Substance Use Disorders in High Risk Pregnancy

BACKGROUND

Prematurity is a birth that occurs before 37 weeks of completed gestation.

- Late pre-term birth is between 34 and 37 weeks of gestation
- Very pre-term birth is between 29 and 33 weeks of gestation
- Extremely per-term birth is at or below 28 weeks of gestation

Premature Infants are defined by birth weight as follows:

- Low birth weight - less than 2500 g
- Very low birth weight - less than 1500 g
- Extremely low birth weight - less than 1000 g

Two serious conditions of pregnancy include **placenta previa** (when the placenta lies near/over the cervix) and **placenta abruption** (when the placenta separates from the uterus). Placenta previa can cause varying degrees of vaginal bleeding and deprive the baby of oxygen and nutrients. In some cases, early delivery is needed. Placental abruption can cause varying degrees of vaginal bleeding and deprive the baby of oxygen and nutrients. Sometimes, early delivery is needed.

Risk factors for preterm labor and delivery include:

- No prenatal care
- Extremes of pre-pregnancy weights and BMI including obesity and low pre-pregnancy weight
- Having diabetes which increases the risk of iatrogenic preterm birth resulting from medical complications
- Smoking (dose-dependent effect)
- Substance abuse (cocaine, alcohol, opiates)

Illicit Substance Use in Pregnancy

- Substance users may not seek prenatal care because of fear, guilt and shame. In addition, there may be concerns about medical and legal intervention.
- Opioid users may not even realize that they are pregnant if they are not planning pregnancy and misinterpret the early signs of pregnancy as opioid withdrawal symptoms (e.g., nausea, vomiting, cramping).
  - Unintended pregnancy is common in these women; in one study, 86 percent of pregnant opioid-using women reported their pregnancy was unintended.
- Substance use assessment, counseling, and support by a nonjudgmental clinician may motivate some women who use illicit drugs other than opioids to abstain.
- Observational studies suggest that combining treatment of substance abuse with comprehensive prenatal care can reduce the frequency of some maternal and neonatal complications of maternal substance use. Components of this care should be individualized based on patient-specific factors, and may include the following:
  - Counsel about the risks associated with each drug the mother is using;
  - Encourage the member to moderate and, ideally, discontinue use of illicit drugs (dependent on specific drug and pattern of use);
  - Identify comorbid conditions (e.g., psychiatric disorders and physical/sexual/emotional abuse) frequently

Original Effective Date: 2/5/2015 - Revised: 5/7/2015, 9/17/2015

found in substance abusers. The interrelationships between these issues and substance use need to be addressed in caring for these patients;
- Address the needs of poorly nourished, homeless, and/or incarcerated pregnant substance abusers. In addition to education about nutrition and weight gain, some of these women may need referral to food assistance programs and shelters, and provision of transportation vouchers and prenatal multivitamins; and
- Assemble a multidisciplinary team to comprehensively assess and participate in the care of these women and their offspring – the team may include obstetrical, medical, pediatric, psychiatric, addiction medicine, and social service providers.

Opiate Use in Pregnancy

Many of the medical risks associated with heroin addiction are the same for both pregnant and non-pregnant women, and similar for addiction to other opiates. Opiate users typically have financial, social, and psychological problems that cause psychosocial stress, expose them to violence, and affect their options and treatment. Multiple obstetrical complications have been associated with opiate-dependence in pregnancy including:

- Placenta abruptio
- Fetal death
- Intra-amniotic infection
- Fetal growth restriction
- Preeclampsia
- Premature labor and delivery
- Premature rupture of membranes
- Placental insufficiency
- Miscarriage
- Postpartum hemorrhagea

Opioid Maintenance Assisted Therapy in Pregnancy

- For opioid-dependent women, medication assisted therapy with methadone or buprenorphine offers overwhelming advantages compared to continued use of heroin (e.g., oral administration, known dose and purity, safe and steady availability, improved maternal/fetal/neonatal outcomes).
- Therapy offers a unique opportunity to bring women into medical and obstetrical care systems.
- Maintenance therapy is preferable to medication-assisted withdrawal (detoxification) because it is safe and associated with a lower rate of resumption of heroin use.
- After delivery, Neonatal Abstinence Syndrome (NAS) is likely to occur.

Methadone / Buprenorpine Use in Pregnancy

Medication assisted therapy can ensure the safety of pregnant women and their infants. Objectives include a reduction in adverse birth and pregnancy outcomes. It is important to note that infant withdrawal is treatable and shows no long-term adverse neurobehavioral consequences *in utero* exposure.

