Pregnancy and Substance Use Disorders

Edward A. Jouney, DO
Clinical Instructor
University of Michigan
Department of Psychiatry

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Addiction Definition

- A primary, chronic disease of brain reward, motivation, memory and related circuitry.
- Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations.
- This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors.

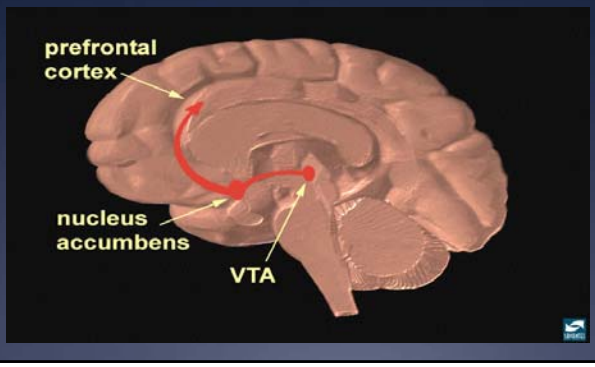
Addiction Definition (cont'd)

- Addiction is characterized by:
  - inability to consistently abstain from drug use
  - impairment in behavioral control
  - craving,
  - diminished recognition of significant problems with one's behaviors and interpersonal relationships
  - a dysfunctional emotional response
- Like other chronic diseases, addiction often involves cycles of relapse and remission.
- Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death.

Addiction Definition

- The 4 "C's"
  - Loss of **C**ontrol
  - **C**ompulsive use
  - Use despite **C**onsequences
  - **C**ravings

What Happening in the Brain?



Drugs of abuse act on:

Amphetamine and **cocaine** elevate DA in NAS

Nicotine acts on cholinergic receptors at cell bodies and terminals of mesolimbic system, increasing DA in NAS

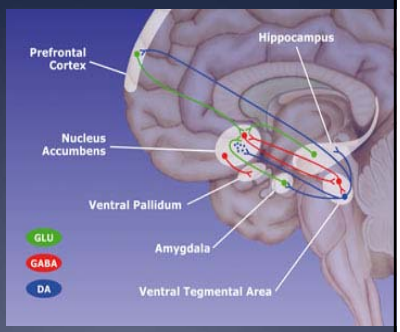
PCP blocks NMDA (GLU) increasing DA in NAS.

Opiates inhibit the GABAergic cells that normally inhibit the mesolimbic system Increasing dopamine in NAS

Barbiturates and **benzos** do the same at some GABAergic level

Ethanol and **marijuana** end with the same results in NAS through unknown mechanisms

Caffeine doesn't involve the same circuit.



Definitions

- DSM IV terminology
  - Addiction = Dependence
  - Do not confuse this definition of "dependence" with "physical dependence"
- DSM-V terminology
  - Addiction = Substance Use Disorder
- NOTE: The word "Addiction" is not used.

Substance Use Disorder

- Is simply another way of saying "addiction."
- Criteria are universal for ALL substances. (ex. Nicotine Use Disorder has the same diagnostic criteria as Cocaine Use Disorder).
  - The behavioral phenotypes of addiction are very similar, regardless of class of drug is being used.
  - Example: Behaviors associated with opiate addiction mirror those of cocaine addiction.
    - This indicates a central and common disease process or pathway.

Substance Use Disorder

- A maladaptive pattern of substance use leading to clinically significant impairment or distress, as manifested by 2 (or more) of the following, occurring within a 12-month period:
- 1. Recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home.
- 2. Recurrent substance use in situations in which it is physically hazardous.
- 3. Continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance.

Substance Use Disorder (cont'd)

- 4. Tolerance
- 5. Withdrawal
- 6. The substance is often taken in larger amounts or over a longer period than was intended.
- 7. There is a persistent desire or unsuccessful efforts to cut down or control substance use.
- 8. A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects.

Substance Use Disorder (cont'd)

- 9. Important social, occupational, or recreational activities are given up or reduced because of substance use.
- 10. The substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
- 11. Craving or a strong desire or urge to use a specific substance.

