

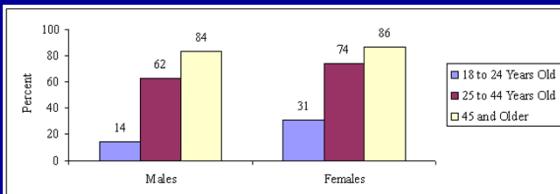
Impact of Parental Substance Abuse on Children's Development

Lauren Swager MD
Child and Adolescent Psychiatrist
West Virginia University

Objectives

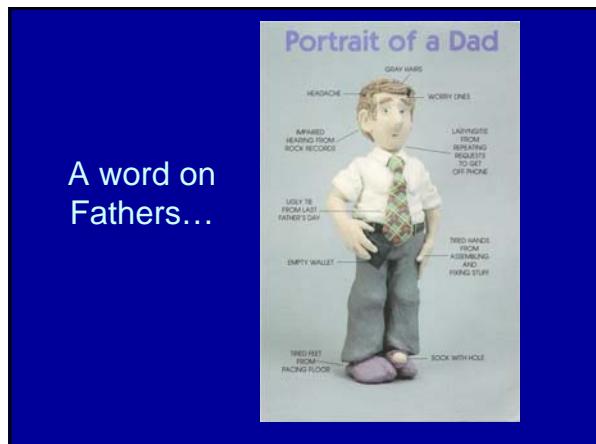
- Review the proposed Mechanisms of How Parental Substance Use Disorder effects Children
- Recognize the physical and cognitive effects that encompass fetal alcohol spectrum disorders
- Review the evidence of prenatal exposure of other substances (tobacco, marijuana, cocaine, opiates) and psychiatric outcomes in childhood
- Discuss how the treatment of parental substance use disorders can benefit childhood pathology

Percentage of adults ages 18 and older who have ever had a biological child: 2000



SOURCE: National Health Interview Survey, 2000





Proposed Mechanisms of How Parental Psychopathology effects Children

- Genetic Transmission
- Development of dysfunctional neuroregulatory mechanisms prenatally
- Exposure to the parent's maladaptive affect
- Contextual stressors associated with the parental illness

Cornell and Goodman, Psychol Bull. 2002, Vol 128 (5), 746-773

Risk of Parental Psychosis?

- Association between alcohol, cannabis, and other illicit substance abuse and risk of developing schizophrenia: a nationwide population based register study.
- Denmark Registry Study of 3,133,968 individuals (204,505 with substance use disorders and 21,305 with schizophrenia)
- A diagnosis of substance abuse increased the overall risk of developing schizophrenia
 - Any Substance Use [hazard ratio (HR) 6.04, 95% confidence interval (CI) 5.84-6.26].
 - Cannabis (HR 5.20, 95% CI 4.86-5.57)
 - alcohol (HR 3.38, 95% CI 3.24-3.53)
 - hallucinogens (HR 1.86, 95% CI 1.43-2.41)
 - sedatives (HR 1.68, 95% CI 1.49-1.90)

Key Points:

- The risk was found to be significant even 10-15 years subsequent to a diagnosis of substance abuse.
- Robust associations between almost any type of substance abuse and an increased risk of developing schizophrenia later in life.

Psychol Med. Nielsen, et al. 2017 Feb 7:1-10. doi: 10.1017/S0033291717000162. [Epub ahead of print]

Some Definitions

- Internalizing Problems
 - Anxiety
 - Depression
 - Self Esteem
- Externalizing Problems
 - ADHD
 - Oppositionality
 - Conduct Problems
 - Aggression



Maternal vs. Paternal Psychopathology



- Difficult to study; studies often contradict
- Gender of the parent and offspring may play a role
- Societal Expectations
- Putting it all together: Most results suggest the presence of disorders in mothers and fathers present equal risks for offspring with 2 exceptions:
 - 1) Depression in mothers was found to be more closely related to children's internalizing (but not externalizing) problems than depression in fathers
 - 2) Alcoholism and substance abuse disorders in mothers were more closely related to externalizing (but not internalizing) problems than were such disorders in fathers.

Connell and Goodman. Psychological Bulletin. 2002; 128 (5) 746-773.

