

Blending Addiction Science and Practice April 23, 2010

Identification of and Treatment for Prenatal Substance Use: From Research to Practice

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Objectives

- To describe screening techniques
- To provide rules of counseling
- To identify current information about specific substances and comorbid conditions
- To mention principles of treatment during pregnancy
- To counsel about newborn assessment and postpartum care

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Screening


Questions to Ask

- WHEN was the substance taken?
- HOW MUCH AND LONG was the substance taken?
- WHAT OTHER substances were taken?
- HOW REGULARLY was the substance taken (daily, binge)?

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Screening

Urine Screening



- History of substance abuse in this pregnancy
- Preterm labor (Not POOC)
- Placental abruption
- Behavior consistent with acute intoxication

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Screening

Drugs in Urine

Alcohol	< 12 hr	Amphetamines	< 48 hr
Opiates		Benzodiazepines	
Codeine	< 48 hr	Single use	< 72 hr
Morphine	< 48 hr	Chronic use	< 6 weeks
Heroin	< 96 hr		
Methadone	< 72 hr	Marijuana	
		Single use	< 72 hr
Cocaine	< 96 hr	Chronic use	< 30 days

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Screening

Screening Accuracy

Self reporting underestimates use: 48% of women with positive urine drug screens denied drug use on hospital admission
(Gillogley AJOG 1990)

Meconium positive in 88% of women admitting use compared to positive urine toxicology in 52%
(Ostrea Pediatrics 1992)

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Individual Susceptibility

- Placental transfer has been documented
- Preimplantation: from fertilization to implantation (abort)
- Embryo, from second through eighth week (anomalies)
- Fetus, from the ninth week until term (shorten gestation, restricted growth, behavior difficulties)

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Information Services

- Computerized databases online and on diskette (ex. Reproductive Toxicology)
- Briggs Drugs in Pregnancy and Lactation, 6th ed
- Poison control centers
- PubMed, Up To Date, DynaMed, Cochrane Library

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Sources of Evidence

- Case reports reporting rare events
- Cohort studies: Dose, duration, and route of administration; retrospective vs. prospective
- Drug exposure registries

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Limitations of Studies

- Confounding variables: Other substances (75%), disorders
- Experience with first trimester is often too limited
- Animal studies do not reliably predict human response
- Results of retrospective and uncontrolled studies can be misleading
- Often involve patient recall
- Usually positive results from cases or small series

Rules for Counseling

- An ultrasound is necessary to confirm dating and to screen for structural defects.
- Serum testing, CVS, amniocentesis, and fetal blood sampling do not assess drug effects.
- Large populations are required to determine the relative teratogenic risk

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Alcohol and Smoking

- Most commonly used alcohol (25%), smoking (22%)
- Paucity of women who report heavy use after pregnancy recognition

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Alcohol

- A clearly defined syndrome of defects has been noted only for regular users
- FAS may be as low as 4%, even among heavy drinkers

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Craniofacial Features of FAS

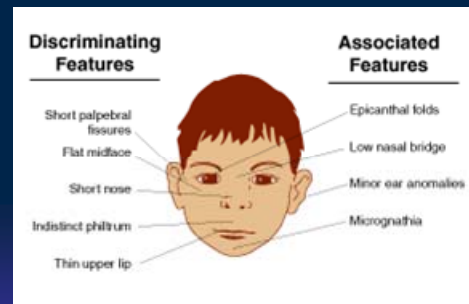


Illustration from Vol. 18, No. 1, 1994 *Alcohol Health & Research World*.¹⁴

Binge Drinking

- Difficult to define the risk
- Often before learning of the pregnancy in the first trimester
- Development: more social disinhibition
- Defects in numeric and language skills that persist into adolescence

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Beer Drinkers

- Focus on drinks per drinking occasion, not average drinks per day
- Birth weight reduction and a significant increase in anatomic abnormalities

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Cigarette Smoking

- Decreased levels of chorionic gonadotropin and increased rates of miscarriage
- Maternal smoking and placenta previa, placental abruption, and bleeding early or late in pregnancy

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Cigarette Smoking

Perinatal mortality has been shown to be higher:

