Learning Objectives

At the end of this presentation the participant will be able to:
1. Characterize the patterns and trends of mortality/survival for critical congenital heart defects.
2. Understand the patterns of microcephaly.
3. Describe the characteristics of infants born to mothers with evidence of Zika virus infection.

Topics Covered

• Prevalence of Birth Defects
• Birth Defects Mortality/Survival
• Critical Congenital Heart Defects Mortality/Survival
• Risk Factors for Birth Defects
• Zika Virus and Microcephaly

Prevalence of Birth Defects

Prevalence of Any Monitored Birth Defect Over Time, Texas, 1999-2013
Prevalence of Two Selected Birth Defects Over Time, Texas, 1999-2013

- Cleft Lip with/without Cleft Palate
- Gastroschisis

Prevalence of Pyloric Stenosis Over Time, Texas, 1999-2013

- Any Monitored Defect, Texas, 1999-2013
- Selected Birth Defects with Statistically Significant Differences in Prevalence among Three Racial/Ethnic Groups, Texas, 1999-2013

Birth Defects that are Higher in Males, Higher in Females, Similar in Both

- Mother's Education, Texas, 1999-2013
Prevalence of Critical Congenital Heart Defects Targeted for Pulse Oximetry Screening, Texas, 2005-2013

In Texas, 1 in every 517 babies is born with a critical congenital heart defect.
Pediatric Grand Rounds - UT Health San Antonio

3/31/2017

Risk Factors for Birth Defects

Differences in Self-reported Preconception Health Indicators, by Medicaid Status, Texas Pregnancy Risk Assessment and Monitoring System, 2002-2010

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Medicaid paid for delivery</th>
<th>% (95% CI)</th>
<th>% (95% CI)</th>
<th>Adj. prevalence ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No daily multivitamin</td>
<td>64.7 (63.1, 66.2)</td>
<td>82.7 (81.0, 83.8)</td>
<td>1.3 (1.2, 1.3)</td>
<td></td>
</tr>
<tr>
<td>Physical inactivity</td>
<td>34.9 (32.7, 37.1)</td>
<td>43.7 (41.7, 45.8)</td>
<td>1.3 (1.2, 1.4)</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>12.5 (11.4, 13.5)</td>
<td>19.3 (18.4, 20.3)</td>
<td>1.5 (1.4, 1.7)</td>
<td></td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>58.4 (56.8, 60.1)</td>
<td>35.9 (34.5, 37.8)</td>
<td>0.6 (0.6, 0.7)</td>
<td></td>
</tr>
<tr>
<td>Binge drinking</td>
<td>21.0 (19.6, 22.4)</td>
<td>16.5 (15.4, 17.6)</td>
<td>0.8 (0.7, 0.9)</td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td>19.1 (17.8, 20.4)</td>
<td>23.3 (22.2, 24.9)</td>
<td>1.2 (1.1, 1.4)</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.4 (1.3, 1.5)</td>
<td>2.2 (1.8, 2.5)</td>
<td>1.5 (1.3, 1.7)</td>
<td></td>
</tr>
</tbody>
</table>

* Reference group

MMWR, July 27, 2012, Vol. 6, No. 29
Risk Factors from the National Birth Defects Prevention Study

- Cooperative agreement grant with CDC
- One of 10 centers in the nation
- National Birth Defects Prevention Study
  - Largest population-based case-control study on birth defects
  - Study includes 30 specific birth defects
  - Additional clinical review and classification of cases
  - Computer-assisted maternal phone interview
  - Cheek cell samples (DNA): mom, dad, infant

States that Participated in the National Birth Defects Prevention Study

- Adjusted Odd Ratios for Pre-pregnancy Obesity and Selected Isolated Birth Defects, 1997–2002

Adjusted Odd Ratios for Pre-pregnancy Obesity and Selected Isolated Birth Defects, 1997–2002
Fever, Antipyretics, and Oral Clefts, 1997-2004: Adjusted Odds Ratios

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>No Antipyretic Use</th>
<th>Antipyretic Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA (IA)</td>
<td>IA (IA)</td>
<td>IA (IA)</td>
</tr>
<tr>
<td>Controls</td>
<td>4074</td>
<td>4074</td>
</tr>
<tr>
<td>CL-I</td>
<td>1098</td>
<td>1098</td>
</tr>
<tr>
<td>CP-L, CP-M</td>
<td>894</td>
<td>894</td>
</tr>
<tr>
<td>CL-I, CP-M</td>
<td>438</td>
<td>438</td>
</tr>
<tr>
<td>CL-I, CP-M</td>
<td>139</td>
<td>139</td>
</tr>
<tr>
<td>CL-I, CP-M</td>
<td>113</td>
<td>113</td>
</tr>
<tr>
<td>CL-I, CP-M</td>
<td>26</td>
<td>26</td>
</tr>
</tbody>
</table>