But remember

- Confounders
 - Genetics
 - Age of offspring & parents
 - Educational/Cognitive Level
 - Socioeconomics
 - Lack of parental models
 - We've been wrong before
 - “Parent bashing” is not helpful



In this lecture...

- Maternal Substance Use and In-utero exposures
 - Fetal Alcohol Exposure and Sequela
 - Tobacco
 - Marijuana
 - Cocaine
 - Methamphetamines
 - Opiates

Review from Lander US Prevalence of the Problem

- NSDUH 2013 illicit drug use
 - Pregnant women age 15-17 – 14.6%
 - Pregnant women age 18-25 – 8.6%
 - Pregnant women 26-44 – 3.2%
 - Stitely, 2010-WV CAMC study
 - 759 samples or chord blood taken
 - 142 + for drugs or alcohol (19.2%)
 - Over 1 million babies are born every year to mothers who abuse substances (Over 4,000 in WV)

International Data on Substance abuse in Pregnancy

- 20-30% of women use tobacco
 - 15% use alcohol
 - 3 to 10% use cannabis
 - 0.5-3% cocaine



- Frequently multiple drugs are being used

Lamy and Thibaut. Encephale 2010 Feb 36(1) 33-8.

Obtaining the History

- Self report questionnaire is not reliable as a screening tool for substance use in mothers
 - Review of Birth records, DHHR or court documents
 - Family collateral
 - Limitations regarding urine drug testing
 - Meconium and maternal hair samples may be more helpful

Questions for Assessing the Effects

- Early Effects of Substance Use
 - Morbidity/mortality
 - NICU care
 - Birth defects
 - Weight/growth
 - Late Effects
 - Neuropsychiatric outcomes
 - Behavioral outcomes
 - School and Learning
 - Cognitive Profiles

Prenatal Alcohol Exposure

- Adverse effects known for centuries
 - Jones and Smith set forth diagnostic criteria in 1973 for fetal alcohol syndrome
 - Today we consider in-utero exposure to convey a spectrum of fetal alcohol effects



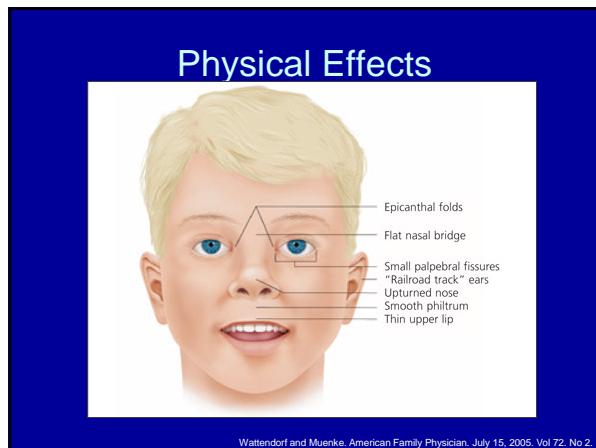
Epidemiology of FAS

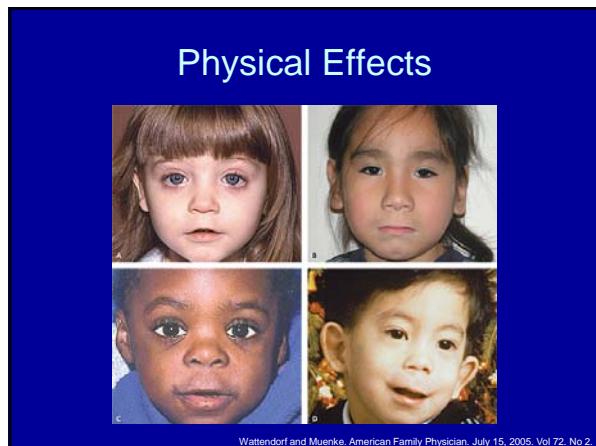
- Identified in all Racial and Ethnic groups
 - Birth Prevalence of FAS in U.S. is 0.5-2 per 1000 births
 - Birth Prevalence for fetal alcohol spectrum disorders (FASD) is estimated at 9-10 per 1000 of live births (approaching 1%)
 - Huge economic impact
 - Rates are considered epidemic in some areas
 - South Africa FAS 39.2-26.4 per 1000 births