Substance Use Disorder (cont'd)

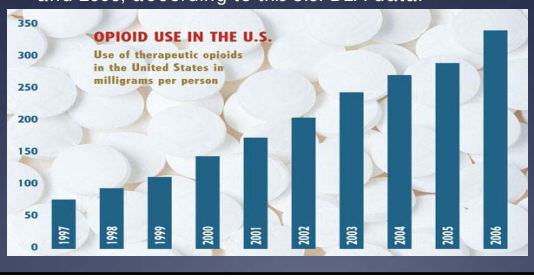
- Severity specifiers:
  - Mild: 2-3
  - Moderate: 4-5 criteria positive
  - Severe: 6 or more criteria positive
- Specify if:
  - With Physiological Dependence: evidence of tolerance or withdrawal (i.e., either Item 4 or 5 is present)
  - Without Physiological Dependence: no evidence of tolerance or withdrawal (i.e., neither Item 4 nor 5 is present)

What Drugs Can Cause Addiction?

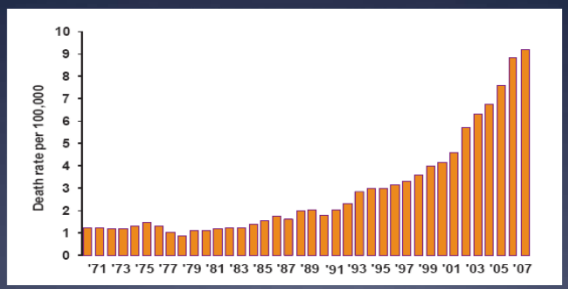
- Only certain drugs are addictive, and are able to stimulate the addiction circuitry.
  - Opiates/opioids
  - Cannabinoids (marijuana)
  - Psycho-stimulants (Adderall, cocaine)
  - Sedative/hypnotics (Benzodiazepines)
  - Nicotine
  - Alcohol
- Relative very few chemical compounds can stimulate the addiction circuitry, in comparison to all the drugs know.

Trends in Opiate Prescribing

- The use of therapeutic opioids-natural opiates and synthetic versions-increased 347% between 1997 and 2006, according to this U.S. DEA data.



Rate of Unintentional Drug Overdose Deaths in US 1970 - 2007



Patient Interpretation of the Problem

- They will minimize or deny the problem.
  - This is a SYMPTOM of the disease, and is to be expected.
  - Patients will "protect" their relationship with the drug, and will block any intervention that attempts to interfere with their drug use.
  - Addiction causes patients to undergo a **personality metamorphosis.**
  - They begin to manipulate, lie, and even steal, in order to satiate their drug craving.

Patient Assessment: What to look for

- Social cues:
  - Lying
  - Stealing
  - Manipulative behaviors
  - Various complaints from family members
  - Relationship turmoil/breakup
  - Family reports large amounts of money missing.
  - Decreased work performance or job termination.
    - If patient has lost their job, always ask: "What happened?" May help you identify a problem.

Patient Assessment

Be empathetic, non-judgmental, and open ended.

Shoe you care

- "How do those around you feel about your drug use?"
- You appear to be struggling to me. What do you think?"
- "It seems like your making some bad choices. What do you think is going on?"
- You don't seem like the type of person who will put others at risk when you drive. What do you think is going on?" (when questioning a patient about a DUI).

Challenges in treating addictive disease in pregnancy

- Negative social stigma is amplified.
- Perceived threat of protective services.
- Patients attempt to "hide" drug use, and fear disclosure.
  - Makes history taking more challenging.

Substance Use in Pregnancy

- Increased risk of associated infectious diseases, including syphilis, gonorrhea, hepatitis, and HIV
- Increased incidence of psychiatric disorders
- Increased incidence of placental abruption
- Hospitalizations for violence found more commonly in women abusing cocaine

Bauer CR, et al.The Maternal Lifestyle Study: drug exposure during pregnancy and short term maternal outcomes. American Journal of Obstetrics and Gynecology. 2002 Mar; 186(3):487-95.

