

# Infants of Mothers with Substance Abuse

Prameela Karimi, MD, FAAP

Nov 13<sup>th</sup>, 2015

Fort Worth Pediatrx Medical Group

# Objectives

- Discuss substance abuse during pregnancy including epidemiology, risk factors, diagnosis
- Describe the use of nicotine and tobacco, alcohol, marijuana, opioids and narcotics, cocaine, amphetamine during pregnancy and neonatal and postnatal outcomes
- Describe fetal alcohol spectrum disorder and Neonatal abstinence syndrome
- To identify resources and support organizations

# Infant of Mothers with Substance Abuse: Epidemiology

- Among surveyed pregnant women aged 15-44 years, reported illicit drug use was 5%, alcohol use 9.4% with 2.6% binge drinking and 0.4% heavy drinking and cigarette use was 17.6% (results from 2011 National survey on Drug Use and Health Summary of National Findings)
- Number of mothers using or dependent on opiates increased from 1/19 to 5.63 per 1000 live births per year. Rate of newborns with NAS increased from 1.2 to 3.39 per 1000 births per year between 2000 and 2009 (JAMA 2012; 307:1934)

# Infant of Mothers with Substance Abuse: Diagnosis

- Maternal screening
- Neonatal screening
  - Urine
  - Meconium
  - Hair
  - Umbilical cord blood and tissue
  - Neonatal nails and vernix (currently experimental)

# Infant of Mothers with Substance Abuse: Management General Approach

- Multidisciplinary team approach
- Careful evaluation of maternal history
- Parental education and support
- Optimal environment
- Drug identification
- Infant assessment
- Maternal therapy

# Infant of Mothers with Substance Abuse: Breastfeeding

- Excreted into breast milk and may have negative effects on nursing infants
- Amphetamine- found in breast milk at concentrations 2.8 to 7.5 times maternal plasma
- Cocaine- possible variability in cocaine levels in breast milk with high concentrations and neonatal intoxication from breastfeeding has been reported.
- Opioids- CNS depression including one infant death reported due to opioid exposure in breast milk due to maternal opioid use including oxycodone and methadone
- Marijuana- THC is concentrated in breast milk at levels up to 8 times plasma in chronic users. Effects include sedation, low tone and poor sucking, delayed motor development at one year of age.
- Phencyclidine- high concentrations noted in breast milk in one case report
- Alcohol- concentration in breast milk is similar to maternal blood levels. Decrease neonatal milk intake, alters neonatal sleep wake cycles and results in a delay in offspring's motor development at one year of age.

# Infant of Mothers with Substance Abuse: Breastfeeding cont'd

- Support decision to breastfeed in women
  - Engaged in substance abuse treatment and consent to discuss progress and plan with counselor
  - Plan to continue in substance abuse treatment in the post partum period
  - Abstinent from illicit drug use or licit drug abuse for 90 days prior to delivery and have demonstrated the ability to maintain sobriety in an outpatient setting
  - Negative UDS at delivery except for prescribed medications
  - Received adequate prenatal care
  - No medical contraindication to breastfeeding (HIV etc)
  - Who are not taking medication that is contraindicated during lactation

# Infant of Mothers with Substance Abuse: Breastfeeding cont'd

- Discourage decision to breastfeed in women
  - No prenatal care
  - Relapsed into illicit drug use or licit substance misuse in the 30 day period prior to delivery
  - Unwilling to engage in substance abuse treatment or not willing to provide consent for contact with the counselor
  - Positive UDS at delivery
  - Who do not have confirmed plans for postpartum substance abuse treatment or pediatric care
  - Who demonstrate behavioral qualities or other indicators of active drug use



# Tobacco and Nicotine



# Tobacco and Nicotine: Pharmacology

- CNS stimulant
- Active constituents of cigarette smoke are nicotine, tar, CO and cyanide
- CO combines with Hb to form carboxyhemoglobin (impairs oxygenation for both the mother and fetus/ fetal hypoxia)
- Placental vasoconstriction and vasospasm
- Dose related response between number of cigarettes smoked and neonatal effects

# Tobacco and Nicotine: Effects on Pregnancy

- Spontaneous abortion
- Placenta previa
- Placental abruption
- Preterm labor
- Premature rupture of membranes
- Cesarean section

# Tobacco and Nicotine: Effects on Fetus and Neonate

- IUGR
- Small increased risk of congenital malformations (CNS malformations, hypospadias, inguinal hernia, eye and ear malformations, polycystic kidneys, aortopulmonary septum defects, gastroschisis, and skull deformities)
- Neurobehavioral effects (perform less well in cognitive, psychomotor, language skills, general academic achievements)
- SIDS
- Increased cost of hospitalization

# Alcohol Use in Pregnancy: Prevalence

- 7.6% of pregnant women used alcohol and 1.4% admitted to binge drinking during the month prior to being interviewed during 2006-2010 (CDC report)
- National Birth Defects Prevention Study
  - 4088 women who delivered live born infants without birth defects
  - 1997-2002
  - 30.3% consumed alcohol at some time during pregnancy
  - 8.3% reported binge drinking

