeptine

- Absence of obstetric exposure data
  - Inhibition of uterine smooth muscle contractions (rat model)
- Paucity of prenatal exposure data
  - Cases (2) of NOWS phenotype treated with morphine
  - Increased dopamine affinity in brain of offspring (rat model)

Bence 2016; Ikeri 2024, Romero 1992; Orescanin-Dusic 2012

A Call for Research

- Toxicology testing
- Evidence - based treatment
- Overdose management
- Neonatal withdrawal management
- Non-pharmacologic support

Edinoff, A. N. et al (2023). Tianeptine, an Antidepressant with Opioid Agonist Effects: Pharmacology and Abuse Potential, a Narrative Review. *Pain and therapy*, *12*(5), 1121–1134.

Takeaways

- Drug supply contaminants and novel substances may be new uses for older compounds
- Naloxone and test strips remain key harm reduction tools
- Patient (and provider) education is key in identifying potential complications of novel substance exposures
- Perinatal research is needed to optimize care for birthing patients and their newborns

Kratom and Pregnancy

Niraj R. Chavan, MD, MPH, FACOG, FASAM
Saint Louis University / SSM Health

Case Discussion

MS is a 23 y/o G3P2002 – currently pregnant at 12 weeks gestation who reports long standing history of off and on use of illicit opioids – since the last 5 years – she has been unable to continue with methadone as medication for opioid use disorder (MOUD) due to access barriers and has been afraid about initiating buprenorphine for fear of having to go through moderate withdrawal.

Of late – she has started using Kratom that she is able to obtain from an online website to supplement her use and this was recommended to her from a friend as a natural organic option to address her opioid use. She presents for initial prenatal care visit and wants to discuss implications for pregnancy management

Case Discussion

- What do you tell MS about impact of Kratom use on implications for pregnancy outcomes?
- What are some of the management options that you can offer this patient?
- From a neonatal standpoint – how do you counsel this patient about potential outcomes and management strategies?

What is Kratom?

- Mitragyna speciosa: tree native to Southeast Asia => products derived from its leaves are marketed as herbal supplements
- Partial opioid agonist: bioactive alkaloids => mitragynine and 7-hydroxymitragynine
- Effects: Analgesia, mood-enhancing, can lead to opioid withdrawal symptoms
- About a fifth to a third of all patients with SUD report use
- Used as treatment for opioid withdrawal - more accessible than structured OUD treatment and illicit opioids

Wright 2023, Smid 2018, Bowman 2023,

Kratom – What do we know?

- Sold as tea, capsules, tablets, raw leaves, herbal supplement as and concentrated extracts.
- Metabolites => do not appear on a standard urine toxicology
- Detection => requires more sophisticated liquid chromatography with tandem mass spectrometry (LCMS) (may take 1-2 weeks)
- Primary reasons for use => stop or reduce opioid use by reduction of withdrawal symptoms, reduce cravings, manage anxiety/depression, chronic pain management

Smid 2018, Bowman 2023, Wright ME 2021

Kratom is everywhere!

Kratom Use in the Perinatal Period

- Pregnancy prevalence unknown
  - 0.8% general population

- Perinatal SUD (single institution survey, n = 80)
  - 32.5% ever use
  - 5% pregnancy
  - 1% lactation
  - 80% used to relieve withdrawal

Bowman 2023

Kratom Effects and Management

- Initial stimulatory effects, mimics opioids with chronic use
- Physiologic withdrawal syndrome – can be similar to opioid withdrawal
- Not detected on standard toxicology
- Has been associated with lethal overdose
- Overdose: respiratory depression, agitation, tachycardia, hypertension
- Case reports of reversal with naloxone

Faucher 2023, Vento 2021, Kalin 2021, Wright 2021

Management

- Case reports / Case series on management of Kratom use with:
  - Buprenorphine
  - Methadone
  - Clonidine
  - Morphine base detoxification
  - Tricyclic antidepressants
  - Contingency Management

Vento 2021, Kalin 2020, Hassan 2021, Khazaeli 2018, Smid 2018

Perinatal Kratom Use

- Data is largely from case reports / case series
- Pregnant patients
  - Often reported opioid withdrawal symptoms upon reducing / stopping kratom use
  - Managed during pregnancy with buprenorphine, methadone, and rapid detoxification with morphine-based weaning
- Neonates
  - May exhibit symptoms of neonatal opioid withdrawal syndrome (NOWS)
  - May require pharmacologic treatment with morphine weaning protocols +/- clonidine