Risk factors

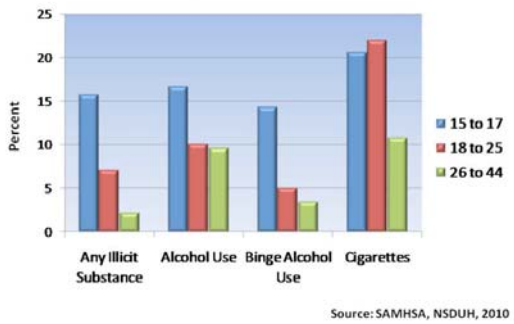
- Sexual abuse
  - increases likelihood of drug addiction 6x
  - 4X the likelihood of alcohol dependence (in female twin studies).
- Major depression
- Positive family history of addictive disease
- Positive history of past use alcohol or other drugs, including tobacco
- Positive history of domestic abuse
- Homelessness, inadequate social support

(Kendler, et al (2000), Prescott, et al (2000)

OB “Red Flags”

- Late prenatal care
- Multiple missed visits
- Impaired work or school performance
- Past OB history of unexplained miscarriage, IUGR, pre-term labor, abruptions, fetal demise
- Neurodevelopmental delay or behavioral problems in children of the patient.

Current Substance Use Among Pregnant Women
Aged 15-44, by Age, 2008-2009 Combined



Source: SAMHSA, NSDUH, 2010

Substance Abuse During Pregnancy

- Substance use is highest in the first trimester.
- The most common form of substance use in pregnancy is smoking among white women.
- Because tobacco, alcohol and drug use in pregnancy occurs across all demographic groups, providers should screen all women.

(SAMHSA, 2005)

Tobacco Use and Pregnancy

Tobacco Use and Pregnancy

- 2 – 4 X increased risk of SIDS
  - Smoking also increases risk of preterm birth & low birth weight, which are independent risk factors for SIDS
- 4 X increased risk of type 2 diabetes with maternal smoking (>10 cig/day)
- Increased risk of vaginal bleeding (placental abruption and placenta previa) and premature delivery
- Inconsistent results from studies on cognitive ability

Sielski, LA. Infants of mothers with substance abuse. UpToDate.com. 2008.

Smoking Cessation

- Advise women to quit smoking
- Advise woman to avoid exposure to second-hand smoke – family/friends should not smoke around pregnant woman or infant, do not allow smoking in home or vehicle
- Educate about effects of smoking in pregnancy
- Offer Nicotine Replacement Therapy (NRT)

Marijuana

- No studies have established safe limits in pregnancy
- No significant neonatal effects
- Heavy users may be at risk for preterm delivery
- Possible neurobehavioural effects in neonate (increased jitteriness, increased tremors)
- Possible long-term effects on school performance among children exposed in utero

Witter, et al. Am J Perinatol. 1990;7(1):36.
Fergusson, et al. BJOG. 2002 Jan;109(1):21-7.

Safe Limits For Alcohol Use

- No clear relationship between amount of prenatal alcohol consumed and the extent of damage in the infant
- There is **NO** safe timing for alcohol use during pregnancy
- There is **NO** confirmed safe limit for alcohol use in pregnancy

Therefore, NO alcohol is the safest choice!

Risks of Prenatal Alcohol Use

- Alcohol crosses the placenta, and the fetus has a limited ability to metabolize
- Alcohol is a known teratogen → can damage developing fetal cells, umbilical cord & placenta
- Prenatal exposure to alcohol results in:

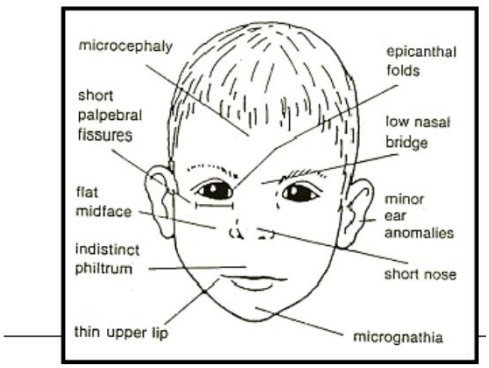
1. Increased risk of spontaneous abortion and stillbirth
2. Increased risk of FASD and FAS, alcohol-related birth defects and alcohol-related neurodevelopmental disorders