# Alcohol : Pharmacology

- Anxiolytic analgesic, CNS depressant
- Absorbed rapidly from the stomach and the intestines; metabolized by the liver and eliminated by the kidneys and lungs
- Fetal ethanol concentration is eliminated only by maternal hepatic biotransformation
- Transfer across the placenta by diffusion and impairs normal placental function by altering the transfer of essential nutrients to the fetus
- Teratogen (effects directly related to quantity and pattern eg binge drinking, daily drinking of alcohol consumption, maternal and fetal genetics, maternal age, maternal nutrition and smoking among other factors)

# Alcohol: Effects on Pregnancy

- Spontaneous abortion
- Placental abruption
- Breech presentation
- IUGR
- Preterm births

# Alcohol: Effects on the Fetus and Neonate



# Alcohol: Neonatal Withdrawal

- Relatively mild in comparison with infant narcotic withdrawal
- Onset: birth up to 12 hours after birth
- Symptoms:
  - Hypertonia
  - Tremors
  - Opisthotonos
  - Weak suck and poor feeding pattern
  - Less sleep, cry more and often engage in exaggerated mouthing behavior

# Fetal Alcohol Spectrum Disorder

- Leading preventable cause of birth defects and developmental disabilities
- FASD encompasses the range of physical, mental, behavioral, and cognitive effects that can occur in individuals with prenatal alcohol exposure
  - Fetal alcohol syndrome
  - Partial fetal alcohol syndrome
  - Neurobehavioral disorder associated with prenatal alcohol exposure (ND-PAE)

# Fetal Alcohol Spectrum Disorder: Pathogenesis

- No safe threshold or pattern of alcohol consumption has been identified
- Fetus is vulnerable to maternal alcohol consumption because of inefficient elimination and prolonged exposure
- Known teratogen with irreversible CNS effects
- Affects at all stages of gestation
  - First trimester: facial and major structural anomalies
  - Second trimester: spontaneous abortions
  - Third trimester: affects weight, length and brain growth
- Neurobehavioral effects may occur with a range of exposures throughout gestation even in the absence of facial or structural brain anomalies

# Fetal Alcohol Spectrum Disorder: Epidemiology

- Estimated prevalence in first grade students
  - FAS 6 to 9 per 1000
  - pFAS 11-17 per 1000
  - FASD 24-28 per 1000
- Increasing prevalence with increasing alcohol consumption during pregnancy
- Risk of FASD in subsequent pregnancies is high if mothers continue to drink alcohol
- Children are at higher risk for FASD if they have a sibling with FASD, have ever lived in an orphanage or been placed in foster care, or have current or past involvement with child protective services

# Fetal Alcohol Spectrum Disorder: Maternal and Psychosocial Risk Factors

- Low education 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

# Fetal Alcohol Spectrum Disorder: Clinical Features

Compilation of diagnostic criteria for fetal alcohol spectrum disorders

FASD	Diagnostic criteria	
Fetal alcohol syndrome	All three characteristic facial features Growth retardation CNS involvement Confirmed or unconfirmed prenatal alcohol exposure	
Partial fetal alcohol syndrome	Two key facial features Growth retardation or CNS impairment Confirmed history of prenatal alcohol exposure	
Neurobehavioral disorder associated with prenatal alcohol exposure*	CNS involvement with functional impairment (eg, social, academic) and onset in childhood Facial features and growth retardation not necessary (but may be present) Not better explained by other teratogens; genetic or medical conditions; or environmental neglect Confirmed history of prenatal alcohol exposure	
Definition of clinical features		
Characteristic facial features	Short palpebral fissures <sup>Δ</sup> Thin vermillion border (University of Washington Lip-Philtrum rank 4 or 5) Smooth philtrum (University of Washington Lip-Philtrum rank 4 or 5)	
Growth retardation	Height and/or weight (adjusted for gestational age) ≤10 <sup>th</sup> percentile for age, sex, race/ethnicity at any point of time (eg, prenatal or postnatal)	
CNS involvement	<b>For FAS and pFAS</b>  Structural abnormalities (one of the following): <ul style="list-style-type: none"><li>■ Head circumference ≤10<sup>th</sup> percentile for age and sex, or, if weight and height are &lt;10<sup>th</sup> percentile, head circumference ≤3<sup>rd</sup> percentile</li><li>■ Significant structural abnormalities on neuroimaging</li></ul> Neurologic abnormalities: <ul style="list-style-type: none"><li>■ Hard or soft neurologic signs<sup>◊</sup></li><li>■ Seizures that are not due to postnatal insult or fever</li></ul> Functional abnormalities (one of the following): <ul style="list-style-type: none"><li>■ Significant global cognitive or intellectual deficits</li><li>■ Significant developmental delay<sup>§</sup></li><li>■ Functional deficits<sup>¥</sup> in at least three of the following domains:<ul style="list-style-type: none"><li>● Cognitive or developmental deficits or discrepancies</li><li>● Executive functioning deficits</li><li>● Motor functioning delays</li><li>● Problems with attention or hyperactivity</li><li>● Social skills</li><li>● Other, such as sensory problems, pragmatic language problems, memory deficits, etc</li></ul></li></ul>	<b>For ND-PAE</b>  NA  NA  Functional impairments/deficits in each of the following domains: Neurocognitive (at least one): <ul style="list-style-type: none"><li>■ Intellectual disability</li><li>■ Executive functioning</li><li>■ Learning</li><li>■ Memory</li><li>■ Visual-spatial reasoning</li></ul> Self-regulation (at least one): <ul style="list-style-type: none"><li>■ Mood or behavioral regulation</li><li>■ Attention</li><li>■ Impulse control</li></ul> Adaptive function (at least two): <ul style="list-style-type: none"><li>■ Communication</li><li>■ Social communication and interaction</li><li>■ Daily living skills</li><li>■ Motor skills</li></ul>

FASD: fetal alcohol spectrum disorder; CNS: central nervous system; FAS: fetal alcohol syndrome; pFAS: partial FAS; ND-PAE: neurobehavioral disorder associated with prenatal alcohol exposure; NA: not applicable.