Adjusted OR (95% CI)

- Secondhand Smoke Exposure (B1P3)

- Formed from incomplete burning of coal, tobacco
- Human exposure common, through:
  - Tobacco smoke
  - Other smoke
  - Air pollution
  - Occupation (coke ovens, foundries, coal tar use, asphalt manufacturing and use)
  - Eating charbroiled foods

Mothers Exposed to Secondhand Smoke Exposure (B1P3) & Selected Isolated Defects

<table>
<thead>
<tr>
<th>Birth Defect</th>
<th>n (No Exposure)</th>
<th>n (Any Exposure)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anomalous hand syndrome-limb body wall complexes (AMBAWBC)</td>
<td>104</td>
<td>40</td>
<td>1.66 (1.10-2.51)</td>
</tr>
<tr>
<td>Neural tube defects</td>
<td>822</td>
<td>219</td>
<td>1.55 (1.10-2.16)</td>
</tr>
<tr>
<td>Nephrotic and/or intracranial defects</td>
<td>247</td>
<td>115</td>
<td>1.56 (1.16-2.09)</td>
</tr>
<tr>
<td>Left palate</td>
<td>1147</td>
<td>245</td>
<td>1.39 (1.00-1.94)</td>
</tr>
<tr>
<td>Left lip +/- cleft palate</td>
<td>1147</td>
<td>245</td>
<td>1.39 (1.00-1.94)</td>
</tr>
<tr>
<td>Bilateral renal agenesis or hypoplasia</td>
<td>45</td>
<td>15</td>
<td>1.99 (1.00-3.86)</td>
</tr>
</tbody>
</table>


Occupational Exposure to Polycyclic Aromatic Hydrocarbons: Some Results

<table>
<thead>
<tr>
<th>Occupational Exposure to Polycyclic Aromatic Hydrocarbons</th>
<th>CLEFT LIP w/o GASTROSCHISIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>No PAH Exp</td>
<td>Low PAH Exp</td>
</tr>
<tr>
<td>&lt; 20 years</td>
<td>20+ years</td>
</tr>
</tbody>
</table>

Langlois et al. The Cleft Palate-Craniofacial Journal 2013

Lupo et al. Environmental Health Perspectives 2012

Socioeconomic Status in Relation to Selected Birth Defects in a Large Multi-centered US Case-Control Study

Formed from incomplete burning of coal, tobacco

Human exposure common, through:
- Tobacco smoke
- Other smoke
- Air pollution
- Occupation (coke ovens, foundries, coal tar use, asphalt manufacturing and use)
- Eating charbroiled foods
Socioeconomic Status in Relation to Selected Birth Defects in a Large Multi-centered US Case-Control Study

- Consistently increased risks of selected birth defects associated with household SES index (parents’ education, parents’ occupation, household income)
- In terms of individual SES measures, elevated but non-significant risks were observed between:
  - Maternal low education and anencephaly and dextro-transposition of the great arteries (dTGA)
  - Paternal low education and anencephaly, cleft palate, Tetralogy of Fallot (TOF), and dTGA
  - Either parent’s unemployment and dTGA

<table>
<thead>
<tr>
<th>Household SES measure</th>
<th>Adjusted odds ratio* (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Spina bifida</td>
</tr>
<tr>
<td>Only one low</td>
<td>1.5 (1.0, 2.2)</td>
</tr>
<tr>
<td>Only two low</td>
<td>1.2 (0.7, 1.9)</td>
</tr>
<tr>
<td>All low</td>
<td>1.5 (0.9, 2.7)</td>
</tr>
</tbody>
</table>

* Household SES index adjusted only by non-SES status covariates (maternal race/ethnicity, age, state of residence, gravidity, obesity, smoking, binge drinking, and folic acid supplementation).

Zika Virus and Microcephaly

- Brain abnormalities with and without microcephaly
- Neural tube defects and other early brain malformations
- Structural eye abnormalities
- Congenital deafness
- Associated limb contractures, hip dislocation, clubfoot

Microcephaly and Head Circumference

- Used to measure “severity”
- Severe: < 3rd percentile for age and sex
- Also called occipital-frontal circumference (OFC)

Explained Microcephaly Cases

- Part of co-occurring malformations
  - Neural tube defects
  - Holoprosencephaly
  - Craniosynostosis
  - Other brain reduction defects
- Documented causes
  - Chromosomal anomalies
  - Infection (cytomegalovirus, toxoplasmosis)
  - Genetic/syndromic
  - Prenatal alcohol exposure
Prevalence of Unexplained Severe Microcephaly*, by Infant Sex and Maternal Education, Texas, 2008-2012