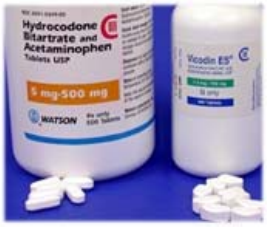
Koren, et al. Fetal alcohol spectrum disorder. CMAJ 2003; 169 (11): 1181-1185.

Fetal Alcohol Spectrum Disorders and Fetal Alcohol Syndrome

- FASD's (0.6 – 4.5% of live births): not a clinical Dx, can include physical, mental, behavioral, and/or learning disabilities with possible lifelong implications.
- FAS (0.2 – 1.5% of live births): most severe, abnormal facial features, growth deficiencies, vision, hearing, attention or memory problems.

Case Presentation: FAS





Opioid Addiction And Pregnancy

- ~7000 infants/year born to opiate using mothers in the US
- ~4.4 % of all pregnant women in the US have misused prescription pain relievers

Management of Maternal Opioid Intoxication

- Supportive only
- NO NARCAN!
- *"Naloxone should not be given to a pregnant woman except as a last resort for severe opioid overdose, because withdrawal precipitated by an opioid antagonist can result in spontaneous abortion, premature labor, or stillbirth."* (Weaver, ASAM 3rd ed, p. 1239)
- Intubation is preferable to naloxone

Case Presentation

- 22 year old G3P2 presents at 18 weeks for first prenatal visit
  - She currently admits taking 6-8 Vicodin tablets per day
    - first prescribed for migraine headaches
    - also prescribed for chronic back pain (herniated disk on MRI)
    - Asking for prescription from you. Primary physician won't prescribe now that she is pregnant.

Case Presentation, Continued

- Review of MAPS reveals multiple ED and offices visits to different prescribers across southeast Michigan and northern Ohio
  - >1000 prescribed oxycodone or hydrocodone doses over the past 4 months!

What Is The Best Course of Action?

1. Refuse to prescribe – detox patient
2. Refer to pain/addiction specialist
3. Refer to methadone clinic
4. Offer buprenorphine (suboxone/subutex)
5. Prescribe methadone
6. Prescribe vicodin on narcotic contract

Opioid Detox During Pregnancy?

- Avoid detox during pregnancy.
- Anecdotal evidence for:
  - Increased fetal loss during 1st trimester
  - Increased fetal distress during 3rd trimester
- May lead to a relapse, due to their inability to remain abstinent

Pagliaro et al, Prin Addiction Med, p 1252

Opioid Withdrawal in Pregnancy

*yawning, restlessness, craving → sweating, chills, mydriasis, rhinorrhea, low grade fever, pallor, nausea, vomiting, diarrhea + myalgia/arthralgias, insomnia.

*Duration depends on half-life of the drug

*Treatment: provide an opiate taper (morphine, methadone, buprenorphine)

most addicts using "street" heroin will not need >40mg methadone to restore equilibrium

Standard of Practice

- Methadone is currently the standard of care in the United States for the treatment of heroin addiction in pregnant women.
- If such specialized services are refused by a patient or are unavailable in the community, maintenance treatment with the buprenorphine may be considered as an alternative.

SAMHSA TIP 40
NIDA – NIH Monograph 149. Printed 1995

Methadone

- Advantages
  - **FDA approved in pregnancy**
  - **No proven adverse fetal effects**
  - **Established network of providers**
  - **Safe in breast feeding**
  - **Fewer positive drug screens? (Jones et al Addiction 2006 Feb; 101(2): 275-81)**
  - **Less legal liability to provider**
  - **Once daily dosing, long T1/2, (mean) 22hrs**

How Much Methadone???

