Maternal-Fetal Substance Use Disorder

August 24, 2022

CSAM Addiction Medicine Board Review Course

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CONFLICT OF INTEREST DISCLOSURE

I Rachel Sussman have nothing to disclose.

I will be discussing “off label” use of drugs or devices in this presentation.

EDUCATIONAL OBJECTIVES

After attending this presentation, participants will be able to:

1. Describe impacts of maternal substance use on fetal development
2. Recognize safety concerns in the treatment of substance use disorder in pregnancy
3. Understand the treatment options for opioid use disorder in pregnancy and for neonatal opioid intoxication and withdrawal, including describing the findings of the MOTHER study

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NEED TO KNOW

1. Effects of the following on fetal development from in utero exposure:
   - Smoking
   - Alcohol
   - Stimulants
   - Barbiturates
   - Benzodiazepines
   - Cannabinoids
   - Opioids & opioid withdrawal
2. Medications used to treat substance use disorder that are contraindicated in pregnancy
3. Effects of pregnancy on metabolism of methadone vs. buprenorphine

NEED TO KNOW

4. Findings of the MOTHER study (compared buprenorphine & methadone in pregnancy): induction issues, treatment retention, & effects on neonatal abstinence syndrome
5. Pain management during labor & postpartum for patients on opioid agonist/partial agonist therapy
6. Signs of neonatal intoxication & withdrawal
7. Timing of onset of neonatal withdrawal after in utero exposure to heroin, methadone, & buprenorphine
8. Compatibility of maternal buprenorphine, buprenorphine/naloxone, & methadone with breastfeeding

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1. You are caring for a 30-year-old woman who was admitted to opioid agonist treatment with methadone during the 3rd trimester of pregnancy. She previously was taking 60 mg of oxycodone & smoking cigarettes daily. She had an uncomplicated delivery after an otherwise uneventful pregnancy. You recommend the newborn be observed in house for:

A. 48 hours
B. 3 days
C. 4 to 7 days
D. 10 days

1. Answer: C. 4 -7 days

	NOWS Onset Time	Common Practice	AAP recommendation
Heroin/Oxycodone	2-3 days	observe & monitor in hospital for 1 week	observe & monitor in hospital for 3-7 days
Methadone	within 4 days		
Buprenorphine	within 4 days		

Note: newer research suggests 5 days may be sufficient

References:

Anbalagan S, Mendez MD. Neonatal Abstinence Syndrome. [Updated 2020 Apr 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2020 Jan. Available from: https://www.ncbi.nlm.nih.gov/books/NBK551498/

Mark L. Hudak, MD, Rosemarie C. Tan, MD, PhD, The committee on Drugs, and the Committee on Fetus and Newborn. PEDIATRICS Volume 129, Number 2, February 2012

2. The infant has some mild irritability and difficult feeding at 3-4 days, but responds well to swaddling in a quiet room with small frequent feeds. On day of life 5, the infant suddenly developed diarrhea & vomiting, increased irritability & increased muscle tone. What is the best response?

A. Start methadone promptly

B. Continue to observe throughout the day & overnight, & round on mother & baby the next day

C. Order blood cultures, hemogram, a chemistry panel, TSH, & consider head imaging

D. Start intravenous fluids & antibiotics

2. Answer C. Order blood cultures, hemogram, a chemistry panel & consider head imaging.

- Neonatal opioid withdrawal syndrome should not be assumed; it is a diagnosis of exclusion.
- The infant should be screened for infectious or metabolic causes, thyroid function abnormalities & brain lesions. These conditions must be ruled out before concluding that neonatal abstinence syndrome is the cause of the changing clinical picture.

2. Answer C. continued

References:

Robert M. Kliegman, Patricia S Lye, Brett J. Bordino, Heather Toth, Donal Basel, Nelson Pediatric Symptom-Based Diagnosis E-Book Google Books, Chapter 26, Irritable Infant Pages 411-420. March 2017

Jansson, L et.al "The Opioid Exposed Newborn: Assessment and 2020 Pharmacologic Management". J Opioid Manag. 2009 ; 5(1): 47–55. Principles of Addiction Medicine 4th Ed. 2009 Chapter 81. pp 1116.