Smid 2018, Wright 2021, Murthy 2019, MacKay 2018, Davidson 2019

Takeaways

- Ask about supplements, other natural interventions – Kratom use is more common than you think!
- Detection requires LCMS – will not be picked by routine urine drug screens
- Effective treatment with buprenorphine has been described in pregnancy => consider standard dose buprenorphine induction
- Untreated and unaddressed perinatal kratom use is a risk for neonatal withdrawal symptoms, similar to NOWS

Harm Reduction for Emerging Substance Use

Maria Manriquez, MD, FASAM, FACOG

University of Arizona College of Medicine Phoenix

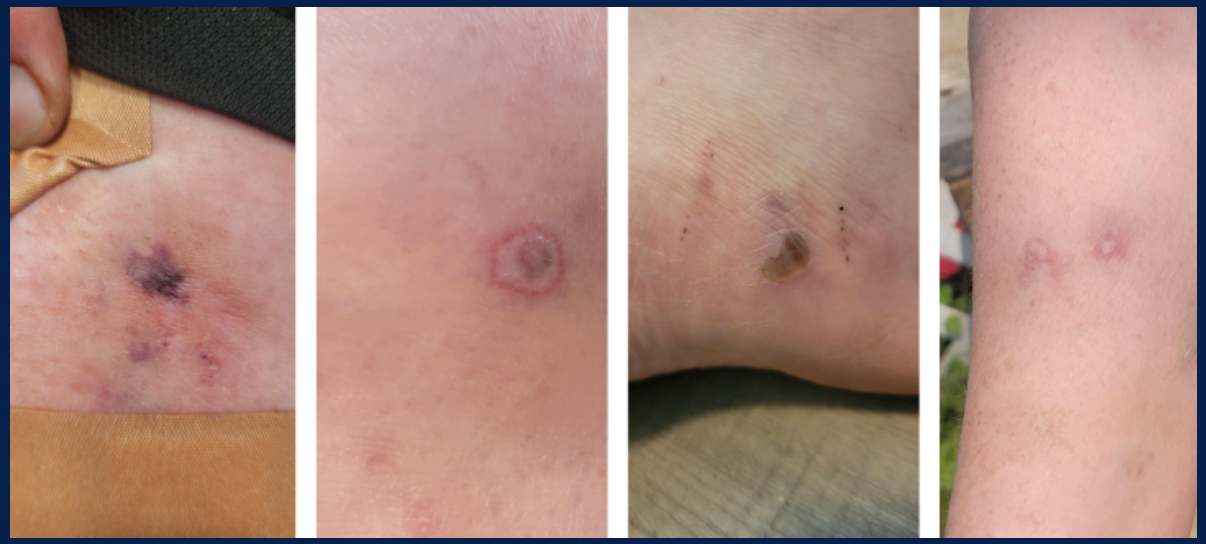
Integrating Harm Reduction into Prenatal Care

- Screening and early identification
  - Universal verbal screening using validated tool, using non stigmatizing language
- Medications for use disorder and withdrawal management
  - Buprenorphine or methadone for patients with OUD, managing withdrawal symptoms safely
- Overdose prevention and harm reduction supplies
  - Distributing naloxone and providing overdose education, access to test strips
- Trauma-informed and culturally competent care
- Social support and legal considerations
  - Housing, food, financial assistance, and legal resources

Xylazine (Tranq or Tranq Dope)

Harm Reduction Strategies

- Patient Education
  - Uses
  - Effects
    - Short and Long term
  - Recognizing Overdose
- Screening and Testing
- Wound Care; Examining the Skin
- Overdose Prevention - Utility of Naloxone
- SUD Treatment - Integrated Prenatal Care
- Social Support and Housing



Reducing the harms of xylazine: clinical approaches, research deficits, and public health context. Zagorski, C et al Harm Reduction Journal 20, 141(2023)

Kratom (Mitragynine)