- Dashe et al: Higher methadone dose predicted longer duration of neonatal withdrawal, higher abstinence score and prolonged treatment. (OB Gyn 2002 Dec; 100 (6): 1244-9).
- Berghella et al: Mothers on doses <80 mg had more illicit drug use. Neonatal abstinence score, duration were similar. (AJOG 2003 Aug; 189(2); 312-7).
- Ostrea 1975: Goal is less than 20 mg methadone qd to avoid NAS! (Addict Dis. 1975; 2(1-2): 187-99.)

Buprenorphine

- partial mu opioid agonist
- potent in non-tolerant patient (~30X > morphine)
- very high binding affinity
- T1/2 (mean) 37hrs

Buprenorphine vs. Methadone

advantages

- Don't have to go to methadone clinic
- Less stigma
- Less sedating, Higher therapeutic index
- Less addictive potential ?
- Harder to abuse

disadvantages

- expensive, $ 5-8/tab (vs. $ 0.10/day for methadone
- Medicaid payment stops post partum (6 mos. or so), relapse likely at this point
- with acute pain, (behaves as partial antagonist at μ opioid receptor)

Buprenorphine versus methadone (MOTHER Study)

- Advantages of buprenorphine
  - Shorter neonatal length of stay for NAS
  - Lower required morphine dose for NAS
- Advantages of methadone
  - Higher treatment retention
  - Greater patient satisfaction with Rx

Jones H.E. et al. Neonatal Abstinence Syndrome after Methadone or Buprenorphine Exposure. NEJM. 2010;363:2320-31.

Buprenorphine in Pregnancy

- Well tolerated by neonates (Fischer 2000)
- "Not inferior" to methadone in maternal and neonatal safety (Jones 2005b)
- Withdrawal symptoms may resolve more quickly with buprenorphine in non-pregnant patients (Gowing 2004)
- Overall safety profile is superior (Soyka 2006)

Cocaine

- Presynaptic DA release = euphoria, decreased. seizure threshold
- In periphery is a local anesthetic, vasomotor stimulant, vasoconstrictor
- Terotogenicity unclear
- Adverse pregnancy outcome very clear
- Crack cocaine most commonly encountered
- Placental abruption secondary to hypertensive response + vasoconstriction

Methamphetamine

- Presynaptic DA release, postsynaptic DA re-uptake blockade
- See cocaine-like effects but much longer lasting
- Rapid placental transfer, see maternal/fetal hypertensive response, dec. fetal O2 sat, inc. umbilical vasc. resistance and dec. uterine blood flow
- Usually smoked, can be “snorted”, injected IV

Management of Stimulant Intoxication During Pregnancy

- Alpha adrenergic blockers for HTN (phentolamine)
- IV NTG. (NO IV nitroprusside→cyanide→ inc. concentration in fetus)
- NO BETA BLOCKERS,NO LABETOLOL! (often “DOC” in L and D) (ASAM 3rd ed)
- Benzos for CNS/CV toxicity
- Evaluate with EKG, watch for rhabdomyolysis

Management of Stimulant Withdrawal in Pregnancy

- Little physical danger during withdrawal
- Pt. shows lethargy, hypersomnia, increased appetite
- Dysphoria and craving may lead to leaving AMA, immediate relapse
- Attempt to engage patient before they leave the floor!

"Crack Baby", Prenatal Complications of Cocaine

- Placental ischemia (i.e., limb reduction defects)
- Placental abruption – most frequent complication
- IUFD
- IUGR
- Fetal distress

"Crack Baby", Postnatal Effects

"Among children 6 years or younger, there is no convincing evidence that prenatal cocaine exposure is associated with developmental toxic effects that are different in severity, scope, or kind from the sequelae of multiple other risk factors."

Frank et al, JAMA 2001 285 (12):1613-1625.

Is There Recovery After Delivery?

- Pregnancy is a “window of opportunity” in addiction treatment
- Patients may be faced with loss of custody of children.
- If they do not succeed, mothers prognosis is felt to be “hopeless”

Thank you!

- Edward Jouney, DO
- ejouney@med.umich.edu