Karen McQueen and Jodie Murphy-Oikonen. Neonatal Abstinence Syndrome. N Engl J Med 2016;375:2468-79.

Anne Johnston, Jerilyn Metayer, Elizabeth Robinson. Management of Neonatal Opioid Withdrawal (aka Vermont Guidelines).

3. When all labs & studies are normal but diarrhea, vomiting, irritability & increased muscle tone persist, you begin pharmacologic treatment for NOWS. Which is the most commonly used medication?

A. Oral morphine: titrate to control signs of withdrawal, then taper gradually.
B. Sublingual buprenorphine: titrate to control signs of withdrawal, then taper gradually.
C. Oral methadone: titrate to control withdrawal symptoms, then taper gradually.
D. Transmucosal fentanyl: titrate to control withdrawal symptoms, then taper gradually.

3. Answer: A. Oral morphine

- Oral morphine is used by ~80% of U.S. centers. Doses are based on the FNASS or the infant's weight. Oral morphine is preferred to tincture of opium as required dilution of the tincture increases risk of dosing error.
- Oral methadone is used by ~20% of U.S. centers. Modest advantage over morphine in terms of length of treatment & hospital stay, but there is no standard treatment regimen.
- Sublingual buprenorphine is used by a small number of centers. Trials have found a shorter length of treatment compared with morphine & methadone. Long-term outcomes studies in newborn infants are needed
- Fentanyl is not used to treat infants with NOWS.

3. Answer: A. continued

References:

AK Mangat, GM Schmölzer, MD, PHD and WK Kraft “Pharmacological and Non-pharmacological treatments for the Neonatal Abstinence Syndrome (NAS).” Semin Fetal Neonatal Med. 2019 April 24(2): 133-141.

WK Kraft, MW Stover, JM Davis “Neonatal abstinence syndrome: Pharmacologic strategies for the mother and infant”. Semin Perinatol. 2016;40(3):203-212. doi:10.1053/j.semperi.2015.12.007.

4. All of the following are true about The Eat Sleep Console (ESC) approach to managing Neonatal Opioid Withdrawal Syndrome (NOWS) EXCEPT:

A. The ESC approach is being used by many hospitals instead of the FNASS – driven approach.

B. The ESC approach requires the scorer to un-swaddle & disturb the infant.

C. The ESC approach limits pharmacologic treatment & may lead to substantial reductions in length of stay.

D. The ESC approach focuses on how symptoms of withdrawal are affecting the infant's ability to function & the overall well-being of the infant, rather than reducing withdrawal signs with attendant exposure to opioids & other medications.

4. Answer: B. The ESC approach requires the scorer to un-swaddle & disturb the infant

- The ESC approach involves hospital staff teaching parents specific methods to nurture infants at risk of NOWS. If signs of NOWS emerge, parents are encouraged to provide increased nurturing & provided detailed guidance on how to do this.
- One advantage of this approach is that it is much less intrusive. Rooming in is a key component.
- This approach has decreased need for medication to treat NOWS & led to shorter hospital stays for infants with NOWS.

4. Answer: B. Continued

Reference:

Grossman MR, Lipshaw MJ, Osborn RR, Berkwitt AK. A Novel Approach to Assessing Infants With Neonatal Abstinence Syndrome. *Hosp Pediatr*. 2018;8(1):1-6. doi:10.1542/hpeds.2017-0128.

5. A 26 y.o. pregnant woman presents to your clinic requesting opioid agonist treatment with methadone. She reports an 8-year history of injection heroin use with 2 years of sustained abstinence while on opioid agonist treatment with methadone. She was tapered off methadone while incarcerated.