Marijuana Use in Pregnancy

Marijuana is the most common illicit substance used during pregnancy. The drug is transferred across the placenta and into breast milk. The impact of prenatal marijuana use on pregnancy outcome is not clear. Adverse effects have not been consistently reported and there is no strong evidence of an increase in congenital anomalies or growth restriction. Observational studies have not reported an association between marijuana use and preterm birth.

Cocaine Use in Pregnancy

- Public and professional interest in prenatal cocaine use is high, although many more pregnant women smoke cigarettes, drink alcohol, or smoke marijuana than use cocaine. Female crack/cocaine users in their thirties

constitute a fast growing group of new users who do not use other substances.

- Cocaine readily crosses the placenta and fetal blood-brain barrier; vasoconstriction is the major purported mechanism for fetal and placental damage.
- The few adequately controlled reports suggest that cocaine's effects are related to dose and stage of pregnancy.
- Studies that evaluated the relationship between maternal cocaine exposure found cocaine use during pregnancy significantly increased the risks of:
  - Preterm birth
  - Low birth weight
  - Small for gestational age infant
  - Shorter gestational age at delivery
  - Reduced birth weight
  - Others have reported increased risks of miscarriage, abruptio placentae, and decreased length and head circumference at birth.

Cocaine and Amphetamine Use in Pregnancy

- Cardiovascular cocaine toxicity is increased in pregnant women.
- Cocaine toxicity usually causes hypertension, which may mimic preeclampsia.
- Amphetamines including methamphetamine — A diagnosis of amphetamine abuse is becoming more common among women of reproductive age, including hospitalized pregnant women.
- Methamphetamine, commonly known as speed, meth, and chalk, or as ice, crystal, and glass when smoked, is a powerfully addictive stimulant. It is a known neurotoxic agent, which damages the endings of brain cells containing dopamine.
- Amphetamines and their byproducts cross the placenta.
- Methamphetamine exposure during pregnancy has been associated with maternal and neonatal morbidity and mortality. In studies that controlled for confounders, methamphetamine exposure was associated with a two- to fourfold increase in risk of fetal growth restriction, gestational hypertension, preeclampsia, abruption, preterm birth, intrauterine fetal demise, neonatal death, and infant death.

Selective Serotonin Reuptake Inhibitors

Mood and anxiety disorders are common in women during their childbearing years. The prevalence of depression has been reported to be between 10% and 16% during pregnancy. The use of selective serotonin reuptake inhibitors during pregnancy or lactation is, to date, not promoted because of lack of safety documentation. There is a growing body of evidence suggesting a link between use of certain SSRI medications in early pregnancy and an increase in some birth defects.[1] However, the off-label use of these drugs has been common for several years. In the treatment of mood and anxiety disorders during pregnancy, the serotonin reuptake inhibitors are often preferred over tricyclic antidepressants because of their relatively few adverse effects and safety in overdose. This has created concern among women planning pregnancies and pregnant women, as well as among their families and physicians.[2]

Fetal Alcohol Spectrum Disorder (FASD)

FASD is an umbrella term that encompasses the range of physical, mental, behavioral, and cognitive effects that can occur in individuals with prenatal alcohol exposure, including:

- Fetal alcohol syndrome
- Partial fetal alcohol syndrome (pFAS)
- Neurobehavioral disorder associated with prenatal alcohol exposure (ND-PAE), sometimes called neurodevelopmental disorder associated with prenatal alcohol exposure

The terminology for FASD continues to evolve to reflect the spectrum of clinical presentations. Terms that have been used in the past to describe clinical or neurodevelopmental effects of prenatal alcohol exposure include “alcohol-related birth defects,” “fetal alcohol effects,” “alcohol-related neurodevelopmental disorder” (ARND), and “neurodevelopmental disorder/alcohol-exposed” or “static encephalopathy/alcohol-exposed”. Facial features of FASD include:

- Small head
- Epicanthal folds
- Low nasal bridge
- Small eye openings
- Flat midface
- Short nose
- Smooth philtrum
- Thin upper lip
- Underdeveloped jaw

