Uncertain Legacy…

Intrauterine Substance Exposure
Impact on Infants and Young Children

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Objectives

- Identify two neonatal complications seen with maternal methamphetamine use.
- Describe the risk of the “meth” environment on infants & children.
- Discuss assessment tools for the mother at risk for intra-uterine substance use.
- Discuss the follow-up needs of the infant with intra-uterine substance exposure.

Disclosure Statement

- Financial Arrangements
  - I am currently on the speakers bureau and receive financial reimbursement from
    - Prolacta Bioscience
    - Abbott Nutrition
- Images & Photographs come from publicly accessed sources
- I will make no “off-label” recommendation of a drug during this presentation
- I am a really fun person

Concepts To Remember

- Denial runs deep!
- Users are not the best of historians!
- Polydrug usage and effects!
- The stuff doesn’t come from Walgreens!
- It’s an addiction!
- Criminal activity vs. public health issue!
- Usage patterns & substances may change over time and by location!

Concepts to Remember

"Globally, drug use is not distributed evenly and is not simply related to drug policy, since countries with stringent user-level illegal drug policies did not have lower levels of use than countries with liberal ones."

Louisa Degenhardt, et al

University of New South Wales, Australia
PLoS Medicine, 2008

Concepts to Remember

"The use of drugs seems to be a feature of more affluent countries. The U.S., which has been driving much of the world's drug research and drug policy agenda, stands out with higher levels of use of alcohol, cocaine, and cannabis, despite punitive illegal drug policies, as well as (in many U.S. states), a higher minimum legal alcohol drinking age than many comparable developed countries."

Louisa Degenhardt, et al

University of New South Wales, Australia
PLoS Medicine, 2008

Evolving Issue of Substance Abuse

1990's	2000	2008
Cocaine	Methamphetamine	Cannabis
Club drugs	Designer drugs	Cocaine
Heroin	Prescription drugs	Methamphetamine
Alcohol	Alcohol	Alcohol
Tobacco	Tobacco	Tobacco

“Designer” or Synthetic Drugs

- “Designer” or “Synthetic” Drugs
  - Relatively new in widespread usage
  - Used by a younger population
  - Used in a “social” or “group” setting
  - Extreme variation in composition, dosage
  - ? Of greater morbidity to user
  - ? Known about long term effects on the fetus, infant and young child

Methamphetamine

- Methamphetamine
  - "Meth, Speed, Ice, Crystal, Crank, Chalk, Tina, Zip, Cristy"
  - Odorless, white, bitter powder
  - "Crystal Meth" – large, chunky, crystals
  - Highly addictive, psychostimulant
  - Snorted, smoked, injected, taken orally & rectally

Methamphetamine

- 12 Million Americans have used it
- Americans spent $5.4 billion on it in 2000
- 6.7% of high school seniors had tried it
- A $5.00 hit last ~ 12 hrs
- Most prevalent synthetic drug used in US
- “Meth” epidemic declared – July 2005

Methamphetamine

- 5.3% of 10th graders – lifetime use
- Adult male arrests + for meth
  - Honolulu 40.3%; Phoenix 38.3%
  - San Diego 36.2%; Los Angeles 28.7%
- Substance abuse treatment admissions
  - Honolulu 59%; San Diego 51%
  - Atlanta 10.6%; Minneapolis/St. Paul 18.7%