- Reduced birth weight or gestational age
- Chronic reduction in placental blood flow
- Fetal hypoxia due to carbon monoxide
- An increase in cadmium levels

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Cigarette Smoking

Associations between maternal smoking:

- Craniosynostosis
- Facial clefting (1/183 vs. 1/500)
- Attention deficit hyperactivity disorder in children

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Cannabis

- Increasing appetite and controlling nausea
- No indication that a pattern of malformations results
- Might be associated with impaired fetal growth even when the possible effects of cigarette smoking were controlled
- Possible effects on complex behaviors such as “executive function”

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Cocaine

- No agreement on whether cocaine use increases the risk of structural malformations
- Increase in urinary tract anomalies and other vascular disruption-type abnormalities (?)
- Premature birth, placental abruption, IUGR, stillbirth
- SIDS, NEC, abnormal behavior

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Methamphetamine

- Rapid increase in use with pregnancy hospitalizations
- Recent multi-center study of pregnancy (IDEAL)
 - Methamphetamine used by 5.2%
 - Alcohol 22.8%
 - Tobacco 25%
- Began prenatal care later



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Amphetamines

- Case reports that associate exposures with various malformations
- Did not uncover a significant association with major or minor birth defects
- Insufficient to evaluate the effects of exposure on neurobehavioral abnormalities
- IDEAL Study : 3.5 (95% CI 1.7-7.4) increased risk of SGA with methamphetamine use in pregnancy

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Hydrocodone

- Structurally similar to codeine
- Interferes with embryo development in hamsters at very high doses
- No increase in congenital malformations

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Heroin

- A birth defect syndrome has not been described
- Diverse nature of the described defects makes definition of a single heroin syndrome difficult
- Premature delivery, premature rupture of the membranes, intrauterine fetal growth restriction, meconium stained amniotic fluid, and perinatal mortality
- A withdrawal syndrome

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Substance Use Disorders: Sex Differences and Psychiatric Comorbidities

- Women with substance use disorders present higher prevalence rates of psychiatric comorbidity than do men with the same diagnosis, making the psychiatric assessment a crucial step in evaluating for a substance use disorder
- Major depression is more often primary to the substance use disorder (with the opposite occurring in men); it is therefore less likely to improve with abstinence from psychoactive substances alone
- Women with primary depression or anxiety disorders should be taught to recognize early signs of recurrence. Vigorously treating a recurrence of depression can prevent full relapse of the substance use disorder

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FDA Prescription Drug Labeling and Demise of “the Letter”

- The long-standing pregnancy letter categories (A, B, C, D, X) will disappear
- They will be replaced by more clinically useful and up-to-date information on prescription drug use during pregnancy and lactation
- Risk Summary will describe data from clinical trials, good quality observational studies, pregnancy exposure registries, and case series reporting a rare event
- <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/Labeling/ucm093307.htm>

Obstet Gynecol 2009 27

Drug Exposure during Pregnancy and Short-Term Maternal Outcomes

	<u>Odd ratios</u>
Syphilis	6.7
Gonorrhea	1.9
HIV	8.2
Hepatitis	4.8
Psychiatric, nervous, emotional disorders	4.0
Abruptio placenta	2.3

NICHD Neonatal Research Network, AJOG 2002 28

Psychosocial Treatments

- Motivational interviewing
- Cognitive behavioral approaches
- 12-step approaches
- Community/social network approaches
- Contingency management

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Psychological and/or Educational Interventions for Reducing Alcohol Consumption in Pregnant Women and Women Planning Pregnancy

- Results were not consistent
- The paucity of studies, the number of total participants, the high risk of bias of some of the studies, and the complexity of interventions limit our ability to determine the type of intervention

Cochrane Review 2009 30

Psychosocial Interventions for Pregnant Women in Outpatient Illicit Drug Treatment Programs

- Psychosocial interventions may help overcome barriers to a treatment program and reduce illicit drug use
- Contingency management uses positive, supportive reinforcement (for example, monetary vouchers or giving work and a salary only when abstaining from drug use or attending treatment to change behavior)
- Insufficient evidence to support motivational interviewing

Cochrane Review 2007 31

Medications: Mechanisms of Action

- Replacement – methadone, buprenorphine, slow morphine (opiate)
- Direct blockade – naloxone, naltrexone (opiod)
- Indirect blockade – naltrexone (alcohol, cocaine), vaccine (cocaine)
- Aversion – disulfiram (alcohol)
- Reduction of craving – nicotine patches, naltrexone?, acamprosate?, amantadine?
- Treatment of psychiatric disorder – SSRIs, thorazine

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Appropriateness of Randomized Control Trials?