\* Sometimes called "Neurodevelopmental disorder associated with prenatal alcohol exposure;" similar to "Alcohol-related neurodevelopmental disorder," a term that is being phased out.

Δ The definition of short palpebral fissures varies according to the diagnostic schema.

◊ "Hard" neurologic signs include abnormal reflexes, abnormal tone, cranial nerve deficits; "soft" neurologic signs include poor coordination or balance, visual-motor difficulties, nystagmus, difficulty with motor sequencing or rapid successive movements, right-left confusion.

§ Performance below the 3<sup>rd</sup> percentile (two standard deviations below the mean) on a validated assessment tool that assesses multiple domains.

¥ Performance below the 16<sup>th</sup> percentile (one standard deviation below the mean) on a validated assessment tool.

Data from:

- American Psychiatric Association. Neurobehavioral disorder associated with prenatal alcohol exposure. In: *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5)*. American Psychiatric Association, Arlington, VA 2013. p.798.
- Astley SJ. *Diagnosis of Fetal Alcohol Spectrum Disorders (FASD): The 4-Digit Diagnostic Code, 3rd edition*. University of Washington Publication Services, Seattle, 2004.
- Bertrand J, Floyd RL, Weber MK, et al. National Task Force on Fetal alcohol syndrome and fetal alcohol effect. *Fetal alcohol syndrome: Guidelines for referral and diagnosis*. Center for Disease Control and Prevention; Atlanta, GA, 2004. Available at: [www.cdc.gov/ncbddd/fasd/documents/fas\\_guidelines\\_accessible.pdf](http://www.cdc.gov/ncbddd/fasd/documents/fas_guidelines_accessible.pdf) (Accessed on February 24, 2014).
- Chudley AE, Conry J, Cook JL, et al. Fetal alcohol spectrum disorder: Canadian guidelines for diagnosis. *CMAJ* 2005; 172:S1.
- Hoyme HE, May PA, Kalberg WO, et al. A practical clinical approach to diagnosis of fetal alcohol spectrum disorders: clarification of the 1996 institute of medicine criteria. *Pediatrics* 2005; 115:39.

# Fetal Alcohol Spectrum Disorder:

## Diagnostic criteria

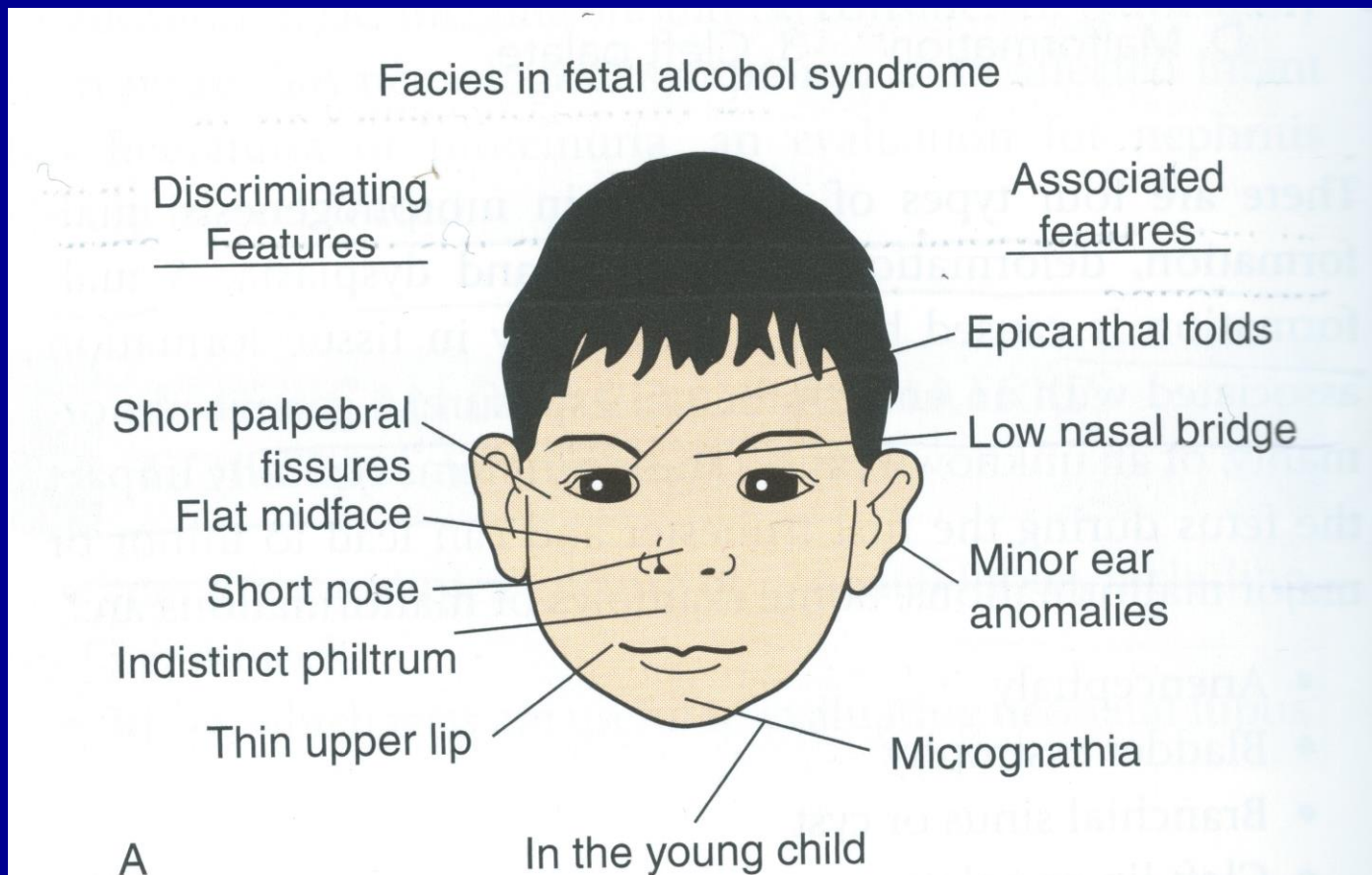
- Fetal alcohol syndrome
  - All three characteristic facial features (short palpebral fissures, thin vermillion border, smooth philtrum)
  - Growth retardation
  - CNS involvement
  - Confirmed or unconfirmed prenatal alcohol exposure
- Partial fetal alcohol syndrome
  - Two key facial features
  - Growth retardation or CNS impairment
  - Confirmed history of prenatal alcohol exposure
- Neurobehavioral disorder associated with prenatal alcohol exposure
  - CNS involvement with functional impairment (eg. Social, academic) and onset in childhood
  - Facial features and growth retardation not necessary (but may be present)
  - Not better explained by other teratogens; genetic or medical conditions; of environmental neglect
  - Confirmed history of prenatal alcohol exposure