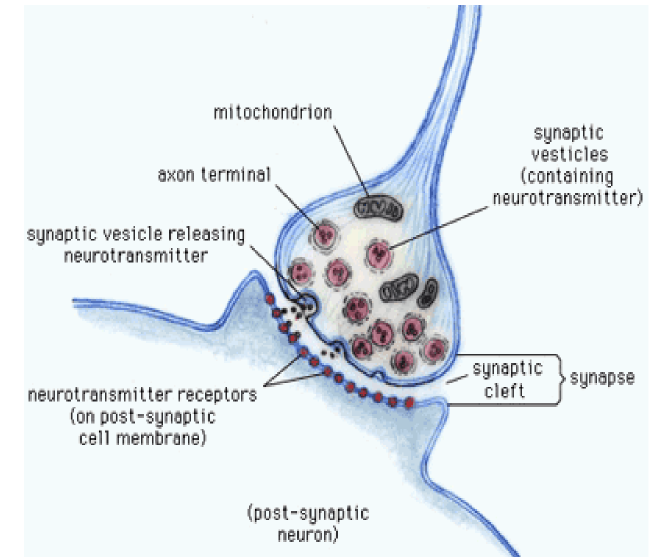
NIDA

Metamphetamine

- Stimulant → effects sympathetic system
- Releases ↑ levels of dopamine
- ↑ HR, BP, hyperthermia
- Wakefulness, activity, euphoria
- Produces extra energy, stamina
- Causes extreme anorexia

Methamphetamine

- Has toxic effect on nerve terminals
  - Both dopamine & serotonin containing neurons
  - Terminals are “pruned back”
  - Re-growth of terminals is limited
  - May activate apoptotic changes
- Long term use → “Parkinson-like” effects



Methamphetamine

- Health Issues
  - Nutrition
  - Lack of prenatal care
  - Poor dental health
  - Skin burns & sores
  - Facial sores & picking
  - STD's

Drug Related ED Visits

Total Number of Drug-Related ED Visits	1,997,993
Methamphetamine related ED Visits	**73,400**
Disposition of methamphetamine related visits	
Treatment	**(20,792)**
Referred to detox/treatment	6,452
ICU/critical care	3,796
Other inpatient unit care	5,471
Transferred	5,073
No treatment	**(43,071)**
Discharged home	36,576
Released to police/jail	3,848
Left against medical advice	1,144
Other/unknown	1,503

Fetal Effects of Methamphetamine

- Maternal Effects
  - 4 fold ↑ usage in pregnant women
  - Placental vasoconstriction
  - ↑ Premature delivery & abruptio placenta
  - Maternal malnutrition, binges
  - Associated use of other substances
  - Limited PNC
  - ↑ Incidence of STD's
  - Risk of toxic "meth environment"

Methamphetamine

- Cocaine
  – Plant derived
  – Smoking produces a high that lasts 20-30 minutes
  – 50% of the drug is removed from the body in 1 hour
- Methamphetamine
  – Man-made
  – Smoking produces a high that lasts 8-24 hrs
  – 50% of drug removed from the body in 12 hours

Neonatal Abstinence

- NAS – a constellation of behavioral and physiologic signs and symptoms that are remarkably similar despite marked differences in the properties of the causative agents

Neonatal Abstinence

- Two Etiologies for NAS
  - NAS due to prenatal exposure from maternal use of substances that result in withdrawal symptoms
  - NAS due to discontinuation of medications such as fentanyl or morphine used in pain therapy

Neonatal Abstinence

- Drugs frequently associated with NAS

Codeine	Heroin
Demerol	Morphine
Cocaine	Diazepam
SSRI's	Barbituates
Caffeine	Marijuana
Nicotine	Methadone

Neonatal Abstinence

- Multi-system Disorder
  - CNS, GI, autonomic, & respiratory system
  - Manifestations dependent on
    - Drug used
    - Dose used
    - Frequency of use
    - Infant's metabolism & excretion
    - Timing of last intra-uterine exposure
    - Drug's half-life

Neonatal Abstinence

- CNS dysfunction
  - High-pitched cry
  - Restlessness with ↓ sleep duration
  - Hyperactive reflexes
  - Jitteriness, tremors
  - Hypertonia
  - Myoclonic jerks
  - Seizures

Neonatal Abstinence

- Metabolic, Vasomotor & Respiratory
  - Sweating
  - Fever
  - Sneezing (> 3 times per interval)
  - Frequent yawning
  - Nasal flaring
  - Tachypnea
  - Apnea
  - Mottling