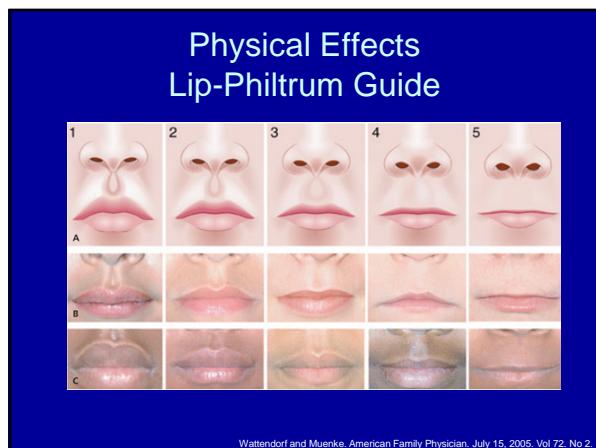
Manning and Hoyme. *Neuroscience and Biobehavioral Reviews* 31 (207) 230-238.

IOM Diagnostic Categories within FASD

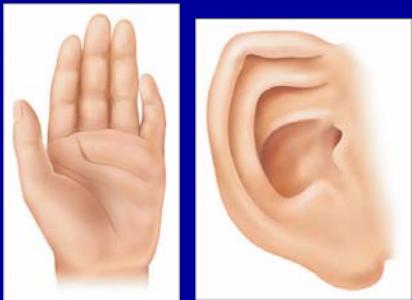
- FAS with confirmed maternal alcohol exposure
 - FAS without confirmed exposure
 - Partial Fetal Alcohol Syndrome with confirmed exposure (PFAS)
 - Alcohol Related Birth Defects (ARBD)
 - Alcohol Related Neurodevelopmental Disorders (ARND)







Physical Effects



Wattendorf and Muenke. American Family Physician, July 15, 2005, Vol 72, No 2.

Physical Effects Criteria for Diagnosis

- Short palpebral fissures (<10%)
- Thin vermillion border (score 4 or 5)
- Smooth philtrum (score of 4 or 5)
- Height and/or weight <10%
- Structural Brain Abnormalities
- Head Circumference <10%

Cognitive/Behavioral Effects

Several studies report 87-97% chance of at least one Axis I diagnosis in children with prenatal alcohol exposure.

Significant effects on frontal lobes (executive function, sustained attention) and HPA axis are felt to contribute.



O'Conor and Paley, Dev Disabilities 15:225-234 (2009)
Green, et al. Journ of Child Psych & Psychiatry 50:6 688-697

Cognitive/Behavioral Effects

Increased Rates of:

- Insecure Attachment
 - 80% of heavy use vs 36% in light use

- Mood and Anxiety
 - 19% of alcohol exposed children in mom's with (3>drinks/occ.) had depression vs. 1% of prevalence in early childhood

O'Conner and Paley. Dev Disabilities 15:225-234 (2009)

Cognitive/Behavioral Effects

Increased Rates of:

- ADHD, ODD, and Conduct
 - 59% of kids have had externalizing disorders
 - More likely view hypothetical ambiguous peer interactions as hostile and their responses to perceived hostility are more likely to involve aggressive physical solutions
 - the ADHD/hyperactivity symptoms appear as a different clinic presentation and respond differently to meds

O'Conner and Paley. Dev Disabilities 15:225-234 (2009)

Cognitive/Behavioral Effects

Increased Rates of:

- Suicide
 - 43% of youth made suicidal threats;
 - 23% to 55% had suicide attempts
- Substance Abuse
 - RR of 2.74 that at age 14 those exposed to prenatal alcohol were more likely to engage in binge drinking of >3 drinks
- Learning and Language Problems
 - 44% had significantly lower IQ and achievement
 - more were likely to be in the borderline or mentally retarded range when compared to controls.