Harm Reduction Strategies

- Patient Education
  - Uses (Kratom as a Harm Reduction Strategy)
  - Effects
  - Recognizing Overdose
- Screening and Testing
- Medication Treatment
  - Buprenorphine
- Monitoring Liver Function
- Evaluation of psychiatric disorder - understanding why mitragynine is being used
- Overdose Prevention - Utility of Naloxone - not proven useful to date
- SUD Treatment - Integrated Prenatal Care
- Social Support and Housing

Kratom as a potential substance use disorder harm reduction agent. Green, M Front. Public Health, Volume 12 - May 2024

Case to consider

- 38 yo G3P0020 presents at 30 weeks gestation with new onset chest and back pain, found confused by family.
- Normotensive with decreased level of consciousness requiring 15 L/min O2 to maintain O2 sat of 88%. Pt was intubated and admitted to ICU.
- FHT Cat 2 then Cat 1 after O2 and uterine displacement.
- Initial laboratory results revealed multiorgan dysfunction. LDH>2500 U/L, ALT 2945 U/L, Creatinine 677, Troponin 44, CK 17,146 U/L.
- Biologic urine testing + for benzodiazepines (Pt known to be on diazepam and SSRI's for anxiety) and cannabis.
- ECHO non-ischemic cardiomyopathy with EF of 35-40%