She has been out of jail for the past 8 months, learned yesterday that she is 8 weeks pregnant & is no longer seeing the father of the baby who is using heroin. She denies opioid use since out of jail but is craving opioids “all the time”. Onsite urine drug test is negative for opioids, stimulants, benzodiazepines, methadone, buprenorphine, oxycodone & marijuana. There are no signs or symptoms of opioid withdrawal.

5. What is the best response to this patient's request?

A. Advise patient that she does not meet regulatory requirements for methadone treatment & recommend she seek a modality of treatment (residential, intensive outpatient or outpatient) that does not involve medication.

B. Suggest opioid agonist treatment with buprenorphine as an alternative & offer to begin treatment today.

C. Submit an online exception request to allow admission to opioid agonist treatment with methadone, & schedule patient to return in a day or two.

D. Admit to opioid agonist treatment with methadone today.

5. Answer: B. Suggest buprenorphine maintenance as an alternative & offer to begin treatment today.

- Avoiding medication would increase patient's risk of relapse to injection heroin use.
- Current physical dependence is not required for initiation of buprenorphine treatment & there is no risk of precipitated withdrawal in this case.
- If buprenorphine is ineffective or is not tolerated, a federal/state exception may be requested for opioid agonist treatment with methadone. Pt does not meet California's regulatory requirements for admission to opioid agonist treatment with methadone (documentation of physical dependence & opioid use for all or most of the preceding year). Use of methadone would require prior federal/state authorization, which usually takes at least a day.

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5. Answer: B. continued

Reference:

JJ McCarthy, D Stephenson, Pregnancy and Neonatal Withdrawal, Chapter 4 pages 47-64, Guidelines for Physicians Working in California Opioid Treatment Programs. W Ling, D Stephenson, E Vasti (editors), California Society of Addiction Medicine, 2019.

6. The MOTHER (Maternal Opioid Treatment: Human Experimental Research) Trial compared methadone versus buprenorphine for treatment of opioid use disorder in pregnancy. The authors concluded that buprenorphine is:

A. Associated with a clinically meaningful reduction in the severity of NOWS.
B. Associated with higher treatment retention rates.
C. Safe in pregnancy when combined with naloxone.
D. Associated with higher doses of morphine for the treatment of neonatal abstinence syndrome.

6. Answer: A. The authors concluded that buprenorphine is associated with clinically meaningful reduction in the severity of NOWS

- The MOTHER trial is the most current & single most comprehensive research effort to investigate the safety & efficacy of maternal & in utero exposure to methadone & buprenorphine & is an important study to review given its seminal nature.
  - ✓ While there was no difference in peak NOWS scores, babies with in-utero exposure to buprenorphine required lower doses of morphine & shorter hospital stays than those exposed to methadone.

6. Answer: A. continued

- ✓ Retention was a problem in the buprenorphine arm, about 33% dropped out, most citing dissatisfaction with the medication.
- ✓ In the study, doses of buprenorphine from 2 to 32 mg were felt to be equivalent to doses of methadone from 20 to 140 mg.

- In clinical practice:
  - ✓ An average dose of buprenorphine for treatment of OUD is 16 mg. Doses above 24 mg are not generally recommended. Twice daily dosing is common in pregnancy.
  - ✓ An average dose of methadone for treatment of OUD is 80-120 mg. Doses of methadone above 140 mg are not unusual. Metabolic rates of methadone generally increase during pregnancy, sometimes dramatically. Most women require twice daily dosing regimens, some more frequent.

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6. Answer: A. continued

- Increasingly less concern about safety of naloxone in pregnancy:
  - ✓ A number of observational studies have now shown equivalent pregnancy outcomes in pregnant women treated with buprenorphine-naloxone compared with buprenorphine only or methadone
  - ✓ Consider continuing buprenorphine-naloxone for patients who are successful with it
  - ✓ Strongly consider continuing buprenorphine-naloxone for patients who present past the window of critical organogenesis (after week 10 of pregnancy)

6. Answer: A. continued

References:

Jones, H.E, et. al., “Neonatal Abstinence Syndrome after Methadone or Buprenorphine Exposure.” N Engl J Med 2010; 363:2320-31.