- The population of pregnant women who participate in RCTs for drug and alcohol treatment is not representative of women who continue to use drugs and alcohol in pregnancy
- Quality cohort studies with appropriate unexposed controls to assess potential confounders such as continued maternal alcohol use and socioeconomic variables would be more appropriate and cost effective

Cochrane Review 2009 33

Outcomes of Smoking Interventions

- Smoking cessation by late pregnancy
 - 34 studies (n=9945)
 - OR = 0.53 (95% CI 0.47-0.60)
- Low birthweight (<2500 gms)
 - 8 studies (n=6854)
 - OR= 0.80 (95% CI 0.67-0.95)
- Preterm birth (<36 or 37 wks)
 - 6 studies (n=8798)
 - OR=0.83 (95%CI 0.69-0.99)

Cochrane Review 2008 34

Nicotine Replacement Therapy in Pregnancy

- Consider in women smoking 20 cigarettes or more per day who have failed behavioral intervention
- Nicotine metabolism increased in pregnancy
- Patch allows avoidance of other components in tobacco smoke

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Nicotine Replacement Therapy in Pregnancy

- Increased metabolism in pregnancy requires use of higher dose patch (e.g. use 21 mg rather than 15 mg patch)
- 16 hr rather than 24 hr patch recommended to reduce fetal exposure
- Not proven of benefit in pregnant women

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Pharmacologic Interventions for Pregnant Women Enrolled in Alcohol Treatment

- Medicines are given to assist with alcohol treatment by lessening the effects during detoxification
 - These include benzodiazepines, phenothiazines and chlormethiazone, used to reduce anxiety and insomnia
 - Antidepressants may also be given after withdrawal
- Disulfiram, naltrexone and acamprosate are used in more severe cases to decrease cravings for alcohol and maintain abstinence
- Given the stigma attached to alcohol use in pregnancy, recruitment for outcomes trials is likely to remain difficult

Cochrane Review 2009 37

Methadone Use in Pregnancy

- Goal is: replacement dose to remove cravings
- Part of comprehensive program with prenatal care, counseling, urine drug monitoring
- Recommendations are towards higher doses and not weaning off during pregnancy
- Most UNM patients on 80-120 mg per day

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Methadone

- The probability of a reactive NST is less when the test is performed 1 to 2 h after a maintenance dose of methadone
- Prematurity, low birth weight, microcephaly, arrhythmias, withdrawal syndrome
- Effects on neurobehavioral development are complicated by environmental and genetic factors

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Buprenorphine in Pregnancy

- Useful where methadone maintenance programs are unavailable
- Patient must be in mild to moderate withdrawal
- Declines methadone and signs consent
- Less neonatal abstinence syndrome

Addiction 2003 40

Bupropion in Pregnancy

- Not proven effective in pregnancy
- Registry advisory: 668 cases is "of insufficient size to reliably compute a birth defect risk"
- Bupropion increases seizure risk at higher doses particularly in women with eating disorders
- Stop if severe nausea/vomiting or preeclampsia

Benowitz 2004 41

Buprenorphine Induction

- May be dispensed by primary care physicians after 8 hour course
(<http://www.aaap.org/buprenorphine/buprenorphine.html#WEB-BASED>)
- Subutex (buprenorphine alone) NOT suboxone (buprenorphine with naloxone)
- Observed in clinic for 3-4 hours
- Prescribe no more than weekly at first (may be up to 2-4 week supply eventually)

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Buprenorphine vs. Methadone Treatment of Opiate Dependence during Pregnancy