https://doi.org/10.1016/j.psycr.2022.100088

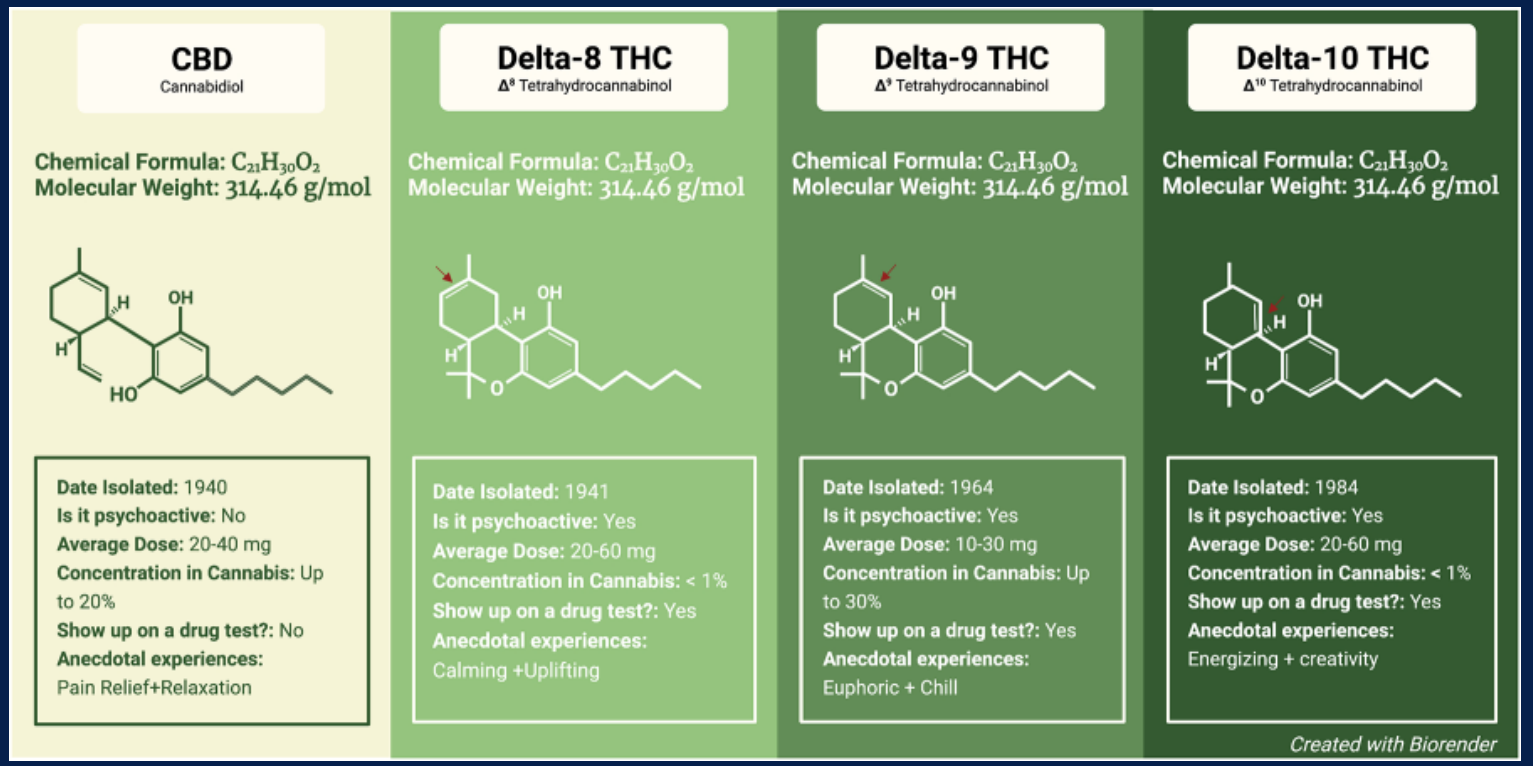
Perinatal Implications of Cannabis

Maria Manriquez, MD, FASAM, FACOG

University of Arizona College of Medicine Phoenix

Cannabis and CBD: Pharmacology and Mechanism of Action

- Differences between THC and CBD
- Interaction with the endocannabinoid system
- Placental transfer of cannabinoids



Prevalence of Cannabis and CBD Use During Pregnancy

- Trends in cannabis and CBD consumption among pregnant individuals
- Reasons for use (nausea, anxiety, pain)

Table. Change in Percentage of Cannabis Use During Pregnancy After the Start of the Pandemic[a]

	Rate ratio (95% CI)	
Interrupted time-series model variables	Unadjusted	Adjusted[b]
Pre-COVID-19 expected trend[c]	1.001 (0.994-1.008)	1.001 (0.993-1.008)
COVID-19 shift	1.268 (1.145-1.405)[d]	1.251 (1.120-1.397)[d]
COVID-19 change in trend	0.989 (0.973-1.006)	0.992 (0.975-1.010)

[a] See the Methods section for the prepandemic period definition.

[b] Adjusted for age (<25, 25 to <35, and ≥35 years) and self-reported race and ethnicity from the electronic health record (see the Methods section definition for race and ethnicity).

[c] See Laboratory Methods in the Supplement for determination of prenatal cannabis use.

[d] Significant at $P < .05$.