JJ McCarthy, D Stephenson, Pregnancy and Neonatal Withdrawal, Chapter 4 pages 47-64, Guidelines for Physicians Working in California Opioid Treatment Programs W Ling, D Stephenson, E Vasti (editors), California Society of Addiction Medicine, 2019

Link, H.M., Jones, H., Miller L., Kaltenbach K., Seligman N. (2020). Buprenorphine-naloxone use in pregnancy: a systematic review and meta-analysis. Amer J Ob Gyn MFM, 2(3).

7. A 24-year-old woman presents to your office with a 6-week history of nausea/vomiting & reports drinking a 12-pack of beer daily for the past year. A routine pregnancy test is positive. Patient is motivated to stop drinking to protect the baby. History is positive for severe alcohol withdrawal symptoms with prior cessation attempts and negative for *delirium tremens &* seizures. In addition to psychosocial treatment, you recommend:

A. Admission and treatment an anticonvulsant, such as carbamazepine.
B. Careful monitoring, but no medical management likely necessary since patient's history is negative for seizures & *delirium tremens.*
C. Admission and treatment with a benzodiazepine.
D. Admission and treatment with clonidine and gabapentin

7. Answer: C. Admission and treatment with a benzodiazepine.

- Given the patient's history of severe alcohol withdrawal, medical management is appropriate.
- Of the choices listed, a benzodiazepine is most appropriate.
- Most anticonvulsants are relatively contraindicated in pregnancy
- Clonidine and gabapentin, while becoming more widely used and studied, are still not first line monotherapy for alcohol withdrawal and in particular are not well studied in pregnancy.

7. Answer: C. continued

References:

UpToDate: "Management of Ambulatory Alcohol Withdrawal", "Gabapentin: Drug Information," "Management of Moderate/Severe Alcohol Withdrawal." Principles of Addiction Medicine, 5th ed., Chapter 83, pp. 1254-1260 and p. 1274.

Kelty, E., Terplan, M., Greenland, M. *et al.* Pharmacotherapies for the Treatment of Alcohol Use Disorders During Pregnancy: Time to Reconsider?. *Drugs* 81, 739–748 (2021). https://doi-org.laneproxy.stanford.edu/10.1007/s40265-021-01509-x

8. In utero alcohol exposure may lead to a range of conditions known as Fetal Alcohol Spectrum Disorders (FASD). Which of the below statements about FASD is most correct?

A. Diagnosis of FAS requires the presence of all 4 cardinal features: characteristic pattern of minor facial anomalies, growth deficiency, deficient brain growth, & neurobehavioral impairment
B. Diagnosis of fetal alcohol syndrome (FAS) requires known, documented in-utero alcohol exposure.
C. Frequent low levels of drinking (0-2 drinks daily) have been shown to be the most detrimental to fetal development.
D. Diagnosis of Alcohol Related Neurodevelopment Disorder (ARND) can be made at any age, with or without documented in-utero alcohol exposure.

8. Answer: A. Diagnosis of FAS requires the presence of all 4 cardinal features: characteristic pattern of minor facial anomalies, growth deficiency, deficient brain growth, & neurobehavioral impairment.

Disorder Name	*Alcohol Exposure*	*Physical Issues*	*Cognitive Issues*
Fetal Alcohol Syndrome (all 4 features present)	does not need to be documented/known	**1. characteristic pattern of minor facial anomalies** **2. growth deficiency (before or after birth)**	**3. deficient brain growth** **4. neurobehavioral impairment**
Alcohol-related neurodevelopment disorder (ARND)	known in-utero exposure, and diagnosed after age 3		• intellectual disabilities • problems with behavior and learning
Alcohol-related birth defects	known in-utero exposure	defects involving heart, kidney, bone, hearing or a combination	
Neurobehavioral disorder associated with prenatal alcohol exposure (NBD-PAE)	known in-utero exposure		problems in 3 areas: thinking & memory behavior & mood issues w/difficulty in attentional task shifts trouble with day-to-day living

8. Answer: D. continued

References:

HE Hoyme, WO Kalberg, Amy J Elliott, et al. Updated Clinical Guidelines for Diagnosing Fetal Alcohol Spectrum Disorders. Pediatrics 2016 138 (2) e20454256, August 2018.