Neonatal Abstinence

- GI Dysfunction
  - Excessive (frantic) sucking or rooting
  - Poor feeding performance
  - Hyperphagia with poor weight gain
  - Regurgitation and vomiting
  - Loose or watery stools

Neonatal Abstinence

- Opiates
  - Produce most dramatic effects
  - Additional signs →LBW, prematurity, IUGR
- Heroin
  - Short half-life; symptoms within 24 hours
  - Some delayed effects → first week of life
- Benzodiazepines/Barbituates
  - Very long half-life
  - Withdrawal may not start until after d/c

Neonatal Abstinence

- Methadone
  - Half-life longer than 24 hours
  - ↑ risk of symptoms if maternal dose > 20 mg/d)
  - Symptoms can appear after first weeks of life
  - ↑ Risk of fetal demise, impaired growth, SIDS
- Cocaine/Amphetamines
  - Stimulants with potent vasoconstrictor effects
  - Hyperactive Moro reflex, jitteriness, excessive sucking & activity, sleep interruption
  - ? Limits head growth, disrupts brain development

Neonatal Abstinence

- Nicotine
  - Crosses placenta & may reach concentrations 15% higher than maternal levels
  - Impairs habituation, orientation, autonomic regulation, orientation to sound
  - Exposure affects infant's ability to be comforted; associated with exaggerated Moro reflex, tremors
  - Risk of IUGR, SIDS, nicotine toxicity

Neonatal Abstinence

- Marijuana
  - No neonatal withdrawal problems associated with maternal use of marijuana
  - Fetal exposure associated with IUGR, hypoglycemia, hypocalcemia, sepsis, ICH
  - Associated signs of nicotine toxicity
  - Cognitive effects may persist to school age
- Caffeine
  - Accumulates in blood of breastfed infants
  - New concerns with “energy drinks” (rage)

Neonatal Abstinence

- SSRI's
  - Exposure during last trimester may exhibit neonatal adaptation syndrome
  - Irritability, agitation, tremors, ↑ respiratory rate, nasal congestion, emesis, diarrhea
  - Manifestations are self-limiting & usually disappear by 2 weeks of age
  - Symptoms more common with fluoxetine Prosac), paroxetine (Paxil)

Lab Analysis for Drug Exposure

- Urine Toxicology
  - Easy to obtain, minimum preparation, analyzed using available techniques, lower cost
  - Detection depends on variables such as drug metabolism, hydration status, route and frequency of ingestion
  - Metabolites may be detectable for only a short time

Urine Drug Screening

Amphetamines	48 hours
Alcohol	12 hours
Barbiturates	10 to 30 days
Valium (Diazepam)	4 to 5 days
Cocaine	24 to 72 hours
Heroin (as Morphine)	24 hours
Marijuana	3 to 30 days
Methaqualone (Quaaludes)	4 to 24 days
Phencyclidine (PCP)	3 to 10 days
Methadone	3 days (depending on dose)

Lab Analysis for Drug Exposure

- Meconium
  - Best method for detecting exposure during pregnancy
  - Provides a wider window of detection (2nd trimester)
- Hair
  - Technique is expensive, not widely available
  - Limited by procedures for quantification
  - Recent exposure may not be detected
  - Maternal hair reveals drug pattern of previous 3 months
  - Metabolites detected in infant hair for 2-3 months after birth

Management of NAS

- Supportive Care
  - Serial surveillance
  - Modify environment
    - Decrease light, noise
    - Decrease unnecessary handling, activity
  - Frequent small feedings (↑ caloric density)
  - Swaddling, pacifiers, oscillating cribs

Management of NAS

- Pharmacologic (Anti-epileptics)
  - Long half-life
  - Can be orally administered
  - Lack of effect on GI symptoms
- Phenobarbital
  - Contain 14-25% alcohol
  - Phenobarbital 5-10 mg/kg PO/IV/IM loading
  - Maintenance: 3-4 mg/kg/d PO qd
  - Increase by 10% when NAS score consistently > 8
  - Wean by decreasing dose by 20% qod

