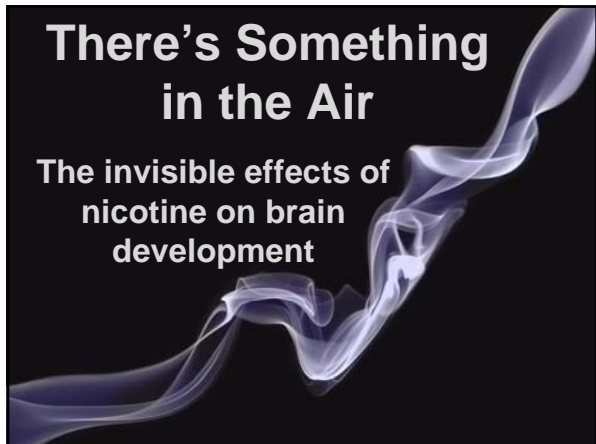


There's Something in the Air

The invisible effects of
nicotine on brain
development



Outline

- Maternal Smoking in Pregnancy
- Second hand smoke exposure
 - For the Fetus
 - For the Child

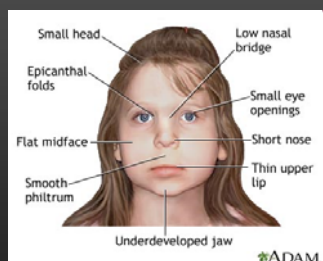
Smoking During Pregnancy



What is Teratology?

- “The science or study of monstrosities or abnormal formations in organisms”
 - “The biological study of birth defects”
- Classifications
 - A: evidence of no harm
 - B: no evidence, but presumed safe
 - C: safety unknown at this time
 - D: evidence of teratogenic potential
 - X: highly unsafe, risk outweighs any benefit

Fetal Alcohol Exposure



A history of cigarette warnings

- Caution: Cigarette Smoking May be Hazardous to your Health (1966)
- Warning: The Surgeon General has Determined Smoking is Dangerous to Your Health (1970)

A history of cigarette warnings

- SURGEON GENERAL'S WARNING: Smoking Causes Lung Cancer, Heart Disease, Emphysema, And May Complicate Pregnancy
- SURGEON GENERAL'S WARNING: Quitting Smoking Now Greatly Reduces Serious Risks to Your Health

Nicotine as a teratogen

SURGEON GENERAL'S WARNING: Smoking By Pregnant Women May Result in Fetal Injury, Premature Birth, And Low Birth Weight.

What is the face of prenatal nicotine exposure?



Fetal Nicotine or Cocaine Exposure: Which One is Worse?

- The incidence of smoking among samples of pregnant substance users is high
- Nicotine mimics endogenous neurotransmitters with critical developmental significance
- Nicotine is typically used to achieve stable blood concentrations

T. A. Slotkin, 1998

What is Neurobehavioral Teratology?

- Any substance that impacts CNS development can impact behavior
- Physical teratogen ≠ behavioral teratogen
- Deficits may not be immediately apparent
- Susceptibility may occur over a range of doses, and may not be equal in all individuals
- Timing is everything

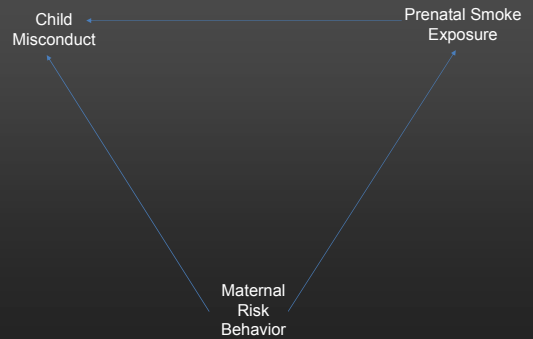
Outcomes of Prenatal Nicotine Exposure: Human Research

- Irritability in infancy (Schuetze & Eiden, 2007)
- Attention Deficit/Hyperactivity Disorder (ADHD) (Linnet et al., 2003; Millberger et al., 1998; Thapar et al., 2003)
- Aggression (Orlebeke et al., 1999)
- Conduct Disorder, Delinquency, Criminality (Wakschlag et al., 1997; Wakschlag et al., 2002; Brennan et al., 1999)

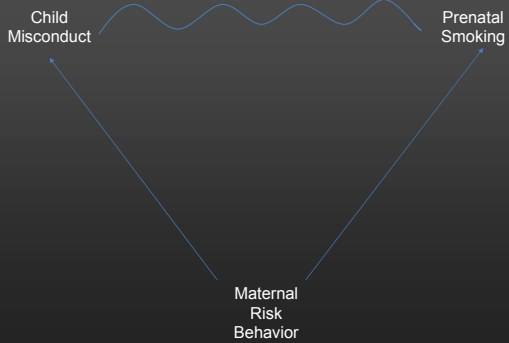
Who's Smoking During Pregnancy?