	Buprenorphine	Methadone	p
Birth weight (g)	3250 ± 528	2941 ± 483	0.008
Infants with birth weight < 2500 g; (%)	3 (6.4)	9 (25)	0.03
Infants with any NAS; (%)	19 (40.4)	28 (77.8)	0.0008
Infants treated for NAS; (%)	7 (14.9)	19 (52.8)	0.0004
Total hospital stay (days)	9.4 ± 8.4	19.7 ± 18.8	0.0009

Kakko, 2008 ⁴³

- ### Methadone/Buprenorphine and Labor
- Continue in labor
 - Analgesia possible with epidural or higher dose parenteral narcotics in labor
 - Spinal for cesarean with post-op need for morphine PCA or higher dose oral narcotics
 - May breastfeed
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- ### Crack Babies Revisited: Neonatal Effects of Prenatal Cocaine Exposure
- Crack babies hysteria of 1980s lacked a scientific basis and had negative effects:
- Massive increase in the rates of incarceration for poor women of color
 - Difficulty placing infants in adoptive and foster homes
 - Dominance of criminal rather than public health approach to maternal substance abuse
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- ### Withdrawal in Newborn
- Irritability, tremors, seizures
 - Fever
 - High-pitched cry
 - Abnormal muscle tone (hypo-, hypertonia)
 - Poor feeding
 - Vomiting, diarrhea
 - Impaired temperature maintenance
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- ### Neonatal Abstinence Syndrome
- Most babies exposed to methadone
 - Mandatory 72 hour observation
 - Usually develops within 72 hours
 - 24 hrs: 42%
 - 48 hrs: 73%
 - 72 hrs: 87%
- 
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- ### Newborn Urine Screening
- 
- Substance abuse in this pregnancy
 - Preterm labor (not premature contractions)
 - Placental abruption, bleeding
 - Unexplained neonatal depression, seizures, jitteriness
 - Possible abstinence syndrome
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Meconium Drug Testing

- Meconium tests more sensitive
 - Identifies use from 28 weeks gestation until delivery
 - Costs about \$150 per test
 - Costs decreasing
 - Results in 14 to 21 days
 - Low impact on decision making
- Negative aspect: less specific
 - Positive even if mother started drug treatment
 - Positive if mother stopped using



Meconium in diaper

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Drugs and Breastfeeding

- Nearly all drugs are excreted in breast milk (often less than 5% of weight-adjusted maternal daily dose)
- The World Health Organization and Am Acad Peds recommend no breastfeeding
- Contraindications are either theoretical or founded by case reports

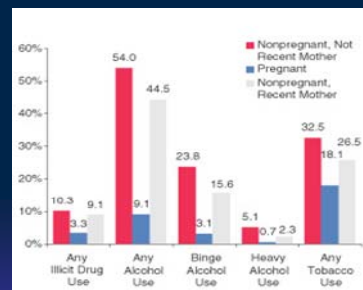
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Breastfeeding and Methadone

- Recommend prenatal breastfeeding consultation
- Must be HIV negative
- No active polysubstance abuse
- Hepatitis C okay if no bleeding from nipples
- Enrolled in monitored program
- Plan to monitor infant if rapid wean occurs

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Postpartum Resumption



Percentages of Women Aged 15 to 44 Reporting Past Month Substance Use, by Pregnancy and Recent Motherhood Status**
Source: SAMHSA 2002 NSDUH

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Contraception and Substance Abuse

- Contraception is primary prevention of the problems of drug-exposed pregnancy
- Treatment programs increase contraception (from 5% to 61% by 12 months)
- IUD: Assess STD risk. Cocaine and opioid use associated with prostitution and "sex for drugs"
- OCPs/Patch/Implanon: Assess liver function if alcohol abuse or hepatitis

Floyd, AJOG 2008 53

Home Visits during Pregnancy and After Birth for Women with an Alcohol or Drug Problem

- There is sufficient evidence to recommend the routine prenatal use of home visits for women with a drug or alcohol problem
- Visits after birth increased the engagement of these women in drug treatment but data are insufficient to say if improved the health of baby or mother.

Cochrane Review 2005 54