# Fetal Alcohol Spectrum Disorder: Clinical Features

- Facial dysmorphisms and minor anomalies
- Structural birth defects
- Growth retardation
- CNS involvement
- Associated problems
- Comorbid mental health conditions

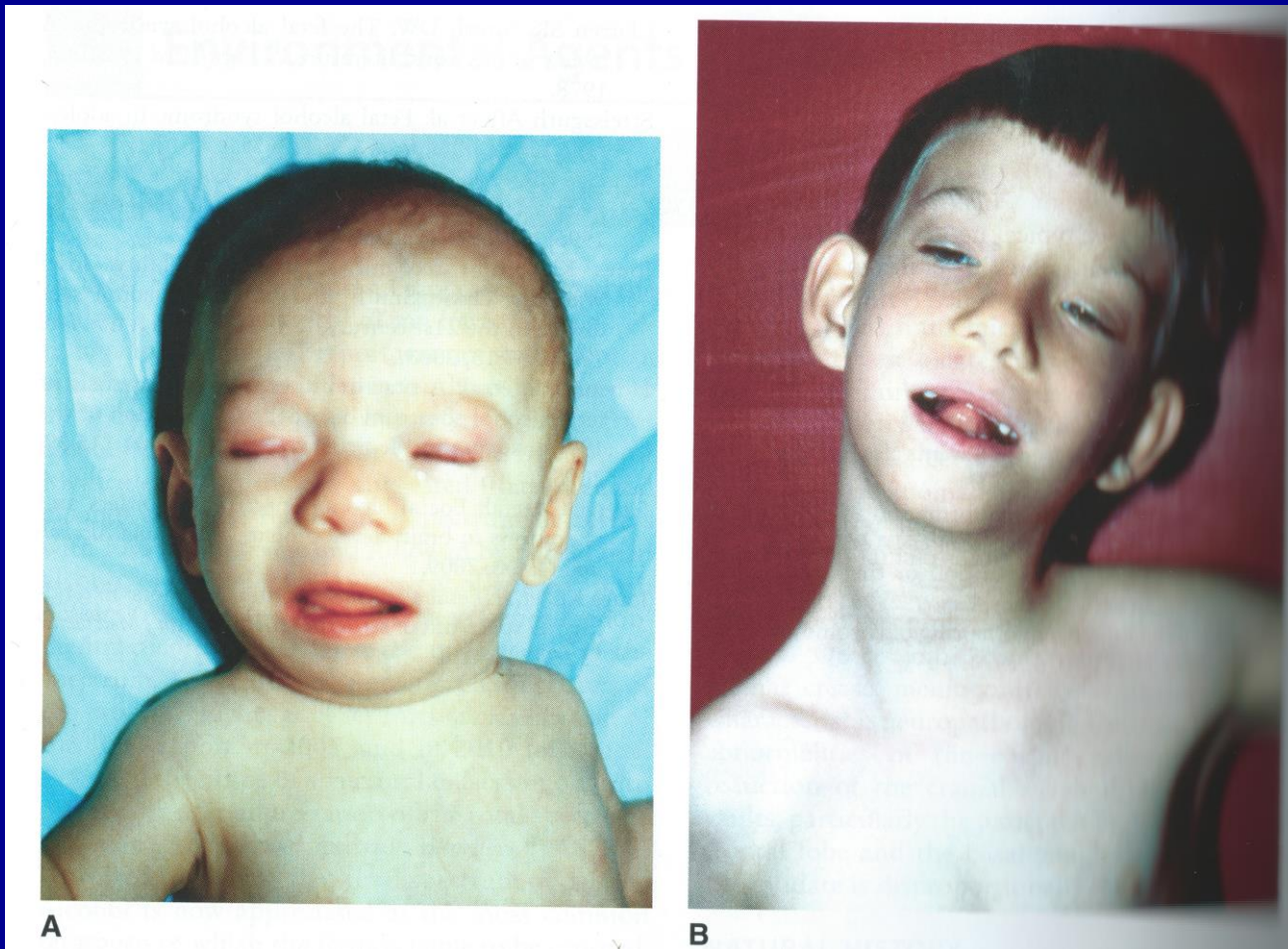


# FASD Clinical Features: Facial dysmorphism and Minor Anomalies



**FIGURE 1.** Characteristic features of a child with *fetal alcohol syndrome*. Modified from Sadler T. *Langman's Medical Embryology*. 9th ed. Image Bank. Baltimore, MD: Lippincott Williams & Wilkins; 2003

# FASD Clinical Features: Facial dysmorphism and Minor Anomalies



*Smith's Recognizable Patterns of Human Malformations, 7th edition*



# FASD Clinical Features: Facial dysmorphism and Minor Anomalies



*Smith's Recognizable Patterns of Human Malformations, 7th edition*

# FASD Clinical Features: Facial dysmorphism and Minor Anomalies

**Characteristic facial features in a child with fetal alcohol spectrum disorder**



Examples of the fetal alcohol syndrome facial phenotype across three races: Caucasian, Native American, and African American. Characteristic facial features include short palpebral fissure length, smooth philtrum, and a thin upper lip.



# FASD Clinical Features: Facial dysmorphism and Minor Anomalies

## Hand anomalies in fetal alcohol spectrum disorders



Clinodactyly of the fifth finger and a "hockey stick" configuration of the upper palmar crease. Note that the upper palmar crease widely curves and terminates between the index and middle fingers.

*Reproduced with permission from: Darryl Leja.*

UpToDate®

## Ear anomalies in fetal alcohol spectrum disorders



"Railroad track" ear is a minor anomaly common among children with fetal alcohol spectrum disorders. Note the upper curve of the outer ear is underdeveloped, folded over, and parallel to the curve beneath it, giving the appearance of a railroad track.

*Reproduced with permission: from Darryl Leja.*

UpToDate®

# FASD Clinical Features: Structural Birth Defects

- Cardiac
  - ASD, VSD, conotruncal heart defects
- Skeletal
  - Flexion contractures, pectus excavatum, pectus carinatum, Klippel-Feil syndrome, hemivertebrae, scoliosis, radioulnar synostosis, hypoplastic nails, shortened fifth digits, clinodactyly of the fifth finger, camptodactyly
- Renal
  - Aplastic, dysplastic, hypoplastic kidney or horseshoe kidney, ureteral duplications, hydronephrosis
- Ocular
