BIRTH DEFECTS
EPIDEMIOLOGY AND
SURVEILLANCE

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Birth Defects Epidemiology and Surveillance Branch
Texas Department of State Health Services
Outline

• Texas birth defects registry
  – Overview
  – Describing the occurrence of birth defects
  – Cluster investigations

• Some research on causes of birth defects

• Zika virus and microcephaly
Texas Birth Defects Registry: Overview
Origin of birth defects a mystery

Officials call for government probe of anencephaly

Anencephalic babies leave mothers devastated

Medical puzzle sounds alarm
Search on for ‘common thread’ in Cameron’s birth defect cases

Brownsville awaits anencephaly study results

1991 Headlines
The Texas Birth Defects Registry: What It Is

• One of the largest active birth defects surveillance systems
  – Passive vs. active surveillance

• Extensive quality control checks
  – Includes review of roughly 50% of records by clinical geneticists

• Computerized database of infants and pregnancies affected by birth defects
The Texas Birth Defects Registry: Case Definition

• Infant/fetus has structural or chromosomal anomaly
• Mother resident in TX at delivery
• Birth defect diagnosed prenatally or within first year of life
• Includes all pregnancy outcomes
The Texas Birth Defects Registry: What It Does With The Data

• Describe occurrence of birth defects in Texas

• Conduct cluster investigations

• Work with others in:
  – Research
  – Prevention
  – Linking families to available services
Texas Birth Defects Registry:

Describing the Occurrence of BDs by Time, Place, and Person
Birth Prevalence of Children With Any Monitored Birth Defect by Year

Cases per 10000 live births

Birth Year

1999 2001 2003 2005 2007 2009 2011 2013
The Increase May Be Due Largely to Better Detection/Ascertainment Over Time

<table>
<thead>
<tr>
<th>Birth Defect Category</th>
<th>Average Annual % Change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Cases</td>
</tr>
<tr>
<td>Least Susceptible to Diagnostic Variability</td>
<td>- 0.2</td>
</tr>
<tr>
<td>e.g. gastroschisis, limb reduction defects</td>
<td></td>
</tr>
<tr>
<td>Somewhat Susceptible</td>
<td>+ 0.5</td>
</tr>
<tr>
<td>e.g. hypospadias, trisomy 21</td>
<td></td>
</tr>
<tr>
<td>Mid Susceptibility</td>
<td>+ 1.4</td>
</tr>
<tr>
<td>e.g. anotia/microtia, tetralogy of Fallot</td>
<td></td>
</tr>
<tr>
<td>Quite Susceptible</td>
<td>+ 0.8</td>
</tr>
<tr>
<td>e.g. VSD, renal agenesis/dysgenesis</td>
<td></td>
</tr>
<tr>
<td>Most Susceptible to Diagnostic Variability</td>
<td>+ 2.0</td>
</tr>
<tr>
<td>e.g. ASD, cataract</td>
<td></td>
</tr>
</tbody>
</table>
Birth Prevalence of Children With Gastroschisis by Year
Ambient Levels of Benzene and Spina Bifida, Texas 1999-2004

<table>
<thead>
<tr>
<th>Benzene Level (ug/m³)</th>
<th>Adj Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.12 – 0.45</td>
<td>1.00 (referent)</td>
</tr>
<tr>
<td>&gt;0.45 – 0.98</td>
<td>1.77 (1.04 - 3.00)</td>
</tr>
<tr>
<td>&gt;0.98 – 1.52</td>
<td>1.90 (1.11 – 3.24)</td>
</tr>
<tr>
<td>&gt;1.52 – 2.86</td>
<td>1.40 (0.82 – 2.38)</td>
</tr>
<tr>
<td>&gt;2.86 – 7.44</td>
<td>2.30 (1.22 – 4.33)</td>
</tr>
</tbody>
</table>

Lupo PJ et al. 2011 Environmental Health Perspectives
Proximity of Children with Birth Defects to Pediatric Genetics Clinics, Texas, 1999-2003

Represents 22,875 cases from the Texas Birth Defects Registry delivered 1999-2003


Cases per 10,000 Live Births

Mother’s Age

<20, 20-24, 25-29, 30-34, 35-39, 40+
For your own queries:
http://healthdata.dshs.texas.gov/Registries/BirthDefects
Texas Birth Defects Registry:

Cluster Investigations
Birth defect cluster

One definition: more than the expected number of cases of a birth defect in a population group for a defined geographic area and a defined time period
What causes birth defect clusters?

- Chance...normal fluctuation over time in the occurrence of birth defects
- Changes in diagnostic practices or hospital referral patterns
- Shared exposure the cases have in common
Why investigate birth defect clusters?

• Generate new clues about causes of birth defects (*RARELY*)

• Respond to the concerns of community members

• Educate/inform the public about birth defects
BIRTH DEFECT CLUSTERS INVESTIGATED IN 2010

cluster
ANENCEPHALY
MICROTIA 1
MICROTIA 2
ASD
DIA. HERNIA
TRISOMY 18
GASTROSCHISIS
A Recent Cluster Investigation: Trisomy 18
In the Bryan/College Station Area

- Cluster of 4 babies conceived during August 2009–February 2010 to residents of Brazos County
  - 2 families from Bryan
  - 2 families from College Station

- Concern about possible relationship to chemical plant fire on July 30, 2009
Trisomy 18
by Estimated Date of Conception

Brazos County

Surrounding Counties

Fire, 7/30/2009
Some Research on Causes of Birth Defects
Texas Center for Birth Defects Research and Prevention, 1996-2013

- 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 to date
- 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
Pre-pregnancy Obesity and Selected Isolated Birth Defects, 1997 – 2002

Waller DK et al. 2007. *Archives Pediatr & Adolesc Med*
# Fever, Antipyretics, and Oral Clefts, 1997-2004: Adjusted Odds Ratios