9. Select the most true statement about alcohol consumption during pregnancy in the United States, 2018 - 2020.

A. 1 in 7 pregnant adults reported drinking alcohol in the past 30 days
B. Fewer pregnant adults reported drinking alcohol in the past 30 days in 2018-2020 compared to the prior 3 year period.
C. Pregnant adults with some college education were less likely to report binge drinking than pregnant adults with a high school diploma or less.
D. Of those pregnant adults who reported drinking alcohol in the past 30 days, only 10% reported binge drinking.

9. Answer: A. 1 in 7 pregnant adults reported drinking alcohol in the past 30 days

Actually, more pregnant adults reported past 30 day drinking in 2018-2020 than the prior study period. Some college education made binge drinking significantly more likely in this sample. Of those pregnant adults who reported past 30 day drinking of any amount, approximately 40% also reported binge drinking.

Reference:
MMWR Morb Mortal Wkly Rep. 2022;71:10-13.

10. During pregnancy, tobacco is the most commonly used substance, & marijuana is the most widely used illegal drug in the U.S. All of the following are true ***except*** :

A. Prenatal marijuana exposure is associated with increased likelihood of a person using marijuana as a young adult.
B. Tobacco use, marijuana use & passive exposure to tobacco increase the risk of stillbirth.
C. Smoking marijuana during pregnancy is associated with long term brain development issues affecting memory, learning, & behavior.
D. Most women who quit smoking during pregnancy remain smoke-free one year after delivery.

10. Answer: D. Most women who quit smoking during pregnancy remain smoke-free one year after delivery.

- Unfortunately, most women who quit smoking during pregnancy resume smoking within the first year after delivery. In one study 70% returned to smoking.

- Prenatal marijuana exposure is associated with increased likelihood of a person using marijuana as a young adult. This has been found to be true when other factors that influence drug use are considered.

10. Answer: D: continued

References:

Forray A. Substance use during pregnancy. *F1000Res*. 2016;5:F1000 Faculty Rev-887. Published 2016 May 13. doi:10.12688/f1000research.7645.1

https://www.samhsa.gov/marijuana/marijuana-pregnancy

Fingerhut LA, Kleinman JC, Kendrick JS. Smoking before, during, and after pregnancy. *Am J Public Health*. 1990;80(5):541-544. doi:10.2105/ajph.80.5.541

NIDA. Substance Use While Pregnant and Breastfeeding. National Institute on Drug Abuse website. https://www.drugabuse.gov/publications/research-reports/substance-use-in-women/substance-use-while-pregnant-breastfeeding. June 6, 2020 Accessed July 14, 2020.

11. Which of the following is true about buprenorphine use during pregnancy?

A. Buprenorphine treatment is more effective than methadone treatment, so women presenting with opioid use disorder should be offered buprenorphine rather than methadone.

B. Buprenorphine should be preferred because it has better treatment retention than methadone treatment.

C. After stabilization on a therapeutic dose, buprenorphine dose adjustments are less likely to be needed than methadone dose adjustments during pregnancy and postpartum

D. Women should be tapered off buprenorphine after the post-partum period.

11. Answer C. After stabilization on a therapeutic dose, buprenorphine dose adjustments are less likely to be needed than methadone dose adjustments during pregnancy and postpartum

- Both medications have advantages & disadvantages. A treatment recommendation should be made after careful consideration of each case.
- Choice C. correctly identifies a key advantage of buprenorphine; due to its long half-life and active metabolites, it does require fewer dose adjustments .
- Methadone may be started with no fear of precipitated withdrawal, a significant advantage for patients at increased risk of miscarriage, preterm labor or delivery & for patients/providers who prefer not to allow withdrawal to progress to the severity necessary to avoid precipitated withdrawal during buprenorphine induction.

