Prenatal Exposures and Low Birthweight

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http://www.emory.edu/MSACD

Percentage of infants weighing less than 2,500 grams (5 pounds, 8 ounces) at birth in the United States and Georgia.

- In Georgia, it is more than 9%.
- The percentage has not been decreasing.

From America’s Health Rankings. 
What is “Low Birthweight (<2500 gm)

Two Factors

- Gestational age <37 weeks
  - Per the March of Dimes, 70% of “low birthweight” results from preterm birth.
- Growth retardation.
  - That is, small for gestational age, SGA, usually < 10th percentile.


- More common in women less than 17 years and greater than 35 years.
- One associated factor is prenatal use of cigarettes, alcohol, other illicit drugs, and misuse of prescription drugs.
Risk Factors for IUGR/SGA

- Maternal weight less than 100 pounds
- Poor nutrition in pregnancy
- Birth defects and chromosomal abnormalities
- Use of drugs, cigarettes and alcohol
- Pregnancy induced hypertension
- Placental abnormalities
- Umbilical cord abnormalities
- Multiple pregnancies
- Gestational diabetes
- Oligohydramnios

http://americanpregnancy.org/pregnancy-complications/intrauterine-growth-restriction/
Rates of Preterm Birth: Georgia, 2015, Showing slight decline in rates from 2010

<table>
<thead>
<tr>
<th>Location</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>US</td>
<td>11.5%</td>
</tr>
<tr>
<td>Georgia</td>
<td>10.8%</td>
</tr>
<tr>
<td>Atlanta</td>
<td>11.5%</td>
</tr>
<tr>
<td>Columbus</td>
<td>13%</td>
</tr>
<tr>
<td>Savannah</td>
<td>11%</td>
</tr>
<tr>
<td>Augusta</td>
<td>12.6%</td>
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<tr>
<td>Athens</td>
<td>10.6%</td>
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</tbody>
</table>

Race/Ethnicity

- White: 9.6%
- African-American: 13.7%
- Hispanic: 8.7%
- Asian: 8.6%

Rates in Europe: 5-10%

Drug Use During Pregnancy (% Women Reporting Use)

What is the Impact of substance use?

How is Fetal Alcohol Syndrome Diagnosed?

1. Prenatal Exposure
2. Face
3. Growth (IUGR)
4. Brain
Meta-analysis of 14 studies showing relative risk (RR) of preterm birth as a function of number of drinks per day in pregnancy.

From Patra et al, 2011
Preterm Birth Rates in Ukrainian Sample

- For whole sample (N=686)
  - Preterm rate (<37 weeks) overall = 7%
  - Alcohol Use Group rate = 9.9% vs No Use = 4.1%
  - RR of preterm birth in Alcohol group = 2.6 (p<.003)

- When the MVM group was removed, leaving 381 cases:
  - Alcohol Use group = 11.1% vs No Use = 4.9%
  - RR of preterm birth in Alcohol group = 2.6% (p<.02)

Thus MVM lowers total rate slightly but doesn’t change the relative proportion.
<table>
<thead>
<tr>
<th>Factor</th>
<th>β</th>
<th>$X^2$</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prenatal Care</td>
<td>-0.075</td>
<td>16.25</td>
<td>1</td>
<td>0.000</td>
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<tr>
<td>Mom Age</td>
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<td>0.90</td>
<td>1</td>
<td>0.342</td>
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<td>SES</td>
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<td>6.75</td>
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<td>0.009</td>
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<tr>
<td>TWEAK</td>
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<tr>
<td>Cigarettes</td>
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<td>0.000</td>
<td>1</td>
<td>0.997</td>
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<tr>
<td>Child Sex</td>
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<td>0.021</td>
<td>1</td>
<td>0.885</td>
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<tr>
<td>Site</td>
<td>0.222</td>
<td>1.758</td>
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<td>0.185</td>
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</table>

Model Statistics: $X^2=50.89$, df=7, $p<0.000$

<table>
<thead>
<tr>
<th>Factor</th>
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<tbody>
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<td>Child Sex</td>
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<td>Site</td>
<td>0.227</td>
<td>1.84</td>
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</table>

Model Statistics: $X^2=50.98$, df=7, $p<0.000$

Results: Less prenatal care, Lower SES and Alcohol Use lead to lower Gestational Age
Increase in Opiate prescriptions in US*

Neonatal abstinence Syndrome in Georgia

*National Institute on Drug Abuse
Effects of Opiates on the Fetus and New Born

- Opiates cross the placental barrier just as they cross the blood/brain barrier.

- **Growth reduction is common. (IUGR, SGA)**

- May be affected by intermittent opiate use (repeated episodes of intoxication and withdrawal).

- Stillbirth

- Methadone maintenance results in development of tolerance/dependence in infant.

- Neonatal withdrawal syndrome (abstinence syndrome) may occur as a result of exposure to any of the narcotics (and other depressive drugs).
Developmental Effects of Heroin and Opiates

- Growth Retardation
  - IUGR
  - SGA
- Prematurity
- SIDS

No persistent developmental effects attributable to teratogenic effects of drugs when confounding factors controlled.
Non-narcotic drugs causing neonatal behavior consistent with withdrawal*

- Alcohol
- Barbiturates
- Caffeine
- Chlordiazepoxide
- Clomipramine
- Diazepam
- Ethchlorvynol
- Glutethimide
- Hydroxyzine
- Meprobamate
- SSRIs

*American Academy of Pediatrics, 2012, Pediatrics, Published on-line, 1/30/12
Increase in Stimulant Prescriptions*

That is,

Amphetamines
Methylphenidate (Ritalin)

Non prescription stimulants include

Cocaine
Methamphetamine

*National Institute on Drug Abuse
Effects on the Fetus—Stimulant Drugs
(cocaine, methamphetamines)

- Growth retardation
- Risk of fetal wastage
  - Miscarriage, stillbirth
- Risk of Preterm birth
Effects on the Fetus

- After alcohol and tobacco, marijuana is the most commonly used drug in pregnancy.
  - No birth defects have been found
  - No growth retardation
  - Infants do not have significant effects in the newborn period.
There are many Teratogenic agents

Known Teratogens include:

- Diseases (CMV, Toxoplasmosis, rubella)
- Environmental Toxins (Lead, Mercury)
- Prescription Medications (Thalidomide, Warfarin, Accutane)
- Drugs of Abuse (Alcohol)

Here is a picture of a child with microcephaly associated with the Zika Virus.