Effects of Alcohol in Pregnancy

- Is teratogenic (interferes with normal development) and may cause irreversible central nervous system effects.
- Abnormalities include reduced brain volume with specific reductions in the frontal lobe, striatum and caudate nucleus, thalamus, and cerebellum; thinning of the corpus callosum; and abnormal functioning of the amygdala. These areas influence impulse control and judgment, transfer of information between the hemispheres, memory and learning, motor coordination, ability work toward goals, and perception of time.
- A "safe" threshold or pattern of alcohol consumption has not been identified. A fetus is particularly vulnerable to maternal alcohol consumption due to inefficient elimination and prolonged exposure. Alcohol is eliminated from the fetal compartment at a rate of only 3 to 4 percent of the maternal rate. In addition, much of the alcohol excreted by the fetus into the amniotic fluid is "recycled" through fetal swallowing of amniotic fluid and intramembranous absorption.
- Alcohol has the potential to cause deleterious effects at all stages of gestation.
  - Significant alcohol exposure during the first trimester is associated with facial anomalies and major structural anomalies, including brain anomalies.
  - Exposure in the second trimester increases the risk of spontaneous abortion.
  - Exposure in the third trimester predominantly affects weight, length, and brain growth. However, neurobehavioral effects may occur with a range of exposures throughout gestation, even in the absence of facial or structural brain anomalies.
- Teratogenic effects vary depending upon the quantity and pattern (e.g., binge drinking, daily drinking) of alcohol consumption, maternal and fetal genetics, maternal age, maternal nutrition, and smoking, among other factors.

Despite the risk factors listed below, all women are at risk of giving birth to a child with FASD if they consume alcohol:

- Low educational attainment
- Higher maternal age
- Higher gravidity and parity
- History of miscarriages and stillbirths
- Poor maternal nutrition during pregnancy
- History of FASD in previous children
- Substance use, including tobacco
- Mental health problems including depression
- History of physical or sexual abuse
- Social isolation including living in a rural area during pregnancy
- Intimate partner violence
- Paternal alcohol and drug use at the time of pregnancy
- Other maternal family members with substance use at the time of pregnancy
- Poverty

Clinical Features of FAS. The characteristic clinical features of FASD include three facial dysmorphisms (short palpebral fissures, thin vermillion border, and smooth philtrum), growth retardation, and central nervous system (CNS) abnormalities. The predominant clinical features may vary with age. Facial dysmorphisms may be apparent at birth (though may not be recognized). Growth retardation may occur prenatally or post-natally. CNS impairment may not be apparent until the child is in school. Most individuals with FASD are diagnosed during childhood. In the CDC Fetal Alcohol Syndrome Surveillance project, the average age at ascertainment of FAS was 48.3 months.

Smoking in Pregnancy

Cigarette smoking during pregnancy is the most important modifiable risk factor associated with adverse pregnancy outcomes. In 2002 in the United States, 5 to 8 percent of preterm deliveries, 13 to 19 percent of term infants with growth restriction, 5 to 7 percent of preterm-related deaths, and 23 to 34 percent of sudden infant death syndrome (SIDS) deaths were attributable to prenatal smoking. In addition, smoking and secondhand smoke exposure increase the risk of infertility, placental abruption, preterm premature rupture of membranes (PPROM), and placenta previa. Other items:

- Despite the known harmful effects of smoking, 23 percent of American women report smoking cigarettes in the three months before pregnancy.
- In the United States, the Pregnancy Risk Assessment Monitoring System (PRAMS) survey reported a prevalence of 11 percent during the last three months of pregnancy in 2010.
- Smoking prevalence was highest in women aged 20 to 24 years (17.6 percent), were American Indians/Alaska Natives (26.0 percent), had <12 years of education (17.4 percent), and had Medicaid coverage during pregnancy or at delivery (17.6 percent).
- The use of biochemical markers, including exhaled carbon monoxide and urinary cotinine, has shown that pregnant women underreport both smoking status and the extent of smoking.

Effects of Smoking in Pregnancy

- Impaired fetal oxygen delivery is the best-studied cause of adverse outcome in pregnant women who smoke. Pathologic evaluations of the placentas of smokers have shown structural changes, including a reduction in the fraction of capillary volume and increased thickness of the villous membrane when compared to nonsmokers.
- Another problem is that carbon monoxide exposure from smoking causes the formation of carboxyhemoglobin, which also impairs fetal oxygen delivery.
- Smoking may also result in direct damage to fetal genetic material.
- Other possible mechanisms responsible for adverse fetal outcomes in mothers who smoke include direct toxicity of the more than 2500 substances found in cigarettes, such as ammonia, polycyclic aromatic hydrocarbons, hydrogen cyanide, vinyl chloride, nitrogen oxide, and carbon monoxide.
- Finally, exposure to nicotine results in sympathetic activation leading to acceleration of fetal heart rate and a reduction in fetal breathing movement.