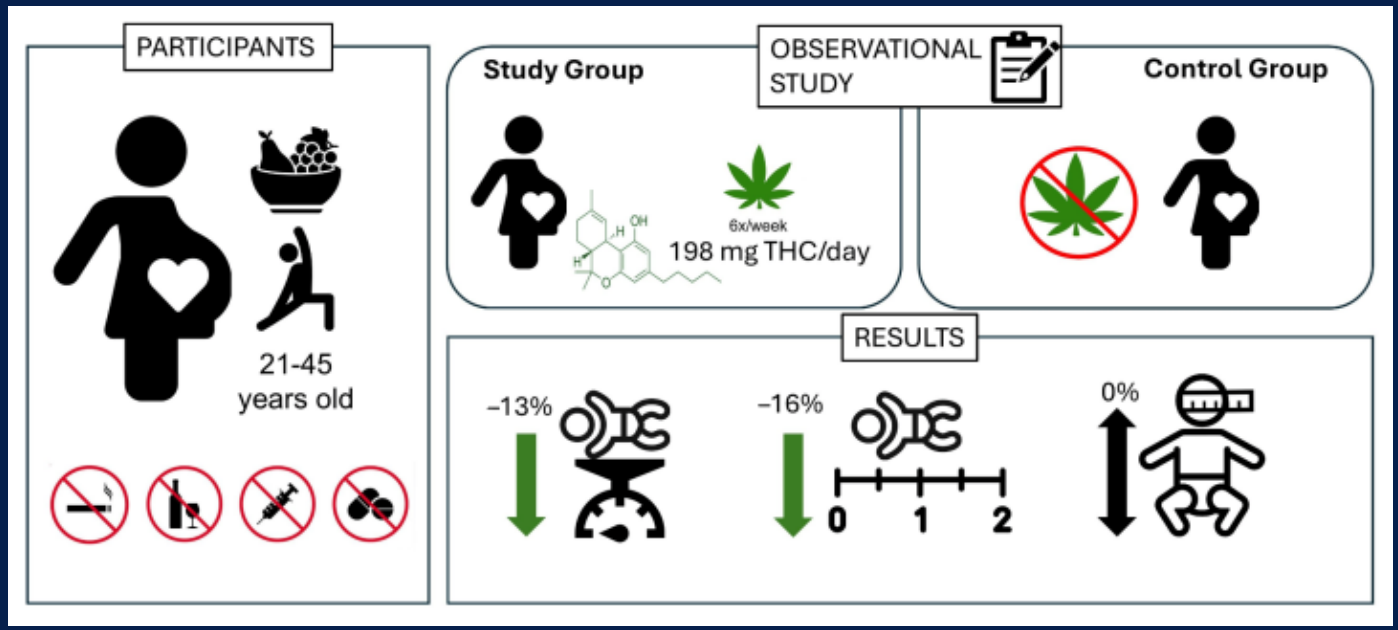
Maternal Health Implications

- **Potential Effects** on Pregnancy Outcomes
  - Increase risk of miscarriage and stillbirth
  - Preterm birth
  - Preeclampsia
  - Low birth weight
- Maternal Mental Health
  - Anxiety and depression
  - Substance Use disorders

Placenta keeps the score of maternal cannabis use and child anxiety. Janine M. LaSalle

Fetal and Neonatal Outcomes

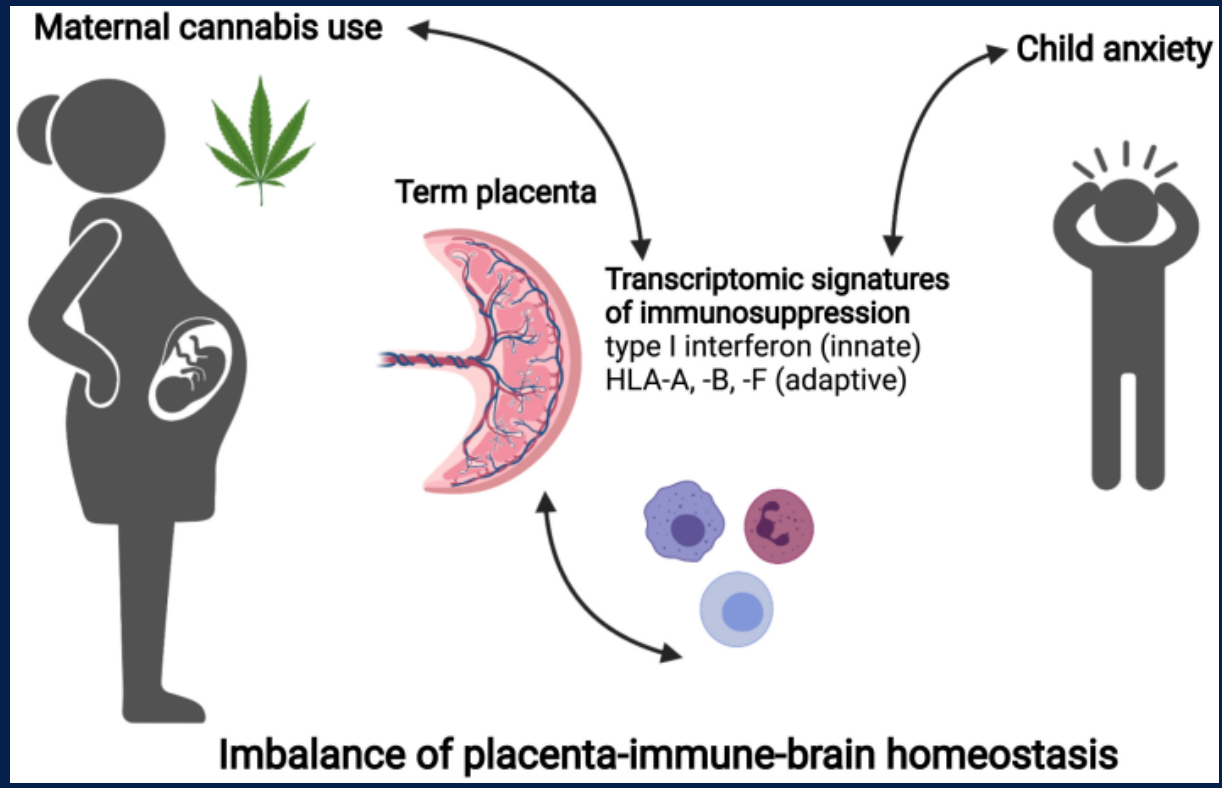
- Cannabis-Related Risks
  - Low Birth Weight
  - Fetal Growth Restriction
  - Neurodevelopmental Impact
  - Increase Risk of Stillbirth