Management of NAS

- Pharmacologic (Opiates)
  - CNS depressants, mild sedatives
  - Oral administration,
- Methadone
  - Long-lasting narcotic analgesic
  - Available in an alcohol-free solution
  - Initial dose: 0.05-0.2 mg/kg/dose PO q 12-24 h
  - Reduce dose by 10-20% per week over a 4-6 wks period

Management of NAS

- Pharmacologic (Opiates)
- Morphine
  - Shorter half-life than Methadone
  - Powerful respiratory depressant
  - Use preservative free product
  - Initial dose:
  - 0.03-0.1 mg/kg PO q 3-4 hrs
  - Gradually wean by 20% qod
  - Associated with ↑ LOS (~ 30 days)

Hamdan, AH, et al (2008). Neonatal Abstinence Syndrome. *emedicine*.

Management of NAS

- Pharmacologic (Sublingial Buprenorphine)
  - Opioid agonist used for treatment of adult detoxification and maintenance
- Randomized, active-control study
  - N =13 term infants with opiate withdrawal
    - 13.2 to 39.0 µg/kg/ per day in 3 divided doses
  - 13 term infants received oral NOS
  - Results
    - Largely effective in controlling NAS
    - 3 infants in buprenorphine group (vs. 1 in NOS group) required adjunct therapy with phenobarbital
    - Mean LOS for NOS was 38 days compared with 22 days for buprenorphine group

Kraft, WK, et al (2008). Pediatrics, 122(3); e601-e607.

Meth Exposure in Infants

- Smith, LM, et al (2001). Brain proton magnetic resonance spectroscopy in children exposed to methamphetamine in utero. *Neurology 57;255-260*.

- N = 12 meth exposed infant and 14 age-matched non-exposed children
- MRI and Child Behavior Checklist
- Meth exposed group
  - Elevated Creatine in striatum & frontal white matter
  - No difference in significant neuronal loss or damage
  - Suggests abnormality in energy metabolism in the brain of children exposed to meth
  - No difference reported in behavioral problems

Methamphetamine

- Neonatal Effects
  - ↑ (4-6 fold) incidence of cardiac defects, cleft lip, biliary atresia, growth restriction
  - Associated in infant with poor feeding, restlessness, seizures
  - Withdrawal responds to phenobarbital
  - ~80% of women with +UDS for "meth" also used alcohol, nicotine, poor nutrition

Merritt , A (2003)

Methamphetamine - UCLA

- N = 134 meth-exposed infants
  - UDS + only for meth
  - Nicotine/ETOH use by self-report
- Controls = 160 non-exposed infants
- + Meth Exposed Infants: Controls
  - Shorter duration pregnancies
  - Average weight 200 grams less
  - Shorter length
  - Smaller head circumference
  - ↑ Exposure to ETOH, tobacco

Smith, LM et al (2003)

Methamphetamine - UCLA

- + Meth Exposed Infants:
  - Controls S/S of withdrawal ~ 40%
  - Only 4% treated pharmacologically for severe Finnegan scores (> 8)
  - 2x length of stay than controls
  - Less + UDS in Hispanic infants than Caucasians, blacks

Smith,LM et al (2003)

Neonatal Effects

- Smith, LM, et al (2006). The infant development, environment, and lifestyle study: effects of prenatal methamphetamine exposure, polydrug exposure, and poverty on intrauterine growth. *Pediatrics; 118;1149-1156.*

- Screened 13,808 infants in CA, OK, HA, IO
- 84 meth exposed; 1534 meth unexposed
- Both groups included infants with tobacco, alcohol, marijuana exposure, but no opiates, cocaine, LSD, PCP
- Meth group
  - 3.5 times more likely to be SGA
  - Increased maternal weight gain in meth exposed group
  - Birth weights lower than unexposed group
  - Decreased head circumference relative to birth weight
  - Incidence of smoking higher than other populations

Outcome of Drug Exposed Children

"... the pre- and post-natal environment and lifestyle of the drug-abusing parent may be associated with factors that adversely influence the children's development perhaps more than the actual drug exposure.