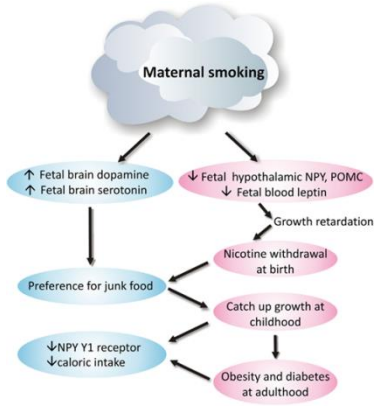

Figure 1. Neurophysiological mechanism of how maternal smoking programs metabolic disorders in offspring[1]

Adverse Outcomes in Pregnant Smokers

- **Reduction in birth weight.** The birth weight deficit associated with smoking is 100-300 grams, depending on the number of cigarettes smoked. Smoking in the third trimester appears to have the greatest impact. Women who smoke are 1.5 to 3.5 times more likely to have a LBW infant; risk increases with increasing cigarette consumption.
- **Stillbirth.** Studies have shown a relative risk ranging from 1.2 to 1.4 in smokers. A dose response curve has been reported, with heavy smokers having the greatest risk.
- **Preterm premature rupture of membranes (PPROM).** There is a consistent increase in risk of PPROM among smokers, with relative risks ranging from 1.9 to 4.2.
- **Placental abruption/placenta previa.** Cigarette smoking increases the risk of placental abruption, with reported adjusted relative risks of 1.4 to 2.5. Dose-response curve analysis has consistently revealed that the risk of abruption is greatest among heavy smokers. Cigarette smoking has also been consistently associated with placenta previa, with reported relative risks ranging from 1.4 to 4.4. A dose-response curve for this complication has not been consistently replicated.

General Principles of Managing Substance Use Disorders in Pregnancy

- Use Motivational Interviewing* to assess the member's readiness to change.
- Provide information when they are ready, to assist them in understanding the consequences of continued substance use during the pregnancy.
- Use medication assisted therapy where available for opiate addictions, not detoxification.
- For most substances there is a dose-response curve; even reductions in drug use have some benefit to the fetus.
- Alcohol is the substance with the most significant, lifelong consequences to the fetus.

* Please see Clinical Practice Guideline *Motivational Interviewing and Health Behavior Change : HS 1047.*

HEDIS AND STAR MEASURES

CMS has not published any measures for this topic. NCQA has published the following measures for this topic:

Follow-Up After Hospitalization for Mental Illness. Members who are hospitalized due to a mental health diagnosis should follow up with a mental health practitioner:

- 7-Day Follow-Up should include an outpatient visit, intensive outpatient visit or partial hospitalization with a mental health practitioner within 7 days after discharge.
- 30 Day Follow-Up should include an outpatient visit, intensive outpatient visit or partial hospitalization with a mental health practitioner within 30 days after discharge.

RELATED CLINICAL PRACTICE GUIDELINES

In addition to the information contained in this document, please reference the following CPGs: Behavioral Health Conditions in High Risk Pregnancy: HS 1040 and Substance Use Disorders : HS 1031.

REFERENCES

1. Reefhuis,J, Devine O, Friedman J, Louik,C, Honein M, Specific SSRIs and birth defects: Bayesian analysis to interpret new data in the context of previous reports, BMJ 2015; 350:h3190.
2. Pär H, Sjöblom V. The use of selective serotonin reuptake inhibitors during pregnancy and breast-feeding: a review and clinical aspects. 2005. Journal of Clinical Psychopharmacology; 25;1:59-73.
3. Chen H., Saad S, Sandow SL, Bertrand PP. Cigarette smoking and brain regulation of energy homeostasis. Front. Pharmacol., 25 July 2012 | doi: 10.3389/fphar.2012.00147.
4. Committee opinion no. 254: opioid abuse, dependence and addiction in pregnancy. American College of Obstetricians and Gynecologists Web site. http://www.acog.org. Published May 2013 (reaffirmed 2014). Accessed August 14, 2015.
5. Guidelines for the identification and management of substance use and substance use disorders in pregnancy. World Health Organization Web site. http://www.who.int/en/. Published 2014. Accessed August 14, 2015.

LEGAL DISCLAIMER

MEDICAL POLICY COMMITTEE HISTORY AND REVISIONS

Date	History and Revisions by the Medical Policy Committee
9/17/2015, 5/7/2015	• Approved by MPC. Added information on SSRIs.
2/5/2015	• Approved by MPC. New.