  - Strabismus, ptosis, retinal vascular anomalies, optic nerve hypoplasia, refractive problems secondary to microphthalmia, vision problems
- Auditory
  - Conductive or sensorineural hearing loss

# FASD Clinical Features: Comorbid Mental Health conditions

- Conduct disorders
- Oppositional defiant disorder
- Anxiety disorder
- Adjustment disorder
- Sleep disorder
- Depression
- Substance use disorder

# FASD Clinical Features: CNS Involvement

- Infancy- Irritability, jitteriness, autonomic instability and problems regulating state eg. Sleep, attention, arousal
- Childhood- Hyperactivity, inattention, cognitive impairment, emotional reactivity, learning disabilities, hypotonia, auditory and visual impairment, seizures, deficits in memory and reasoning
- Adolescence and young adulthood- adverse effects related to primary deficits in social skills, adaptive function, and executive function (eg. School disruption, inability to maintain employment, inappropriate sexual behavior)
- CNS involvement classified as
  - Structural
  - Neurologic
  - Functional



# FASD Clinical Features: CNS Structural and Neurologic Abnormalities

- Structural abnormalities
- Decreased head circumference
- Structural abnormalities on neuroimaging eg reduction in size of change in shape of the corpus callosum, cerebellum or basal ganglia
- Neurologic abnormalities
- Abnormal reflexes, abnormal tone, cranial nerve deficits
- Poor coordination or balance, visual motor difficulties, nystagmus, difficulty with motor sequencing or rapid successive movements, right- left confusion, seizures that are not related to postnatal insult or infection

# FASD Clinical Features: CNS Functional Abnormalities

- Cognitive
- Executive function
- Motor function
- Problems with hyperactivity, attention or concentration
- Social skills and adaptive function

# FASD Clinical Features: Associated Problems

- Difficulty getting along with peers related to poor social skills and vulnerability to bullying and abuse
- Unrealistic expectations or being labelled as lazy or oppositional
- Difficulty with activities of daily living
- Disrupted school experience
- Problems with impulse control and judgement
- Participation in criminal activity and encounters with law enforcement
- Problems with alcohol or drugs

# FASD Clinical Features: Comorbid Mental Health conditions

- Conduct disorders
- Oppositional defiant disorder
- Anxiety disorder
- Adjustment disorder
- Sleep disorder
- Depression
- Substance use disorder