Kleinhans, N. et al High-Potency Prenatal Cannabis Exposure and Birth Outcome Measures

Long-Term Neurodevelopmental

- Potential cognitive and behavioral concerns
  - Attention deficits
  - Impaired executive functioning
  - Increase risk anxiety



Placenta keeps the score of maternal cannabis use and child anxiety. Janine M. LaSalle

Breastfeeding and Cannabis

- THC present in breastmilk
- THC is fat soluble and can remain in infants systems for days
- Cannabis smoke has chemicals that can harm infants brain and lungs
- Second hand smoke increases risk for SIDS

Cannabinoid Hyperemesis Syndrome

- Persistent nausea
- Intense abdominal pain
- Loss of appetite
- Repeated vomiting

Treatment

- IV fluids and electrolytes may be needed for dehydration
- Antiemetics (don’t usually work)
- Alternative therapies; capsaicin cream, benzodiazepines, haloperidol
- Hot showers decrease symptoms
- ONLY CURE is to STOP using cannabis

ACOG Recommendations

- Preconception and early pregnancy - Universal Screening
- Screen positive for cannabis use - counsel regarding potential adverse health consequences
- Encourage discontinuation
- Encourage alternative therapies for those using medical cannabis
- Insufficient data to evaluate the effects of cannabis use on infant breastfeeding

Marijuana Use During Pregnancy and Lactation ACOG Committee Op #722

Cannabis and Perinatal Legislative Advocacy

Cresta W Jones, MD, FASAM, FACOG
University of Minnesota

Postpartum inpatient rounds

25 year old G1 P1001, one day after vaginal birth at term

Patient-infant dyad underwent toxicology testing - indication - fetal growth restriction

Toxicology indicated cannabis metabolites - you are asked to discuss

Patient used legal THC seltzers to help with insomnia and states was never discussed by her OB care team

Cannabis and Perinatal Legislative Advocacy

- Rapid expansion of legal access to cannabis
- Rapid changes in formulations
- Rapid changes in THC concentrations

Limited perinatal research and patient education

Cannabis and Perinatal Legislative Advocacy

As cannabis legalization advances across the country, what do we need to improve patient outcomes?

Cannabis Policy and Advocacy

- Know your laws
  - Perinatal toxicology testing
  - Substance use reporting
  - Prenatal substance exposure and family regulation

Levels of Engagement

FEDERAL

STATE

HEALTH SYSTEM

COUNTY/CITY

MEDICAL SOCIETY

SCHOOL BOARD

WHAT YOU NEED

- COMMUNICATION SKILLS
- EMPATHY
- ORGANIZATIONAL SKILLS
- PROBLEM SOLVING
- AN ABILITY TO SUSPEND THE NEED TO PRESENT DATA

MY EXPERIENCE IN POLICY CHANGE

MINNESOTA MANDATORY PERINATAL SUBSTANCE USE REPORTING

WHAT I LEARNED

- PRESENT AN IDEA THAT WORKED IN A “COMPETITOR” SPACE
- CULTIVATE PARTNERSHIPS WITH DIFFERENT PERSPECTIVES
- COMPELLING STORIES CHANGE POLICY
- BE PATIENT AND EMBRACE SETBACKS

DON'T BE AFRAID TO ADVOCATE

START WITH A LETTER TO YOUR ELECTED OFFICIALS

VOICE YOUR IDEAS TO ASAM, AAP, ACOG, AAFP

YOU ARE THE EXPERT VOICE WHEN YOUR PATIENT CAN'T BE

Cannabis Policy and Advocacy

- Modifications of perinatal statute to address legalization and inequities in testing, reporting and family separation
- Ongoing evaluation of hospital and system level screening and reporting
- Advocating for universal screening and brief intervention
- Developing educational materials for healthcare professionals and patients
- Funding for research

Session Summary

- Emerging substances may play a significant role in perinatal complications
- Education of providers (and patients!) on new substances in key to ongoing care optimization
- We are the experts that are needed to advocate for our patients when they don’t have a voice

Thank you!

Questions?

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