- Moms who quit when pregnant are different from those who don't
 - Poor relationships
 - Low adaptive functioning
 - Risky health behaviors
 - Personal history of antisocial behavior
- When genes and environments are correlated– identifying the source is very difficult

Direct Nicotine Effect



Correlated Third Variable



Criteria for Causality

- Temporal relationship
- Dose-response relationship
- Consistency
- Plausibility
- Consideration of Alternative Explanations
- Experiment
- Specificity

Criteria for Causality

- Temporal relationship
 - Cause must precede effect in time
- Smoke exposure → Antisocial outcome

Criteria for Causality

- Dose response relationship
 - Loss of teeth, stroke risk, cardiovascular disease, lung cancer
 - Adult intelligence, antisocial symptoms

Criteria for Causality

- Consistency
 - Replications across the life span
 - Replications across a range of outcomes
 - Replications across ethnicity, culture, and nationality
 - Replications across cohorts

Plausibility

- Nicotine used by the mother reaches fetal circulation (Luck et al., 1985)
- Fetal concentration may reach higher levels than maternal concentration (Luck et al., 1985)
- Nicotine mimics normal developmental signals (Oloff & Gallardo, 1999)

Plausibility

- Timing is everything (Slotkin, 2008)
 - Cell replication
 - Differentiation
 - Growth
 - Elimination
 - Threshold sensitivity
- Impacts mesolimbic and nigrostriatal dopamine networks

Plausibility

- Changes in brain development occur at doses *lower* than those needed to affect physical growth (Navarro et al., 1989; Slotkin, 1998)
- Maximal vulnerability is in 2nd and 3rd trimesters
- Majority of studies find strongest effects for exposure occurring in the 3rd trimester

Criteria for Causality

- Consideration of Alternative Explanations
 - Not solely a function of culture, socioeconomic status, or maternal characteristics
 - Genes may contribute to risk rather than account for it

Criteria for Causality

- Experiment
 - Not feasible in humans
 - Animal research demonstrates that the primary teratogenic effect derives from nicotine, and not other components of smoke
 - Animal experiments do not support selection hypothesis

Criteria for Causality

- Specificity
 - Neurocognitive effects– IQ
 - “Hot” but not “cool” executive function deficits
 - Behavioral effects– externalizing disorders
 - Effect on internalizing disorders less apparent
 - No apparent gender dichotomy

Implications and Recommendations

- Quitting should be prioritized
- Techniques for maximal success should be employed
 - Nurse-managed smoking cessation (Barron et al., 2007)
- Avoid replacement “smokeless” products as a long term alternative
- 1st trimester may be a “buffer” zone for quitting (Slotkin et al., 1993)



Second Hand Smoke

Second hand smoke

- Surgeon General’s Report
- Environmental smoke exposure can reach concentrations in non-smokers that are comparable to smokers
- Environmental exposure impacts the same brain systems are direct exposure

Second hand smoke

- The same physical risks are noted for environmental exposure
- Few studies conducted with humans
 - Cognitive deficits intermediate to direct-exposed and non-exposed children (Makin et al., 1991)
 - Externalizing symptoms comparable to direct-exposed

Implications and Recommendations

- Controlled through legal policy
 - Arizona, Delaware, Washington DC, Hawaii, Illinois, Iowa, Maryland, Massachusetts, New Jersey, New York, Ohio, Rhode Island, Washington.

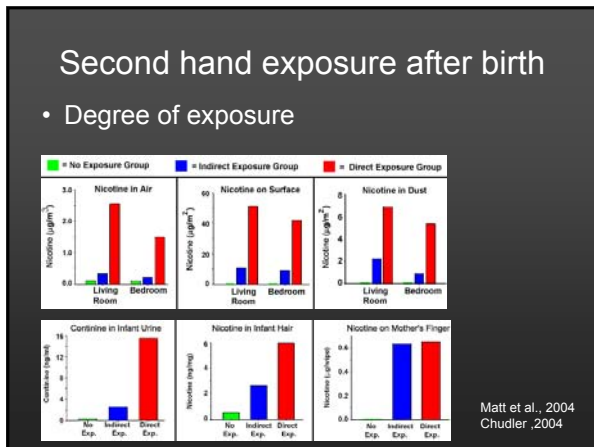
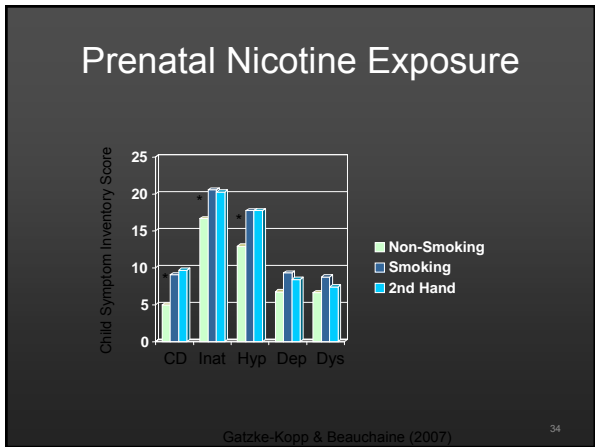


Second hand exposure after birth

- Physical effects
 - Sudden infant death
 - Asthma
 - Ear infections
 - Increased frequency of illness

Second hand exposure after birth

- Neurobehavioral effects
 - Continuity of smoking from pre- to postnatal time periods may be a factor in aggressive and hyperactive outcomes
 - Postnatal smoke exposure may impart incremental risk to the child above prenatal exposure



Implications and Recommendations

- Quit smoking
- Prohibit smoking in the home
- Wash hands and clothes after smoking
- Nicotine replacement should be used with caution

Summary and Conclusions

- Evidence is accumulating that nicotine exposure early in neurodevelopment has a direct effect on brain development that impacts cognitive and behavioral outcomes
- Causality can not be definitively determined