# FASD: Management

- Role of the primary care provider
  - Early identification
  - Education and anticipatory guidance
  - Family support
  - Medical home
- Individualized interventions according to the needs of the patient and family
- General Strategies
  - Increasing the predictability and structure of the environment
  - Using visual prompts and sequences to reinforce and remind children how to perform activities of daily living
  - Developing behavior plans built on positive reinforcement and healthy discipline strategies
  - Simplifying the environment (e.g. Avoiding multi step commands, reducing distractions)
- Specific interventions
  - May be used to target academic, social and adaptive skills

# FASD: Referral Services

- < 3 years
  - May benefit from speech and language, occupational and physical therapy
- Preschool and school age
  - May benefit from physical therapy, speech and language therapy, occupational therapy (adaptive skills training), social skills training and special education services
- Adolescents and young adults
  - May benefit most from adaptive (e.g daily living) and employment skills (e.g. Job coach)
  - May need additional support with transportation and housing and continued assistance managing money, scheduled and unpredictability

# FASD: Prognosis

- High risk for adverse life outcomes from “secondary disabilities”
  - Inappropriate sexual behavior, disrupted school experience, trouble with the law and incarceration, homelessness, unemployment, substance abuse problems, chronic mental health problems, and premature death most likely from impulsivity and poor judgement such as car accidents or HIV infection; or from comorbidities such as substance abuse, unhealthy lifestyle, suicide or homicide
- Factors associated with fewer adverse outcomes include
  - Diagnosis before 6 years of age
  - Eligibility for social and educational services
  - Stable and nurturing living environment
  - Absence of exposure to physical, sexual, or other types of violence
  - Diagnosis of FAS rather than one of the other FASDs probably related to earlier diagnosis and intervention

# FASD: Prevention

- Leading preventable cause of birth defects and developmental disorders in the US
- Education of students of all ages, women of child bearing age and mothers and their partners about the effects of alcohol on a fetus and about FASD
- Promotion of abstinence from drinking alcohol before conception and during pregnancy
- Screening to identify high risk mothers who are pregnant and referring to appropriate programs



# FASD: Additional Resources

- American Academy of Pediatrics Fetal Alcohol Spectrum Disorders Program
- The Centers for Disease Control and Prevention
- Fetal Alcohol Spectrum Disorders Center for Excellence
- National Organization on Fetal Alcohol Syndrome
- University of Washington FAS Diagnostic and Prevention Network

# Marijuana (Cannabinoids)



# Marijuana (Cannabinoids)

- Most commonly used illicit drug
- Has both depressant and mild hallucinogenic effects on the CNS
- Cannabis sativa (dried leaves and flowering tops of the plant)
- Usually smoked (also cooked in biscuits or cakes)
- Principal active ingredient is tetrahydrocannabinol (THC)
- Readily crosses the placenta (highest in the first trimester of pregnancy)
- Smoking marijuana increases the blood CO level and may result in hypoxia

# Marijuana: Effects on Pregnancy, Fetus and Neonate

- Does not independently affect somatic fetal growth and results in no known congenital anomalies
- No known neonatal signs of withdrawal from marijuana exposure
- Maternal marijuana use is a relative contraindication to breastfeeding
- No known independent effect of prenatal marijuana exposure on childhood growth through adolescence
- Prenatal marijuana exposure exerts long term effects on behavior (inattention and impulsivity), problem solving skills, and underachievement in reading and spelling, but not on IQ or language



# Opioids and Narcotics



# Opioids and Narcotics: Epidemiology

- Rising incidence of maternal use of opioid pain relievers (1.9 to 5.63 per 1000 live births from 2000 to 2009)
- Rising incidence of NAS (1.2 to 5.8 per 1000 live births from 2000 to 2012)
- Increasing NICU admissions (7 to 27 per 1000 admission rate to 299 NICUs from 2004 to 2013)
- NAS requiring pharmacotherapy in infants with prenatal exposure to opioids 42 to 94%
- Antenatal cumulative prescription exposures, type of opioid used, tobacco use and SSRI use increase the risk of NAS
- No evidence there is a relationship between maternal methadone dose and neonatal severity

# Opioids and Narcotics: Pharmacology

- CNS depressant
- Derived from the opium poppy, *Papaver somniferum*
- Activates mu-opioid receptors in the CNS and GIT
- Heroin
  - Semisynthetic opiate that may be sniffed, smoked or injected
  - Quick acting and produces a sense of euphoria within 10 sec after injection
  - Stronger than morphine and readily passes the placental barrier
- Methadone
  - Absorbed slowly, long duration of action making it suitable for treatment of heroin addicts
  - Drug level delivered to the fetus is more stable and reduces the risk fo fetal withdrawal

# Opioids and Narcotics: Effects on Pregnancy

- May be polydrug users
- May present with medical complications related to drug use (anorexia, anemia, cardiac disease, thrombosis, abscesses)
- STDs (Gonorrhea, Syphilis, Hepatitis B and C, HIV)
- Spontaneous abortions
- Obstetric complications (toxemia, placental abruption, premature labor, shorter than average labor, precipitous delivery, breech delivery, fetal distress, stillbirth)
- Many of the effects of opiate use in pregnancy are correlated directly to the amount of prenatal care received and the maternal lifestyle rather than drug itself