O'Conner and Paley. Dev Disabilities 15:225-234 (2009)

DSM5: Proposed Criteria

Neurobehavioral Disorder Associated With Prenatal Alcohol Exposure

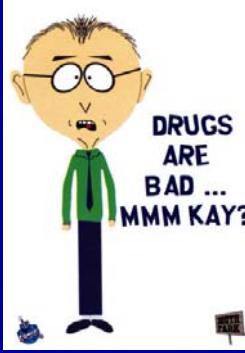
- A. More than minimal Exposure to alcohol during Gestation
- B. Impaired Neurocognitive Functioning
 - Impairment in global intellectual performance (i.e. IQ)
 - Impairment in executive functioning (planning, organization, inflexibility, difficulty with behavioral inhibition)
 - Impairment in learning
 - Memory impairment
 - Impairment in visual-spatial reasoning
- C. Impaired Self-Regulation
 - Impairment in Mood or behavioral regulation
 - Attention deficit
 - Impairment in impulse control
- D. Impaired Adaptive Functioning
- E. Onset of Disorder in Childhood
- F. Causes significant Distress

FAS and Foster Care/Adoption

- Lots in the news about psychotropic use in Foster Care populations reaching alarming levels. Average 4-5 psychotropic meds per some reports.
- Russian orphanage and Eastern European adoptees by Families in Sweden showed 29-68% of children showed severe alcohol related damage
- Recent review suggests of kids in care of child well fare system:
 - 6.0% had fetal alcohol syndrome
 - 16.9% had a fetal alcohol spectrum disorder

Prevalence of Fetal Alcohol Spectrum Disorders in Child Care Settings: A Meta-analysis.
Pediatrics 2013; Oct; 132(4): e980-995

A word about other drugs...



Tobacco

- Strong Association data as clear risk for Development of ADHD in multiple studies
- >10 cigarettes a day increases risk



Marijuana

- 3 longitudinal studies
 - Ottawa Prenatal Prospective Study (1970s)
 - Maternal Health Practices and Child Development (1982)
 - Generation R Study (2001)
- Findings in Child behaviors
 - OPPS (age 6) and MHPDC (age 6 and 10) higher rates of impulsivity, hyperactivity, and delinquency. Some evidence of impaired executive functioning
 - Awaiting the Generation R study with neuropsychological testing results.

Huizink, 2013 Prenatal Cannabis Exposure and Infant outcomes. Progress in Neuropsychopharmacology and Biological Psychiatry

Marijuana and IQ

Prenatal marijuana exposure and intelligence test performance at age 6.
J Am Acad Child Adolesc Psychiatry. 2008 Mar;47(3):254-63.

Abstract

OBJECTIVE: This is a prospective study of the effects of prenatal marijuana exposure on the intelligence test performance of 648 children at a 6-year follow-up.

METHOD: Women were interviewed about the amount and frequency of their marijuana use at 4 and 7 months of pregnancy and at delivery. Participants were light to moderate users of marijuana and represented a lower income population. Children were assessed with the Stanford-Binet Intelligence Scale by examiners blind to exposure status. Multiple regression was applied to examine the effects of prenatal marijuana exposure on children's intelligence after partialing out the effects of other significant predictors.

RESULTS: There was a significant nonlinear relationship between marijuana exposure and child intelligence. Heavy marijuana use (one or more cigarettes per day) during the first trimester was associated with lower verbal reasoning scores on the Stanford-Binet Intelligence Scale. Heavy use during the second trimester predicted deficits in the composite, short-term memory, and quantitative scores. Third-trimester heavy use was negatively associated with the quantitative score. Other significant predictors of intelligence included maternal IQ, home environment, and social support.

CONCLUSIONS: These findings indicate that prenatal marijuana exposure has a significant effect on school-age intellectual development.

6-8 IQ points, on average difference

Marijuana and Depression

Prenatal marijuana exposure: effect on child depressive symptoms at ten years of age.
Neurotoxicol Teratol. 2005 May-Jun;27(3):439-48.

Abstract : Studies of the consequences of prenatal marijuana use have reported effects predominantly on the behavioral and cognitive development of the children. This study examines the relations between prenatal marijuana exposure (PME) and child depressive symptoms at 10 years of age. Data are from the 10-year follow-up of 633 mother-child dyads who participated in the **Maternal Health Practices and Child Development Project**. Maternal prenatal and current substance use, measures of the home environment, demographic status, and psychosocial characteristics were ascertained at prenatal months four and seven, at delivery, and at age 10. At age 10, the children also completed the Children's Depression Inventory (CDI) [M. Kovacs, *The Children's Depression Inventory*, Multi-Health Systems, Inc., North Tonawanda, NY, (1992).], a self-report measure of current depressive symptoms. Multivariate regressions were used to test trimester-specific effects of marijuana and their associations with the CDI total score, while controlling for significant prenatal predictors and significant current covariates of childhood depression.