11. Answer C. continued

- Treatment retention has been found to be higher with methadone.
- While some patients will need a higher buprenorphine dose as pregnancy progresses & a lower one after delivery, this is much less common than with methadone because of buprenorphine's active metabolite.
- Discontinuation of opioid agonist treatment (methadone or buprenorphine) has a very high risk of relapse (80% or higher within the first year). Parenting an infant/child is stressful, which further increases the risk of relapse if the support of opioid agonist treatment is withdrawn. Relapse poses the added risk of loss of custody of the baby.

11. Answer C. continued

Reference:

JJ McCarthy, D Stephenson, Pregnancy and Neonatal Withdrawal, Chapter 4 pages 47-64, Guidelines for Physicians Working in California Opioid Treatment Programs W Ling, D Stephenson, E Vasti (editors), California Society of Addiction Medicine, 2019

12. During a monthly follow-up visit with a 24-year-old pregnant woman on opioid agonist treatment with methadone for management of heroin use disorder, she asks whether it would be okay for her to breastfeed. Which aspect of this patient's case would cause you to recommend against breastfeeding?

A. Patient's methadone dose is 140 mg at the time of delivery.
B. Patient has had two brief relapses to binge drinking, but none since starting on escitalopram for treatment of her anxiety.
C. Patient's partner just tested positive for HIV, and her own confirmatory test comes back positive.
D. Patient has hepatitis C.

12. Answer C. Patient's partner just tested positive for HIV, and her own confirmatory test comes back positive.

- The American Academy of Obstetrics & Gynecology & the American Academy of Pediatrics agree that methadone at any therapeutic dose is compatible with breastfeeding.
- While HIV is a contraindication to breastfeeding, Hepatitis B & C are not. Hepatitis C is not found in breastmilk. Hepatitis B DNA can be detected in breast milk, but breastfeeding has not been found to be a risk factor for mother-to-child transmission. Newborns are further protected from Hepatitis B by beginning the vaccination series at delivery. Mothers with Hepatitis B &/or C should pump & discard in the event of cracked & bleeding nipples, until the condition resolves.

12. Answer: C. continued

- Maternal infectious diseases such as active tuberculosis & HTLV I & II should be considered. (HTLV I & II are retroviral infections; I associated with leukemia/lymphoma and a neurodegenerative disease; II has no associated diseases but the two are not easily distinguished by screening tests. I is passed through blood exposure, sex, and breastfeeding; it is endemic in Japan and the Caribbean).
- Escitalopram is compatible with breastfeeding. Rare past binge drinking episodes are not a contraindication to breastfeeding, with ongoing monitoring.

12. Answer: C continued

References:

Academy of Breastfeeding Medicine Protocol Committee, Jansson LM. ABM clinical protocol #21: Guidelines for breastfeeding and the drug-dependent woman. *Breastfeed Med*. 2009;4(4):225-228. doi:10.1089/bfm.2009.9987.

Chen X, Chen J, Wen J, et al. Breastfeeding is not a risk factor for mother-to-child transmission of hepatitis B virus. *PLoS One*. 2013;8(1):e55303. doi:10.1371/journal.pone.0055303.

Carneiro-Proietti AB, Amaranto-Damasio MS, Leal-Horiguchi CF, et al. Mother-to-Child Transmission of Human T-Cell Lymphotropic Viruses-1/2: What We Know, and What Are the Gaps in Understanding and Preventing This Route of Infection. *J Pediatric Infect Dis Soc*. 2014;3 Suppl 1(Suppl 1):S24-S29. doi:10.1093/jpids/piu070

13. A 36 year-old G3P2 presents to your clinic for her first prenatal care visit at 5 weeks and 4 days. She has been smoking cigarettes on and off since age 14. Although she tried to quit smoking during her previous pregnancies, she did not tell her doctor about it and had limited success with abstinence, though she says she "cut way down" at the time. She asks for your help quitting smoking now. Prior to this pregnancy, she participated in your clinic's smoking cessation program, but stopped going after 3 sessions and states she didn't like it. What do you suggest to her?