# Opioids and Narcotics: Effects on Fetus and Neonate

- Hypoxia
- Lower APGAR scores
- Meconium aspiration and aspiration pneumonia
- IUGR
- Lower incidence of respiratory distress syndrome and hyperbilirubinemia
- Congenital infections
- Increased incidence of SIDS
- LBW
- Microcephaly
- Increased chromosomal aberrations (heroin only exposed infants)

# Opioids and Narcotics: Neonatal Abstinence Syndrome

- Drug withdrawal from maternal dependency of opioids or other substances
- Variable, complex and incompletely understood spectrum of signs of neonatal behavior dysregulation
- Other substances such as cigarettes, benzodiazepines and SSRIs can potentiate the severity of NAS

# Neonatal Abstinence Syndrome: Timing of Withdrawal

- Depends upon the recent history of drug dose and the half life of drug elimination
  - Heroin (short half life) within 24 hours of birth
  - Methadone (long half life) begins 24 to 72 hours after birth
- Risk of acute signs of withdrawal low if more than one week has lapsed between the last maternal opioid use and delivery of the infant
- Late onset NAS
- Duration ranges from 8 to 16 weeks or longer

# Neonatal Abstinence Syndrome: Premature Infants

- Premature infants <35 weeks gestation are at a lower risk for developing NAS compared with term infants
- Risk diminishes as gestational age decreases
  - Developmental immaturity of the preterm CNS
  - Limited ability to express the signs of motor function dysfunction
  - Reduced total drug exposure during the intrauterine period
  - Lower amounts of fat deposition of drug
  - Difficulty in identifying signs in premature infants

# Neonatal Abstinence Syndrome: Clinical Presentation

- Neurologic
  - Tremors
  - Irritability
  - Increased wakefulness
  - Hypertonia
  - Hyperreflexia
  - Exaggerated Moro reflex
  - High pitched cry
  - Seizures
- Autonomic
  - Yawning
  - Nasal stuffiness
  - Sweating
  - Sneezing
  - Temperature instability
  - Skin mottling
- Gastrointestinal
  - Poor feeding
  - Uncoordinated and constant sucking
  - Vomiting
  - Diarrhea
  - Dehydration
  - Poor weight gain
- Other
  - Tachypnea
  - Skin excoriation

# Neonatal Abstinence Syndrome: Scoring

- Three methods:
  - Finnegan's Neonatal Abstinence Score (Modified Finnegan Score)
  - Neonatal Drug Withdrawal Scoring System (Lipsitz, 1975)
  - Neonatal Withdrawal Inventory (Zahorodny, 1998)

## NEONATAL ABSTINENCE SCORE

Date: \_\_\_\_\_

Weight: \_\_\_\_\_

Date: \_\_\_\_\_Weight: \_\_\_\_\_

System	Signs & Symptoms	Score	Time												Comment	
			AM						PM							
Central Nervous System Disturbances	Excessive High Pitched Cry	2														
	Continuous High Pitched Cry	3														
	Sleeps < 1 Hour After Feeding	3														
	Sleeps < 2 Hours After Feeding	2														
	Sleeps < 3 Hours After Feeding	1														
	Hyperactive Moro Reflex	2														
	Markedly Hyperactive Moro Reflex	3														
	Mild Tremors Disturbed	1														
	Moderate - Severe Tremors Disturbed	2														
	Mild Tremors Undisturbed	3														
	Moderate - Severe Tremors Undisturbed	4														
	Increased Muscle Tone	2														
	Excoriation (Specific Area)	1														
	Myoclonic Jerks	3														
	Generalized Convulsions	5														
Metabolic / Vasomotor / Respiratory Disturbances	Sweating	1														
	Fever < 101° F (37.2° - 38.2° C)	1														
	Fever ≥ 101.1° F (≥38.4° C)	2														
	Frequent Yawning ( > 3 - 4 Times/Interval)	1														
	Mottling	1														
	Nasal Stuffiness	1														
	Sneezing ( > 3 - 4 Times/Interval)	1														
	Nasal Flaring	2														
	Respiratory Rate - 60/min	1														
	Respiratory Rate - 60/min with Retractions	2														
Gastrointestinal Disturbances	Excessive Sucking	1														
	Poor Feeding	2														
	Regurgitation	2														
	Projectile Vomiting	3														
	Loose Stools	2														
	Watery Stools	3														
	TOTAL SCORE															
	Initials of Scorer															



# Neonatal Abstinence Syndrome: Lipsitz Neonatal Drug Withdrawal Scoring System

■ TABLE 3-3

■ ■ Neonatal Abstinence Scoring System

Signs	Score			
	0	1	2	3
Tremors (muscle activity of limbs)	Normal	Minimally ↑ when hungry or disturbed	Moderately or markedly ↑ when undisturbed, subside when fed or held snugly	Marked even when undisturbed, going on to seizure-like movements
Irritability (excessive crying)	None	Slightly ↑	Moderate to severe when disturbed or hungry	Marked even when undisturbed
Reflexes	Normal	Increased	Markedly increased	
Stools	Normal	Explosive, but normal frequency	Explosive, more than 8/day	
Muscle tone	Normal	Increased	Rigidity	
Skin abrasions	No	Redness of knees and elbows		Breaking of skin
Respiratory rate/minute	<55	55 to 75	76 to 95	
Repetitive sneezing	No	Yes		
Repetitive yawning	No	Yes		
Vomiting	No	Yes		
Fever	No	Yes		

Scoring: Identification of newborn with narcotic withdrawal when score >17 (78% probability).