PME in the first and third trimesters predicted significantly increased levels of depressive symptoms. This finding remained significant after controlling for all identified covariates from both the prenatal period and the current phase at age 10. These findings reflect an association with the level of depressive symptoms rather than a diagnosis of a major depressive disorder. Other significant correlates of depressive symptoms in the children included maternal education, maternal tobacco use (prenatal or current), and the child's composite IQ score. These findings are consistent with recent reports that identify specific areas of the brain and specific brain functions that are associated with PME.

Marijuana and the Immune System

- Epigenetic Regulation of Immunological Alterations Following Prenatal Exposure to Marijuana Cannabinoids and its Long Term Consequences in Offspring.

Abstract

Use of marijuana during pregnancy is fairly commonplace and can be expected increase in frequency as more states legalize its recreational use. The cannabinoids present in marijuana have been shown to be immunosuppressive, yet the effect of prenatal exposure to cannabinoids on the immune system of the developing fetus, its long term consequences during adult stage of life, and transgenerational effects have not been well characterized. Confounding factors such as co-existing drug use make the impact of cannabis use on progeny inherently difficult to study in a human population. Data from various animal models suggests that *in utero* exposure to cannabinoids results in profound T cell dysfunction and a greatly reduced immune response to viral antigens. Furthermore, evidence from animal studies indicates that the immunosuppressive effects of cannabinoids can be mediated through epigenetic mechanisms such as altered microRNA, DNA methylation and histone modification profiles. Such studies support the hypothesis that parental or prenatal exposure to cannabis can trigger epigenetic changes that could have significant immunological consequences for offspring as well as long term transgenerational effects.

J Neuroimmune Pharmacol. Zumberg EE¹, et al. 2015 Jun;10(2):245-54. doi: 10.1007/s11481-015-9586-0. Epub 2015 Jan 25.

Crack Baby Scare?



Cocaine

- Prenatal Cocaine Exposure (PCE) increases risk of needing an Individualized education plan (IEP)
- Review article of effects of PCE in school-age children:
 - Through 6 years no long term direct effects on physical growth, developmental test scores, or language outcomes and all attenuated by environmental variables.
 - But Significant negative associations with sustained attention and behavioral self-regulation**
- Studies show a similar trend into Adolescence
 - Yale study showed **lower gray matter volumes in key brain regions involved in emotion, reward, memory and executive function in PCE brains**

"A review of the Effects of Prenatal Cocaine Exposure Among School Age Children". Pediatrics. March 2010; 125: 554-565.
Psychopathology and special Education enrollment in children with PCE. J Dev Behav Pediatr. 2012; 33(5): 377-86.
Systematic review of prenatal cocaine exposure and adolescent development. Pediatrics. 2013 June; 131 (6) e1917-36.

Methamphetamines

- IDEAL study: Infant Development, Environment, and Lifestyle Study**
- 7.5 year at follow-up**
- 412 mother-infant pairs, 4 sites**
- 204 exposed infants**
- CBCL and early adversity indexes**
- Results**
 - Increased externalizing, rule-breaking behavior and aggression**
 - Direct association between PME and early adversity**

J Pediatr. 2016 Mar;170:34-8.e1. doi: 10.1016/j.jpeds.2015.11.070. Epub 2016 Jan

Opiates

- Neonatal Abstinence Syndrome**
- Long term consequences?**
 - One study of methadone exposure in 20 women vs. controls suggested lower IQ in school age children and higher rates of aggression and anxiety and rejection (1993)
 - Otherwise very little beyond first 3 years.
- Unique issues:**
 - Medication Assisted Treatment vs. Abstinence Models



Treatment for Families- Multimodal

- Treatment for the parents for their substance use disorder
- Permanency and stability in home environment-meeting basic needs
- Parent Child Dyad therapy
- Individual therapy
- Family Based Therapy
- Hearing, Vision, and Language assessments

Treatment for Families- Multimodal

- Medical needs
 - Sleep, growth, nutrition
 - Speech, Occupational, Physical therapy
- School services:
 - IEP, 504 plans
 - Psychoeducational testing &/or neuropsychological testing
- Evaluation for medication
 - attention and focus
 - impulse control issues
 - Depression/anxiety/PTSD

Questions....