A. Prescription of nicotine-replacement therapy, after discussion of the risks and benefits.
B. Prescription of bupropion, after discussion of the risks and benefits
C. Prescription of varenicline, after discussion of the risks and benefits
D. Recommendation to switch to e-cigarettes to avoid prenatal exposure to tar in cigarettes, after discussion of the risks and benefits

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13. Answer A. Prescription of nicotine-replacement therapy, after discussion of the risks and benefits.

- Note that the treatment of choice for smoking cessation in pregnancy would be behavioral therapy, however this patient declined that option.
- NRT in pregnancy may result in higher chance of quitting compared to no medication. Limited quality evidence suggests that there is no increased risk of fetal harm from NRT.
- Although there is still limited safety evidence, more recent systematic reviews suggest that a trial of NRT should be considered for pregnant persons, particularly when an individual patient has not been successful in quitting with behavioral support alone and when individual risks are especially high from continued smoking, as is the case with this patient due to her age.

13. Answer A continued.

- There is insufficient evidence of efficacy for bupropion for smoking cessation during pregnancy, and to a lesser extent limited evidence of safety, so choice B is not the best choice, although it could be considered on a case-by-case basis. (Note that use of bupropion as an antidepressant, though still not a preferred agent for that indication, is better studied).
- Neither the safety nor efficacy of varenicline during pregnancy has been established, so choice C is not the best choice.
- There is inconclusive evidence in adults for the role of e-cigarettes in smoking cessation, and even less evidence regarding safety and efficacy in pregnant persons, so choice D is not the best choice.

13. Answer A. continued

References

Claire R, Chamberlain C, Davey MA, Cooper SE, Berlin I, Leonardi-Bee J, Coleman T. Pharmacological interventions for promoting smoking cessation during pregnancy. Cochrane Database Syst Rev. 2020 Mar 4;3(3):CD010078. doi: 10.1002/14651858.CD010078.pub3. PMID: 32129504; PMCID: PMC7059898.

Taylor L, Claire R, Campbell K, Coleman-Haynes T, Leonardi-Bee J, Chamberlain C, Berlin I, Davey MA, Cooper S, Coleman T. Fetal safety of nicotine replacement therapy in pregnancy: systematic review and meta-analysis. Addiction. 2021 Feb;116(2):239-277. doi: 10.1111/add.15185. Epub 2020 Oct 1. PMID: 32621526.

Patnode CD, Henderson JT, Coppola EL, Melnikow J, Durbin S, Thomas RG. Interventions for Tobacco Cessation in Adults, Including Pregnant Persons: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA. 2021 Jan 19;325(3):280-298. doi: 10.1001/jama.2020.23541. PMID: 33464342.

Kranzler HR, Washio Y, Zindel LR, Wileyto P, Srinivas S, Hand DJ, Hoffman M, Oncken C, Schnoll RA. Placebo-controlled trial of bupropion for smoking cessation in pregnant women. Amer J of Ob & Gyn MFM. 2021 Nov; 3(6).

14. A 24-year-old G1P1 presents to L&D in early labor. She appears withdrawn and somewhat somnolent. A urine toxicology screen is positive for methamphetamine. Which of the following treatment approaches would NOT be recommended?

A. Offer referral to a local residential treatment center for pregnant and postpartum mothers
B. Counsel her about the importance of frequent early breastfeeding to increase maternal-infant bonding and improve newborn outcomes.
C. Offer take-home naloxone at the time of discharge given high probability of encountering methamphetamine laced with fentanyl in many communities.
D. Send urine for confirmatory GC/MS testing to clarify which substances the patient and fetus were exposed to, and consider meconium tox testing after delivery.