- By Infant Sex:
  - Male: 2.8 per 10,000 live births
  - Female: 3.5 per 10,000 live births

- By Maternal Education:
  - < High School: 4.1 per 10,000 live births
  - High School: 2.0 per 10,000 live births

*Head circumference at delivery <3rd percentile for infant sex and gestational age

Unexplained Severe Microcephaly Cases, by Maternal Race and Education, Texas, 2008-2012

- Male
  - Less than high school: 1.9 per 10,000 live births
  - High school: 1.2 per 10,000 live births
  - Greater than high school: 0.4 per 10,000 live births

- Female
  - Less than high school: 3.2 per 10,000 live births
  - High school: 3.0 per 10,000 live births
  - Greater than high school: 1.0 per 10,000 live births


- Hispanic: 11.9 per 10,000 live births
- Non-Hispanic Black: 11.2 per 10,000 live births
- Non-Hispanic White: 8.5 per 10,000 live births
- Total: 9.7 per 10,000 live births

*Includes data from 14 state surveillance programs

Microcephaly*: Total Definite Cases, Texas, 1999-2012 (n=5,774)

- Prevalence of Microcephaly in the United States*, 2009-2013 Deliveries, by Maternal Race/Ethnicity

Unexplained Cases of Definite Microcephaly, by Percentile of Head Circumference (HC), Texas, 1999-2012

- 3rd percentile (Severe)
- 3rd to 5th percentile (Less severe)
- ≥ 5th percentile (Normal HC)
Zika in Texas (as of Mar. 1, 2017)

- **Biggest concern**: adverse birth outcomes among pregnant women with Zika (microcephaly and other birth defects; risk = 1 to 30%)
- Texas has had 314 reported, confirmed cases of Zika virus disease
  - 2 sexually transmitted
  - 6 mosquito-borne cases (Cameron Co. bordering Mexico)
  - All others travel-related (mostly Central America/Caribbean)
- Focusing on pregnancy and birth outcomes:
  - 162 women with evidence of Zika infection during pregnancy
  - 9 fetuses/infants with evidence of Zika infection (3 with microcephaly)

Zika Pregnancy Outcomes in Texas

162 pregnant women with evidence of Zika virus infection
104 with completed pregnancies
49 pregnancy outcomes with known status

Zika Virus Disease Cases by County, Texas (as of March 1, 2017)

- 314 cases of Zika virus disease reported as of March 1, 2017
- 162 pregnant women with symptomatic or asymptomatic Zika virus infection reported as of March 1

Country of Travel for Pregnant Women with Evidence of Zika Virus Infection with Known Pregnancy Outcomes, Texas 2015 – 2017*, N = 49

- Mexico and Central America, 79%
- South America, 10%
- Caribbean, 8%
- Other, 2%

Zika Pregnancy Outcomes in Texas: Testing Completed

162 pregnant women with evidence of Zika virus infection
104 with completed pregnancies
49 pregnancy outcomes with known status
28 infants with completed testing
9 with evidence of Zika virus infection
19 with no evidence of Zika virus infection

Zika Pregnancy Outcomes in Texas: Testing Completed

162 pregnant women with evidence of Zika virus infection
104 with completed pregnancies
49 pregnancy outcomes with known status
21 infants with testing not completed
Summary: Zika Pregnancy Outcomes in Texas

- As of March 1, 2017, 162 women in Texas with evidence of a Zika infection during pregnancy
- Reported to U.S. Zika Pregnancy Registry, CDC

<table>
<thead>
<tr>
<th>BIRTH DEFECT STATUS</th>
<th>FETUS/INFANT LAB TESTING</th>
<th>LAB TESTING NOT COMPLETED</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zika-related birth defects</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>No apparent birth defects</td>
<td>6</td>
<td>18</td>
<td>19</td>
</tr>
<tr>
<td>Total</td>
<td>9</td>
<td>19</td>
<td>21</td>
</tr>
</tbody>
</table>

Percent of infant/fetuses with Zika-related birth defects = 12%

Percentage of Infants/Fetuses Delivered with Birth Defects from 442 Mothers with Evidence of Possible Recent Zika Infection, U.S. Zika Pregnancy Registry, Dec. 2015 – Sept. 2016*

- 6% overall (26/442): trimester of exposure/symptoms not discernible
  - Microcephaly (4%), other brain anomalies (1%), other (1%)
  - 21 cases were live born; 5 cases were fetal deaths
  - Same percentage for symptomatic and asymptomatic pregnant women
- 11% (9/85): first trimester/periconceptional exposure or symptoms only
- No reports of birth defects among fetuses/infants with Zika exposure only in second or third trimesters

*Honein MA et al., JAMA. 2017;317(1):59-68.

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THANK YOU

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