Source: Lipsitz, P.J.: A proposed narcotic withdrawal score for use with newborn infants: A pragmatic evaluation of its efficacy. *Clinical Pediatrics*, 14(6):592-594, 1975.



# Neonatal Abstinence Syndrome: Management

- Non pharmacologic supportive care
  - Swaddling
  - Allow infant to PO ad lib on demand feeds (consider small feeds as a comfort measure, consider higher calorie feeds due to increased metabolic demand of up to 150-250 cal/kg/day)
  - Low light and low noise environment
- Pharmacologic therapy
  - Oral morphine
  - Oral methadone
  - Phenobarbital
  - Clonidine

# Cocaine



# Cocaine: Pharmacology

- Benzoylmethyl-ecgonine is a CNS stimulant
- Derived from Erythroxylon coca shrub leaves
- Oral, Sublingual, Intranasal, Intravenous, Inhaled (“crack”)
- Inhibits the reuptake of norepinephrine, dopamine and serotonin neurotransmitter pathways
- Peripheral vasoconstriction, tachycardia, hypertension and hyperthermia (MI, CVA, pulmonary edema, renal and bowel infarction)
- Metabolized by plasma and liver cholinesterases and excreted by the kidneys
- Crosses the placenta readily and is excreted in breast milk

# Cocaine: Effect on Pregnancy, Fetus and Neonate

- Placental abruption, fetal hypoxia and stillbirth, meconium staining, spontaneous abortion, precipitous delivery, PIH, preterm labor
- No consistent teratogenic effect found
- Multiorgan dysfunction
  - CNS: Abnormal sleep patterns/ EEG; seizures/ tremors; cerebral infarction
  - Sensory organs: Abnormal ABER
  - CVS: atrial/ ventricular arrhythmia, hypertension, decreased cardiac output
  - Respiratory: apnea, abnormal breathing patterns
  - Renal: ectopia
  - GI: Increased risk of early onset NEC, intestinal perforation not related to NEC
  - Eye: vascular, disruptive lesions; retinal hemorrhage

# Cocaine: Neonatal Withdrawal

- Not clearly defined
- Most frequently on the 2<sup>nd</sup> or 3<sup>rd</sup> postnatal days
- Irritability, hyperactivity, tremors, high pitched cry, excessive sucking and poor alertness and orientation
- Cocaine or its metabolites may be detected in the neonatal urine for as long as 7 days after delivery; may reflect drug effect rather than withdrawal

# Cocaine: Long Term Outcomes

- Beginning evidence for significant however relatively subtle cocaine associated deficits in a number of domains of neurobehavioral and neuropsychologic functioning such as sustained attention, language functioning and external behaviors

# Amphetamines: Pharmacology

- CNS stimulant
- Used to treat narcolepsy, ADHD and obesity (short term)
- Most widely used forms
- Methylenedioxymethamphetamine (MDMA, ecstasy)
- Methamphetamine (ice, crystal)
- Methylenedioxyamphetamine (MDA, the love pill)
- Methylenedioxymethamphetamine (MDEA, Eve)
- Can be inhaled, smoked or taken orally
- Neurotoxic
- Vasoconstriction and hypertension
- Intense physical and psychologic exhilaration (duration 2-14 hours)

# Amphetamines: Effects on Pregnancy, Fetus and Neonate

- Prematurity, placental abruption, hypertension, cardiac arrhythmias, myocardial infarction, clefting and fetal growth restriction
- CNS and cardiac anomalies/ defects, cleft palate, limb reduction and/ or musculoskeletal anomalies
- IUGR
- Neonatal withdrawal
  - Abnormal sleep patterns, poor feeding, tremors, abnormal weight gains, diaphoresis, episodes of agitation alternating with lassitude, miosis and vomiting



# Phencyclidine

- PCP or angel dust
- CNS stimulant and depressant
- Risk of prematurity or IUGR (conflicting reports)
- Neurodevelopmental abnormalities (hypertonicity, irritability, sleep problems, temperature instability)

# Barbiturates

- Prenatal barbiturate exposure associated with neonatal drug withdrawal symptoms and congenital malformations (cleft lip and palate, cardiac, increased risk of hemorrhagic disorder of the newborn)
- Median age of withdrawal 7 days (2-14 days)
- Two stages
  - Acute stage- Irritability, constant crying, sleeplessness, tremors, hiccups and mouthing motions
  - Subacute stage- voracious appetite, frequent regurgitation, gagging, episodic irritability, sweating, sleep disturbances and increased sensitivity to sound
- Treatment:
  - Supportive
  - Phenobarbital

# References

- Jansen, L.M. Infants of mothers with substance abuse. UpToDate 2015
- Jansen, L.M. Neonatal abstinence syndrome. UpToDate 2015
- Weitzman. Fetal alcohol spectrum disorder. UpToDate 2015
- AAP committee on Drugs. Neonatal Drug Withdrawal. Pediatrics. Jan 2012
- Mark L Hudak. Infants with Antenatal Exposure to Drugs. Fanaroff and Martin's Neonatal-Perinatal Medicine. 10<sup>th</sup> edition
- Kathleen Pitts. Perinatal Substance Abuse. Core Curriculum for Neonatal Intensive Care Nursing. Fourth Edition