14. Answer: B. Counsel her about the importance of frequent early breastfeeding to increase maternal-infant bonding and improve newborn outcomes.

- Standard of care for women using methamphetamine during pregnancy is behavioral treatment. Postpartum residential treatment allows substance use treatment to occur alongside developmental and parenting interventions for the mother-infant pair.
- Methamphetamine is relatively concentrated in breast milk--to levels even higher than that of the maternal serum level--and therefore breastfeeding is contraindicated for mothers with recent or ongoing methamphetamine use.
- Take-home naloxone should be given to patients who use methamphetamine given high frequency of fentanyl co-positivity in urine specimens that are positive for methamphetamine

14. Answer B continued.

- Sending confirmatory urine testing and meconium testing to confirm methamphetamine use, and look for fentanyl exposure in patient, and to confirm the infant's exposure is indicated .

- In California, there is no mandated reporting for *prenatal* substance use, however for "an infant born and identified as being affected by substance abuse or withdrawal symptoms resulting from prenatal drug exposure, or a fetal alcohol spectrum disorder (FASD)", an *assessment of needs* must be conducted (usually by hospital social worker) prior to discharge; this assessment usually includes referral to child welfare services (CPS).

14. Answer B continued.

References:

Putnam-Hornstein E, Prindle JJ, Leventhal JM. Prenatal Substance Exposure and Reporting of Child Maltreatment by Race and Ethnicity. Pediatrics. 2016;138(3): e20161273

Methamphetamine abuse in women of reproductive age. Committee Opinion No. 479. American College of Obstetricians and Gynecologists. Obstet Gynecol 2011;117:751–5.

Larue L, Twillman RK, Dawson E, Whitley P, Frasco M. Rate of fentanyl positivity among urine drug test results positive for cocaine or methamphetamine. JAMA Network Open, 201, 2(4).

California Citation: DSS All County Letter No. 17-92. Accessed on 7/78/22 at: https://www.childwelfare.gov/pubPDFs/safecare.pdf

15. You are seeing a 32 yo G2P1 patient in the clinic for her first prenatal visit, at 14 weeks by LMP. What should you do to screen for substance use?

A. Use the patient's provided sample to check a urine tox screen and then ask for further history if it is positive

B. If certain high-risk conditions are present (e.g. history of abruption, preterm labor, late to prenatal care), then screen with a validated instrument and urine tox screen

C. Ask for consent to check a urine tox screen, and collect further history from the patient if it is positive

D. With patient consent, use a valid screening instrument to ask about substance use, and if positive seek consent for urine tox screen

15. D. With patient consent, use a valid screening instrument to ask about substance use, and if positive seek consent for urine tox screen

Research has shown that selective screening leads to increased rates of urine tox screening in Black and Hispanic patient, and misses many patients who might benefit from treatment, so universal screening is recommended.

Both ACOG and ASAM guidelines recommend the use of a validated screening tool for substance use in pregnant patients and caution that informed consent must be obtained prior to screening or sending urine toxicology testing. No screening tool or toxicology testing should be administered to a patient who refuses consent.

15. D. With patient consent, use a valid screening instrument to ask about substance use, and if positive seek consent for urine tox screen

Validated screening tools include:

Tobacco	5 A's – Tailored Approach	If positive, use 3-question AUDIT-C or T-ACE (validated in pregnancy
Alcohol	Universal screening question: How much beer, wine, or other alcoholic beverages do you consume in an average week?	If positive, use 3-question AUDIT-C or T-ACE (both validated in pregnancy)
Cannabis, opioids, stimulants, benzodiazepines	4P's Plus or 5P's NIDA Quick Screen ASSIST SURP-P CRAFFT (age <= 26) WIDUS	

Ref: Table from Smid and Terplan, Ob & Gyn, 2022

15. D. With patient consent, use a valid screening instrument to ask about substance use, and if positive seek consent for urine tox screen

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Thank you & Good Luck!