Giusti, Children With Drug Exposure

Meth Environment

- Riverside County, CA
  - 85% of children removed from labs tested positive for methamphetamine
  - Authorities found children or evidence of children at ~ 50% of meth labs they raided
  - Authorities report at 30% increase in presence of children at meth labs

David Schwartz, PsychCorp/Harcourt, Inc.

Methamphetamine

- Key ingredient is ephedrine
- Pseudoephedrine is available in OTC cold products, diet pills
- Lithium camera batteries, muriatic acid, lye
- Matches, lighter fluid, paint thinner
- Tincture of iodine, hydrogen peroxide
- Anhydrous ammonia in fertilizer

Methamphetamine

- Typical Midwestern “cooker” is
  - A white male
  - Between 15 - 30 years old
  - Poorly educated
  - Living in poverty
  - Usually unemployed

Meth: What’s Cooking in Your Neighborhood

“Meth” and Children

- Many of the following slides were shared with me by and used by permission from:
  - Dr. Deanna St. Germain
  - SIU School of Medicine
  - Dept. of Pediatrics
  - Children’s Medical Resource Network
  - drstgerm@msn.com

“Meth” and Children

- Risks to Children Living in Meth Houses
  - Chemical contamination from fumes, ingestion, skin contact, surfaces

“Meth” and Children

- Risks to Children Living in Meth Houses
  - Chemical contamination from fumes, ingestion, skin contact, surfaces

“Meth” and Children

- Risks to Children Living in Meth Houses
  - Fires & explosions – 15% of meth houses are discovered due to fire or explosion

“Meth” and Children

- Abuse & neglect – caregivers are irritable, violent, neglectful; physical, sexual abuse

“Meth” and Children

- Hazardous lifestyle – criminal activity, booby traps, weapons, dangerous animals

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Improving Treatment for Drug Exposed Infants

- Early Interventions for Drug Exposed Infants
  - Psychomotor assessment
  - Vision & hearing assessment
  - Speech & language assessment
  - Assessment of emotional development
  - Play therapy
  - Early educational needs assessment
  - Physical therapy
  - Immunizations
  - Appropriate referrals

US Dept of HHS; DHHS Publication # SMA 93-2011

Common Symptoms in Drug Exposed *Infants*

- Diagnosis: Hypertonicity
- Causes: Overdrive of brain's response for muscle action
- Course: Birth – 12 months or longer
- Treatments:
  - Passive ROM
  - May require referral to therapy services
  - Avoid walkers at any age
  - Exersaucers & jumpers when tone is stabilized

R Shah & B Deiter, Blank Children's Hospital

Common Symptoms in Drug Exposed *Infants*

- Diagnosis: Tremors of arms & legs
- Causes: Overdrive of brain's response for muscle action
- Course: Birth – 12 months or longer
- Treatments:
  - Minimize overstimulation
  - Stress reduction
  - May refer to PT/OT

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Common Symptoms in Drug Exposed *Infants*

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  - Stress reduction
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Common Symptoms in Drug Exposed *Infants*

- Diagnosis: Irritability & excessive crying
- Causes: Poorly organized brain response to external stimuli
- Course: Birth – 12 months or longer
- Treatments:
  - Avoid overstimulation
  - Provide a consistent, stable environment
  - Swaddle in blanket, pacifier

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Common Symptoms in Drug Exposed *Infants*

- Diagnosis: Poor self-regulation of feeding – infant wanting to eat all the time
- Causes: Poorly organized brain function
- Course: Birth – 4 months of age
- Treatments:
  - Determine optimal caloric needs
  - Offer bottled water between feedings
  - Swaddle in blanket, pacifier, nonnutritive suck