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>Fever no ill</th>
<th>Fever febrile ill</th>
<th>No antipyretic use aOR (CI)</th>
<th>Antipyretic use aOR (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>4074</td>
<td>73</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CL+-/P</td>
<td>1089</td>
<td>37</td>
<td>2.04 (1.36-3.07)</td>
<td>1.07 (0.82-1.40)</td>
</tr>
<tr>
<td>CL+/P_I</td>
<td>950</td>
<td>29</td>
<td>1.81 (1.17-2.82)</td>
<td>1.14 (0.87-1.50)</td>
</tr>
<tr>
<td>CLP_I</td>
<td>604</td>
<td>21</td>
<td>2.06 (1.25-3.40)</td>
<td>1.01 (0.72-1.44)</td>
</tr>
<tr>
<td>CL_I</td>
<td>346</td>
<td>8</td>
<td>1.39 (0.66-2.94)</td>
<td>1.35 (0.91-2.00)</td>
</tr>
<tr>
<td>CL+/P_M</td>
<td>139</td>
<td>8</td>
<td>3.87 (1.80-8.32)</td>
<td>0.52 (0.19-1.42)</td>
</tr>
<tr>
<td>CLP_M</td>
<td>113</td>
<td>6</td>
<td>3.77 (1.57-9.01)</td>
<td>0.33 (0.08-1.33)</td>
</tr>
<tr>
<td>CL_M</td>
<td>26</td>
<td>2</td>
<td>4.48 (1.02-19.76)</td>
<td>1.26 (0.29-5.42)</td>
</tr>
<tr>
<td>CP_I</td>
<td>433</td>
<td>11</td>
<td>1.45 (0.76-2.77)</td>
<td>1.01 (0.68-1.50)</td>
</tr>
<tr>
<td>CP_M</td>
<td>116</td>
<td>6</td>
<td>3.00 (1.26-7.12)</td>
<td>1.02 (0.49-2.13)</td>
</tr>
</tbody>
</table>

_I: Isolated defects;  _M: Multiple defects

Zika Virus and Microcephaly
Current Zika Virus Outbreak

• **Fall 2015:** NE Brazil reported a twenty-fold microcephaly increase that coincided with local transmission of Zika virus

• **February 2016:** World Health Organization declares Zika to be a global Emergency

• **August 2016:** First cases of Zika virus infection locally spread by mosquitos in continental US
Reported occurrence of Aedes aegypti & albopictus by county in the United States

Maps showing the reported occurrence of Ae. aegypti (A) and of Ae. Albopictus (B) by county between 1 January 1995 and March 2016 in the United States.

Micah B. Hahn et al. J Med Entomol 2016;jme.tjw072
Definition

• Clinical finding of a small head (when compared with infants of the same sex and age).

• CONGENITAL MICROCEPHALY: present prenatally or at birth/delivery.
Head Circumference

• Used to measure “severity”
• Severe: < 3\textsuperscript{rd} percentile for age and sex
• Also called occipital-frontal circumference (OFC)
Some Challenges for Public Health Surveillance

• Some clinicians use different cut-points
  – < 5th percentile, < 10th percentile
  – Based on standard deviations below average
  – Subjective assessment

• HC measurement sometimes missing

• Cause in many cases can be explained
  – Can be a feature of other birth defects
  – Several known causes (in utero infections, maternal conditions, teratogens)
## Microcephaly Cases in Texas 2008-2012

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>CASES</th>
<th>% OF TOTAL CASES</th>
<th>BIRTH PREVALENCE (CASES/10,000 LIVE BIRTHS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Explained Cases</td>
<td>856</td>
<td>30%</td>
<td>4.4</td>
</tr>
<tr>
<td>Unexplained Cases</td>
<td>2,013</td>
<td>--</td>
<td>10.3</td>
</tr>
<tr>
<td>Unexplained Severe Cases</td>
<td>615</td>
<td>21%</td>
<td>3.2</td>
</tr>
<tr>
<td>Unexplained Less Severe Cases</td>
<td>1,398</td>
<td>49%</td>
<td>7.2</td>
</tr>
<tr>
<td>Total Cases</td>
<td>2,869</td>
<td>100%</td>
<td>14.7</td>
</tr>
</tbody>
</table>
Microcephaly by Year and Subgroup
TX 1999-2012

- Total Cases
- Unexplained Cases
- Severe Microcephaly (<3 Percentile)
## MICROCEPHALY AND WHAT ELSE?

<table>
<thead>
<tr>
<th>BIRTH DEFECT</th>
<th># CASES/YR</th>
</tr>
</thead>
<tbody>
<tr>
<td>MICROCEPHALY (causal association)</td>
<td>819</td>
</tr>
<tr>
<td>OTHER BRAIN AND SKULL ANOMALIES</td>
<td>2438</td>
</tr>
<tr>
<td>Abnormal brain cortex, corpus callosum</td>
<td></td>
</tr>
<tr>
<td>Fetal brain disruption sequence</td>
<td></td>
</tr>
<tr>
<td>NEURAL TUBE DEFECTS + HOLOPROSENCEPHALY</td>
<td>337</td>
</tr>
<tr>
<td>Anencephaly, spina bifida, encephalocele</td>
<td></td>
</tr>
<tr>
<td>Holoprosencephaly</td>
<td></td>
</tr>
<tr>
<td>OTHERS</td>
<td>591</td>
</tr>
<tr>
<td>Eye abnormalities</td>
<td></td>
</tr>
<tr>
<td>Congenital contractures (e.g. arthrogryposis)</td>
<td></td>
</tr>
<tr>
<td>Congenital deafness</td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td>3550</td>
</tr>
</tbody>
</table>
Thanks

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