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Common Symptoms in Drug Exposed *Infants*

- Diagnosis: Poor self-regulation of feeding – difficult to get infant to feed
- Causes: Infant too sleepy or tuned out; does not wake for feeding, takes too long too feed, poor suck/swallow
- Course: Birth – 4 months of age
- Treatments:
  - Determine optimal caloric needs
  - Wake child every four hours to feed
  - Try different nipples
  - Feeding evaluation

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Common Symptoms in Drug Exposed *Infants*

- Diagnosis: Poor self-regulation of sleep-wake cycle (infant sleeps all of the time)
- Causes: Poor brain regulation
- Course: Birth – 6 months of age
- Treatments:
  - Minimize overstimulation
  - Establish sleep routines

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Common Symptoms in Drug Exposed *Infants*

- Diagnosis: Trunkal muscle weakness
- Causes: CNS injury; positional effect from back to sleep position
- Course: Varied
- Treatments:
  - Encourage supervised play on tummy
  - Supportive positioning
  - May refer to PT/OT

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Common Symptoms in Drug Exposed *Toddlers*

- Diagnosis: Speech problems (speech unclear or child not using appropriate number of words for age)
- Causes: Toxic effect on brain centers for speech
- Course: Varied
- Treatments:
  - Refer for speech & hearing evaluation as indicated
  - Encourage interactive reading at home
  - Encourage child to use words before honoring his request
  - Encourage sign language communication

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Common Symptoms in Drug Exposed *Toddlers*

- Diagnosis: Temper tantrums & aggressive behavior
- Causes: Normal toddler behavior
  Poor communication, speech delays
  Response to stress in environment
  Toxic effects of drug exposure
- Course: Varied
- Treatments:
  - Teach sign language for expression of feelings
  - Redirect behavior
  - Use positive, non-punitive reinforcement
  - Reframe the behavior as a mode of expression

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Common Symptoms in Drug Exposed *Toddlers*

- Diagnosis: Sensory integration issues (aversion to cuddling, touching, issues around clothes, shoes, bath, new environment)
- Causes: Poor development of sensory brain function
- Course: Varied
- Treatments:
  - Refer for sensory integration evaluation
  - Treatment through OT
  - Avoid triggers for sensory defensiveness

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Common Symptoms in Drug Exposed *Children*

- Diagnosis: Attention Deficit Hyperactivity Disorder
- Causes: Direct result of drugs on brain function
  Environmental factors
- Course: Varied
- Treatments:
  - AAP Recommendation for ADHD
    - Medical treatment with behavioral therapy most effective
    - Efficacy of medical treatment in drug-exposed children not studied
    - Each individual case needs risk/benefit analysis
    - Medication alone is not recommended

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Common Symptoms in Drug Exposed *Children*

- Diagnosis: Social Maladjustment
- Causes: Sensory integration problems
  Developmental disorders (PPD)
  Secondary to environmental deprivation
  Direct toxic effect of drugs (alcohol)
- Course: Varied
- Treatments:
  - Individual and group therapy
  - Neuropsychological evaluation
  - Assessment of underlying psychiatric disorders
  - Interventions to improve environment
  - Sensory integration therapy

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Common Symptoms in Drug Exposed *Children*

- Diagnosis: Academic Failure
- Causes: Intellectual delay
  Learning disability
- Course: Varied
- Treatments:
  - Individual and group therapy
  - Neuropsychological evaluation
  - Assessment of underlying psychiatric disorders
  - Interventions to improve environment
  - Sensory integration therapy
  - Classroom modification

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Literature Review

- “Effects of Prenatal Substance Exposure on Infant and Early Childhood Outcomes”
- “Lessons Learned: Assessing and Supporting Parenting in Families Affected by Substance Abuse and HIV”

National Abandoned Infants Assistance Resource Center

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